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Original Article

Expression and prognostic correlation of extravascular lung water index and blood lactic acid clearance rates in patients with septic shock

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Abstract: Objective: The current study aimed to investigate the expression and prognostic correlation of extravascular lung water index (EVLWI) and blood lactic acid clearance rates (BLACR) in patients with septic shock. Methods: Retrospective analysis was performed on the data of 72 patients with septic shock, admitted to the ICU. Patients were divided into the survival group, with 49 patients, and the death group, with 23 patients, according to outcomes. Blood lactic acid (BLA) levels and BLACR of the patients were measured at the time of ICU stay, as well as the 6th, 12th, 24th, and 72nd hour after ICU stay. EVLWI was measured on the day of ICU stay and at the 72nd hour after ICU stay, aiming to analyze the relationship between BLACR, EVLWI, and patient prognosis. Results: There were no significant differences in gender composition, age, and source of infection between the two groups (P>0.05). Acute physiology and chronic health evaluation scoring system and sequential organ failure assessment scores were higher in the death group than those in the survival group (P<0.05). At the 6th, 12th, 24th, and 72nd hour after ICU stay, compared with patients in the death group, patients in the survival group had significantly lower BLA levels (P<0.05), but significantly higher BLACR (P<0.05). At the time of ICU stay, there were no significant differences in EVLWI between the two groups (P>0.05). At the 72nd hour after ICU stay, EVLWI in the survival group was significantly decreased (P<0.05), while that in the death group was significantly increased (P<0.05), with significant differences between the two groups (P<0.05). BLACR was negatively correlated with mortality of patients with septic shock (P<0.05). EVLWI was positively correlated with mortality (P<0.05). Conclusion: Hyperlactacidemia and an increase in EVLWI in patients with septic shock in the early stages of ICU stays may indicate poor prognosis. Strengthening the monitoring of EVLWI and BLACR is of great value for judging prognosis and guiding clinical early intervention.

Keywords: Extravascular lung water index, blood lactic acid clearance rate, septic shock, prognosis, correlation

Introduction

Septic shock is a common complication in critically ill patients. In infection and inflammatory reactions, blood vessels of the body dilate and blood in the capillaries vessels oozes out through the blood vessel walls. This results in insufficient circulating blood volume, shock, and even death [1]. With the rapid development of current medical technology, early rapid fluid resuscitation, strict and effective fluid management, and early effective antibiotic treatments are the most important means of diagnosis and treatment of septic shock. However, even if positive and effective treatment is given, the mortality of the patients is still 20%-63%. Therefore, septic shock remains a very difficult problem in clinical practice [2].

Patients with septic shock often have elevated hydrostatic pressure of pulmonary capillaries, which eventually develops into pulmonary edema. Excessive fluid replacement for tissue perfusion increases the risk of acute respiratory distress syndrome (ARDS) in patients, causing a large area of edema in the pulmonary interstitium and pulmonary alveoli and increasing the mortality of patients with septic shock. Therefore, the key issue is effectively and sufficiently expanding capacity and ensuring the success of fluid resuscitation, while avoiding occurrence or aggravation of pulmonary edema. Extravascular lung water index (EVLWI), an important indicator for pulmonary edema, reflects the prognosis of elderly patients with septic shock and pulmonary capillary leakage, as well as the severity of lung injuries, with a high prognostic predictive value, according to a study [3, 4].

In addition, reduction in circulating blood volume and deficiencies in the blood and oxygen supply lead to tissue ischemia, hypoxia, and metabolic disorders in patients with septic shock. These are more able to reflect hemodynamics levels prior to changes in clinical hemodynamic parameters. Blood lactic acid (BLA) is an important indicator that reflects body metabolism, systemic perfusion, and changes in oxygen metabolism [5]. One study shows that, since patients with septic shock are detected with increased arterial BLA concentrations and patients with low blood lactic acid clearance rates (BLACR) have a poor prognosis, BLA levels can be an important indicator judging the prognosis of patients with septic shock [6-8]. However, at present, there are few reports on the correlation of the combined detection of EVLWI and BLACR with prognosis of patients with septic shock. Therefore, 72 patients with septic shock were enrolled in this study to investigate the correlation.

Materials and methods

General information

Retrospective analysis was performed on the data of 72 patients with septic shock, admitted to Binzhou Center Hospital, from June 2015 to June 2018. Inclusion criteria: (1) All patients met the diagnostic criteria for septic shock of American College of Chest Physicians and Society of Critical Care Medicine in 2001 [9]; (2) Patients with an ICU treatment time >72 hours; (3) Patients aged 18-79 years old; and (4) Patients with a good prognosis for underlying diseases. Exclusion criteria: (1) Patients with a contraindication to venipuncture or peripherally inserted central catheter; (2) Patients with heart, liver, and kidney dysfunction; (3) Patients with a contraindication to liquid load test; (4) Pregnant or lactating women; and (5) Patients using immunosuppressants. The patients were divided into the survival group, with 49 patients, and the death group, with 23 patients, according to outcomes.

The study was in accord with medical ethical standards and was approved by the Ethics Committee of Binzhou Center Hospital. Family members of the patients were informed of and agreed with the study, providing informed consent.

Methods

Patient clinical data

Patient clinical data was counted, including age, gender, acute physiology and chronic health evaluation scoring system (APACHEII) scores, source of infection, sequential organ failure assessment (SOFA) scores, and laboratory indexes. APACHEII was mainly composed of acute physiology, age, and chronic health scores, with a total score of 0-71 points and a final score being the sum of the three scores [10, 11]. Higher scores indicate worse conditions. The severity of the disease was evaluated by quantified scoring. SOFA scores consisted primarily of a functional status assessment of six types of organs, including respiratory, coagulation, liver, cardiovascular, nervous, and kidney systems, with a score of 0-4 points for each item. Any organ function score ≥2 points was diagnosed as organ dysfunction, while scores ≥3 points were diagnosed as organ failure.

EVLWI and BLA determination

(1) Determination of EVLWI: Internal jugular vein or subclavian vein puncturing was carried out on the patient and an Arrow 7Fr single needle double gun (AERO, USA) was used for deep venous catheterization. Femoral artery puncture was performed and a 4Fr catheter (Pulsion Medical Systems, Germany) for pulse indicator continuous cardiac output (PiCCO) was inserted to connect to the PiCCO monitor. Approximately 10-15 mL of normal saline at <4°C was injected into the temperature probe to measure EVLWI 3 consecutive times on the day of ICU stay and at the 72nd hour after ICU stay. This was to obtain average values.

(2) Determination of BLA: A total of 3 mL of venous blood was collected from the patients for examination using a vacuum blood collector with heparin anticoagulation. BLA levels were measured using a RAPIDPoint 500 blood gas analyzer (Siemens AG, Japan) at the time of ICU stay, as well as the 6th, 12th, 24th, and 72nd hour after ICU stay. BLACR = (BLA level at the time of ICU stay - BLA level measured)/BLA level at the time of ICU stay * 100%.

Table 1. Comparison of demographic data

	Survival group (n=49)	Death group (n=23)	χ^2/t	P
Gender (case)			0.192	0.662
Male	36	18		
Female	13	5		
Age (year)	68.3±4.2	70.6±6.7	1.727	0.089
Source of infection (case)				
Lung	29	13	0.046	0.831
Urinary system	10	5	0.017	0.897
Enterocoelia	5	2	0.041	0.840
Others	5	3	0.128	0.721
APACHE II (score)	22.61±3.42	28.29±2.86	7.780	<0.001
SOFA (score)	7.85±3.09	12.53±4.21	5.765	<0.001
Scr (μmol/L)	71.74±12.53	76.21±13.63	1.514	0.170
LVEF (%)	0.45±0.12	0.45±0.10	0.000	1.000

Note: APACHE II, acute physiology and chronic health evaluation scoring system; SOFA, sequential organ failure assessment; Scr, serum creatinine; LVEF, left ventricular ejection fractions.

Table 2. Comparison of EVLWI (mL/kg)

	Survival group (n=49)	Death group (n=23)	t	P
On the day of ICU stay	11.51±3.34	11.27±3.65	0.276	0.783
At the 72nd hour after ICU stay	9.46±3.28	14.03±2.96	4.961	<0.001
t	3.065	2.817		
P	0.003	0.007		

Note: EVLWI, extravascular lung water index; ICU, intensive care unit.

72nd hour after ICU stay; APACHEII score within 24 hours of ICU stay.

Statistical analysis

SPSS19.0 statistical software was used for analysis. Measurement data are expressed as mean ± standard deviation ($\overline{x}$ ± sd) and t-test was carried out. Count data are expressed as the number of cases/percentage (n/%) and an χ^2 test was carried out. Pearson's correlation analysis was used for correlation of EVLWI and BLACR with the mortality of patients. For multivariate analysis, BLACR at the 6th, 12th, 24th, and 72nd hour after ICU stay and EVLWI were used as independent variables. Whether the patient died or not was used as a dependent variable. Logistic regression analysis was used to analyze risk factors for patients with septic shock. P<0.05 indicates statistical significance.

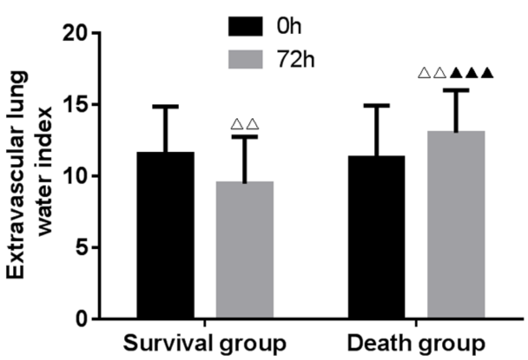

Figure 1. Comparison of extravascular lung water index. 0 h: On the day of ICU stay; 72 h: At the 72nd hour after ICU stay. Compared with 0 h, $^{\triangle\triangle}$P<0.01; compared with survival group, $^{\blacktriangle\blacktriangle\blacktriangle}$P<0.001.

Outcome measures

BLA levels at the time of ICU stay, as well as the 6th, 12th, 24th, and 72nd hour after ICU stay; BLACR; EVLWI on the day of ICU stay and the

Results

Comparison of demographic data

There were no significant differences in gender composition, age, and source of infection between the two groups (P>0.05). APACHEII and SOFA scores were higher in the death group than those in the survival group (P<0.05). See **Table 1**.

Comparison of EVLWI

On the day of ICU stay, there were no significant differences in EVLWI between the two groups (P>0.05). In the survival group, EVLWI at the 72nd hour after ICU stay was significantly lower than that on the day of ICU stay (P<0.05). In the death group, it was the opposite. At the 72nd hour after ICU stay, EVLWI in the survival group was significantly lower than that in the death group (P<0.05). See **Table 2** and **Figure 1**.

Table 3. Comparison of BLA levels (mmol/L)

	Survival group (n=49)	Death group (n=23)	t	P
On the day of ICU stay	6.14±2.26	6.22±2.53	0.135	0.893
At the 6th hour after ICU stay	5.05±1.82	6.13±2.15	2.214	0.030
At the 12th hour after ICU stay	4.43±1.25	5.57±2.33	2.706	0.009
At the 24th hour after ICU stay	2.92±1.32	5.39±2.04	6.177	<0.001
At the 72nd hour after ICU stay	2.01±1.15	5.18±2.08	8.331	<0.001

Note: BLA, blood lactate acid; ICU, intensive care unit.

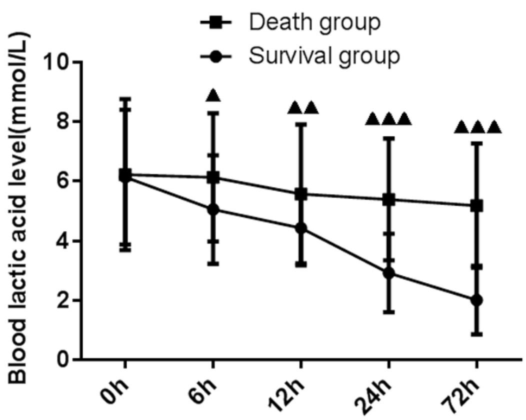

Figure 2. Comparison of blood lactic acid levels. 0 h: On the day of ICU stay; 6 h, 12 h, 24 h, 72 h represents at the 6th, 12th, 24th, 72nd hour after ICU stay. Compared with survival group, ▲P<0.05, ▲▲P<0.01, ▲▲▲P<0.001.

Comparison of BLA level

There were no significant differences between the two groups with respect to BLA levels (P>0.05). With ICU stays prolonged, BLA levels were significantly lower in the survival group than in the death group at the 6th, 12th, 24th, and 72nd hour after ICU stay (P<0.05). See **Table 3** and **Figure 2**.

Comparison of BLACR

With ICU stays prolonged, BLACR was increased. It was significantly higher in the survival group than in the death group at the 6th, 12th, 24th, and 72nd hour after ICU stay (P<0.05). See **Table 4** and **Figure 3**.

Analysis of BLACR, EVLWI, and prognosis in patients with septic shock

Higher BLACR levels indicate lower mortality rates of patients with septic shock. Greater differences in EVLWI levels indicate higher mortality rates of patients with septic shock. Differences showed statistical significance (P<0.05). See **Table 5** and **Figure 4**.

Correlation analysis

BLACR was negatively correlated with mortality of patients with septic shock (P<0.05), while EVLWI was positively correlated with mortality of the patients (P<0.05). See **Table 6**.

Analysis of risk factors for patients with septic shock

BLACR, at the 6th, 12th, 24th, and 72nd hour after ICU stay, and EVLWI were used as independent variables. Whether the patient died or not was used as a dependent variable. These were included in the multivariate logistic regression model. Results showed that BLACR, at the 6th and 12th hour, and EVLWI were independent risk factors for death in patients with septic shock. See **Table 7**.

Discussion

Septic shock is an important cause of death in critically ill patients, with a high mortality. It involves complex physiological processes [12, 13]. Generalized infections and inflammatory reactions lead to cellular dysfunction, coagulation disorders, and circulatory disturbance, causing ARDS, lung injury, and even organ failure in patients [14-16]. In recent years, related studies have shown that BLACR and EVLWI have higher predictive values for prognosis of patients with septic shock [17-19].

Extravascular lung water that contains a large amount of intracellular fluid, pulmonary interstitial fluid, and alveolar fluid reflects the degree of lung injuries [20]. Previous studies have confirmed that EVLWI is closely related to the degree of lung injuries and higher EVLWI predicts more severe lung injuries [18, 19]. This study showed that, in the survival group of patients with septic shock, EVLWI at the 72nd hour after ICU stay was lower than that on the day of ICU stay. In the death group, EVLWI at the 72nd hour after ICU stay was higher. Further

Table 4. Comparison of blood lactic acid clearance rates (%)

	Survival group (n=49)	Death group (n=23)	t	P
At the 6th hour after ICU stay	13.58±4.86	-2.56±0.68	15.796	<0.001
At the 12th hour after ICU stay	27.13±7.49	4.89±2.63	13.802	<0.001
At the 24th hour after ICU stay	36.57±14.68	9.76±4.55	8.540	<0.001
At the 72nd hour after ICU stay	48.38±13.79	9.97±4.67	12.971	<0.001

Note: ICU, intensive care unit.

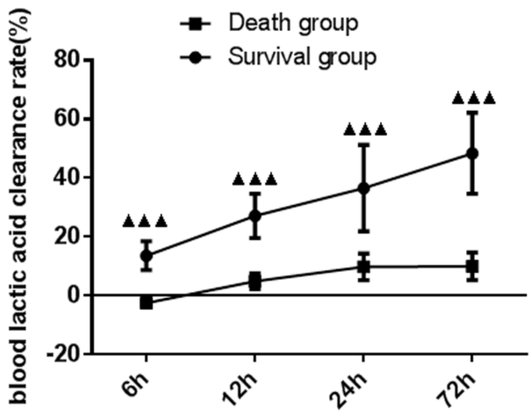

Figure 3. Comparison of blood lactic acid clearance rates. 6 h, 12 h, 24 h, 72 h represents at the 6th, 12th, 24th, 72nd hour after ICU stay. Compared with survival group, ▲▲▲P<0.001.

analysis showed that patients with septic shock, with a difference in EVLWI >0, had a higher risk of death. Moreover, EVLWI was positively correlated with mortality of the patients, suggesting that EVLWI reflects the prognosis of patients with septic shock, at least to some extent. The key to treatment of patients with septic shock is early fluid resuscitation and later effective fluid management, aiming to improve deficiencies in blood circulatory volume. However, due to different degrees of pulmonary edema in patients, fluid resuscitation and fluid management may cause the aggravation of pulmonary edema. Improper treatment makes conditions worse. One study showed that PiCCO technology was administered to patients with septic shock to monitor EVLWI. The sensitivity of prognostic evaluation is 83.3% when EVLWI >7.5 mL/kg, suggesting that if EVLWI is significantly decreased in the early stages of treatment, fluid is negatively balanced and prognosis may be better. Thus, the indicators have an accurate prognostic evaluation [21]. This is consistent with the results of the current study, demonstrating that PiCCO technology for monitoring EVLWI reflects pulmonary edema of patients at all times. Therefore, it is of great significance for guiding early fluid resuscitation treatment and the rate and volume of fluid replacement in fluid management. This can replenish enough fluid while not significantly increasing pulmonary edema.

BLA is produced by the interaction of pyruvic acid and lactic dehydrogenase. Its physiological role is mainly involved in the metabolism of fatty acids and proteins [20]. It reflects oxygen supply, metabolism, and perfusion in the body [22]. Patients with septic shock, under systemic inflammatory reactions, have abnormal tissue perfusion that leads to insufficient oxygen supply to the tissue [23]. Therefore, BLA reflects patient conditions to a certain extent. The study showed that, compared with patients with septic shock in the death group, patients in the survival group had lower BLA levels, but higher BLACR at each time point after ICU stay. Related studies have reported that BLA levels in patients with septic shock are higher, which is basically consistent with present results [24]. Further analysis showed that BLACR was negatively correlated with the mortality of patients with septic shock. Lower BLACR levels indicate a higher risk of patient death and lower survival rates.

In terms of drug treatment, the increase in BLACR and EVLWI suggests that patients have symptoms of metabolic acidosis and aggravated pulmonary edema. Therefore, the therapeutic effects can be judged through BLACR and EVLWI during medication treatment. Adjusting the treatment plan in time can improve efficacy. Hydrostatic pressure and permeability of the pulmonary capillary in patients with septic shock may be increased during weaning from mechanical ventilation, causing pulmonary interstitial edema and even alveolar edema. This may eventually lead to dyspnea, cyanosis, insufficient blood and oxygen supply to the body, metabolic disorders, and increased BLA. Therefore, monitoring changes in EVLWI and BLACR during weaning is important in predicting the success or failure of weaning, as well as subse-

Table 5. Analysis of BLACR, EVLWI, and prognosis in patients with septic shock

	n	Survival group (n=49)	Death group (n=23)	Mortality (%)	χ^2	P
BLACR					39.834	<0.001
≤0%	9	0	9	100.00		
0%-10%	6	1	5	83.33		
10%-30%	10	5	5	50.00		
≥30%	47	43	4	8.51		
Difference in EVLWI					23.837	<0.001
≤0	44	39	5	11.36		
0-0.5	15	7	8	53.33		
0.5-1.0	9	2	7	77.78		
≥1.0	4	1	3	75.00		

Note: BLACR, blood lactic acid clearance rate; EVLWI, extravascular lung water index; ICU, intensive care unit.

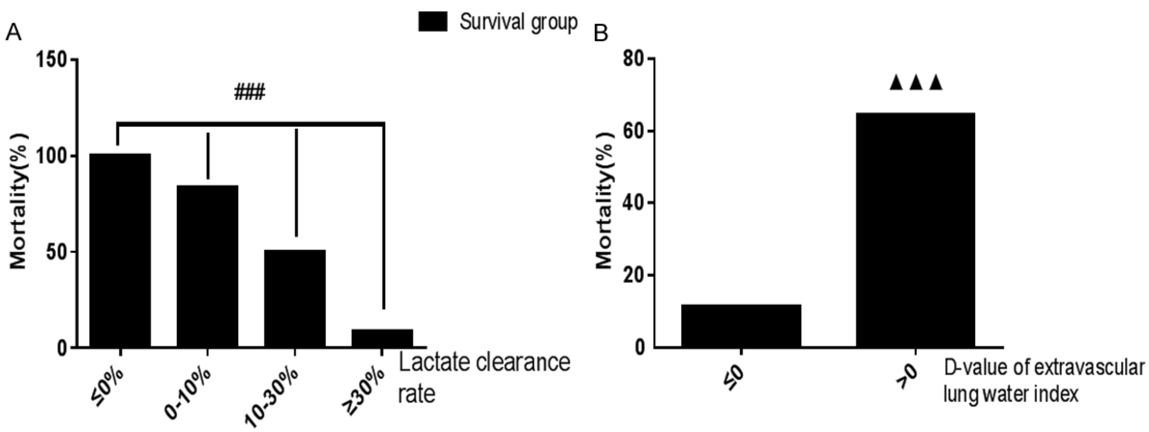

Figure 4. Correlation between lactate clearance rate, extravascular lung water index, and mortality. A: Correlation between lactate clearance rate and mortality. B: Correlation between extravascular lung water index and mortality. Comparison between groups, ###P<0.01; Compared with ≤0 group, ▲▲▲P<0.001.

Table 6. Correlation analysis (%)

	BLACR	EVLWI
r	-3.269	2.473
P	0.006	0.009

Note: BLACR, blood lactic acid clearance rate; EVLWI, extravascular lung water index.

quent treatment. One study showed that, in patients with sepsis, EVLWI was positively correlated with APACHEII scores, while BLACR was negatively correlated with the score [25]. This suggested that BLACR and EVLWI can reflect the severity and prognosis of sepsis, with higher EVLWI and lower BLACR indicating worse conditions and poorer prognosis. This is consistent with present results. In conclusion, monitoring EVLWI and BLACR provides important guiding value in judging the prognosis of patients with septic shock, as well as for drug treatment, fluid resuscitation, fluid management, and weaning from mechanical ventilation.

However, there were shortcomings to the current study. The sample size was small and should be enlarged. Therefore, cutoff values, sensitivity, specificity, and accuracy of EVLWI and BLACR values in predicting prognosis of patients with septic shock require further investigation.

In summary, EVLWI and BLACR are closely related to prognosis of patients with septic shock. Clinically strengthening the monitoring of EVLWI and BLACR is of great reference value in predicting disease outcomes and guiding clinical timely intervention.

Disclosure of conflict of interest

None.

Table 7. Analysis of risk factors in patients with septic shock

	β	Wald	P	95% CI
BLACR				
At the 6th hour after ICU stay	1.037	6.892	0.007	1.468-4.671
At the 12th hour after ICU stay	2.681	8.674	0.001	1.572-4.119
At the 24th hour after ICU stay	0.479	2.025	0.069	-0.635-1.343
At the 72nd hour after ICU stay	0.326	1.968	0.074	-0.961-1.071
EVLWI	1.745	8.133	0.003	1.156-3.242

Note: BLACR, blood lactic acid clearance rate; EVLWI, extravascular lung water index; ICU, intensive care unit; CI, confidence interval.

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References

[1] Simpson SQ, Gaines M, Hussein Y and Badgett RG. Early goal-directed therapy for severe sepsis and septic shock: a living systematic review. J Crit Care 2016; 36: 43-48.

[2] Terayama T, Yamakawa K, Umemura Y, Aihara M and Fujimi S. Polymyxin B hemoperfusion for sepsis and septic shock: a systematic review and meta-analysis. Surg Infect (Larchmt) 2017; 18: 225-233.

[3] Fujii T, Ganeko R, Kataoka Y, Furukawa TA, Featherstone R, Doi K, Vincent JL, Pasero D, Robert R, Ronco C and Bagshaw SM. Correction to: polymyxin B-immobilized hemoperfusion and mortality in critically ill adult patients with sepsis/septic shock: a systematic review with meta-analysis and trial sequential analysis. Intensive Care Med 2018; 44: 279-280.

[4] Wu XY, Zhuang ZQ and Zheng RQ. Evaluation of extravascular pulmonary water index in the prognosis of elderly patients with septic shock complicated with pulmonary capillary leakage. Chinese Journal of Geriatrics 2015.

[5] Wernly B, Haumann S, Masyuk M, Muessig J, Lichtenauer M, Bäz L, Franz M, Pfeil A, Lauten A, Schulze PC, Hoppe UC, Kelm M, Westenfeld R, Jung C and Renz D. Extravascular lung water index and Halperin score to predict outcome in critically ill patients. Wien Klin Wochenschr 2018; 130: 505-510.

[6] Liu SX, Liu KX, Wang YL, Kang XW and Chen XB. Study on the prognosis in patients with septic shock by dynamic monitoring the lactate level of arterial blood. Chinese General Practice 2010; 13: 4141-4142.

[7] Chung FT, Lee CS, Lin SM, Kuo CH, Wang TY, Fang YF, Hsieh MH, Chen HC and Lin HC. Alveolar recruitment maneuver attenuates extravascular lung water in acute respiratory distress syndrome. Medicine 2017; 96: e7627.

[8] Zhou M, Dai J, Du M, Wang W, Guo C, Wang Y, Tang R, Xu F, Rao Z and Sun G. Effect of dobutamine on extravascular lung water index, ventilator function, and perfusion parameters in acute respiratory distress syndrome associated with septic shock. Artif Cells Nanomed Biotechnol 2016; 44: 1326-1332.

[9] Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, Cohen J, Opal SM, Vincent JL, Ramsay G; SCCM/ESICM/ACCP/ATS/SIS. 2001 SCCM/ESICM/ACCP/ATS/SIS international sepsis definitions conference. Crit Care Med 2003; 31: 1250-1256.

[10] Knaus WA, Draper EA, Wagner DP and Zimmerman JE. APACHE II: a severity of disease classification system. Critical Care Medicine 1985; 13: 818-829.

[11] Vincent JL, Moreno R, Takala J, Willatts S, De Mendonca A, Bruining H, Reinhart CK, Suter PM and Thijs LG. The sepsis-related organ failure assessment (SOFA) score to describe organ dysfunction/failure. Intensive Care Med 1996; 22: 707-710.

[12] Meng JB, Lai ZZ, Xu XJ, Ji CL, Hu MH and Zhang G. Effects of early continuous venovenous hemofiltration on E-Selectin, hemodynamic stability, and ventilatory function in patients with Septic-Shock-Induced acute respiratory distress syndrome. Biomed Res Int 2016; 2016: 7463130.

[13] Tagami T and Ong MEH. Extravascular lung water measurements in acute respiratory distress syndrome: why, how, and when? Curr Opin Crit Care 2018; 24: 209-215.

[14] Polat G, Ugan RA, Cadirci E and Halici Z. Sepsis and septic shock: current treatment strategies and new approaches. Eurasian J Med 2017; 49: 53-58.

[15] Kellum JA, Chawla LS, Keener C, Singbartl K, Palevsky PM, Pike FL, Yealy DM, Huang DT, Angus DC; ProCESS and ProGReSS-AKI Investigators. The effects of alternative resuscitation strategies on acute kidney injury in patients with septic shock. Am J Respir Crit Care Med 2016; 193: 281-287.

[16] Leisman D, Wie B, Doerfler M, Bianculli A, Ward MF, Akerman M, D'Angelo JK and Zemmel D'Amore JA. Association of fluid resuscitation initiation within 30 minutes of severe sepsis and septic shock recognition with reduced mortality and length of stay. Ann Emerg Med 2016; 68: 298-311.

[17] Liu X, Ji W, Wang J and Pan T. Application strategy of PiCCO in septic shock patients. Exp Ther Med 2016; 11: 1335-1339.
[18] David S, Thamm K, Schmidt BMW, Falk CS and Kielstein JT. Effect of extracorporeal cytokine removal on vascular barrier function in a septic shock patient. J Intensive Care 2017; 5: 12.
[19] Brenner T, Uhle F, Fleming T, Wieland M, Schmoch T, Schmitt F, Schmidt K, Zivkovic AR, Bruckner T, Weigand MA and Hofer S. Soluble TREM-1 as a diagnostic and prognostic biomarker in patients with septic shock: an observational clinical study. Biomarkers 2017; 22: 63-69.
[20] Hong Y, Chi D, Wang S and Liu B. Effect of early goal-directed therapy on mortality in patients with severe sepsis or septic shock: a meta-analysis of randomised controlled trials. BMJ Open 2016; 6: 8330.
[21] Yang CS, Qiu HB, Liu SQ, Yang Y, Huang YZ and Liu L. The prognostic value of extravascular lung water index in critically ill septic shock patient. Chin J Intern Med 2006; 145: 192-195.
[22] Whitson MR, Mo E, Nabi T, Healy L, Koenig S, Narasimhan M and Mayo PH. Feasibility, utility, and safety of midodrine during recovery phase from septic shock. Chest 2016; 149: 1380-1383.
[23] Cronhjort M, Hjortrup PB, Holst LB, Joelsson-Alm E, Mårtensson J, Svensen C and Perner A. Association between fluid balance and mortality in patients with septic shock: a post hoc analysis of the TRISS trial. Acta Anaesthesiol Scand 2016; 60: 925-933.
[24] Wang T, Xia Y, Hao D, Sun J, Li Z, Han S, Tian H, Zhang X, Qi Z, Sun T, Gao F and Wang X. [The significance of lactic acid in early diagnosis and goal-directed therapy of septic shock patients]. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue 2014; 26: 51-55.
[25] Zhu XH and Hu XF. The expression of extravascular pulmonary water index and lactate clearance rate in sepsis and their correlation with prognosis. Zhejiang Practical Medicine 2017; 22: 398-400.