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Clinical characteristics and mortality-related risk factors of septic shock in Emergency Intensive Care Unit

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Abstract

Objective: To discuss the clinical characteristics and mortality-related risk factors of septic shock in Emergency Intensive Care Unit (EICU).

Method: The clinical data of 201 patients with septic shock hospitalized in the EICU of our hospital from June 2017 to June 2019 were studied retrospectively. Combined with the summery of the clinical characteristics, univariate analysis and multivariate stepwise Logistic regression analysis were applied to identify risk factors in mortality of septic shock.

Result: In the 201 cases of septic shock patients, there were 121 males (60.2%) and 80 females (39.8%), with the mean age of 57.15 ± 16.54 years old. The mean number of dysfunctional organ was 3.29 ± 1.60. The abdomen was the most common site of infection (45.3%), and cardiovascular disease was the most common underlying one (41.7%). The overall mortality of septic shock was 53.2% (107/201). The mortality of male was higher than that of female (60.4% vs. 42.9%, P<0.05). The multivariate logistic regression analysis showed that the number of dysfunctional organ and intravenous use of sodium bicarbonate were the independent risk factors associated with death. Hemopurification and length of stay were the protective factors.

Conclusion: The mortality of septic shock is extremely high. It may play a key role in decreasing mortality of septic shock by use of early and active rescue, the use of hemopurification and other rescue measures to prevent organ function impairment.

Keywords: septic shock, EICU, clinical characteristic, risk factor.

1. Introduction

Septic shock, as a common critical disease in care emergency department, is a shock caused by sepsis. Its mortality is up to 30% to 70% (Napoli A.M. et al., 2010), and its incidence rate increases by 1.5% every year (Nee P.A., 2006). Septic shock is usually caused by gram-negative bacilli (Hanberger H. et al., 2011), mainly found in acute obstructive suppurative cholangitis, gangrenous cholecystitis, pyelonephritis, acute pancreatitis and some nosocomial infections (Guignant C. et al., 2012), which is mainly manifested with tissue hypoperfusion, namely sustained hypotension state or blood lactate concentration larger than or equal to 4 mmol/L after capacity test. Emergency department is the center for the rescue of emergency critical diseases. Emergency patients usually show the characteristics of acute onset, disease diversification, fast change and a wide variety of pathogenetic conditions. Early diagnosis and treatment of sepsis patients is a key factor in mortality reduction. However, there are few studies on the clinical characteristics and mortality-related risk factors for septic shock patients in EICU. To this end, retrospective summary was conducted on the clinical

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data of 201 patients with septic shock admitted to the EICU of our hospital to analyze its risk factors of death.

2. Materials and Methods

2.1. Subjects

A total of 201 septic shock patients who were admitted to the EICU of our hospital from June 2017 to June 2019 and met the standards were selected. The cases which did not meet the requirements, with unavailable history and incomplete information were not included in this study.

2.2. Clinical diagnosis basis

Basis of septic shock diagnosis: the septic shock diagnostic criteria in the severe sepsis rescue and septic shock treatment guidelines in 2008 (Venkatesh B. & Cohen J., 2011); multiple organ dysfunction syndrome: referring to the diagnostic criteria of Wang et al.: respiratory failure: acute dyspnea, assisted respiration > 24 h, arterial partial pressure of oxygen/fraction of inspired oxygen (PaO2/FiO2) <200; hepatic failure: total bilirubin (Tbil) >34.2 μmol/L, alanine aminotransferase (ALT) twice greater than the normal level; renal failure: serum creatinine (Scr) >176.8 μmol/L; central function failure: Glasgow score <6 points; blood coagulation failure: platelet < 5×104/μl, prothrombin time > 15 s, fibrin <2 g/L and fibrin degradation products >20 μg/ml (Wang C. et al., 2009).

2.3. Survey contents

The clinical data of 201 patients with septic shock were studied with retrospective analysis, listed as follows: general items: gender, age, etiology, hospitalization time; past history: trauma history, surgical history, dysimmunity (malignant tumor, radiotherapy, chemotherapy history), chronic disease, bad habit (smoking, drinking), etc.; current disease history: onset time, incentive, symptom, state of consciousness, site of infection, complications, time and number of occurring organ failure; treatment: antibiotic, vasoactive agent, glucocorticoid, anticoagulation, fluid resuscitation, blood transfusion/blood product, blood purification, sodium bicarbonate, invasive diagnosis and treatment (central venous catheter, endotracheal intubation, tracheotomy, invasive mechanical ventilation, blood purification therapy, floating catheterization), etc.; main biochemical indicators: biochemical parameters at the time of admission and incidence of shock (albumin, total protein, bilirubin, transaminase, blood gas analysis, serum creatinine, platelet, prothrombin time, etc.); prognosis: improvement includes discharge or department transfer after condition is stable, and mortality contains hospital death and self-determined discharge for irreversible organ failure.

2.4. Statistical analysis

All data were analyzed by SPSS 18.0. Measurement data were subjected to normality analysis. The normal distribution data were expressed as mean ± standard deviation, and the abnormal distribution data were expressed as median and quartet median spacing. Numeration data were subjected to the $\chi 2$ test. The factors with $P<0.05$ were subjected to non-conditional Logistic regression. $P<0.05$ was considered statistically significant.

3. Results

3.1 Basic clinical characteristics of septic shock patients

The basic clinical characteristics of septic shock patients are summarized in Table 1.

Risk factors associated with septic shock death

3.2 Univariate analysis

16 factors in total were considered in the analysis. The differences were statistically significant ($P <0.05$) between the septic shock survival and death groups in terms of ten factors, namely gender, total hospitalization time, EICU stay time, underlying disease, number of dysfunctional organ, deep venous catheterization, blood purification, mechanical ventilation, sodium bicarbonate and use of blood product, $P <0.01$ in the following six factors: EICU stay time, number of dysfunctional organ, deep venous catheterization, mechanical ventilation, sodium bicarbonate and use of blood product (Table 2).

3.3 Multivariate stepwise Logistic regression analysis

Multivariate stepwise Logistic regression analysis was conducted on the ten factors which were screened by the above univariate analysis and significantly correlative with septic shock prognosis (for-ward LR method, $\alpha in = 0.10$, $\alpha out = 0.15$) to obtain the regression equation (Table 3).

Table 1: **Basic clinical characteristics of septic shock patients**

Item	Case No. [n (%)]	Mortality rate (%)
	Gender	
male	121(60.2)	60.3
female	80(39.8)	42.5
	Organ function failure	
respiratory system	84(41.8)	76.2
cardiovascular system	198(98.5)	48.5
kidney	76(37.8)	61.8
blood system	112(55.7)	52.7
central nervous system	48(23.9)	83.3
liver	118(58.7)	65.3
	Infection position	
respiratory tract	52(25.9)	53.8
urinary tract	26(12.9)	15.4
abdomen	91(45.3)	50.5
limb	17(8.5)	76.5
bacteremia	28(13.9)	50.0
multiple infections	31(15.4)	54.8
undefined	24(11.9)	87.5
	Underlying disease	
respiratory system	19(12.2)	47.4
cardiovascular system	65(41.7)	60.0
digestive system	15(9.6)	80.0
urinary system	15(9.6)	33.3
blood system	8(5.13)	75.0
endocrine system	43(27.6)	53.5
autoimmunity system	6(3.8)	50.0
hepatic disease	22(14.1)	81.8
malignant tumor	10(6.4)	50.0
mental disease	6(3.8)	50.0

Table 2: **Univariate analysis of risk factors associated with septic shock death**

Item		Survival	Death	*P*
Case No.		94	107	0.000
Age (years old)		56.68±16.81	57.99±15.87	0.375
Gender	male	48	73	0.029
	female	46	34	
Total inpatient time (day)		19.15±19.18	5.24±7.89	0.000
EICU stay time (day)		5.63±11.78	3.72±4.41	0.039
Underlying disease	yes	65	91	0.019
	no	29	16	
Organ failure No.		2.56±1.30	4.08±1.41	0.000
Deep venous catheterization	yes	45	81	0.000
	no	49	26	
Tracheotomy	yes	1	3	0.549
	no	93	104	
Blood purification	yes	17	6	0.019
	no	77	101	
Mechanical ventilation	yes	20	58	0.000
	no	74	49	
Surgical history	yes	12	25	0.065
	no	82	82	
Hormone	yes	50	67	0.221
	no	44	40	
Acidosis	yes	60	62	0.452
	no	34	45	
Sodium bicarbonate	yes	14	53	0.000
	no	80	54	
Blood product	yes	55	84	0.005
	no	39	23	
Albumin		31.4±2.72	28.4±4.16	0.481

Table 3: **Multivariate stepwise Logistic regression analysis of risk factors associated with septic shock death**

Risk factor	Regression coefficient	Standard error	*Wald*	*P*	*OR*	95%CI
Sodium bicarbonate	2.329	0.679	11.679	0.001	10.281	2.696~39.104
Organ failure	1.296	0.413	9.714	0.002	3.648	1.618~8.243
Blood purification	-2.519	0.887	8.038	0.005	0.079	0.014~0.461
Total inpatient time	-4.236	0.665	40.543	0.000	0.035	0.004~0.054
Constant	1.980	1.103	3.219	0.072	7.229	

4. Discussion

The study results showed that the mortality of septic shock patients was 53.2% (107/201), male higher than female; abdomen was the most common site of infection, followed by lung; in the patients with septic shock, except the failure of cardiovascular system, liver was the most common dysfunctional organ, and blood system the most common dysfunctional system, however, the failure of the central nervous system had the highest mortality rate. 77.6% (156 cases) of the patients suffered with underlying diseases, the most common of which were cardiovascular diseases, hypertension mainly. The results of Logistic regression suggested that the use of sodium bicarbonate and the number of dysfunctional organs were the risk factors in septic shock mortality, and blood purification and hospitalization time were protective factors.

A domestic retrospective survey studied 143 cases of septic shock patients from 1991 to 2001, and its statistical results showed that the total mortality rate of the patients was 69.2% (99/143) , which was 53.2% (107/201) in this study, similar to the SOAP results (Sakr Y. et al., 2006) (54.1%); the data was lower than 61.2% of mortality rate reported by Kobayashi, et al. The reasons for these differences may be relative with the adoption of different septic shock diagnostic criteria, patient compositions, underlying diseases, types of infection, numbers of dysfunctional organ, treatment programs and other factors (Herzum I. & Renz H. et al., 2008). Many studies have indicated that the respiratory tract is the most common source of infection in septic shock, while in this study, the most common source of infection was abdomen (45.3%), followed by respiratory tract (25.9%), the reason of which might be related with the different sources of patients; there were 164 patients found shock during the emergency medical treatment in this study, who were sent to EICU for rescue immediately after vital signs were stable; only 37 patients were transferred department; intestinal infection accounted for 70.33% (64/91) in abdominal infections. Intestine is the largest bacteria and endotoxin reservoir in the human body. In case of shock, systemic inflammatory response syndrome can be caused due to intestinal mucosal ischemia, hypoxia, microcirculation disturbance, intestinal apoptosis, DNA fragmentation and the production of a variety of cytokines (Kannan K.B. et al., 2011); at the same time, both the endotoxemia caused by the increase of intestinal permeability (Sharma M. et al., 2012) and the final occurrence of intestinal bacteria translocation play an indispensable role in sepsis and MODS (Schietroma M. et al., 2006). In this study, the fatality rate of urinary tract infection was relatively low (15.4%), while the fatality rate of unknown site infection was the highest (87.5%). The difference in mortality rate was statistically significant (15.4% vs. 87.5%, P = 0.001), which was similar to the result reported in literatures (Van Dyck E. et al., 2011). This suggested that prognosis could be roughly judged through understanding infection sites during the admission of patients with septic shock.

In this study, 77.6% of the septic shock patients suffered from underlying diseases, and the mortality rate of the patients with diseases in blood, digestive, endocrine and cardiovascular systems and the patients with chronic liver disease were higher than the total mortality rate (53.2%), in which that of the chronic liver patients was the highest; the mortality rate of septic shock patients with autoimmune, urinary, respiratory, mental diseases or malignant tumors was less than 53.2%, in which that of the patients with urinary system disease was the lowest. The mortality rate of the patients with underlying diseases (De Kock I. et al., 2010) was higher than those without the diseases (58.3% vs. 35.5%, P = 0.019). The septic shock patients with cardiovascular and endocrine system diseases accounted for 69.2% of those with underlying diseases (108/201), with the fatality rate of 57.4%; hypertension and diabetes are the most common. If septic shock occurs on a patient with long-term poor control in blood pressure, large fluctuations of blood pressure will lead to insufficient blood supply to the heart, brain and kidney or dysfunction, so as to aggravate the patient's condition and increase mortality; diabetic patients are prone to secondary infection, which may aggravate infection due to more difficult glycemic control in emergency, so that rescue difficulty will be increased (Levine A.B. et al., 2012). Liver, as the most important organ for synthesis and metabolism in the body, has the functions of immunization, coagulation, detoxification, metabolism, bile production and excretion. The immunity of patients with cirrhosis and other chronic liver diseases is lower than that of normal persons, showing a high incidence of secondary infections. In the event of septic shock, its prognosis is often poor; at the same time, such patients usually have hypofunctional liver reserves, so in case of shock, the live is in a state of ischemia and hypoxia, hepatic function is prone to deterioration so as to emerge hepatic failure, as well as many complications rapidly, such as hepatic encephalopathy, hepatopulmonary syndrome and hepatorenal syndrome, etc. (MODSBenard G. et al., 2012). The mortality of septic shock with the blood system underlying disease was up to 75.0%. Studies have reported that PT abnormality and PLT reduction indicate a critically pathogenetic condition (Irmak K. et al., 2006).

For circulatory failure, septic shock patients are usually conducted with fluid supplement through the deep venous catheterization, the use of vasopressor drugs, and monitoring the hemodynamic status to guide clinical treatment; univariate analysis showed that the mortality rate of patients receiving deep venous catheterization was significantly increased; literatures have reported that deep venous catheterization may increase the risk of kidney failure, and is also an independent risk factor in death of patients with septic shock (Buiter H.J. et al., 2008). The data of this study suggested that respiratory failure

accounted for 41.8% (84/201) in septic shock patients, and mechanical ventilation was an important method for rescuing shock patients with respiratory failure. The univariate analysis showed that the mortality of mechanically ventilated patients increased. Previous studies have stated that mechanical ventilation is an independent risk factor of death in patients with septic shock (White A.C. et al., 2009). Therefore, prognosis can be judged through observing whether septic shock patients are treated with deep venous catheterization and mechanical ventilation or not, and at the same time, it also suggests that it is necessary to pay close attention that deep venous catheterization may be complicated by thrombosis, hemopneumothorax, infection, etc., and mechanical ventilation may bring pressure injury, nosocomial infection, increased circulation disorder and other complications. In case of septic shock, the decrease in effective circulating blood volume may lead to tissue and organ hypoperfusion, ischemia and hypoxia, increased anaerobic metabolism and lactic acid accumulation which may cause metabolic acidosis. The data showed that 122 cases in the 201 cases of septic shock patients (60.7%) were complicated with metabolic acidosis, in which 67 cases were given 5% sodium bicarbonate solution with the dose of 192.78 ± 58. 09ml, resulting in 53 cases of death. The pH value was measured before the use and a half hour after the use of 5% sodium bicarbonate solution respectively, which increased from 7.19 ± 0.18 to 7.31 ± 0.31. The study found that in the critically ill patients with lactic acidosis, the use of sodium bicarbonate could not improve cardiac output, blood pressure, and other hemodynamic indicators, nor improve the activity of the cardiovascular system on catecholamine drugs. On the contrary, it may reduce the plasma-free calcium concentration, weaken the cardiac excitability - contraction coupling, and can also increase intracellular acidosis. The data showed that the use of sodium bicarbonate was correlative with fatality, so its clinical use should be strictly controlled. The guidelines are recommended as follows: the septic shock patients with lactic acidosis (pH $\geqslant$ 7.15) caused by hypoperfusion are not recommended to use sodium bicarbonate to achieve the purpose of improving hemodynamics or reducing dose of vasoactive agents (Boyd JH. & Walley KR., 2008).

This study found that the number of dysfunctional organ was the mortality-related risk factor in septic shock, which was consistent with the literature (Klein Klouwenberg PM. et al., 2012). In the 201 cases of septic shock patients, the mortality rate of patients with circulatory failure alone was 33.3% (3/9), however, the mortality in the patients associated with one, two or three dysfunctional organs were 36.8% (14/38), 46.2% (30/65) and up to 69.7% (62/89) respectively. It suggests that once patients with septic shock are complicated with organ dysfunction, the risk of death may be significantly increased. Thus, focusing on the protection of vital organ functions and actively controlling the primary disease and infection at the same time are conducive to the improvement of the survival rate of patients with septic shock (Oliveira NS. et al., 2008).

In this study, all blood purifications adopted continuous venous-venous hemofiltration (CVVH) (Piazza O. et al., 2012). There were 23 patients in total receiving CVVH, in which 17 cases were cured, 6 died. Regression analysis showed that blood purification was the protection factor in death of patients with septic shock, OR = 0.079. By the mechanism of filtration and adsorption generated by dispersion or convection, CVVH can eliminate a variety of inflammatory mediators causing organ dysfunction in septic shock, such as interleukin (IL)-1, IL-6, IL-8, tumor necrosis factor (TNF), etc., and it can also remove nitrogen metabolites and toxins accumulated in the body due to acute renal injury, correct metabolic acidosis, improve and stabilize internal environment, and have less impact on hemodynamics; there are also studies showing that CVVH has an immunomodulatory function for patients with septic shock (de Pablo R. et al., 2011). Septic shock features acute onset, rapid progression and high mortality (Frank A.J. et al., 2012). The results of this study showed that the mortality rate was 87.0% (87/100) for the patients with hospitalization time $\leqslant$1 week; 73.1% (98/134) for those with 2-week hospital stay; 58. 0% (101/174) for those with hospital stay $\leqslant$3 week, which indicated that the first week of hospitalization was the peak period for death of septic shock patients. Logistic regression showed that the OR value of hospitalization time was 0.035, suggesting that the mortality rate was lower in patients with long hospital stay than those with short one. Therefore, septic shock patients should be rescued actively and monitored closely in their early hospitalization for the prevention and treatment of organ failure, so as to reach the goal of mortality rate reduction.

In short, this study indicated that septic shock was a high mortality disease in EICU. The use of sodium bicarbonate and the number of dysfunctional organ were mortality-related risk factors for septic shock patients, and hemopurification and length of stay were

the protective factors (Kollef M. et al., 2012). If patients with septic shock are treated with sodium bicarbonate and complicated with multiple organ failure, they should be given close surveillance, and actively applied with blood purification and many other treatment and cure methods in the early shock period, to prevent the occurrence of organ failure, in order to improve the survival rate.

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