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Ultrasound-guided fluid resuscitation combined with esmolol in the treatment of septic shock

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Abstract: Objective To investigate the effect of ultrasound-guided fluid resuscitation combined with esmolol on oxygen metabolism indicators and inflammatory levels in patients with septic shock. **Methods** A total of 122 patients with septic shock admitted to Affiliated Hospital of Hebei University of Engineering from June 2021 to June 2023 were selected and randomly divided into a control group and a treatment group, with 61 cases in each group. All patients received conventional treatments including fluid resuscitation for anti-shock, application of vasoactive drugs, anti-infection, immune regulation, and organ function support. The control group was treated with ultrasound-guided fluid resuscitation, while the treatment group was additionally treated with esmolol based on the control group. Oxygen metabolism indicators [oxygen consumption (VO_2), oxygen delivery (DO_2)], inflammatory factors [interleukin-6 (IL-6), C-reactive protein (CRP)], 6-hour lactate clearance rate, mortality rate during treatment, hemodynamic indicators [mean arterial pressure (MAP), central venous pressure (CVP)], and myocardial related indicators [creatinine kinase-MB (CK-MB), brain natriuretic peptide (BNP), cardiac troponin I (cTnI)] were compared between the two groups. **Results** After treatment, the levels of IL-6, CRP, CK-MB, BNP, and cTnI decreased in both groups, and those in the treatment group were significantly lower than those in the control group ($P < 0.05$). The levels of VO_2 , DO_2 , MAP, and CVP increased in both groups, and those in the treatment group were significantly higher than those in the control group ($P < 0.05$). The 6-hour lactate clearance rate in the treatment group was significantly higher than that in the control group [(86.21±9.35)% vs (81.52±8.69)%, $t=2.870$, $P=0.005$]. There was no significant difference in mortality rate during treatment between the two groups ($P > 0.05$). **Conclusion** Ultrasound-guided fluid resuscitation combined with esmolol can effectively improve oxygen supply-consumption balance, enhance tissue oxygen delivery capacity, stabilize hemodynamics, inhibit the release of inflammatory factors, reduce systemic inflammatory response, and improve myocardial function in patients with septic shock, which has clinical application value.

Keywords: Esmolol; Ultrasound guidance; Fluid resuscitation; Septic shock; Oxygen metabolism; Inflammation; Hemodynamics
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Septic shock is a critical clinical syndrome caused by the body's uncontrolled response to infection, which leads to circulatory dysfunction and cellular metabolic disorder. It can induce multiple organ dysfunction, accompanied by refractory hypotension and insufficient tissue perfusion, posing a serious threat to the life safety of patients [1]. According to reports, the global annual number of sepsis cases exceeds 19 million, with 6 million deaths [2]. Clinical treatments such as fluid replacement for anti-shock, application of vasoactive drugs and antibiotics can alleviate the symptoms, but the overall efficacy is limited and the prognosis is poor [3]. With the unique advantage of real-time dynamic monitoring, ultrasound technology can closely track the hemodynamic status of patients, and comprehensively evaluate cardiac pumping function, vascular elasticity, blood flow velocity and tissue perfusion of the whole body. Implementing fluid resuscitation under precise ultrasound guidance allows timely adjustment of the fluid replacement regimen according to the patient's unique physiological characteristics and real-time hemodynamic changes, which can effectively avoid the risks that may be brought by traditional empirical fluid replacement, and ensure the accuracy and safety of treatment [4]. Esmolol can improve microcirculation

disturbance, effectively increase the perfusion volume of tissues and organs, ensure that tissue cells obtain sufficient blood supply, so as to restore normal physiological functions. It can also effectively relieve microvascular spasm, maintain the patency of the microvascular network, provide a smooth channel for material exchange between blood and tissues, and further optimize the microcirculation state [5]. This study analyzed the effects of ultrasound-guided fluid resuscitation combined with esmolol on oxygen metabolism indexes and inflammatory levels in patients with septic shock, and the report is presented as follows.

1 Materials and Methods

1.1 Sample Size Calculation

The minimum required sample size was estimated according to the formula:
$$n = \frac{\pi_1(100-\pi_1) + \pi_2(100-\pi_2)}{(\pi_2 - \pi_1)^2} f(\alpha, \beta)$$
, where π_1 represents the expected total effective rate of the control group (60.66%), π_2 represents the expected total effective rate of the

treatment group (81.97%), α is the type I error probability (set as 0.05 in this study), and β is the type II error probability (set as 0.20 in this study). According to the formula calculation, at least 53 cases were required in each group. Considering possible loss to follow-up, 61 patients were included in each group.

1.2 General Information

A total of 122 patients with septic shock admitted to the Affiliated Hospital of Hebei University of Engineering from June 2021 to June 2023 were selected as the research subjects. **Inclusion criteria:** (1) meeting the diagnostic criteria for septic shock [6]; (2) aged 18 to 60 years old; (3) having a clear focus of infection or a highly suspected focus of infection; (4) the patient's family members were informed of the research purpose and signed the informed consent form. **Exclusion criteria:** (1) combined with severe trauma or burns; (2) allergic to the drugs used in this study; (3) combined with valvular heart disease or hepatic and renal dysfunction; (4) patients with intellectual disability, dementia, or mental illness; (5) combined with malignant tumors or immune system diseases; (6) pregnant or lactating women. **Drop-out criteria:** Patients who died within 24 hours after admission or whose vital signs could not be maintained.

1.3 Grouping

The 122 patients were divided into a control group and a treatment group using a random number table method, with 61 cases in each group. In the control group, the age was (47.33 ± 5.13) years, the body mass index (BMI) was (22.30 ± 2.43) kg/m^2 , with 37 males and 24 females; in the treatment group, the age was (48.03 ± 5.21) years, the BMI was (22.67 ± 2.49) kg/m^2 , with 33 males and 28 females. There was no statistically significant difference in general data such as age, BMI, and gender between the two groups ($P > 0.05$). This study has been reviewed by the Ethics Committee of the Affiliated Hospital of Hebei University of Engineering [Ethics Approval No.: 2021(K)025].

1.4 Treatment Methods

All patients received conventional treatment including fluid replacement, anti-shock therapy, administration of vasoactive drugs, anti-infection treatment, immunomodulation, and organ function support, while vital signs monitoring and disease condition assessment were completed simultaneously.

The ultrasound-guided fluid resuscitation process for the control group was as follows.

Preparation stage: the patient was placed in the supine position, the skin under the xiphoid process was exposed, and a phased-array probe ultrasound machine (Model: Mindray ME7, Manufacturer: Shenzhen Mindray Bio-Medical Electronics Co., Ltd.) was used. Inferior vena cava (IVC) measurement: M-mode ultrasound was used to measure the IVC diameter at the expiratory and inspiratory

phases in the straight segment of the IVC approximately 2 cm from the right atrial opening, and the collapsibility index was calculated.

Cardiac ultrasound assessment: transthoracic ultrasound was performed through the apical four-chamber view and parasternal left ventricular long-axis view to evaluate cardiac systolic function and cardiac cavity size. The left ventricular end-diastolic diameter (LVEDD) was measured, and cardiac output (CO) was calculated.

Lung ultrasound monitoring: the BLUE protocol was used to perform standardized scanning of the bilateral anterior chest, lateral chest, and back, and the number and distribution characteristics of B-lines in each region were recorded. Diffuse bilateral B-lines indicate the risk of pulmonary edema, and dynamic monitoring is recommended to guide fluid management.

Fluid resuscitation implementation: initial fluid resuscitation was started at 10-15 $\text{mL}/(\text{kg}\cdot\text{h})$, and then the rate was adjusted every 15-30 minutes according to the IVC status. The specific volume was individually adjusted according to the patient's clinical background, and fluid responsiveness was dynamically evaluated.

Dynamic adjustment: ultrasound and clinical indicators were rechecked every 0.5-1 hour. If the IVC diameter was $>2\text{cm}$ or the number of B-lines increased, fluid infusion was slowed down. For spontaneously breathing patients, if the end-expiratory IVC diameter was $<1.5\text{cm}$ or the collapsibility index was $>50\%$, it indicated good volume responsiveness, and fluid infusion could be accelerated; if the end-expiratory IVC diameter was $>2.5\text{cm}$ and the collapsibility index was $<20\%$, it indicated volume overload, and fluid infusion should be restricted.

Small-dose fluid challenge test: when ultrasound indicated unclear volume responsiveness, 50-100 mL of fluid was rapidly infused within 1-2 minutes, and stroke volume (SV) or CO was remeasured within 5 minutes after infusion. If the increase was $\geq 10\%$ -15%, it was considered responsive, and fluid infusion could be continued; if there was no response, fluid was restricted.

Comprehensive monitoring: vital signs, urine output, blood lactate and other indicators of the patients were continuously monitored until shock was reversed, to ensure the effect of fluid resuscitation.

In addition to the above treatment steps, the treatment group additionally received intravenous drip of esmolol (Qilu Pharmaceutical, National Medicine Approval No. H19991059, 10 mL: 0.1 g). The initial dose of esmolol was usually $7.5\ \mu\text{g}/(\text{kg}\cdot\text{min})$, and the dose was gradually adjusted according to the patient's response. During the treatment, the patient's heart rate was closely monitored to maintain the heart rate between 60 and 100 beats per minute.

1.5 Observation Indicators

The following indicators were observed and recorded before and after treatment.

Primary indicators

(1) oxygen metabolism indexes [7]: oxygen consumption (VO_2) and oxygen delivery (DO_2) were

detected by respiratory measurement; (2) inflammatory factors [8]: the levels of interleukin-6 (IL-6) and C-reactive protein (CRP) were detected by enzyme-linked immunosorbent assay (ELISA); (3) 6-hour lactate clearance rate [9]: the 6-hour lactate clearance rate was detected by a blood gas analyzer, with the formula: 6 h lactate clearance rate = (initial lactate concentration - lactate concentration at 6 h) / initial lactate concentration × 100%; (4) mortality: The proportion of deaths during treatment in the total number of patients was calculated.

Secondary indicators

(1) hemodynamic indexes [10]: mean arterial pressure (MAP) was detected by an automatic sphygmomanometer, and central venous pressure (CVP) was detected by central venous pressure measurement technology; (2) myocardial related indexes [11]: The levels of creatine kinase MB (CK-MB), brain natriuretic peptide (BNP), and cardiac troponin I (cTnI) were detected by ELISA.

1.6 Statistical Methods

SPSS 25.0 software was used for data analysis. Count data were expressed as cases (%), and comparison between groups was performed using the chi-square test. Measurement data conforming to normal distribution were expressed as $\bar{x} \pm s$. Comparison between groups was performed using independent samples t-test, and intra-group comparison was performed using paired samples t-test. A $P < 0.05$ was considered statistically significant.

2 Results

2.1 Comparison of Oxygen Metabolism Indexes

After treatment, the levels of oxygen consumption (VO_2) and oxygen delivery (DO_2) increased in both the control group and the treatment group, and the levels in the treatment group were higher than those in the control group, with statistically significant differences ($P < 0.05$). [Table 1]

Tab.1 Comparison of oxygen metabolism indicators before and after treatment between two groups [$n=61$, mL/(min·m²), $\bar{x} \pm s$]

Group	DO ₂		VO ₂	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Treatment group	531.24±55.36	814.35±85.37 ^a	196.38±20.15	265.78±29.68 ^a
Control group	534.84±56.12	758.24±80.18 ^a	198.65±20.98	231.27±25.41 ^a
<i>t</i> value	0.357	3.742	0.609	6.898
<i>P</i> value	0.722	<0.001	0.543	<0.001

Note: ^a $P < 0.05$, compared with the same group before treatment.

2.2 Comparison of Inflammatory Factor Levels

After treatment, the levels of interleukin-6 (IL-6) and C-reactive protein (CRP) decreased in both the control group and the treatment group, and the levels in the

treatment group were lower than those in the control group, with statistically significant differences ($P < 0.05$). [Table 2]

Tab.2 Comparison of inflammatory factors levels before and after treatment between two groups ($n=61$, $\bar{x} \pm s$)

Group	IL-6 (pg/mL)		CRP (mg/L)	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Treatment group	112.56±14.51	43.26±5.67 ^a	89.68±10.34	30.28±4.35 ^a
Control group	109.98±13.84	59.69±6.84 ^a	87.61±9.84	43.15±5.68 ^a
<i>t</i> value	1.005	14.443	1.133	14.050
<i>P</i> value	0.317	<0.001	0.260	<0.001

Note: ^a $P < 0.05$, compared with the same group before treatment.

2.3 Comparison of 6-hour Lactate Clearance Rate and Mortality

After treatment, the 6-hour lactate clearance rate in the treatment group was higher than that in the control group ($P < 0.05$); there was no statistically significant difference in mortality between the two groups during the treatment period ($P > 0.05$). [Table 3]

Tab. 3 Comparison of 6-hour lactate clearance rate and mortality before and after treatment between two groups ($n=61$)

Group	6 h lactate clearance rate (% , $\bar{x} \pm s$)	fatality rate[case(%)]
Treatment group	86.21±9.35	5 (8.20)
Control group	81.52±8.69	9 (14.75)
<i>t</i> / χ^2 value	2.870	1.291
<i>P</i> value	0.005	0.256

2.4 Comparison of Hemodynamic Parameters

After treatment, the MAP and CVP increased in both the control group and the treatment group, and the levels in the treatment group were higher than those in the control group ($P < 0.05$). [Table 4]

Tab. 4 Comparison of hemodynamic parameters before and after treatment between two groups ($n=61$, $\bar{x} \pm s$)

Group	MAP (mmHg)		CVP (cmH ₂ O)	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Treatment group	64.59±7.22	98.68±10.27 ^a	5.21±0.85	10.24±1.63 ^a
Control group	65.41±7.68	92.15±9.62 ^a	5.36±0.91	8.16±1.13 ^a
<i>t</i> value	0.608	3.624	0.941	8.191
<i>P</i> value	0.545	<0.001	0.349	<0.001

Note: ^a $P < 0.05$, compared with the same group before treatment.

2.5 Comparison of Myocardial-Related Indexes Between the Two Groups

After treatment, the levels of CK-MB, BNP and cTnI decreased in both the control group and the treatment group, and the levels in the treatment group were lower than those in the control group ($P < 0.05$). [Table 5]

Tab. 5 Comparison of myocardial function before and after treatment between two groups ($n=61, \bar{x}\pm s$)

Group	CK-MB (ng/mL)		BNP (pg/mL)		cTnI (ng/L)	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Treatment group	2.12±0.35	1.21±0.23 ^a	172.32±19.25	124.32±13.56 ^a	164.29±18.52	95.64±10.27 ^a
Control group	2.06±0.31	1.49±0.28 ^a	169.58±18.24	152.21±16.38 ^a	162.32±17.54	103.57±11.14 ^a
<i>t</i> value	1.002	6.035	0.807	10.244	0.603	4.088
<i>P</i> value	0.318	<0.001	0.421	<0.001	0.548	<0.001

Note: ^a $P<0.05$, compared with the same group before treatment.

3 Discussion

Septic shock is the result of an excessive inflammatory response of the body to severe infection, which can cause systemic toxic symptoms, lead to myocardial dysfunction, and endanger the lives of patients [12]. Arterial vasodilation can lead to insufficient vascular filling, while the reactivity of the renal microvascular system to vasoconstrictors is enhanced, which in turn reduces renal blood flow and glomerular filtration rate [13-14]. Critically ill patients may develop cardiovascular system dysfunction and myocardial depression, leading to insufficient perfusion of vital organs such as the brain, lungs, kidneys, and gastrointestinal tract, which can further cause coma, and even multiple organ damage in severe cases [15-16].

Previous studies have reported that ultrasound-guided fluid resuscitation and esmolol have certain therapeutic effects in the treatment of septic shock [17-18]. Echocardiography can comprehensively evaluate the size, morphology and structural characteristics of the heart, accurately distinguish the functional status of the right and left ventricles, monitor the dynamic changes of cardiac pumping function in real time, and simultaneously assess vascular resistance characteristics and compliance. This helps to optimize treatment regimens, ensure the safety and effectiveness of drug therapy, and prevent the occurrence of fluid overload [19]. Esmolol can reduce heart rate, effectively alleviate cardiac load and optimize cardiac function, improve cardiac compliance by regulating the myocardial diastolic process, and promote sufficient ventricular filling during diastole. In addition, esmolol can also inhibit the release of inflammatory mediators, reduce tissue and cell damage, and promote tissue repair and regeneration [20]. Based on the above characteristics of the two interventions, this study aims to explore the application value of ultrasound-guided fluid resuscitation combined with esmolol in the treatment of septic shock.

VO_2 and DO_2 are important indexes for evaluating tissue metabolic status [21]. The level of IL-6 is closely related to the severity of disease in patients with sepsis, and the elevation amplitude of CRP is positively correlated with the degree of infection [22]. The results of this study showed that after treatment, VO_2 and DO_2 levels increased, while IL-6 and CRP levels decreased in both groups, and the changes were more significant in the treatment group, indicating that the combined therapy can effectively improve oxygen metabolism indexes and reduce the inflammatory response in patients. The underlying mechanism may be as follows: Ultrasound-guided fluid

resuscitation can accurately evaluate hemodynamic status, guide the dose and rate of fluid resuscitation, and ensure effective circulating blood volume; esmolol can reduce heart rate and myocardial contractility, decrease myocardial oxygen consumption, attenuate excessive sympathetic excitation, and indirectly alleviate sympathetic-mediated excessive inflammatory activation and tissue damage under sepsis/stress conditions. The synergistic effect of the two interventions can optimize fluid resuscitation and regulate the inflammatory response, thereby more significantly reducing the levels of IL-6 and CRP. The 6-hour lactate clearance rate is one of the important indexes for evaluating the resuscitation effect and prognosis of patients with septic shock [23]. The results of this study showed that the 6-hour lactate clearance rate in the treatment group was higher than that in the control group after treatment, while there was no statistically significant difference in mortality between the two groups during the treatment period, indicating that the combined therapy can improve the 6-hour lactate clearance rate of patients. The possible reason is that the combination of ultrasound-guided fluid resuscitation and esmolol can synergistically optimize the balance between oxygen supply and oxygen consumption, reduce lactate production, and promote metabolic clearance by tissues and organs. MAP monitoring is helpful to clarify the goal of fluid resuscitation and evaluate the resuscitation effect, while CVP is an important index reflecting right atrial pressure and systemic blood volume status, which can be used to evaluate the volume status of patients with septic shock and guide fluid resuscitation decisions [24-25]. The results of this study showed that MAP and CVP levels increased in both groups after treatment, and the elevation was more significant in the treatment group, indicating that the combined therapy can effectively improve the hemodynamic status of patients. During septic shock, systemic inflammatory response and microcirculation dysfunction can lead to myocardial cell injury, which in turn causes an increase in CK-MB level. Meanwhile, increased cardiac load and myocardial cell damage can raise BNP level. Meanwhile, cTnI is released into the blood when myocardial cells are damaged, and its elevated level usually indicates severe myocardial cell injury [26-27]. The results of this study showed that the levels of CK-MB, BNP and cTnI decreased in both groups after treatment, and were lower in the treatment group than in the control group, indicating that the combined therapy can effectively ameliorate myocardial injury in patients. The mechanism is reflected in the synergistic effect of ultrasound-guided fluid resuscitation and esmolol: Ultrasound-guided fluid resuscitation precisely controls volume load, reduces

ventricular wall tension, decreases BNP secretion, and avoids aggravating myocardial injury caused by volume overload; esmolol slows heart rate, reduces myocardial contractility and myocardial oxygen consumption through β 1-blockade, prolongs coronary diastolic perfusion time, and alleviates myocardial ischemic injury. The combination of the two interventions can more significantly reduce the levels of myocardial injury markers such as CK-MB, BNP and cTnI.

In conclusion, ultrasound-guided fluid resuscitation combined with esmolol can optimize the balance between oxygen supply and oxygen consumption, stabilize hemodynamics, inhibit inflammatory response, and protect the metabolic function of the myocardium and tissue organs, thereby improving the therapeutic effect on septic shock. However, this study still has certain limitations: restricted by factors such as inclusion and exclusion criteria and research funding, the sample size of enrolled patients is limited and all subjects are from the same region. In the future, we will expand the sample size and geographical coverage, and carry out multicenter, large-sample studies to further verify the conclusions.

Conflict of interest None

Reference

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· 脓毒症专题·论著·

超声引导下液体复苏联合艾司洛尔治疗脓毒症休克

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摘要: **目的** 探讨超声引导下液体复苏联合艾司洛尔对脓毒症休克患者氧代谢指标及炎症水平的影响。**方法** 选取河北工程大学附属医院于2021年6月至2023年6月收治的122例脓毒症休克患者为研究对象,采用随机数字表法分为对照组和治疗组,各61例。所有患者均接受补液抗休克、应用血管活性药物、抗感染、免疫调节、器官功能支持等常规救治。对照组给予超声引导下液体复苏治疗,治疗组在对照组基础上联合艾司洛尔治疗。比较两组氧代谢指标[氧耗(VO_2)、氧输送(DO_2)]、炎症因子[白细胞介素-6(IL-6)、C-反应蛋白(CRP)]、6 h乳酸清除率、治疗期间病死率、血流动力学指标[平均动脉压(MAP)、中心静脉压(CVP)]及心肌相关指标[肌酸激酶同工酶MB(CK-MB)、脑利钠肽(BNP)、心肌肌钙蛋白I(cTnI)]。**结果** 治疗后,两组IL-6、CRP、CK-MB、BNP、cTnI水平均降低,且治疗组低于对照组($P<0.05$);两组 VO_2 、 DO_2 、MAP、CVP水平均升高,且治疗组高于对照组($P<0.05$)。治疗组6 h乳酸清除率高于对照组[(86.21±9.35)% vs (81.52±8.69)%], $t=2.870$, $P=0.005$], 两组治疗期间病死率比较差异无统计学意义($P>0.05$)。**结论** 超声引导下液体复苏联合艾司洛尔可有效优化脓毒症休克患者氧供氧耗平衡,提升组织氧输送能力,稳定血流动力学,同时抑制炎症因子释放,减轻全身炎症反应,改善心肌功能,具有临床应用价值。

关键词: 艾司洛尔; 超声引导; 液体复苏; 脓毒症休克; 氧代谢; 炎症; 血流动力学

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Ultrasound-guided fluid resuscitation combined with esmolol in the treatment of septic shock

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Abstract: Objective To investigate the effect of ultrasound-guided fluid resuscitation combined with esmolol on oxygen metabolism indicators and inflammatory levels in patients with septic shock. **Methods** A total of 122 patients with septic shock admitted to Affiliated Hospital of Hebei University of Engineering from June 2021 to June 2023 were selected and randomly divided into a control group and a treatment group, with 61 cases in each group. All patients received conventional treatments including fluid resuscitation for anti-shock, application of vasoactive drugs, anti-infection, immune regulation, and organ function support. The control group was treated with ultrasound-guided fluid resuscitation, while the treatment group was additionally treated with esmolol based on the control group. Oxygen metabolism indicators [oxygen consumption (VO_2), oxygen delivery (DO_2)], inflammatory factors [interleukin-6 (IL-6), C-reactive protein (CRP)], 6-hour lactate clearance rate, mortality rate during treatment, hemodynamic indicators [mean arterial pressure (MAP), central venous pressure (CVP)], and myocardial related indicators [creatinine kinase-MB (CK-MB), brain natriuretic peptide (BNP), cardiac troponin I (cTnI)] were compared between the two groups. **Results** After treatment, the levels of IL-6, CRP, CK-MB, BNP, and cTnI decreased in both groups, and those in the

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treatment group were significantly lower than those in the control group ($P<0.05$). The levels of VO_2 , DO_2 , MAP, and CVP increased in both groups, and those in the treatment group were significantly higher than those in the control group ($P<0.05$). The 6-hour lactate clearance rate in the treatment group was significantly higher than that in the control group [(86.21±9.35)% vs (81.52±8.69)%, $t=2.870$, $P=0.005$]. There was no significant difference in mortality rate during treatment between the two groups ($P>0.05$). **Conclusion** Ultrasound-guided fluid resuscitation combined with esmolol can effectively improve oxygen supply-consumption balance, enhance tissue oxygen delivery capacity, stabilize hemodynamics, inhibit the release of inflammatory factors, reduce systemic inflammatory response, and improve myocardial function in patients with septic shock, which has clinical application value.

Keywords: Esmolol; Ultrasound guidance; Fluid resuscitation; Septic shock; Oxygen metabolism; Inflammation; Hemodynamics

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脓毒症休克是机体对感染产生的失控性应答,引发循环功能障碍、细胞代谢紊乱的危重临床综合征,可诱发多器官功能障碍,同时伴随顽固性低血压与组织灌注不足,严重威胁患者生命安全^[1]。据报道,全球每年脓毒症发病人数超过1 900万,其中死亡病例达600万^[2]。临床予以补液抗休克,应用血管活性药物及抗生素等治疗,虽可缓解其症状,但整体疗效有限,预后欠佳^[3]。超声技术凭借实时动态监测的独特优势,能够密切追踪患者血流动力学状态,全面评估心脏泵血功能、血管弹性、血流速度及全身各组织灌注情况,在超声精准引导下实施液体复苏,可根据患者独特生理特征和即时血流动力学变化及时调整补液方案,有效避免传统经验性补液可能带来的风险,确保治疗的精准性和安全性^[4]。艾司洛尔可改善微循环障碍,有效提升组织器官灌注量,确保组织细胞获得充足血液供应,从而恢复正常生理功能,还能有效缓解微血管痉挛,保持微血管网络通畅,为血液和组织间物质交换提供顺畅通道,进一步优化微循环状态^[5]。本研究分析超声引导下液体复苏联合艾司洛尔对脓毒症休克患者氧代谢指标、炎症水平的影响,现报道如下。

1 资料与方法

1.1 样本量计算 根据公式 $n = \frac{\pi_1(100 - \pi_1) + \pi_2(100 - \pi_2)}{(\pi_2 - \pi_1)^2}$

$f(\alpha, \beta)$ 估算所需最小样本量, π_1 表示对照组预期疗效总有效率(60.66%), π_2 表示治疗组预期临床疗效总有效率(81.97%), α 表示 I 类错误概率(本研究中取0.05), β 表示 II 类错误概率(本研究中取0.20)。根据公式计算,每组至少需要53例,考虑到失访,每组纳入患者61例。

1.2 一般资料 选取河北工程大学附属医院2021年6月至2023年6月收治的122例脓毒症休克患者

为研究对象。纳入标准:(1)符合脓毒症休克诊断标准^[6];(2)年龄18~60岁;(3)有明确感染灶或高度怀疑的感染灶;(4)患者家属对研究目的知情,且签署同意书。排除标准:(1)合并严重创伤或烧伤;(2)对本研究药物过敏;(3)合并心脏瓣膜病或肝肾功能障碍;(4)患者智力障碍、痴呆、罹患精神疾病;(5)合并恶性肿瘤或免疫系统疾病;(6)妊娠或哺乳期妇女。脱落标准:入院后24 h内死亡或生命体征无法维持者。

1.3 分组 采用随机数字表法将122例患者分为对照组和治疗组,各61例。对照组年龄(47.33±5.13)岁,身体质量指数(body mass index, BMI)(22.30±2.43) kg/m²,男37例,女24例;治疗组年龄(48.03±5.21)岁, BMI(22.67±2.49) kg/m²,男33例,女28例。两组年龄、BMI、性别等一般资料比较差异无统计学意义($P>0.05$),本研究已通过河北工程大学附属医院伦理委员会审查[伦理审批号:2021(K)025]。

1.4 治疗方法 所有患者均接受补液、抗休克、应用血管活性药物、抗感染、免疫调节、器官功能支持等常规救治,同时完善生命体征、病情监测与评估。

对照组超声引导下液体复苏过程如下。准备阶段:患者平卧位,暴露剑突下皮肤,选择相控阵探头超声机(型号:迈瑞 ME7,厂家:深圳迈瑞生物医疗电子股份有限公司);下腔静脉(inferior vena cava, IVC)测量:采用M型超声在下腔静脉距右房开口处约2 cm的平直段测量呼气相和吸气相IVC直径,计算塌陷率;心脏超声评估:经胸超声行心尖四腔心及胸骨旁左室长轴切面,评估心脏收缩功能、心腔大小,测量左心室舒张末期内径(left ventricular end-diastolic diameter, LVEDD),计算心输出量(cardiac output, CO);肺部超声监测:采用BLUE方案对双侧前胸、侧胸及背部进行标准化扫查,记录各区域B线数量及分布特征,弥漫性双侧B线提示肺水肿风险,建议动态监测以指导液体管理;液体复苏实施:初始液体复苏

以10~15 mL(kg·h)起始,然后根据IVC每15~30 min调整速度,具体计量根据患者临床背景进行个性化调整,并动态评估液体反应性。动态调整:每0.5~1 h复查超声及临床指标,若IVC直径>2 cm或B线增多,减慢补液;自主呼吸患者若IVC呼吸末内径<1.5 cm或塌陷率>50%,提示容量反应性良好,可加快补液;若IVC呼气末内径>2.5 cm且塌陷率<20%,提示容量超负荷,应限制补液。小剂量补液试验:当超声提示容量反应性不明确时,1~2 min内快速输注50~100 mL,输注后5 min内复测SV或CO,若增加≥10%~15%则为有反应,可继续补液;若无反应则限制液体。综合检测:持续监测患者生命体征、尿量、血乳酸等指标,直至休克逆转,确保液体复苏效果。

治疗组除上述治疗步骤外,还增加静脉滴注艾司洛尔(齐鲁制药,国药准字H19991059,10 mL:0.1 g)治疗,艾司洛尔初始剂量通常为7.5 μg/(kg·min),根据患者反应逐渐调整剂量;在治疗过程中,密切监测患者心率变化,使心率维持在60~100次/min。

1.5 观察指标 于治疗前、治疗后观察并记录以下指标。主要指标:(1) 氧代谢指标^[7],通过呼吸测量法检测氧耗(oxygen consumption, VO₂)和氧输送(oxygen delivery, DO₂);(2) 炎症因子^[8],应用酶联免疫吸附(enzyme-linked immunosorbent assay, ELISA)法检测白细胞介素-6(interleukin-6, IL-6)、C-反应蛋白(C-reactive protein, CRP)水平;(3) 6 h乳酸清除率^[9],通过血气分析仪检测6 h乳酸清除率,6 h乳酸清除率=[(初始乳酸浓度-6 h乳酸浓度)/初始乳酸浓度]×100%;(4) 病死率,统计治疗期间病死人数在总人数中的占比。

次要指标:(1) 血流动力学指标^[10],应用自动血压计检测平均动脉压(mean arterial pressure, MAP),通过中心静脉压测定技术检测中心静脉压(central venous pressure, CVP);(2) 心肌相关指标^[11],通过ELISA法检测肌酸激酶同工酶MB(creatin kinase MB, CK-MB)、脑利尿钠肽(brain natriuretic peptide, BNP)、心肌肌钙蛋白I(cardiac troponin I, cTnI)。

1.6 统计学方法 采用SPSS 25.0软件分析数据。计数资料以例(%)表示,组间比较采用χ²检验;计量资料符合正态分布,以 $\bar{x} \pm s$ 表示,组间比较采用独立样本t检验,组内比较采用配对样本t检验。P<0.05为差异有统计学意义。

2 结果

2.1 氧代谢指标比较 治疗后,对照组和治疗组VO₂、

DO₂均升高,且治疗组高于对照组,差异有统计学意义(P<0.05)。见表1。

2.2 炎症因子水平比较 治疗后,对照组和治疗组IL-6和CRP均降低,且治疗组低于对照组,差异有统计学意义(P<0.05)。见表2。

2.3 6 h乳酸清除率及病死率比较 治疗后,治疗组6 h乳酸清除率高于对照组(P<0.05);两组治疗期间病死率比较差异无统计学意义(P>0.05)。见表3。

表1 两组治疗前后氧代谢指标比较
[n=61, mL/(min·m²), $\bar{x} \pm s$]

Tab.1 Comparison of oxygen metabolism indicators before and after treatment between two groups
[n=61, mL/(min·m²), $\bar{x} \pm s$]

组别	DO ₂		VO ₂	
	治疗前	治疗后	治疗前	治疗后
治疗组	531.24±55.36	814.35±85.37*	196.38±20.15	265.78±29.68*
对照组	534.84±56.12	758.24±80.18*	198.65±20.98	231.27±25.41*
t值	0.357	3.742	0.609	6.898
P值	0.722	<0.001	0.543	<0.001

注:与同组治疗前比较,*P<0.05。

表2 两组治疗前后炎症因子水平比较 (n=61, $\bar{x} \pm s$)

Tab.2 Comparison of inflammatory factors levels before and after treatment between two groups (n=61, $\bar{x} \pm s$)

组别	IL-6(pg/mL)		CRP(mg/L)	
	治疗前	治疗后	治疗前	治疗后
治疗组	112.56±14.51	43.26±5.67*	89.68±10.34	30.28±4.35*
对照组	109.98±13.84	59.69±6.84*	87.61±9.84	43.15±5.68*
t值	1.005	14.443	1.133	14.050
P值	0.317	<0.001	0.260	<0.001

注:与同组治疗前比较,*P<0.05。

表3 两组患者治疗前后6 h乳酸清除率及治疗期间病死率比较 (n=61)

Tab.3 Comparison of 6-hour lactate clearance rate and in-treatment mortality before and after treatment between two groups (n=61)

组别	6 h乳酸清除率(% , $\bar{x} \pm s$)	治疗期间病死率(%)
治疗组	86.21±9.35	8.20
对照组	81.52±8.69	14.75
t/χ ² 值	2.870	1.291
P值	0.005	0.256

表4 两组患者治疗前后血流动力学比较 (n=61, $\bar{x} \pm s$)

Tab.4 Comparison of hemodynamic parameters before and after treatment between two groups (n=61, $\bar{x} \pm s$)

组别	MAP(mmHg)		CVP(cmH ₂ O)	
	治疗前	治疗后	治疗前	治疗后
治疗组	64.59±7.22	98.68±10.27*	5.21±0.85	10.24±1.63*
对照组	65.41±7.68	92.15±9.62*	5.36±0.91	8.16±1.13*
t值	0.608	3.624	0.941	8.191
P值	0.545	<0.001	0.349	<0.001

注:与同组治疗前比较,*P<0.05。

2.4 血流动力学比较 治疗后,对照组的MAP和CVP均升高,且治疗组高于对照组($P<0.05$)。见表4。

2.5 两组患者心肌相关指标比较 治疗后,对照组的CK-MB、BNP、cTnI降低,且治疗组低于对照组($P<0.05$)。见表5。

表5 两组患者治疗前后心肌相关指标比较 ($n=61, \bar{x}\pm s$)
Tab.5 Comparison of myocardial related indicators before and after treatment between two groups ($n=61, \bar{x}\pm s$)

组别	CK-MB(ng/mL)		BNP(pg/mL)		cTnI(ng/L)	
	治疗前	治疗后	治疗前	治疗后	治疗前	治疗后
治疗组	2.12±0.35	1.21±0.23*	172.32±19.25	124.32±13.56*	164.29±18.52	95.64±10.27*
对照组	2.06±0.31	1.49±0.28*	169.58±18.24	152.21±16.38*	162.32±17.54	103.57±11.14*
<i>t</i> 值	1.002	6.035	0.807	10.244	0.603	4.088
<i>P</i> 值	0.318	<0.001	0.421	<0.001	0.548	<0.001

注:与同组治疗前比较,* $P<0.05$ 。

3 讨论

脓毒症休克是机体对严重感染产生过度炎症反应的结果,可引发机体中毒症状,导致心肌功能减退,危及患者生命^[12]。动脉血管舒张可导致血管充盈不足,同时肾脏微血管系统对血管收缩物质的反应性增强,进而引起肾脏血流量及肾小球滤过率下降^[13-14]。重症患者可出现心血管系统功能障碍及心肌抑制,导致大脑、肺、肾、胃肠道等重要器官灌注不足,进而引发昏迷,严重时可能造成多器官功能损害^[15-16]。

研究报道,超声引导液体复苏和艾司洛尔在治疗脓毒症休克中有一定的疗效^[17-18]。超声心动图可全面评估心脏大小、形态及结构特征,精准区分右心室与左心室功能状态,实时监测心脏泵血功能的动态变化,同时评估血管阻力特性与顺应性,有助于优化治疗方案、保障药物治疗的安全性与有效性,并预防液体超负荷的发生^[19]。艾司洛尔可降低心率,有效地减轻心脏负荷并优化心功能,通过调节心肌舒张过程提升心脏顺应性,促进舒张期心室充分充盈;此外,艾司洛尔还可抑制炎症介质释放,减轻组织细胞损伤,促进组织修复与再生^[20]。基于二者的作用特点,本研究旨在探讨超声引导液体复苏联合艾司洛尔在脓毒症休克治疗中的应用价值。

VO_2 和 DO_2 是评估组织代谢状态的重要指标^[21]。 $IL-6$ 水平与脓症患者病情严重程度密切相关,CRP升高幅度与感染程度呈正相关^[22]。本研究显示,治疗后两组 VO_2 、 DO_2 均升高, $IL-6$ 、CRP水平均降低,且治疗组变化更显著,表明联合治疗可有效改善氧代谢指标、减轻患者炎症反应。其机制可能为:超声引导液体复苏可精准评估血流动力学状态,指导液体复苏剂量与速度,保障有效循环血容量;艾司洛尔可降低心率与心肌收缩力,减少心肌氧耗,降低交感过

度兴奋,间接减轻脓毒症/应激下的交感介导的炎症过度激活与组织损伤;二者协同作用,可优化液体复苏并调控炎症反应,进而更显著地降低 $IL-6$ 和CRP水平。6h乳酸清除率是评估脓毒症休克患者复苏效果与预后的重要指标之一^[23]。本研究结果显示,治疗后治疗组6h乳酸清除率高于对照组,两组治疗期间病死率比较差异无统计学意义,表明联合治疗可提高患者6h乳酸清除率。其原因可能为超声引导液体复苏联合艾司洛尔二者协同可优化氧供氧耗平衡,减少乳酸生成,并促进组织脏器代谢清除。MAP监测有助于明确液体复苏目标并评估复苏效果,CVP则是反映右心房压力及机体血容量状态的重要指标,可用于评估脓毒症休克患者的容量状态,指导液体复苏决策^[24-25]。本研究显示,治疗后两组MAP、CVP均升高,且治疗组升高更显著,表明联合治疗可有效改善患者血流动力学状态。脓毒症休克时,全身炎症反应与微循环障碍可导致心肌细胞损伤,进而引起CK-MB水平升高;同时,心脏负荷增加及心肌细胞受损可使BNP水平上升;而cTnI在心肌细胞受损时会释放进入血液,其水平升高通常提示心肌细胞存在严重损伤^[26-27]。本研究结果显示,治疗后两组CK-MB、BNP、cTnI水平均降低,且治疗组低于对照组,表明联合治疗可有效改善患者心肌损伤。其机制体现为超声引导液体复苏与艾司洛尔的协同作用:超声引导液体复苏精准控制容量负荷,降低心室壁张力,减少BNP分泌,同时避免容量过负荷加重心肌损伤;艾司洛尔通过 β_1 阻滞减慢心率、降低心肌收缩力与心肌氧耗,延长冠状动脉舒张灌注时间,减轻心肌缺血损伤,二者协同可更显著地降低CK-MB、BNP及cTnI等心肌损伤标志物水平。

综上所述,超声引导液体复苏联合艾司洛尔可优化氧供氧耗平衡、稳定血流动力学、抑制炎症反

应、保护心肌及组织脏器代谢功能,从而提升脓毒症休克治疗效果。但本研究仍存在一定局限性:受纳入与排除标准、研究经费等因素限制,入组样本量有限且均来自同一地域。后续将扩大样本量及地域范围,开展多中心、大样本研究进一步验证结论。

利益冲突 无

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