Body Composition Analysis in Septic Shock Patients Receiving Protocol-Driven Resuscitation Bundle Therapy: A Prospective Observational Study

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Abstract

Background: Bio-electrical impedance analysis (BIA) is a rapid, simple, and noninvasive tool for assessing volume status in various diseases. Body composition analysis using BIA may identify factors associated with poor outcomes in critically ill patients. Little is known, however, about the relationship between the results of body composition analysis in the emergency department (ED) and mortality in septic shock patients.

Objectives: This study assessed the association between parameters identified by body composition analysis and mortality in patients with septic shock who underwent protocol-driven resuscitation bundle therapy in the ED.

Methods: Data were prospectively collected on adult patients with septic shock who underwent protocol-driven resuscitation bundle therapy between December 2019 and December 2020. Body composition was determined in the ED using BIA with the patient in the supine position. Septic shock was defined by sepsis-3 criteria, and the primary outcome was 30-day mortality.

Results: The study included 218 patients, of whom 58 (26.6%) died within 30 days. The mean time from ED admission to the measurement of body composition was 5.4 hours. The average ratio of extracellular water (ECW) to total body water (TBW) was significantly higher in non-survivors than in survivors (0.412 vs. 0.400, p=0.001). The optimal ECW/TBW cutoff for predicting 30-day mortality was 0.40, with mortality rates being significantly higher in patients with ECW/TBW >0.4 than in patients with ECW/TBW≦0.4 (37.8% vs. 17.5%, p=0.001). Multivariate analysis showed that ECW/TBW >0.4 (odds ratio [OR], 2.11; 95% confidence interval [CI], 1.05–4.23, p = 0.036), active cancer (OR, 2.39; 95% CI, 1.06–5.38, p=0.036), prothrombin time (OR, 2.77; 95% CI, 1.29–5.93, p=0.009), and initial lactate level (OR, 1.15; 95% CI, 1.03–1.28, p=0.010) were significantly associated with 30-day mortality.

Conclusions: The ECW/TBW>0.40 is the only body composition parameter associated with 30-day mortality in patients with septic shock.

Background

Septic shock, which is caused by dysregulation of a host response to infection, is a life-threatening medical condition with high morbidity and mortality rates. In addition to early recognition, guidelines for the management of septic shock recommend the application of protocol-driven resuscitation bundle therapy, which includes fluid resuscitation, blood culturing, and the administration of broad-spectrum antibiotics.[1]

Despite these supportive therapies, mortality rates remain high, suggesting the need to identify modifiable factors or targets for adjuvant therapies in patients with septic shock.[2, 3] Bio-electrical impedance analysis (BIA) of body composition is a non-invasive method of differentiating among fats, proteins, and minerals. In addition, multifrequency BIA is a rapid, simple, and noninvasive method of for assessing volume status in critically ill patients.[4–6]

Body composition analysis using BIA may provide useful information in patients undergoing dialysis, in burn patients, and in patients with malnutrition, trauma, and other critical illnesses.[7–11] Little is known, however, about the relationship between the results of body composition analysis and mortality in septic shock patients. This study hypothesized that body composition analysis might provide information regarding abnormal fluid and nutritional status associated with mortality, particularly during the early resuscitation period. The aim of this study was to determine the association between parameters identified by body composition analysis and mortality in patients with septic shock who underwent protocol-driven resuscitation bundle therapy in the emergency department (ED).

Methods

Study design and population

This prospective observational study included adult patients, aged ≥ 18 years, with septic shock who were admitted to the ED of a tertiary referral center in Seoul, South Korea, between December 2019 and December 2020 and underwent protocol-driven resuscitation care bundle therapy and measurements of body composition by BIA. Septic shock was based on sepsis-3 criteria, defined as refractory hypotension, hyperlactatemia (≥ 2 mmol/L), and suspected or confirmed infection.[12] Refractory hypotension was defined as persistent hypotension with systolic blood pressure < 90 mmHg or mean arterial pressure < 70 mmHg or the need for vasopressors despite adequate intravenous fluid resuscitation (20–30 mL/kg or ≥ 1 L of crystalloid solution administration).[13, 14] Active cancer was defined as a histologically confirmed solid or hematologic malignancy that had been diagnosed or treated within the previous 6 months, or as a recurrent, regionally advanced, or metastatic cancer treated within the previous 6 months. [15, 16] If a patient visited the ED multiple times during the study period, only the first visit was included. The study design was approved by the Institutional Review Board of Asan Medical Center, which waived the requirement for informed consent.

Data collection

Patients’ electronic medical records were reviewed, and their demographic, clinical, and laboratory test results on ED admission were recorded. Details of each patient’s medical history, including hypertension, diabetes mellitus, chronic renal disease, chronic liver disease, heart failure, cardiovascular disease, and active cancer, were also recorded. Laboratory test results during ED stay included leukocyte and platelet counts; prothrombin time (PT); and hemoglobin (Hb), creatinine, total bilirubin, C-reactive protein (CRP), and lactate levels. Mental status was assessed using the alert/responsive to voice/responsive to pain/unresponsive scale, and patients who were not alert were considered to have altered mental status.[17] Sequential Organ Failure Assessment (SOFA) scores were calculated based on physiological and laboratory data collected in the ED.[18]

BIA was performed using a portable multifrequency bio-impedance device (InBody S10, InBody Co. Ltd., Seoul, Korea). This analyzer measured segmental resistance at multiple frequencies (1, 5, 50, 250, 500 kHz, and 1 MHz) with the 8-point touch type electrodes prepared according to the manufacturer's instructions. Body composition data were measured as soon as patients were recognized as having septic shock. The primary outcome of this study was 30-day mortality, and all patients were followed up for more than 30 days.

Statistical analysis

Categorical variables were reported as numbers and percentages and compared using the chi-square test or Fisher's exact test, as appropriate. Continuous variables were reported as means ± standard deviations due to their normal distribution and compared using Student's t-test or the Wilcoxon rank-sum test. Factors associated with 30-day mortality were assessed by univariate and multivariate logistic regression analyses. Variables with $p < 0.1$ on univariate analyses were included in the multivariable analyses. The logistic model of goodness of fit was evaluated using the Hosmer–Lemeshow test. The results of multivariate logistic regression analysis were reported as odds ratios (OR) and 95% confidence intervals (CI). The optimal cutoff value of variables for predicting 30-day mortality was estimated by receiver operating characteristic (ROC) curves. For all tests, P values were two tailed, and those < 0.05 were considered statistically significant. All analyses were performed using IBM SPSS Statics for Windows, version 21.0 (IBM Corp., Armonk, NY, USA).

Results

Baseline characteristics of total patients

During the study period, from December 2019 to December 2020, 218 patients with septic shock and who underwent BIA in the ED were enrolled. Their mean age was 66.3 years, and 58.3% were male. The overall 30-day mortality rate was 26.6%.

The demographic and clinical characteristics of 30-day survivors and non-survivors are compared in Table 1. Age, gender, and medical history did not differ significantly in the two groups, but active cancer was significantly lower in survivors than in non-survivors (61.3% vs. 81.0%, p = 0.006). Altered mental status was more common in non-survivors than in survivors, but the difference was not statistically significant (24.1% vs. 15.0%, p = 0.116). Evaluation of laboratory data showed that Hb levels were significantly lower (9.80 vs. 10.89 g/dL, p = 0.003), whereas while PT (1.85 vs. 1.31 international normalized ratio (INR), p = 0.001), initial lactate levels (5.81 vs. 3.47 mmol/L, p = 0.000), and SOFA scores (6.28 vs. 4.69, p = 0.000) were significantly higher, in non-survivors than in survivors. Ventilator use (27.6% vs. 14.4%, p = 0.025) and the application of continuous renal replacement therapy (CRRT; 22.4% vs. 6.9%, p = 0.001) were significantly more frequent in non-survivors than in survivors.

Table 1
Comparison of the clinical characteristics between the 30-day non-survivor group and the 30-day survivor group

	Total (n = 218)	30-day survivors (n = 160)	30-day non-survivors (n = 58)	P value
Age (years)	66.28 ± 11.53	66.11 ± 11.30	66.76 ± 12.22	0.716
Gender - Male	127 (58.3)	93 (58.1)	34 (58.6)	0.948
Height (cm)	162.5 ± 9.10	162.4 ± 9.27	162.8 ± 8.66	0.750
Weight (kg)	57.02 ± 11.15	57.04 ± 11.22	56.97 ± 11.05	0.968
BMI (kg/m^2)	23.40 ± 37.36	21.59 ± 3.45	28.40 ± 52.74	0.329
Comorbidities				
Hypertension	74 (33.9)	55 (34.4)	19 (32.8)	0.824
Diabetes mellitus	60 (27.5)	48 (30.0)	12 (20.7)	0.174
Chronic renal disease	22 (10.1)	17 (10.6)	5 (8.6)	0.664
Cardiovascular disease	23 (10.6)	16 (10.0)	7 (12.1)	0.660
Heart failure	7 (3.2)	5 (3.1)	2 (3.4)	0.905
Chronic liver disease	27 (12.4)	19 (11.9)	8 (13.8)	0.704
Active cancer	145 (66.5)	98 (61.3)	47 (81.0)	0.006
Vital sign				
SBP (mmHg)	89.49 ± 22.48	89.69 ± 22.64	88.93 ± 22.19	0.825
DBP (mmHg)	58.00 ± 15.48	58.41 ± 14.77	56.90 ± 17.37	0.526
Heart rate (bpm)	110.50 ± 23.73	108.73 ± 23.30	115.38 ± 24.42	0.067
Body temperature (°C)	37.94 ± 4.35	37.86 ± 1.36	38.17 ± 8.16	0.774
SpO2 (%)	94.55 ± 5.98	94.73 ± 4.60	94.04 ± 8.76	0.571
Altered mental status	38 (17.4)	24 (15.0)	14 (24.1)	0.116

Values are expressed as the mean ± standard deviation, the median [interquartile range] or number (%).

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; SpO2, saturation of percutaneous oxygen; WBC, white blood cell; PT, prothrombin time; INR, international normalized ratio.; CRP, c-reactive protein; SOFA, sequential organ failure assessment; CRRT, continuous renal replacement therapy

	Total (n = 218)	30-day survivors (n = 160)	30-day non-survivors (n = 58)	P value
Laboratory data				
WBC ($x10^3/\mu L$)	10.92 ± 9.59	10.55 ± 8.79	11.96 ± 11.55	0.401
Hemoglobin (g/dL)	10.60 ± 2.43	10.89 ± 2.36	9.80 ± 2.47	0.003
Platelet ($x10^3/\mu L$)	149.14 ± 108.17	154.02 ± 97.89	135.69 ± 132.52	0.339
PT (INR)	1.45 ± 0.70	1.31 ± 0.32	1.85 ± 1.15	0.001
Creatinine (mg/dL)	1.99 ± 1.70	1.90 ± 1.67	2.25 ± 1.77	0.178
Total bilirubin (mg/dL)	2.70 ± 4.63	2.26 ± 3.51	3.90 ± 6.73	0.081
CRP (mg/dL)	14.70 ± 10.29	14.01 ± 10.04	16.61 ± 10.80	0.099
Lactate (mmol/L)	4.09 ± 3.27	3.47 ± 2.86	5.81 ± 3.72	0.000
SOFA	5.11 ± 2.80	4.69 ± 2.57	6.28 ± 3.08	0.000
SOFA, maximum	9.56 ± 3.97	8.76 ± 3.42	11.79 ± 4.52	0.000
Ventilator	39 (17.9)	23 (14.4)	16 (27.6)	0.025
CRRT	24 (11.0)	11 (6.9)	13 (22.4)	0.001

Values are expressed as the mean ± standard deviation, the median [interquartile range] or number (%).

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; SpO2, saturation of percutaneous oxygen; WBC, white blood cell; PT, prothrombin time; INR, international normalized ratio.; CRP, c-reactive protein; SOFA, sequential organ failure assessment; CRRT, continuous renal replacement therapy

Table 2 summarizes the results of body composition analysis in 30-day survivors and non-survivors. The mean time from ED admission to the measurement of body composition was 5.4 hours. The average ratio of extracellular water (ECW) to total body water (TBW) was significantly higher in non-survivors than in survivors (0.412 ± 0.027 vs. 0.400 ± 0.023, $p = 0.001$). ROC analysis found that the optimal ECW/TBW cutoff for predicting 30-day mortality was 0.40. The prevalence of patients with ECW/TBW > 0.4 was significantly higher in the non-survivor than in the survivor group (63.8% vs. 38.1%, $p = 0.001$). No other body composition parameter differed significantly between survivors and non-survivors.

Table 2
Comparison of the body composition between the 30-day non-survivor group and the 30-day survivor group

	Total (n = 218)	30-day Survivors (n = 160)	30-day non-survivors (n = 58)	P value
Mean time to body composition (hour)†	5.36 ± 3.44	5.35 ± 3.45	5.39 ± 3.45	0.933
ICW	20.92 ± 17.18	19.95 ± 4.28	23.60 ± 32.59	0.398
ECW	14.12 ± 11.33	13.31 ± 2.96	16.34 ± 21.39	0.288
TBW	35.04 ± 28.45	33.26 ± 7.08	39.94 ± 53.94	0.351
Protein	9.04 ± 7.42	8.62 ± 1.85	10.19 ± 14.08	0.401
Mineral	3.14 ± 0.74	3.16 ± 0.64	3.11 ± 0.98	0.669
Fat	12.09 ± 7.91	12.01 ± 7.48	12.33 ± 9.08	0.790
Soft lean mass	44.62 ± 35.99	42.42 ± 9.02	50.70 ± 68.21	0.361
Fat free mass	45.38 ± 11.86	45.05 ± 9.46	46.30 ± 16.87	0.493
Skeletal muscle mass	45.38 ± 11.86	24.02 ± 5.58	28.79 ± 42.50	0.398
Percent body fat	20.57 ± 11.64	20.50 ± 11.28	20.76 ± 12.68	0.884
Waist-hip ratio	0.75 ± 0.12	0.76 ± 0.11	0.73 ± 0.16	0.152
ECW/TBW	0.403 ± 0.024	0.400 ± 0.023	0.412 ± 0.027	0.001
ECW/TBW > 0.4	98 (45.0)	61 (38.1)	37 (63.8)	0.001
Body cell mass	29.97 ± 24.60	28.58 ± 6.13	33.81 ± 46.68	0.399
Bone mineral content	2.61 ± 0.64	2.62 ± 0.54	2.58 ± 0.87	0.710
AC	27.04 ± 19.01	26.26 ± 5.56	29.10 ± 35.83	0.551
BMR	1344.6 ± 270.3	1335.4 ± 277.7	1370.0 ± 364.2	0.405

Values are expressed as the mean ± standard deviation, the median [interquartile range] or number (%).

ICW, intracellular water; ECW, extracellular water; TBW, total body water; AC, abdominal circumference; BMR, basal metabolic rate

† Mean time to body composition, time duration from the emergency department admission to the measurement of body composition.

Characteristics of septic shock patients with higher ECW/TBW

Table 3 compares the baseline characteristics of patients with ECW/TBW > 0.4 and ≤ 0.4. The percentage of patients with active cancer (73.5% vs. 60.8%, p = 0.049) was higher in the group with ECW/TBW > 0.4 than in that with ECW/TBW ≤ 0.4. Systolic blood pressure (92.48 vs. 85.83 mmHg, p = 0.029), diastolic blood pressure (60.18 vs. 55.34 mmHg, p = 0.016), and Hb levels (9.87 vs. 11.19 g/dL, p = 0.000) were significantly lower in the ECW/TBW > 0.4 than in the ECW/TBW ≤ 0.4 group. PT levels (1.59 vs. 1.34 INR, p = 0.008) and initial SOFA scores (5.61 vs. 4.70 mmol/L, p = 0.016) were significantly higher in patients with ECW/TBW > 0.4 than in patients with ECW/TBW ≤ 0.4, whereas maximum SOFA scores did not differ significantly.

Table 3
Comparison of the clinical characteristics based on the ECW/TBW

	Total (n = 218)	ECW/TBW ≤ 0.4 (n = 120)	ECW/TBW > 0.4 (n = 98)	P value
Age (years)	66.28 ± 11.53	66.04 ± 11.46	66.58 ± 11.67	0.732
Gender - Male	127 (58.3)	76 (63.3)	51 (52.0)	0.093
Comorbidities				
Hypertension	74 (33.9)	39 (32.5)	35 (35.7)	0.618
Diabetes mellitus	60 (27.5)	30 (25.0)	30 (30.6)	0.356
Chronic renal disease	22 (10.1)	12 (10.0)	10 (10.2)	0.960
Cardiovascular disease	23 (10.6)	16 (13.3)	7 (7.1)	0.139
Heart failure	7 (3.2)	5 (4.2)	2 (2.0)	0.376
Chronic liver disease	27 (12.4)	12 (10.0)	15 (15.3)	0.237
Active cancer	145 (66.5)	73 (60.8)	72 (73.5)	0.049
Vital sign				
SBP (mmHg)	89.49 ± 22.48	92.48 ± 24.69	85.83 ± 18.90	0.029
DBP (mmHg)	58.00 ± 15.48	60.18 ± 17.77	55.34 ± 11.64	0.016
Heart rate (bpm)	110.50 ± 23.73	108.83 ± 22.98	112.54 ± 24.59	0.251
Body temperature (°C)	37.94 ± 4.35	38.44 ± 5.69	37.32 ± 1.37	0.058
SpO2 (%)	94.55 ± 5.98	94.77 ± 6.49	94.28 ± 5.32	0.544
Altered mental status	38 (17.4)	18 (15.0)	20 (20.4)	0.295
Laboratory data				
WBC (x10^3/μL)	10.92 ± 9.59	10.20 ± 7.73	11.81 ± 11.45	0.237
Hemoglobin (g/dL)	10.60 ± 2.43	11.19 ± 2.36	9.87 ± 2.34	0.000
Platelet (x10^3/μL)	149.14 ± 108.17	159.64 ± 9.84	136.29 ± 107.79	0.113
PT (INR)	1.45 ± 0.70	1.34 ± 0.62	1.59 ± 0.75	0.008

Values are expressed as the mean ± standard deviation, the median [interquartile range] or number (%).

SBP, systolic blood pressure; DBP, diastolic blood pressure; SpO2, saturation of percutaneous oxygen; WBC, white blood cell; PT, prothrombin time; INR, international normalized ratio.; CRP, c-reactive protein; SOFA, sequential organ failure assessment; CRRT, continuous renal replacement therapy

	Total (n = 218)	ECW/TBW ≤ 0.4 (n = 120)	ECW/TBW > 0.4 (n = 98)	P value
Creatinine (mg/dL)	1.99 ± 1.70	2.07 ± 1.89	1.89 ± 1.43	0.438
Total bilirubin (mg/dL)	2.70 ± 4.63	2.79 ± 4.96	2.59 ± 4.22	0.754
CRP (mg/dL)	14.70 ± 10.29	14.31 ± 10.61	15.17 ± 9.90	0.541
Lactate (mmol/L)	4.09 ± 3.27	3.85 ± 3.06	4.38 ± 3.51	0.235
30-day mortality	58 (26.6)	21 (17.5)	37 (37.8)	0.001
SOFA	5.11 ± 2.80	4.70 ± 2.64	5.61 ± 2.91	0.016
SOFA, maximum	9.56 ± 3.97	9.18 ± 4.06	10.03 ± 3.83	0.117
Ventilator	39 (17.9)	22 (18.3)	17 (17.3)	0.850
CRRT	24 (11.0)	13 (10.8)	11 (11.2)	0.927

Values are expressed as the mean ± standard deviation, the median [interquartile range] or number (%).

SBP, systolic blood pressure; DBP, diastolic blood pressure; SpO2, saturation of percutaneous oxygen; WBC, white blood cell; PT, prothrombin time; INR, international normalized ratio.; CRP, c-reactive protein; SOFA, sequential organ failure assessment; CRRT, continuous renal replacement therapy

Risk factors for 30-day mortality in patients with septic shock

Univariate and multivariate logistic regression analyses were performed to identify the risk factors for 30-day mortality in patients with septic shock (Table 4). Variables with $p < 0.1$ in univariate analysis, such as ECW/TBW > 0.40, active cancer, Hb levels, PT, and initial lactate levels, were included in the multivariable analyses. Multivariate analysis found that ECW/TBW > 0.40 (OR, 2.11; 95% confidence interval [CI], 1.05–4.23, p = 0.036), active cancer (OR, 2.39; 95% CI, 1.06–5.38, p = 0.036), PT (OR, 2.77; 95% CI, 1.29–5.93, p = 0.009), and initial lactate level (OR, 1.15; 95% CI, 1.03–1.28, p = 0.010) were independently associated with 30-day mortality.

Table 4
Univariate and multivariate logistic regression analysis for the association of mortality in septic shock

	Univariate		Multivariate	
	OR (95% CI)	P value	OR (95% CI)	P value
ECW/TBW > 0.40	2.561 (1.333–4.920)	0.005	2.109 (1.050–4.233)	0.036
Active cancer	2.719 (1.312–5.634)	0.007	2.387 (1.059–5.381)	0.036
Hemoglobin	0.822 (0.719–0.939)	0.004		
PT (INR)	4.995 (2.231–11.181)	0.000	2.766 (1.290–5.931)	0.009
Lactate	1.231 (1.121–1.353)	0.000	1.149 (1.033–1.278)	0.010

OR, odds ratio; CI, confidence interval; ECW, extracellular water; TBW, total body water; PT, prothrombin time; INR, international normalized ratio

* Adjusted for variables with a p-value < .10 in univariate analysis.

Hosmer and Lemeshow Goodness of Fit test: $\chi2 = 10.601$, df = 8, p-value 0.225

Discussion

The present study found that the ECW/TBW was significantly higher in 30-day non-survivors than in 30-day survivors of septic shock (0.412 vs. 0.400, p = 0.001) and that the optimal cutoff value for predicting 30-day mortality was 0.40. ECW/TBW > 0.40 was the only parameter of body composition analysis associated with 30-day mortality in patients with septic shock. Septic shock patients with higher ECW/TBW were more likely to have active cancer, lower Hb concentrations, and higher PT than patients with lower ECW/TBW. To our knowledge, this is the first study to investigate the association between ECW/TBW and mortality of patients with septic shock.

BIA is an objective method that measures and analyzes body composition by sending a weak electrical current through the body. It is also a reproducible method that can be performed at the bedside. Its efficacy and accuracy in predicting body water composition are comparable to those of more classic methods.[19, 20] Thus, multi-frequency BIA can be used to assess the volume and nutritional status of patients with various diseases.[21–23] Furthermore, several studies have reported significant relationships between BIA-determined imbalances in body fluid and clinical outcomes in patients with, for example, chronic renal failure, chronic liver disease, and chronic obstructive pulmonary disease.[23–25] Extracellular fluid retention may play an important role in the progression and deterioration of diseases, indicating that pathophysiologic alterations in body fluid composition are associated with poor clinical outcomes.[26–28]

ECW/TBW as determined by BIA is frequently used to assess abnormal fluid status,[22, 29] and is a sensitive indicator of hydration changes.[30] Higher ECW/TBW ratios have been reported to predict clinical outcomes in patients with heart failure, liver diseases, renal disorders, and malignancies.[21–23, 31] Alterations in body fluid distribution without effective volume expansion result in excess fluid retention in the extracellular space, which can cause poor outcomes in critically ill patients.[32, 33] The present study found that ECW/TBW was the only statistically significant body composition variable associated with mortality in patients with septic shock.

Inflammatory processes during septic shock induce endothelial damage, increasing vascular permeability and shifting fluid from the intracellular to the extracellular space.[34–36] These alterations in body water distribution, such as ECW expansion, exacerbate the deterioration of cell membrane function.[37] In responding to cardiac dysfunction during septic shock, fluid retention volume may be increased by fluid resuscitation.[38] This accumulation of fluid in a third space leads to a vicious cycle, in which the patient's condition deteriorates, further contributing to fluid retention during septic shock.

The normal range of ECW/TBW is between 0.360–0.390, with ratios ≥ 0.400 indicating an overhydrated state.[39, 40] The present study found that the optimal ECW/TBW cutoff value was 0.4, with ratios > 0.400 significantly associated with mortality in septic shock patients. The optimal cutoff was determined by calculating the area under the ROC curve, which showed that ECW/TBW > 0.4 was 1.67 times more frequent in 30-day non-survivors than in 30-day survivors. A previous study reported the average of ECW/TBW in patients with bacteremia was 0.510, suggesting that ECW/TBW can be higher in various conditions associated with reduced lean muscle mass, not only in septic shock.[41–44] The average ECW/TBW was found to be 0.42 in non-survivors admitted to the ICU, patients who tended to be malnourished.[32] Average ECW/TBW ratios were found to be 0.412 in patients with acute heart failure [23] and 0.40 in chronic dialysis patients.[45] Although these averages were higher than the normal reference value, they were lower in patients with chronic diseases than in those who were critically ill.

Fluid resuscitation and administration of multiple drugs to septic shock patients can result in faster and more dynamic hemodynamic changes. BIA is not only a prognostic tool but may be an effective and objective method of assessing real-time hemodynamic parameters at the bedside. Most importantly, BIA can repeatedly provide useful information about body fluid distribution or hydration status. Further studies are required to evaluate co-morbidities that can affect body fluid composition, enabling more accurate prediction of patient prognosis and determining whether fluid resuscitation is warranted in patients with septic shock.

The major limitation of this study was that it involved patients at a single-center. Local patterns of illness and racial characteristics may differ at other centers. In addition, it is unclear whether factors other than those considered can affect the results of BIA. The timing of fluid loading or BIA measurement, the presence of other electrical devices, and skin temperature or sweating could be sources of data disruption. Furthermore, the results of BIA may have been confounded by co-morbidities, such as chronic liver disease, chronic renal disease, and malignancies.

Conclusion

ECW/TBW > 0.4 was significantly associated with 30-day mortality in patients with septic shock receiving protocol-driven resuscitation bundle therapy in the ED. Further studies considering factors that affect the results of BIA are needed to determine appropriate fluid resuscitation strategies for septic shock.

Abbreviations

BIA	Bio-electrical impedance analysis
ED	Emergency department
PT	Prothrombin time
Hb	Hemoglobin
CRP	C-reactive protein
SOFA	Sequential Organ Failure Assessment
OR	Odds ratios
CI	Confidence intervals
ROC	Receiver operating characteristic
INR	International normalized ratio
CRRT	Continuous renal replacement therapy
ECW	Extracellular water
TBW	Total body water

Declarations

- Ethics approval and consent to participants

The study design was approved by the appropriate institutional ethics review board (No. 2020-1592), which waived the requirement for informed consent.

- Consent for publication: Not applicable.

- Availability of data and materials: The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.
- Competing interests: The authors declare that they have no competing interests.
- Funding: *No funding to declare.*
- Authors’ contributions

W.Y.K.: provided the concept and design of the study, analysis and interpretation of data, drafting the article, and gave final approval of the version to be submitted; B.C.: supplied the acquisition of data, analysis and interpretation of data, and drafting of manuscript; Y.S.S.: supplied the acquisition of data; S.H.: supplied the acquisition of data; S.M.K.: supplied the acquisition of data; Y.K.: provided the article for intellectual content; S.M.R.: provided the conception and design of the study.

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