Heliyon 10 (2024) e32948

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Association of bioimpedance analysis parameters trajectories with clinical outcomes in neurocritical patients

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ARTICLE INFO

Keywords:
Bioimpedance analysis
Clinical outcome
Group-based trajectory model
Neurocritical patients
Phase angle

ABSTRACT

Background and objective: Neurocritical patients often experience uncontrolled high catabolic metabolism state during the acuta phase of the disease. The complex interactions of neuroendocrine, inflammation, and immune system lead to massive protein breakdown and changes in body composition. Bioelectrical impedance analysis (BIA) evaluates the content and proportions of body components based on the principles of bioelectricity. Its parameters reflect the overall health status of the body and the integrity of cellular structure and function, playing an important role in assessing the disease status and predicting prognosis of such patients. This study explored the association of BIA parameters trajectories with clinical outcomes in neurocritical patients.

Methods: This study prospectively collected BIA parameters of 127 neurocritical patients in the Department of Neurology admitted to the NICU for the first 1–7 days. All these patients were adults (≥18 years old) experiencing their first onset of illness and were in the acute phase of the disease. The group-based trajectory modeling (GBTM), which aims to identify individuals following similar developmental trajectories, was used to identify potential subgroups of individuals based on BIA parameters. The short-term prognosis of patients in each trajectory group with variations in phase angle (PA) and extracellular water/total body water (ECW/TBW) over time was differentially analyzed, and the logistic regression model was used to analyze the relationship between potential trajectory groups of PA and ECW/TBW and the short-term prognosis of neurocritical patients. The outcome was Glasgow Outcome Scale (GOS) score at discharge.

Results: Four PA trajectories and four ECW/TBW trajectories were detected respectively in neurocritical patients. Among them, compared with the other latent subgroups, the "Low PA rapidly decreasing subgroup" and the "High ECW/TBW slowly rising subgroup" had higher incidences of adverse outcomes at discharge (GOS:1–3), in-hospital mortality, and length of neurology intensive care unit stay (all $P < 0.05$). After correcting for potential confounders, compared with the "Low PA rapidly decreasing subgroup", the risk of adverse outcome (GOS:1–3) was lower in the other three PA trajectories, with OR values of 0.0003, 0.0004, and 0.003 respectively (all $P < 0.05$). Compared with the "High ECW/TBW slowly rising subgroup", the risk of adverse outcome (GOS:1–3) was lower in the other three ECW/TBW trajectories, with OR values of 0.013, 0.035 and 0.038 respectively (all $P < 0.05$).

Conclusion: Latent PA trajectories and latent ECW/TBW trajectories during 1–7 days after admission were associated with the clinical outcomes of neurocritical patients. The risk of adverse

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https://doi.org/10.1016/j.heliyon.2024.e32948
Received 25 December 2023; Received in revised form 12 June 2024; Accepted 12 June 2024
Available online 13 June 2024
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outcomes was highest in the "Low PA rapidly decreasing subgroup" and the "High ECW/TBW slowly rising subgroup". These results reflected the overall health status and nutritional condition of neurocritical patients at the onset of the disease, and demonstrated the dynamic change process in body composition caused by the inflammatory response during the acute phase of the disease. This provided a reference basis for the observation and prognostic evaluation of such patients.

List of abbreviations

APACHE	II Acute Physiology and Chronic Health Evaluation II
Alb	albumin
ALC	absolute lymphocyte count
AIC	akaike information criterion
AVEPP	average posterior probability
BCM	body cell mass
BIA	bioimpedance analysis
BIC	bayesian information criterion
BMI	body mass index
CCI	Charlson Comorbidity Index
CNS	central nervous system
ECM	extracellular mass
ECW	extracellular water
FDR	False Discovery Rate
FFM	fat-free mass
GBTM	group-based trajectory model
GCS	Glasgow Coma Scale
GOS	Glasgow Outcome Scale
HALP	Hemoglobin, Albumin, Lymphocyte and Platelet score
NICU	neurology intensive care unit
NIHSS	National Institutes of Health Stroke Scale
PA	phase angle
PNI	prognostic nutritional index score
Post	Hoc post hoc comparisons
RDW	red blood cell volume distribution width
SMM	skeletal muscle mass
TBW	total body water

1. Background

The mortality and disability rates are high among neurocritical patients, and the serious disease burden resulting from their poor prognosis has been an urgent issue worldwide [1–3]. With the progress of aging, these patients are often characterized by advanced age, multiple comorbidities, and rapid changes in their condition. The prognostic assessment is crucial for the comprehensive understanding of patients' conditions, formulating scientifically reasonable treatment plans, and promptly implementing effective treatment measures. Many prognostic scoring systems have been established in previous studies and are widely used in clinical practice. These systems include the Acute Physiology and Chronic Health Evaluation II (APACHE II), National Institutes of Health Stroke Scale (NIHSS), etc., which contain a variety of indicators such as symptoms, signs, and blood and urine composition, etc. [4–6]. However, these assessment systems usually have many entries and are time-consuming. Some indicators require invasive operations, making real time and dynamic acquisition impossible, lacking dynamic monitoring and rapid assessment of disease progression in the acute phase. The prognosis of neurocritical patients is influenced by pre-existing physical health status, the severity of primary brain injury and the trend of secondary brain injury development. In particular, the dynamic changes in inflammatory response and nutritional status in the acute phase (1–7 days after onset) play a key role in the mechanism of secondary brain injury and disease progression [7–10]. The identification of acute phase nutritional and inflammatory status within 1–7 days after admission for neurocritical patients and the observation of trends in their changes may have positive implications for adjusting their treatment plans and improving clinical outcomes. Previous studies have indicated a significant overlap between assessment tools for nutrition and inflammation [11]. Therefore, the selection of a comprehensive indicator that can simultaneously reflect both states is particularly important in clinical practice to improve the effectiveness of assessment. BIA is an objective, noninvasive, portable, and reliable method for measuring bioelectrical characteristics, initially used for the estimation of body composition and the assessment of

nutritional status [12–14]. In recent years, BIA has gained widespread attention from clinical medical staff along with the growing demand in the healthcare field for accurate, cost-effective, and noninvasive clinical status monitoring and disease diagnosis systems. It is considered a promising tool for clinical prognostic assessment. In various clinical conditions, BIA parameters such as PA is associated with several clinical outcomes including: functional status at discharge in acute stroke patients [15]; short-term outcomes and long-term survival in breast cancer, pancreatic cancer and colorectal cancer patients post-surgery [16–18]; frailty mortality, morbidity, and length hospital of stay in patients after major cardiac surgery [19]. In the intensive care unit (ICU) setting, PA and ECW/TBW are associated with worse clinical outcomes such as mortality rate and length of ICU stay [20–22]. In addition, PA and ECW/TBW are also considered to be closely related to nutritional and inflammatory status, serving as comprehensive indicators that can simultaneously reflect both states [23,24]. However, previous studies have mostly focused on the relationship between the measurement values of these indicators at a given moment and prognosis, failing to continuously measure and dynamically assess changes in clinical status. To the best of our knowledge, there is limited research on the application of BIA in monitoring the condition of neurocritical patients, and the relationship between the dynamic change trends in relevant parameters and clinical outcomes in such patients remains unclear.

Therefore, in order to explore the application value of BIA in the clinical environment of neurocritical patients and to identify specific BIA parameters that can be used for prognostic assessment in this patient population, we hypothesized that the BIA parameters of neurocritical patients within 1–7 days of admission would be associated with their clinical outcomes. The group-based trajectory modeling (GBTM) was constructed for these parameters to clarify the distribution and change trends of their continuous measurement values, understand the process of changes in physical condition with disease progression, and achieve the goal of dynamically observing the patient's condition. Meanwhile, the development trends of each trajectory group and their relationship with prognosis were analyzed to elucidate the relationship between dynamic changes in BIA parameter trajectories and clinical outcomes in neurocritical patients.

2. Methods

2.1. Study design and participants

This is an observational study of neurocritical patients admitted to the neurology intensive care unit (NICU) of the First Affiliated Hospital of Chongqing Medical University from July 2022 to December 2022. Consecutive BIA measurements were performed from 1 to 7 days after admission in patients who met the inclusion criteria, while clinical data were prospectively collected during the hospitalization of this group of patients. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Medical Ethics Committee of the First Affiliated Hospital of Chongqing Medical University (Ethics review batch number 2022–198). This study is available from the Chinese clinical trials registry at www.chictr.org/cn/(clinical trial number ChiCTR2300069198).

Inclusion criteria:

1) Age ≥18 years old;
2) First presentation to the NICU and in the acute phase of the disease, i.e., within 1–7 days [25];
3) All patients or their guardians provide written informed consent.

Exclusion criteria:

1) Patients with neuromuscular disorders;
2) Patients who are unable to undergo BIA measurements due to hemodynamic instability, amputation, implantation of a metallic device (such as a pacemaker or artificial femoral head), skin damage in the area where the BIA electrodes are attached, etc;
3) BIA continuous measurement times≦4 times.

2.2. Outcome indicators

Glasgow Outcome Scale (GOS) at discharge [26]. Patients were evaluated for neurological prognosis at discharge using the GOS. The GOS is a functional outcome assessment tool which classifies patients into one of five categories based on their recovery: 1) dead, 2) vegetative state, 3) awake but severely disabled and dependent on others for daily living, 4) disabled but able to live independently, and 5) good functional recovery with possible minor neurological deficits but able to return to normal life. A score of 1–3 indicates an adverse functional outcome, while a score of 4–5 indicates a good functional outcome.

2.3. Data collection methods

1) Demographic indicators: including age and gender;
2) Disease characteristics: including day 1 admission-related indicators body mass index (BMI), APACHE II, Glasgow Coma Scale (GCS), Charlson Comorbidity Index (CCI) and diagnosis in neurocritical patients;
3) Biochemical indicators on day 1 of admission: including albumin (Alb), absolute lymphocyte count (ALC), red blood cell volume distribution width (RDW), prognostic nutritional index (PNI) and Hemoglobin, Albumin, Lymphocyte and Platelet score (HALP);

4) BIA parameters from 1 to 7 days after admission: including PA, skeletal muscle mass (SMM), fat-free mass (FFM), body cell mass (BCM), extracellular mass/body cell mass (ECM/BCM) and ECW/TBW.

All clinical data were recorded and collected by 2 dedicated research assistants through an electronic medical record system. All BIA data were measured and recorded by 2 dedicated dietitians using the BIA (InBody S10) instrument (see Appendix 1 for detail), and data entry was performed separately. Following data entry, the patient's name and medical record number were removed and the patient was given a unique study number. A designated study coordinator organized and confirmed the accuracy of all data, and manually verified inconsistent or out-of-range values. The data set was validated and cleaned prior to statistical analysis to prevent any further changes and to ensure consistency and integrity of statistical reporting and analysis data. All researchers who collected and collated the data were unaware of the study.

2.4. Definition of clinical and laboratory indicators

Definitions of relevant disease characteristics, biochemical indicators and BIA parameters in the study are presented in detail in the appendix (see Appendix A).

2.5. Group-based trajectory model

The group-based trajectory model (GBTM) is a specialized application of finite mixture modeling and is designed to identify groups of individuals following similar developmental trajectories. This method assumes that the population is heterogeneous and is composed of a finite number of distinct groups. In this study, we applied latent mixture modeling to identify trajectories of various BIA parameter from 1 to 7 days after admission in patients with neurocritical illnesses. The latent mixture modeling estimated the model parameters using the maximum likelihood method and assigned each individual to the corresponding group with maximum posteriori probability. Cubic, quadratic and linear tests were performed for each trajectory to select the most appropriate estimates. Bayesian information criterion (BIC) and Akaike information criterion (AIC) were used to evaluate the trajectory model, and the best-fit was considered when the average posterior probability >0.7, the minimum sample size per group >15.0 % and Entropy >0.8 were satisfied trajectory model [27]. Latent mixture modeling was performed using the proc-traj program in SAS9.4 to estimate the trajectory of BIA parameters [28]. Finally, each trajectory group was named and described according to the pattern and characteristics of the BIA parameters over time.

2.6. Description of statistical methods

Normally distributed measures in this study were described by mean ± standard deviation, and comparisons between groups were made by independent-samples T test for two groups and one-way ANOVA for three or more groups, and post hoc comparisons (Post Hoc) were made by SNK-q test. The measures of skewed distribution were described by median (25th, 75th percentile ranges), and the Mann-Whitney *U* test (for two groups) and Kruskal-Wallis test (for three or more groups) were used for comparison between groups, and the Dunn-Bonferroni method was used to adjust *P* values for post hoc comparisons (Post Hoc). Categorical data were described using cases and rates, and comparisons between groups were made using chi-squared test or Fisher exact test, and post hoc comparisons (Post Hoc) were adjusted for *P* values using False Discovery Rate (FDR) method.

A logistic regression model was used to analyze the relationship between BIA parameters trajectories and adverse clinical

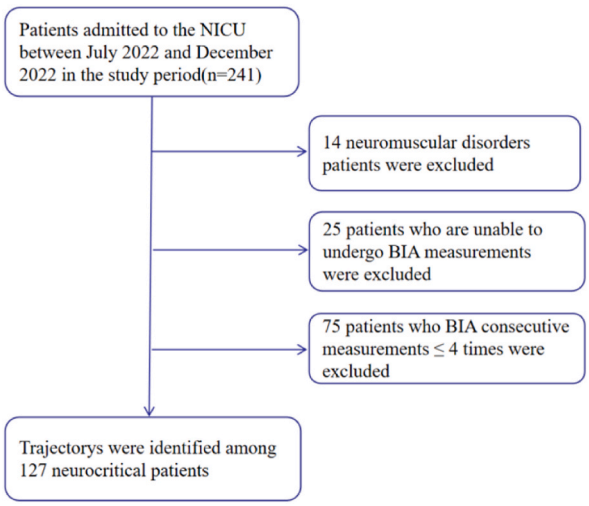

Fig. 1. Patient recruitment flowchart. NICU, Neurological intensive care unit; BIA, Bioelectrical Impedance Analysis.

outcomes. The strength of the association was determined by estimating the odds ratios (OR) and their 95 % confidence intervals. A two-side P value of <0.05 were considered statistically significant. All statistical analyses were performed using SAS9.4 (Copyright ©2016 SAS Institute Inc. Cary, NC, USA).

3. Results

3.1. Baseline characteristics between good and adverse clinical outcomes patients

A total of 241 patients were admitted to the NICU during the study period, 114 were excluded for reasons such as neuromuscular disorders and inability to apply accurate measurements by BIA, and 127 patients were finally analyzed, as shown in Fig. 1. Table 1 shows the comparison of demographic indicators, disease characteristics and biochemical indicators between the two groups of patients. Among demographic indicators and disease characteristics, compared with the good outcomes group, age, APACHE II and CCI were higher, while BMI and GCS were lower in the adverse outcomes group, with statistically significant differences between both groups (all $P < 0.05$). There were no statistically significant differences between the two groups for gender and diagnosis (all $P > 0.05$). Among the biochemical indicators (24 h of admission), RDW was higher in the adverse outcomes group, and the difference between the good and adverse outcomes groups was statistically significant ($P < 0.001$); while other biochemical indicators, including Alb, ALC, PNI and HALP, were not statistically significant between the two groups (all $P > 0.05$).

3.2. Trajectory modeling grouping process

The latent mixture modeling was applied to identify the trajectories of BIA parameters (PA,SMM,FFM,BCM,ECM/BCM and ECW/TBW) within 1–7 days of admission on a case-by-case basis, and the model evaluation indexes and the distribution of patients within the group are shown in Table 2. When the trajectories of PA and ECW/TBW were divided into 4 groups respectively, and the trajectories of SMM, FFM, BCM and ECM/BCM were divided into 3 groups respectively, the minimum sample size of each group was >15.0 %, and the AVEPP was >0.7 and Entropy was >0.8 for each group. The missing values of each BIA parameters and the fit of the trajectory analysis model for different subgroups are detailed in Appendix B (Table A1 and Table A2).

3.3. Trajectory diagram and trend analysis of trajectory groups

The changes over time were statistically significant ($P < 0.05$) for the PA and ECM/TBW trajectory groups, while there were no significant changes over time ($P > 0.05$) for the SMM, FFM, BCM and ECM/BCM trajectory groups (Table A3 in Appendix B).

Table 1
Comparison of demographic indicators, disease characteristics and biochemical parameters between the two groups.

Characteristics	Total (n = 127)	Group		χ2/t/Z	P value
		Good (GOS 4–5) (n = 60)	Adverse (GOS 1–3) (n = 67)		
Demographic indicators					
Age (years)	62.94 ± 17.75	59.17 ± 17.95	66.33 ± 16.99	−2.309	0.023
Gender					
Male	75 (59.06)	32 (53.33)	43 (64.18)	1.540	0.215
Female	52 (40.94)	28 (46.67)	24 (35.82)		
Disease characteristics					
BMI	23.44 ± 3.95	24.4 ± 3.77	22.57 ± 3.93	2.662	0.009
APACHE II	13.11 ± 7.06	8.58 ± 4.29	17.16 ± 6.59	−8.786	<0.001
GCS	12 (7,15)	15 (13,15)	7 (6,12)	7.676	<0.001
CCI	0 (0,2)	0 (0,1)	1 (0,2)	−3.334	0.001
Diagnosis (classification)					
Ischemic stroke	60 (47.24)	29 (48.33)	31 (46.27)	/	0.459
Intracerebral hemorrhage	22 (17.32)	10 (16.67)	12 (17.91)		
Status epilepticus	10 (7.87)	4 (6.67)	6 (8.96)		
CNS infectious diseases	25 (19.69)	13 (21.67)	12 (17.91)		
Metabolic encePAlopathy	6 (4.72)	4 (6.67)	2 (2.99)		
Others	4 (3.15)	0 (0.00)	4 (5.97)		
Biochemical indicators on day 1 of admission					
Alb(g/L)	39.34 ± 5.56	39.87 ± 5	38.87 ± 6.02	1.013	0.313
ALC (10^9/L)	1.28 ± 0.8	1.43 ± 0.71	1.15 ± 0.86	1.970	0.051
RDW (%)	13.57 ± 1.5	13.06 ± 1.06	14.03 ± 1.68	−3.955	<0.001
PNI(g/L+10^9/L)	45.69 ± 7.64	46.88 ± 7.05	44.62 ± 8.04	1.676	0.096
HALP $(g/L)^2$	35.93 ± 22.82	39.18 ± 19.89	33.01 ± 24.95	1.529	0.129

Note:/No statistic by Fisher's exact test. Abbreviation: BMI body mass index; APACHE II Acute Physiology and Chronic Health Evaluation II score; GCS Glasgow Coma Scale; CCI Charlson Comorbidity Index; CNS Central nervous system; CNS infectious diseases which include N-methyl-D-aspartate receptors, tuberculous meningitis, viral encephalitis, purulent meningitis; Others which include brain lymphoma, neuronal intranuclear inclusion disease and parkinsonism; Alb albumin; ALC absolute lymphocyte count; RDW red blood cell volume distribution width; PNI prognostic nutritional index score; HALP Hemoglobin, Albumin, Lymphocyte and Platelet score.

Table 2
Parameters associated with trajectory modeling of BIA parametes 1–7 days after admission in neurocritical patients.

BIA parameters	Number of subgroups	LL	BIC	AIC	Entropy	Participants per group , N (%)	AVEPP
PA (°)	4	−658.80	−687.87	−670.80	0.98	C1 = 30 (23.62 %)/C2 = 49 (38.58 %)/C3 = 28 (22.05 %)/C4 = 20 (15.75 %)C1 = 0.98/C2 = 0.99/C3 = 0.98/C4=>0.99	
SMM(kg)	3	−1882.35	−1904.15	−1891.35	0.95	C1 = 38 (29.92 %)/C2 = 52 (40.94 %)/C3 = 37 (29.13 %)	C1 = 0.99/C2 = 0.97/C3 = 0.98
FFM(kg)	3	−2266.68	−2288.47	−2275.68	0.95	C1 = 36 (28.35 %)/C2 = 55 (43.31 %)/C3 = 36 (28.35 %)	C1 = 0.98/C2 = 0.97/C3 = 0.98
BCM(kg)	3	−1948.35	−1970.15	−1957.35	0.95	C1 = 38 (29.92 %)/C2 = 52 (40.94 %)/C3 = 37 (29.13 %)	C1 = 0.98/C2 = 0.98/C3 = 0.99
ECM/BCM	3	1622.44	1600.64	1613.44	0.88	C1 = 26 (20.47 %)/C2 = 78 (61.42 %)/C3 = 23 (18.11 %)	C1 = 0.94/C2 = 0.95/C3 = 0.95
ECW/TBW	4	2757.25	2728.19	2745.25	0.95	C1 = 24 (18.90 %)/C2 = 58 (45.67 %)/C3 = 20 (15.75 %)/C4 = 25 (19.69 %)	C1 = 0.99/C2 = 0.96/C3 = 0.96/C4=>0.99

Note : BIC Bayesian information criterion; AIC Akaike information criterion; AVEPP average posterior probability; PA phase angle; SMM skeletal muscle mass; FFM fat-free mass; BCM body cell mass; ECM extracellular mass; ECW extracellular water; TBW total body water.

PA trajectory analysis showed that the initial values (day 1 of admission) for each trajectory group of PA were Class1 (6.48 ± 0.53), Class2 (5.18 ± 0.42), Class3 (4.12 ± 0.42), and Class4 (2.96 ± 0.61), and each trajectory group gradually decreased over time (all $P < 0.05$) (Table A4 in Appendix B). Class4 showed the fastest decline ($\beta = -0.083$, $P < 0.001$) compared to Class1 ($\beta = -0.038$, P = 0.031), Class2 ($\beta = -0.039$, $P = 0.005$) and Class3 ($\beta = -0.048$, $P = 0.009$) (Table A3 in Appendix B). Therefore, Class1, Class2, Class3 and Class4 were named as "High PA slowly decreasing subgroup", "Medium PA slowly decreasing subgroup", "Low PA slowly decreasing subgroup" and "Low PA rapidly decreasing subgroup" respectively according to the initial value and descent speed of each trajectory group. Each class of patients accounted for 23.62 %, 38.58 %, 22.05 % and 15.75 % of the total number of patients, respectively (Fig. 2A).

ECW/TBW trajectory analysis showed that the initial values (day 1 of admission) for each ECW/TBW trajectory group were Class1 (0.373 ± 0.005), Class2 (0.387 ± 0.008), Class3 (0.397 ± 0.006), and Class4 (0.413 ± 0.007) respectively (Table A5 in Appendix B). Class1 ($\beta = 0.0005$, $P = 0.054$) did not change significantly over time, and Class2 ($\beta = 0.0007$, $P < 0.001$), Class3 ($\beta = 0.0010$, $P < 0.001$) and Class4 ($\beta = 0.0009$, $P < 0.001$) all increased slowly over time (Table A3 in Appendix B). Based on the initial value and rising trend of each trajectory group, considering the fluctuation range of normal value of human water ratio (0.360–0.390), Class1, Class2, Class3 and Class4 were named as "Normal ECW/TBW stable subgroup", "Normal ECW/TBW slowly rising subgroup", "Medium-high ECW/TBW slowly rising subgroup" and "High ECW/TBW slowly rising subgroup". Each class of patients accounted for 18.90 %, 45.67 %, 15.75 % and 19.69 % of the total number of patients, respectively (Fig. 2B).

3.4. Association of PA and ECW/TBW trajectories with clinical outcomes

Comparison of the clinical outcomes of the PA trajectories showed that the length of NICU stay was prolonged in the "Low PA

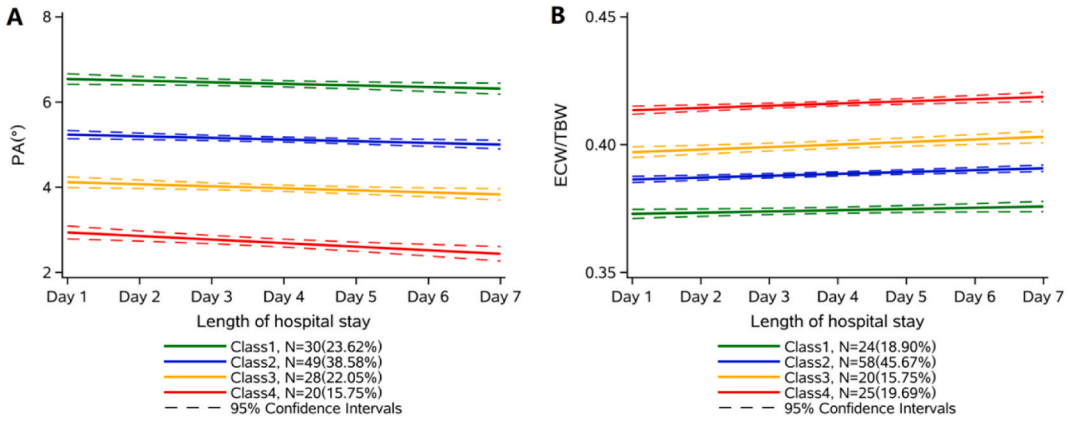

Fig. 2. PA and ECW/TBW trajectory patterns within the first 1–7 days of admission to the NICU. Trajectory models identified 4 distinct trajectory subgroups of PA (A) and ECW/TBW (B) in the neurocritical patients cohort. Solid lines show the mean PA (A) and mean ECW/TBW (B) levels for specific categories as a function of hospital stay. Dashed lines indicate estimated 95 % confidence intervals. Green, blue, orange, and red indicate the different trajectory groups respectively, which are arranged sequentially in increasing order of the trajectory group hierarchy. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

slowly decreasing subgroup" (Class3) compared to the "High PA slowly decreasing subgroup" (Class1) and the "Medium PA slowly decreasing subgroup" (Class2) ($P = 0.003$). Compared with the "High PA slowly decreasing subgroup" (Class1), the "Medium PA slowly decreasing subgroup" (Class2) and the "Low PA slowly decreasing subgroup" (Class3), the "Low PA rapidly decreasing subgroup" (Class4) had higher incidence of adverse outcome (GOS:1–3) at discharge (95 %), higher in-hospital mortality (45 %), longer NICU length of stay of 9 (5.5–20) days and more average daily hospitalization cost of RMB 3600 (2300–5000). Furthermore, the analysis showed a statistically significant difference between the groups (all $P < 0.05$) (Table 3).

Comparison of the clinical outcomes of the ECW/TBW trajectories showed that compared with the "Normal ECW/TBW stable subgroup" (Class1), the "Normal ECW/TBW slowly rising subgroup" (Class2) and the "Medium-high ECW/TBW slowly rising subgroup" (Class3), the "High ECW/TBW slowly rising subgroup" (Class4) had higher incidence of adverse outcome (GOS:1–3) at discharge (88 %), higher in-hospital mortality (40 %) and longer NICU stay of 8 (6,18) days. Furthermore, the analysis showed a statistically significant difference between the groups (all $P < 0.05$) (Table 4).

To reduce the effect of confounding factors, logistic regression models were used to determine the association of each trajectory group of PA and ECW/TBW with adverse outcome at hospital discharge in neurocritical patients. In model I, no parameter adjustment was performed. In Model II, after correcting for potential confounders (age, gender, BMI, diagnosis, APACH II, GCS, CCI, and RDW), it was found that the "High PA slowly decreasing subgroup" (Class1) (OR = 0.0003, 95 % CI = 0.000003–0.032, $P = 0.001$), the "Medium PA slowly decreasing subgroup" (Class2) (OR = 0.0004, 95%CI = 0.000004–0.036, $P = 0.001$) and the "Low PA slowly decreasing subgroup" (Class3) (OR = 0.003, 95%CI = 0.000043–0.142, $P = 0.004$) all had a lower risk of adverse outcome than the "Low PA rapidly decreasing subgroup" (Class4). The "Normal ECW/TBW stable subgroup" (Class1) (OR = 0.013, 95%CI = 0.0004–0.414, $P = 0.014$), the "Normal ECW/TBW slowly rising subgroup" (Class2) (OR = 0.035, 95 % CI = 0.002–0.698, $P = 0.028$) and the "Medium-high ECW/TBW slowly rising subgroup" (Class3) (OR = 0.038, 95 % CI = 0.002–0.713, $P = 0.029$) all had a lower risk of adverse outcome than the "High ECW/TBW slowly rising subgroup" (Class4) (see Table 5).

4. Discussion

A total of 127 neurocritical patients were included in this study, and group-based trajectory modeling of their BIA parameters from 1 to 7 days of admission were performed to analyze the differences and correlations between BIA parameters (PA and ECW/TBW) trajectories and patients' clinical outcomes respectively. It was found that neurocritical patients with lower PA at admission tended to experience a faster decrease over time during the first 1–7 days of admission and had worse outcomes. Conversely, patients with higher ECW/TBW at admission tended to experience a slower increase over time during the first 1–7 days of admission and had worse outcomes. PA and ECW/TBW can be used as valid indicators for the observation of the condition in neurocritical patients. Neurocritical patients who experience a faster decrease in low PA and a slower increase in high ECW/TBW on days 1–7 of admission may be in a coexistent state of malnutrition and inflammation and may be at a greater risk of adverse clinical outcomes.

PA is the ratio of reactance (Xc) to resistance (R) obtained from BIA measurements and expressed as an angle [28]. PA is a valid indicator of cell membrane integrity and cell function, where lower PA is associated with impaired cell structure and increased cell death [29]. In disease states, PA is reduced mainly as a result of malnutrition, inflammation, or both [30]. A recent meta-analysis of the prognostic value of PA in critically ill patients noted that low PA was strongly associated with higher mortality, poorer functional outcomes, and longer ICU stays [31]. However, there is a great deal of heterogeneity in the PA thresholds used to define adverse outcomes in previous studies [32–34], leading to limitations in their clinical application. The main reasons for this are that most of these studies focused on static results of PA indicators at one time point, which are inherently vulnerable to multiple factors and only reflect the disease status of the patient at the time of measurement, and cannot assess the course and trend of the disease with pathophysiological development. In this study, for the first time, the dynamic data of PA were collected by continuous measurement of

Table 3
Clinical outcomes of the study patients with different PA trajectory groups.

Characteristics	Total (n = 127)	PA trajectory groups				χ2/Z	P value
		Class 1 (n = 30)	Class 2 (n = 49)	Class 3 (n = 28)	Class 4 (n = 20)		
GOS at discharge							
4–5 score	60 (47.24)	20 (66.67)	29 (59.18)	10 (35.71)	1 (5.00)	23.157	<0.001
1–3 score	67 (52.76)	10 (33.33)	20 (40.82)	18 (64.29)	19 (95.00)[abc]		
In-hospital death							
No	105 (82.68)	29 (96.67)	41 (83.67)	24 (85.71)	11 (55.00)[a]	/	0.003
Yes	22 (17.32)	1 (3.33)	8 (16.33)	4 (14.29)	9 (45.00)		
Length of NICU stay (day)	6 (3,12)	3 (2,5)	6 (2,10)	7.5 (3.5,12.5)a	9 (5.5,20)[a]	14.287	0.003
Length of hospital stay (day)	17 (11,31)	16 (14,23)	17 (10,27)	24 (13.5,33.5)	15.5 (7.5,41.5)	2.823	0.420
Total hospitalization cost (million)	4.4 (2.22,9.74)	2.72 (1.84,9.14)	4.77 (1.97,7.66)	5.81 (2.66,10.53)	5.71 (3.77,11.54)	5.245	0.155
Average daily hospitalization cost (million)	0.23 (0.13,0.41)	0.15 (0.12,0.28)	0.21 (0.13,0.37)	0.25 (0.17,0.42)	0.36 (0.23,0.5)a	8.539	0.036

Note:/No statistic by Fisher's exact test; *P*-values were adjusted by the FDR method for pairwise comparisons of categorical data, and the Dunn Bonferroni method for measurements with skewed distribution, a compared with class 1, $P < 0.05$; b compared with class 2, $P < 0.05$; c compared with Class 3, $P < 0.05$.

Table 4
Clinical outcomes of the study patients with different ECW/TBW trajectory groups.

Characteristics	Total (n = 127)	ECW/TBW trajectory groups				χ2/Z	P value
		Class 1 (n = 24)	Class 2 (n = 58)	Class 3 (n = 20)	Class 4 (n = 25)		
GOS at discharge							
4–5 score	60 (47.24)	15 (62.50)	33 (56.90)	9 (45.00)	3 (12.00)	16.909	0.001
1–3 score	67 (52.76)	9 (37.50)	25 (43.10)	11 (55.00)	22 (88.00)[abc]		
In-hospital death							
No	105 (82.68)	24 (100.00)	48 (82.76)	18 (90.00)	15 (60.00)	/	0.002
Yes	22 (17.32)	0 (0.00)	10 (17.24)	2 (10.00)	10 (40.00)[a]		
Length of NICU stay (day)	6 (3,12)	3 (2,5.5)	5.5 (2,10)	7.5 (4,12)	8 (6,18)[a]	13.290	0.004
Length of hospital stay (day)	17 (11,31)	16.5 (14,23.5)	15.5 (10,27)	26.5 (13,43.5)	16 (10,35)	3.236	0.357
Total hospitalization cost (million)	4.4 (2.22,9.74)	3.15 (2.04,8.84)	4.01 (1.89,7.66)	6.4 (2.48,10.07)	5.48 (3.83,13.33)	4.327	0.228
Average daily hospitalization cost (million)	0.23 (0.13,0.41)	0.16 (0.13,0.3)	0.22 (0.12,0.35)	0.24 (0.17,0.39)	0.35 (0.23,0.46)	5.941	0.115

Note:/No statistic by Fisher's exact test; *P*-values were adjusted by the FDR method for pairwise comparisons of categorical data, and the Dunn Bonferroni method for measurements with skewed distribution, a compared with class 1, $P < 0.05$; b compared with class 2, $P < 0.05$; c compared with Class 3, $P < 0.05$.

Table 5
Association of each trajectory group of PA and ECM/TBW with adverse outcome in neurocritical patients in different logistic regression models.

BIA parameters	Model I			Model II	
	OR (95%CI)	P value		OR (95%CI)	P value
PA			.		
Trend	2.518 (1.641,3.862)	<0.001	.	5.618 (1.971,16.012)	0.001
Class 1	0.039 (0.006,0.254)	0.001	.	0.0003 (0.000003,0.032)	0.001
Class 2	0.053 (0.009,0.322)	0.001	.	0.0004 (0.000004,0.036)	0.001
Class 3	0.136 (0.021,0.878)	0.036	.	0.003 (0.000043,0.142)	0.004
Class 4	1.0 (reference)		.	1.0 (reference)	
ECW/TBW			.		
Trend	2.089 (1.399,3.121)	<0.001	.	2.929 (1.077,7.964)	0.035
Class 1	0.095 (0.023,0.392)	0.001	.	0.013 (0.0004,0.414)	0.014
Class 2	0.118 (0.034,0.418)	0.001	.	0.035 (0.002,0.698)	0.028
Class 3	0.188 (0.044,0.801)	0.024	.	0.038 (0.002,0.713)	0.029
Class 4	1.0 (reference)		.	1.0 (reference)	

Model I: No other parameter adjustment was performed.
ModelII: Adjusted for age, gender, BMI, diagnosis, APACHE II, GCS, CCI, RDW.

BIA, and its distribution and trends in the acute phase of neurocritical patients' morbidity were restored by modeling the trajectory of PA dynamic data. In this study, patients in both the "Low PA slowly decreasing subgroup" and the "Low PA rapidly decreasing subgroup" had PA values at admission that were lower than the critical PA values for malnutrition in critically ill patients [35], and the lower the initial PA, the faster their PA values decreased over time (1–7 days of admission), and the higher their risk of adverse outcomes. This result suggests that pre-hospital malnutrition has led to a reduction in muscle mass, a decrease in cellular function and a decrease in total body water, which is manifested by low PA on admission [36]. Conversely, the acute phase inflammatory response and oxidative stress lead to further damage to the cellular structure and cell membrane integrity of the affected organ, which accelerates cell death and manifests as a rapid decrease in PA. Therefore, low PA on admission and the rate of its decrease are positively correlated with the degree of organ involvement, thus affecting patient prognosis [37,38]. Notably, the "High PA slowly decreasing subgroup" and the "Medium PA slowly decreasing subgroup" exhibited initially higher PA, indicating good nutritional status, and their PA values also showed a slow decrease over time within 1–7 days of admission, but the risk of adverse outcomes occurred was lower in both the "High PA slowly decreasing subgroup" and the "Medium PA slowly decreasing subgroup" compared to the "Low PA rapidly decreasing subgroup". This result suggests that patients with good nutritional status at admission may have a better prognosis or benefit more from aggressive treatment in this group because of their better ability to recover from stressors, although PA shows a tendency to decrease in response to the inflammation in the acute phase. Therefore, PA at admission and its dynamic trends can help in the observation and prognostic evaluation of neurocritical patients. PA levels on admission reflects the patient's pre-hospital nutritional status. Pre-hospital nutritional status is related to the patient's ability to resist stress and prognosis. Low PA in patients at admission indicates low immune function, and early interventions should be taken to improve their ability to resist stress and improve their clinical outcome. Notably, PA showed a decreasing trend in all trajectory groups from 1 to 7 days of admission and showed a cascading relationship with the risk of adverse outcomes, indicating that the faster the rate of PA decrease, the greater the degree of inflammatory response and organ function impairment, and the greater the risk of adverse prognosis.

ECW/TBW, or edema index, is the ratio of extracellular water to total body water. This ratio is thought to be associated with the prognosis of several diseases. Previous studies have pointed out that high ECW/TBW is a valid predictor of adverse outcomes such as

longer duration of mechanical ventilation and death in critically ill patients, cancer patients and hemodialysis patients [39]. In this study, patients in the high ECW/TBW trajectory group at admission had the worst prognosis, and the results were consistent with previous studies. Notably, through trajectory modeling and correlation analysis, we observed that the high ECW/TBW trajectory group showed a slow and sustained elevated course of change in the trend from 1 to 7 days of admission. The sustained increase in ECW/TBW may reflect a loss of muscle mass [24]. Meanwhile, a study by Unal A [24]et al. noted that the ECW/TBW ratio was positively correlated with the inflammatory index hypersensitivity C-reactive protein. Therefore, the persistent increase in ECW/TBW in the acute phase may reflect a process of malnutrition and an increased degree of inflammatory response, which in turn affects patient' clinical outcomes. However, BIA measurements cannot distinguish the distribution space (intravascular or intertissue) of ECW in humans, and the increase in ECW/TBW may also be associated with increased plasma due to excessive transfusions or cardiac or renal disease [39]. Thus, to make a comprehensive judgment, it is necessary to interpret this index in conjunction with other relevant clinical indicators.

4.1. Limitation

The main limitation of our study was as follows: it was a case-control study with a relatively small sample size, resulting in limited information acquisition and the inability to directly estimate the causal relationship between BIA parameter trajectories in neurocritical patients and their prognosis. Therefore, it is still necessary to expand the sample size and conduct prospective cohort studies to validate the causal inference of BIA parameter trajectories and prognosis at a later stage. To control for biases and address potential confounding factors, we adopted a prospective data collection method in this study and adjusted for all variables that differed in the baseline comparison between the two groups of patients during the data analysis stage. Considering that this study was conducted in a single medical unit, future multicenter and multiregional studies are needed to further validate the generalizability and external validity of the findings, while avoiding the influence of regional-specific factors. In addition, the following issues should be explored in future studies: 1) the assessment of the effectiveness of relevant intervention treatments based on dynamic change trends in PA during hospitalization; 2) the relationship between other hydration assessment parameters measured serially (such as BIVA) and clinical outcomes; and 3) the clinical application value of BIA parameter trajectories in predicting the prognosis of neurocritical patients.

5. Conclusion

This study has been the first to apply continuous measurement of BIA to the observation and prognostic assessment of neurocritical patients in the acute phase, and the first to restore the dynamic change process of body composition with disease progression during the acute phase of these patients by modeling the trajectory of BIA parameters. Our study found that different trajectories of PA and ECW/TBW within 1–7 days of admission were associated with patient prognosis. Neurocritical patients with low PA and rapidly declining trajectories upon admission and high ECW/TBW and slowly increasing trajectories upon admission were at the highest risk of poor prognosis. Our study provided a more efficient and convenient assessment tool for early prognosis evaluation in this patient population.

Funding disclosure

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

Ethics declarations

This study was reviewed and approved by the Medical Ethics Committee of the First Affiliated Hospital of Chongqing Medical University, with the approval number:2022–198. All patients (or their legal guardians) provided informed consent to participate in the study.

Data availability

The datasets used and analyzed during the current study are not publicly available due to the authors do not have permission to share data, but are available from the corresponding author on reasonable request.

CRediT authorship contribution statement

Jingjing Peng: Writing – review & editing, Writing – original draft, Validation, Formal analysis, Data curation, Conceptualization. **Jiajia Yang:** Validation, Software, Methodology, Investigation, Data curation. **Feng Li:** Writing – review & editing, Supervision, Resources, Project administration, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

We thank all of the patients in this study for their cooperation.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e32948.

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