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Original Article

Bioimpedance Analysis for Fluid Status Assessment in Critically Ill Septic Patients

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Abstract

Aim: The aim of this study was to assess the usefulness of bioimpedance analysis in fluid status evaluation in patients with sepsis and septic shock admitted to the adult ICU.

Materials and methods: This is a prospective, observational, clinician-blind study. The inclusion criteria were a diagnosis of sepsis at admission to ICU, a stay in ICU of at least 72 hours, and the first BIA measurement to be conducted within the first three hours of ICU admission. We took whole-body BIA measurements upon admission and every 24 hours thereafter for at least four consecutive measurements. All enteral and parenteral fluids administered to the patients were recorded, as well as the losses through drains, tubes, aspiration, and urine. The cumulative fluid balance (CFB) was calculated every 24 hours.

Results: A total of 51 patients with a mean age of 62 years were included in the final analysis. CFB gradually increased during the first 72 hours of ICU stay from 2003±1331 mL at 24 hours to 3680±2368 mL at 48 hours and 5217±2642 mL at 72 hours. There was a statistically significant positive correlation between the increase in CFB and the increase in total body water, extracellular water, and overhydration. The daily changes of vector length and impedance ratio, as well as the overall 72-hour changes showed statistically significant correlation with the CFB.

Conclusion: Bioimpedance analysis is a non-invasive, easy-to-use, inexpensive, portable, and fast tool for fluid status assessment. In critically ill septic patients it can be a useful tool in fluid therapy management.

Keywords

bioimpedance, fluid status, sepsis

INTRODUCTION

Sepsis is defined as a life-threatening organ dysfunction due to dysregulated host response to an infection. In the pathophysiology of sepsis, endothelial dysfunction plays a most significant role. It leads to generalized vasodilation due to the increased NO production and increased capillary permeability leading to the loss of intravascular fluid into the interstitial space. The net result is severe intravascular hypovolemia and hypotension. Fluid resuscitation and vasopressors are the cornerstones in treating septic patients. According to Surviving Sepsis Campaign (SSC) international guidelines for management of sepsis and septic shock from 2021 for patients with sepsis, induced

hypoperfusion or septic shock at least 30 mL/kg of IV crystalloid fluid should be given within the first three hours of resuscitation. This recommendation is downgraded from strong (2016 guidelines) to weak with low quality of evidence after a serious criticism and the lack of patient benefit from goal-directed therapy.[1,2] The exact amount, type, or rate of fluid administration in septic patients admitted to the ICU is still unclear and fluid therapy recommendations are based mainly on expert opinions. Although intravascular volume expansion is the main treatment option in septic patients, if applied inadequately it can lead to major complications and can be associated with increased ICU mortality.[3] The main reason for the ambiguity is the lack of universal monitoring technique for fluid status assessment in sepsis. The bioelectrical impedance analysis (BIA) is a non-invasive, easy-to-use, inexpensive, portable, and fast tool for body composition and body fluids evaluation. In critically ill patients, it is used to assess the nutrition and hydration status and is used also in perioperative risk assessment and prognostication.

AIM

The aim of this study was to assess the usefulness of bioimpedance analysis in fluid status evaluation in patients with sepsis and septic shock admitted to the adult ICU.

MATERIALS AND METHODS

We conducted a prospective, observational, clinician-blind study from April 2023 to January 2024 for patients admitted to the adult ICU. The inclusion criteria were a diagnosis of sepsis at admission to ICU, a stay in ICU of at least 72 hours, and the first BIA measurement to be conducted within the first three hours of ICU admission. We performed whole-body BIA measurements upon admission and every 24 hours thereafter for at least four consecutive measurements. We used BodyStat MultiScan 5000 bioimpedance analyzer with self-adhesive disposable electrodes provided by the manufacturer. Four electrodes were attached to the right hand and right foot - behind the knuckles, on the wrist, behind the toes, and on the ankle as recommended by the manufacturer. All enteral and parenteral fluids administered to the patients were recorded, as well as the loses through drains, tubes, aspiration, and urine. The cumulative fluid balance (CFB) was calculated every 24 hours for every patient without the insensible losses. The treating physicians were unaware of the bioimpedance measurements results. Determination of the volume of fluid therapy was based on constant monitoring of heart rate and invasive or non-invasive pressure measurements, CFB, standard ICU daily lab tests, but was also based on individual judgement. Dynamic parameters of fluid responsiveness were unavailable to use.

RESULTS

A total of 51 patients (30 men and 21 women) with a mean age of 62 years were included in the final analysis. Their mean ICU stay was 12 days, and the mortality rate was 48%. Baseline patient characteristics on admission are shown in **Table 1**. Biochemical data and hydration evaluation on admission are shown in **Table 2**.

Table 1. Baseline patient characteristics on admission. Results are displayed as means

	All (n=51)
Age (mean)	62 years
Weight (mean)	89 kg
BMI (mean)	29.3 kg/m^2
Women (n)	21
Men (n)	30
SOFA score (mean)	9
ICU length of stay (mean)	12 days
Comorbidities (n)	
Hypertension	36
Coronary artery disease	14
Diabetes	10
Obesity	14
COPD	8
Others	12
Infection source (n)	
Respiratory tract	14
Intra-abdominal	24
Urinary tract	5
Others	8

Table 2. Biochemical data and hydration evaluation on admission. Results are displayed as means

	All (n=51)
SOFA score (mean)	8
MAP	80 (mmHg)
GCS	14 (points)
PLT	285 (×10^3/mm^3)
Bilirubin	29 (μmol/L)
Pa/FiO$_2$ ratio	211
Creatinine	158 (μmol/L)
BIA measurements (mean)	
TBW	46.7 l
ECW	22.5 l
ECW/TBW	0.48
ICW	24.2 l
OHY	5.4 l
IR	0.8555
VL	228.42

SOFA: Sequential Organ Failure Assessment; MAP: mean arterial pressure; GCS: Glasgow Coma Scale; PLT: platelet count; TBW: total body water; ECW: extracellular water; ICW: intracellular water; OHY: overhydration; IR: impedance ratio; VL: vector length

CFB gradually increased during the first 72 hours of ICU stay from 2003±133 mL at 24 hours to 3680±2368 mL at 48 hours, and 5217±2642 mL at 72 hours. The bioimpedance measured parameters also showed a gradual increase. **Tables 3-7** show the total body water (TBW), extracellular water (ECW), the ECW/TBW ratio, intracellular water (ICW), and overhydration (OHY) and their changes during the first 72 hours. There was a statistically significant positive correlation between the increase in CFB and the increase in TBW, ECW and OHY. **Table 8** displays Pearson's correlation coefficient and the corresponding *p*-value for the calculated CFB and BIA measured hydration parameters. Changes in the measured ICW did not correlate with CFB. The scatter plots displayed in **Figs 1-3** show the correlation between the calculated total CFB and the overall changes in the BIA measured TBW, ECW, and OHY.

Table 3. Changes in TBW during the first 72 hours

	TBW at admission	TBW at 24 hours	TBW at 48 hours	TBW at 72 hours
Mean	46.73	48.78627451	52.172549	53.64901961
Standard error	1.66	1.661933718	1.59762588	1.612972831
Median	45.90	48.8	51.1	52.3
Mode	32.30	49.1	52.3	69.4
Standard deviation	11.86	11.8685807	11.4093309	11.51893003
Sample variance	140.76	140.8632078	130.172831	132.685749
Kurtosis	−0.39	−0.299225104	−0.6115498	−0.50146043
Skewness	0.38	0.318348532	0.1169272	0.112132201
Range	52.10	54	46.2	49.5
Minimum	22.70	24.2	28.7	29
Maximum	74.80	78.2	74.9	78.5
Sum	2383.10	2488.1	2660.8	2736.1
Count	51.00	51	51	51
Confidence level (95.0%)	3.34	3.338092113	3.20892602	3.239751277
Upper CI (95%)	50.06	52.12	55.38	56.89
Lower CI (95%)	43.39	45.45	48.96	50.41

Table 4. Changes in ECW during the first 72 hours

	ECW at admission	ECW at 24 hours	ECW at 48 hours	ECW at 72 hours
Mean	22.5	23.8254653	26.06563945	27.9715218
Standard error	0.721436476	0.75638034	0.788964348	0.79578465
Median	22.4	23.5918033	25.75942623	27.7
Mode	21.4	24.1	25.2	27.7
Standard deviation	5.152086956	5.40163609	5.634332427	5.68303911
Sample variance	26.544	29.1776725	31.7457019	32.2969335
Kurtosis	−0.327902406	−0.0676012	−0.060300893	−0.1258803
Skewness	0.050057089	-0.0194208	0.053215746	0.05328169
Range	23.3	23.6948431	24.9	25.3
Minimum	10.4	10.6337079	13.3	15.5
Maximum	33.7	34.3285509	38.2	40.8
Sum	1147.5	1215.09873	1329.347612	1426.54761
Count	51	51	51	51
Confidence level (95.0%)	1.449047807	1.51923463	1.584681531	1.59838051
Upper CI (95%)	23.94904781	25.3446999	27.65032098	29.5699023
Lower CI (95%)	21.05095219	22.3062307	24.48095792	26.3731413

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Table 5. Changes in ECW/TBW during the first 72 hours

	ECW/TBW at admission	ECW/TBW at 24 hours	ECW/TBW at 48 hours	ECW/TBW at 72 hours
Mean	0.49111402	0.4970974	0.5081126	0.53033208
Standard error	0.01147943	0.01172349	0.01254418	0.01236866
Median	0.5	0.50409836	0.51368421	0.53789053
Mode	-	-	-	-
Standard deviation	0.08197952	0.08372245	0.08958333	0.08832987
Sample variance	0.00672064	0.00700945	0.00802517	0.00780217
Kurtosis	0.92985234	1.12370152	1.06110951	0.95101434
Skewness	−0.4351254	−0.4134692	−0.3063746	−0.2358526
Range	0.41552178	0.4248463	0.4902595	0.4772665
Minimum	0.29213483	0.29213483	0.25876011	0.28535032
Maximum	0.70765661	0.71698113	0.74901961	0.76261682
Sum	25.046815	25.3519674	25.9137424	27.0469358
Count	51	51	51	51
Confidence level (95.0%)	0.02305711	0.02354732	0.02519572	0.02484318
Upper CI (95%)	0.51417113	0.52064472	0.53330831	0.55517525
Lower CI (95%)	0.46805691	0.47355008	0.48291688	0.5054889

Table 6. Changes in OHY during the first 72 hours

	OHY at admission	OHY at 24 hours	OHY at 48 hours	OHY at 72 hours
Mean	5.40196078	7.56078431	10.6196078	12.054902
Standard error	0.62418882	0.56037157	0.47920702	0.4420923
Median	5.1	7.3	9.9	12.2
Mode	3.2	4.6	10.2	9.2
Standard deviation	4.45759981	4.00185349	3.42222265	3.15717049
Sample variance	19.8701961	16.0148314	11.7116078	9.96772549
Kurtosis	1.15488996	1.0275812	0.20396621	−0.4711069
Skewness	-0.4066507	0.36674068	0.67639376	0.18054579
Range	23.8	21.7	14.5	12.7
Minimum	−8.1	−3.4	4.4	6.2
Maximum	15.7	18.3	18.9	18.9
Sum	275.5	385.6	541.6	614.8
Count	51	51	51	51
Confidence level (95.0%)	1.25372015	1.12553943	0.96251563	0.88796851
Upper CI (95%)	6.65568093	8.68632375	11.5821235	12.9428705
Lower CI (95%)	4.14824063	6.43524488	9.65709221	11.1669335

The parameters for assessment of the hydration status measured by bioimpedance vector analysis (BIVA) – the vector length (VL) and impedance ratio (IR) were also analyzed. The daily changes of VL and IR as well as the overall 72-hour changes showed statistically significant correlation with the CFB. **Table 9** shows Pearson's correlation coefficient and the corresponding *p*-value for the calculated CFB and the IR and the BIVA-measured VL. The scatter plots displayed in **Figs 4, 5** show the correlation between the calculated total CFB and the overall changes in the BIVA-measured VL and IR.

DISCUSSION

Fluid status assessment in critically ill septic patients is extremely challenging. Dynamic tests for predicting fluid responsiveness are not always applicable. This may leave the static fluid status assessment parameters as the only option. Due to pathogenetic changes, the intravascular hypovolemia and extravascular fluid overload are common in septic patients. Balanced crystalloid solutions as a first-line treatment for intravascular hypovolemia show a relatively low plasma-expanding effect and worsen the interstitial tis-

Table 7. Changes in ICW during the first 72 hours

	ICW at admission	ICW at 24 hours	ICW at 48 hours	ICW at 72 hours
Mean	24.227451	24.9608092	26.1069096	25.6774978
Standard error	1.21563184	1.22243269	1.24629451	1.2545966
Median	23	23.4540984	24.948182	24.2854077
Mode	-	-	-	37.9
Standard deviation	8.76604587	8.8150875	8.98715754	9.04702473
Sample variance	76.8435602	77.7057676	80.7690006	81.8486564
Kurtosis	0.71941491	0.63700521	1.13552696	1.45268971
Skewness	0.876863	0.84752248	0.84555785	0.93071887
Range	38.5	39.0734743	43.6	45.5
Minimum	9.3	9.91453744	11.4	10.6
Maximum	47.8	48.9880117	55	56.1
Sum	1259.82745	1297.96208	1357.5593	1335.22989
Count	52	52	52	52
Confidence level (95.0%)	2.44048275	2.45413603	2.50204064	2.51870777
Upper CI (95%)	26.6679337	27.4149452	28.6089502	28.1962056
Lower CI (95%)	21.7869682	22.5066732	23.6048689	23.15879

Table 8. Pearson's correlation coefficient and the corresponding p-value for the calculated CFB and BIA measured hydration parameters

	CFB 24 hours	CFB 48 hours	CFB 72 hours
TBW	r=0.47 (p<0.001)	r=0.37 (p<0.01)	r=0.31 (p<0.05)
ECW	r=0.41 (p<0.01)	r=0.49 (p<0.001)	r=0.42 (p<0.01)
OHY	r=0.4 (p<0.01)	r=0.47 (p<0.001)	r=0.49 (p<0.001)

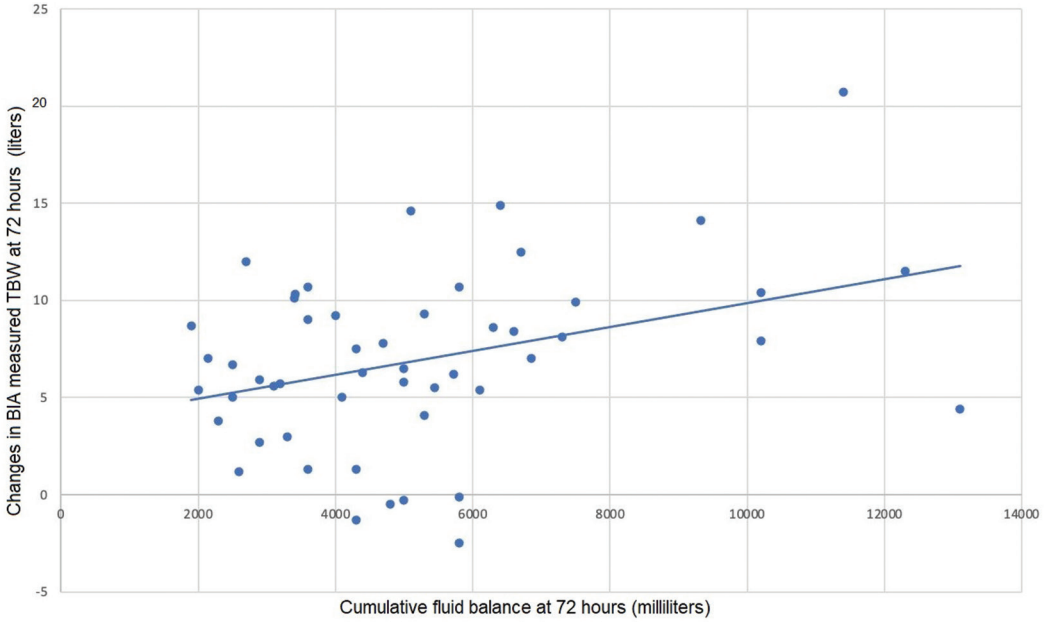

Figure 1. A scatter plot showing the positive correlation between the CFB at 72 hours and the change in the BIA-measured TBW (r=0.36, p<0.01).

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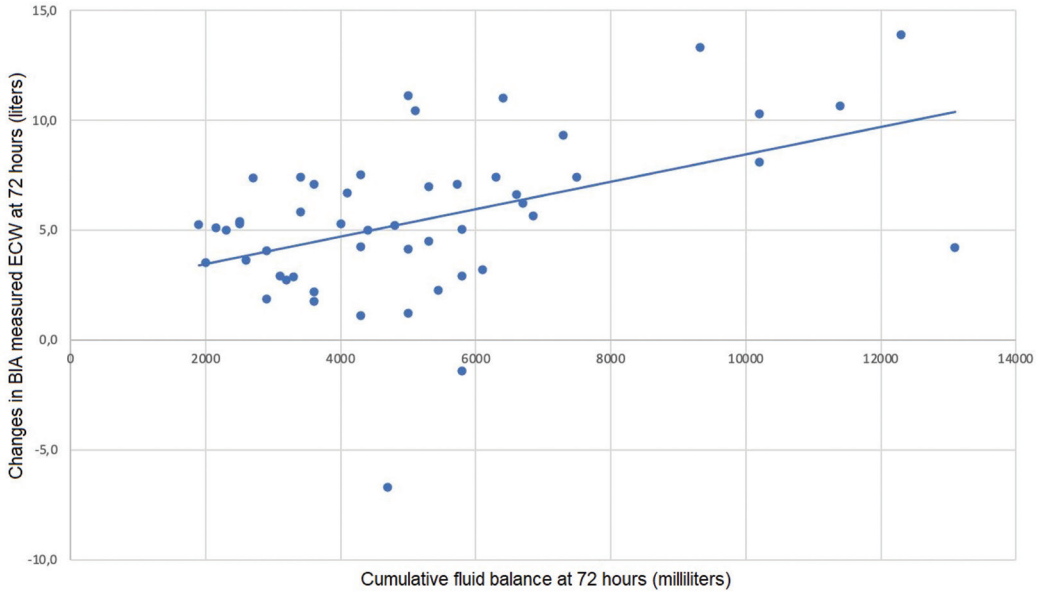

Figure 2. A scatter plot showing the positive correlation between the CFB at 72 hours and the change in the BIA-measured ECW (r=0.46, p<0.001).

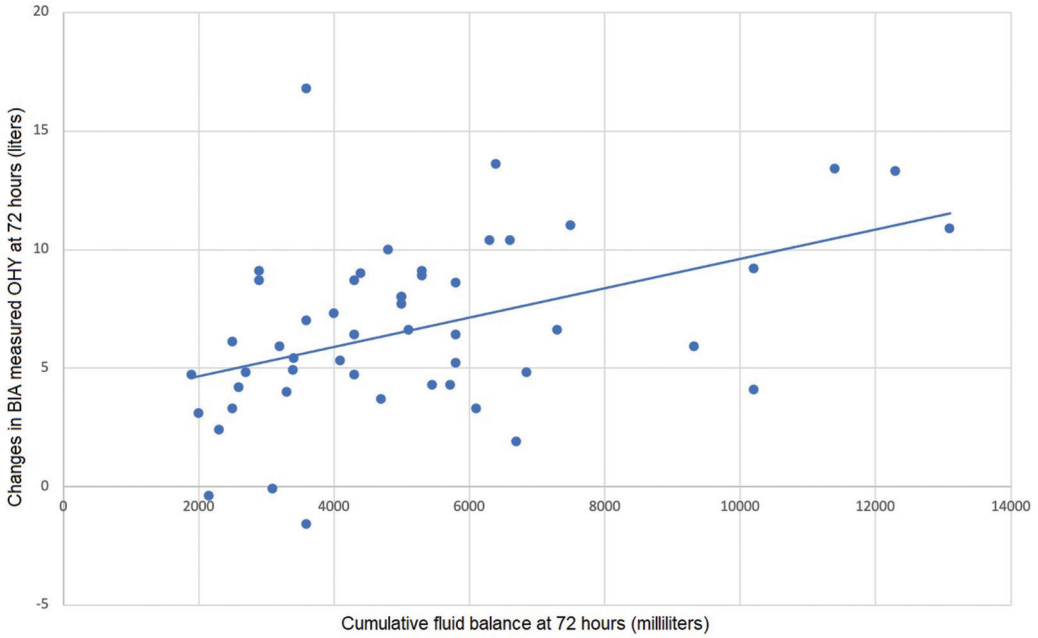

Figure 3. A scatter plot showing the positive correlation between the CFB at 72 hours and the change in the BIA-measured OHY (r=0.45, p<0.001).

Table 9. Pearson's correlation coefficient and the corresponding p-value for the calculated CFB and the BIVA-measured VL and IR

	CFB at 24 hours	CFB at 48 hours	CFB at 72 hours
VL	r=−0.51 (p<0.001)	r=−0.48 (p<0.001)	r=−0.44 (p<0.01)
IR	r=0.37 (p<0.01)	r=0.52 (p<0.001)	r=0.37 (p<0.01)

sue edema.[4] The results in our study show a clear trend towards increase in the measured TBW and ECW during the resuscitation phase of critically ill septic patients. The increased ECW/TBW ratio is associated with higher mortality.[5] Using BIA during initial resuscitation, we can monitor the extent of extravascular fluid overload occurring during large-volume resuscitation with balanced crystalloid solutions. BodyStat MultiScan 5000 uses spectros-

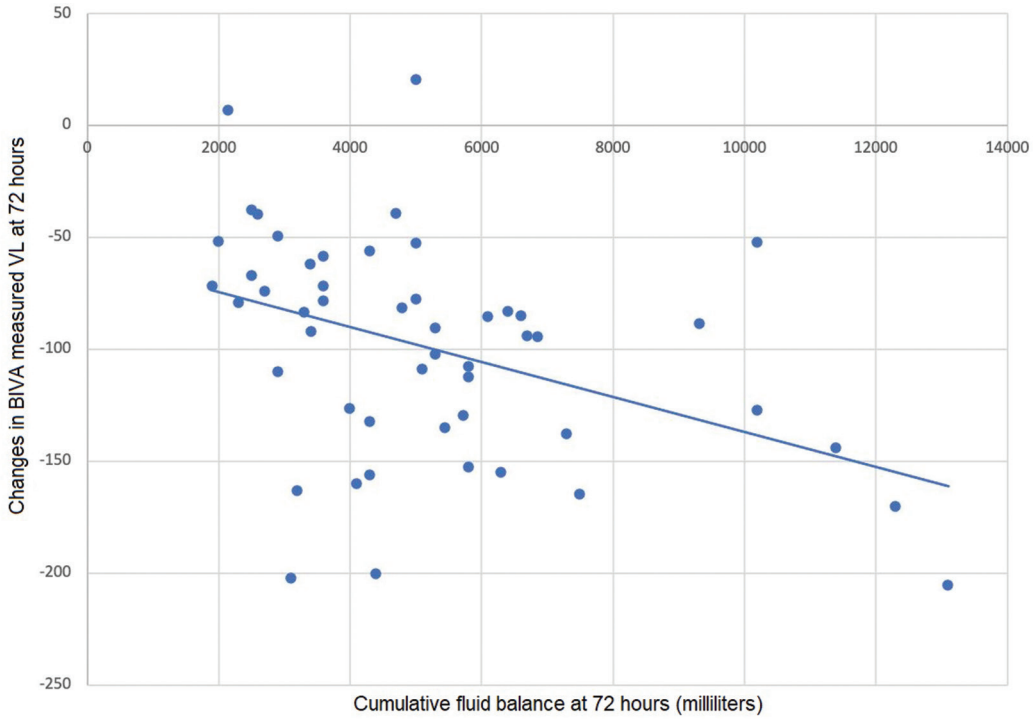

Figure 4. A scatter plot showing the negative correlation between the CFB at 72 hours and the change in the BIVA-measured VL (r=-0.41, p<0.01).

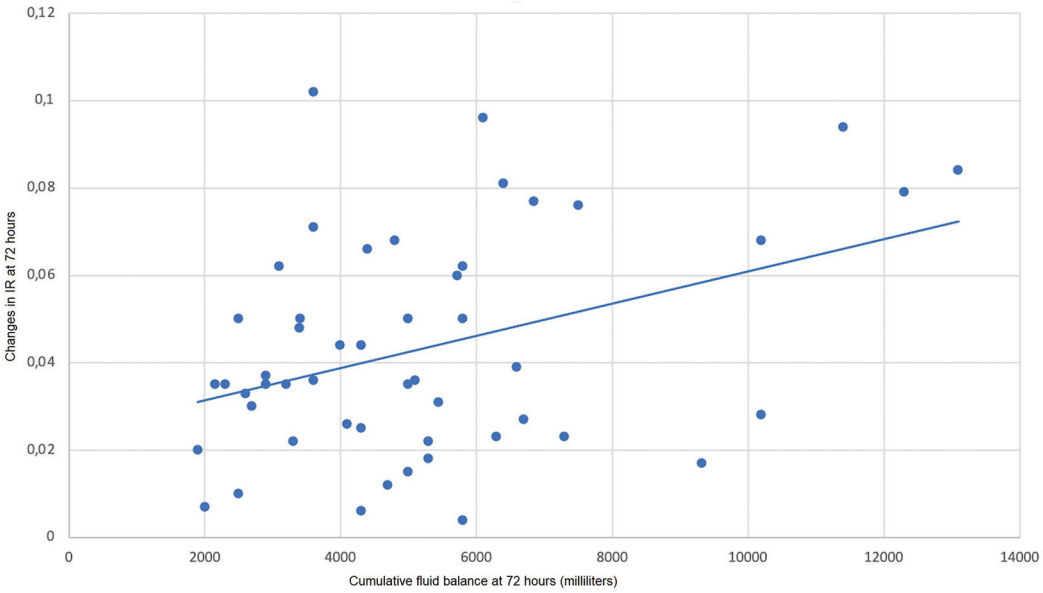

Figure 5. A scatter plot showing the positive correlation between the CFB at 72 hours and the change in IR (r=0.39, p<0.01).

copy to calculate the volume of fluid overload in liters and is displayed as OHY. This is of particular importance when assessing or monitoring dry or target weight for individual dialysis patients. OHY is a parameter showing extracellular fluid overload. In our study, OHY in critically ill septic patients showed good correlation with the CFB.

When patients' body weight is not known, the IR can still be used. In critically ill septic patients, body weight and composition change significantly during their ICU stay. Monitoring body weight is also not available in all ICU beds. IR is the ratio between the impedance measured at 200 kHz and 5 kHz. In a healthy individual, at 5 kHz the resistance to the flow of the current will be higher because the current cannot penetrate the cell membrane (so it can only measure the ECW). At 200 kHz, the current can penetrate the cell membrane wall (the impedance is lower and measures TBW). IR, known also as prediction marker, can be used as fluid status assessment and as a prognostic marker.

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The maximum value of IR is 1.00 and higher values are interpreted as less cellular health or excess amount of ECW. In our study, IR showed good correlation with the increase in ECW and CFB.

BIVA (or 'Rxc Graph') uses no complex mathematical equations. It uses only the Resistance (R) and Reactance (Xc) at 50 kHz and is standardized to the subject's height (weight is not required). The results are illustrated as dots on the vector. The line from the beginning to the dot indicates the VL. The shorter line indicates more tissue edema (as water and electrolytes have good conductivity, so the resistance to flow is less). In our study population, the increase in CFB showed a good correlation with the shortening of VL.

Our study has two major limitations. Firstly, daily CFB can be affected by a variety of factors due to the increase in insensible losses. Some examples include fever, open wounds, mechanical ventilation, etc., all of which are relatively common in septic patients. Adjusting the CFB with the insensible losses (those that we cannot measure) is merely impossible at the bedside. Nevertheless, CFB was used to compare the BIA-measured hydration parameters. The reason is that most clinicians adjust their fluid therapy empirically in cases of increased insensible losses. The aim of our study was to see if the BIA-measured parameters can track changes in body fluids, not to validate the method. In septic patients with generalized endothelial dysfunction, it is expected from physiology that with fluid therapy ECW will increase to a greater extent than ICW which is fairly supported by the results of our study.

The second limitation is that BIA provides static volume status parameters. Changes of these parameters over time showed moderate correlation with CFB. Like the central venous pressure (CVP), guiding fluid therapy based on static parameters would be too optimistic. Dynamic measures of fluid responsiveness (stroke volume variation [SVV], pulse pressure variation [PPV], echocardiography, etc.) should be used in critically ill septic patients. Although noninvasive and minimally invasive, access to modern devices and the availability of trained ICU personnel are still not universal, including in our department.

CONCLUSIONS

Guiding fluid therapy in septic patients is based on complex assessment of a variety of parameters. BIA is a non-invasive, easy-to-use, inexpensive, portable, and fast tool for fluid status assessment. In critically ill septic patients, it can be a useful tool in fluid therapy management.

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Биоимпедансный анализ для оценки состояния жидкости у пациентов с тяжёлым сепсисом

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Резюме

Цель: Целью данного исследования была оценка полезности анализа биоимпеданса при оценке состояния жидкости у пациентов с сепсисом и септическим шоком, поступивших в отделение интенсивной терапии для взрослых.

Материалы и методы: Это проспективное, наблюдательное, слепое для клиницистов исследование. Критериями включения были диагноз сепсиса при поступлении в отделение интенсивной терапии, пребывание в отделении интенсивной терапии не менее 72 часов и первое измерение биоимпедансным анализом (BIA), проведённое в течение первых трёх часов после поступления в отделение интенсивной терапии. Мы проводили измерения BIA всего тела при поступлении и каждые 24 часа после этого в течение как минимум четырёх последовательных измерений. Регистрировались все энтеральные и парентеральные жидкости, введённые пациентам, а также потери через дренажи, трубки, аспирацию и мочу. Кумулятивный баланс жидкости (КБЖ) рассчитывался каждые 24 часа.

Результаты: В окончательный анализ были включены в общей сложности 51 пациент со средним возрастом 62 года. КБЖ постепенно увеличивался в течение первых 72 часов пребывания в отделении интенсивной терапии с 2003±1331 mL за 24 часа до 3680±2368 mL за 48 часов и 5217±2642 mL за 72 часа. Была статистически значимая положительная корреляция между увеличением КБЖ и увеличением общей воды организма, внеклеточной воды и гипергидратации. Ежедневные изменения длины вектора и соотношения импеданса, а также общие 72-часовые изменения показали статистически значимую корреляцию с КБЖ.

Заключение: Анализ биоимпеданса является неинвазивным, простым в использовании, недорогим, портативным и быстрым инструментом для оценки состояния жидкости. У тяжелобольных септических пациентов он может быть полезным инструментом в управлении инфузионной терапией.

Ключевые слова

биоимпеданс, состояние жидкости, сепсис