ORIGINAL ARTICLE

Resuscitation of Septic Patients with Target-and-endpoint Protocol: A Retrospective Study from a Chinese Tertiary Hospital ICU

Hongmin Zhang, Xiaoting Wang, Qing Zhang, Dawei Liu*

Department of Critical Care Medicine, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100730, China

Key words: sepsis; septic shock; lactate; central venous pressure

Objective To investigate the effect of target-and-endpoint protocol on the resuscitation of septic patients.

Methods This is a retrospective study performed at the Peking Union Medical College Hospital Intensive Care Unit. We enrolled 545 septic patients who needed vasopressors on at least the first day of ICU admission. The general characteristics, blood lactate level, mean arterial pressure (MAP), central venous pressure (CVP) and saturation of central venous oxygen (ScvO₂) at admission and 6, 24 hours after admission were collected. The parameters at different time points were compared. Lactate clearance rate and in-hospital mortality were analyzed.

Results The 6-hour lactate clearance rate was 21.6% (IQR, 8.6%-39.0%), and in-hospital mortality was 9.4%. For patients with low CVP values (<8 mm Hg, 1 mm Hg=0.133 kPa) at admission, CVP increased significantly at 6 hours after admission (5.4 ± 1.6 mm Hg vs. 7.7 ± 2.6 mm Hg, $P<0.001$). For patients with low MAP (<75 mm Hg) at admission, the MAP values increased significantly at 6 hours (64.2 ± 7.1 mm Hg vs. 82.2 ± 13.1 mm Hg, $P<0.001$). For patients with low ScvO₂ value (<70%) at admission, the ScvO₂ value increased significantly at 6 hours ($61.9\%\pm7.0\%$ vs. $71.9\%\pm7.8\%$, $P<0.001$). No difference was found between the values at 6 hours and the corresponding values at 24 hours after admission. For patients with high CVP values (≥ 8 mm Hg) at admission, CVP decreased significantly at 6 hours (11.3 ± 4.0 mm Hg vs. 10.3 ± 2.9 mm Hg, $P<0.001$). For patients with high MAP (≥ 75 mm Hg) at admission, the MAP values decreased significantly at 6 hours (94.2 ± 13.9 mm Hg vs. 89.4 ± 11.4 mm Hg, $P<0.001$). For patients with high ScvO₂ value ($\geq 70\%$) at admission, the ScvO₂ values decreased significantly at 6 hours ($76.8\%\pm4.2\%$ vs. $72.9\%\pm7.3\%$, $P<0.001$). No difference was found between the values at 6 hours and the corresponding values at 24 hours.

Conclusions This study suggested that in the resuscitation of sepsis and septic shock patients in the ICU, the

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*Corresponding author Tel: 86-10-69152300, E-mail: dwliu98@163.com

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target values did not need to be within the “normal range” recommended by early-goal directed therapy. The “target-and-endpoint” protocol, which aimed for personalized goals, deserves more consideration.

SEPSIS and septic shock are major health problems, affecting millions of people around the world each year. It has been demonstrated that increased compliance with the Surviving Sepsis Campaign (SSC) resuscitation bundles is associated with a reduction in mortality rates.¹ However, sepsis and septic shock remain a challenge, with their high morbidity and mortality.²

Early goal-directed therapy (EGDT) has been constantly discussed and questioned by researchers since its publication.³⁻⁴ Several studies have noted that EGDT was not superior to “usual care” in the treatment of early septic shock.⁵⁻⁷ Nonetheless, it remains the cornerstone for the management of sepsis and septic shock patients.⁸ Head and Coopersmith⁹ suggested that although the specific EGDT protocol is not beneficial if applied to all patients with sepsis, key tenets of sepsis management are indicated in all septic patients, and the management of sepsis could evolve from EGDT to personalized care.

We also believe in the tenets of EGDT and developed a novel protocol based on them. We thought the goal should be personalized and, most importantly, should be managed on the basis of timing.¹⁰ The protocol, called “target and endpoint”, has been in development and implementation for up to 5 years in our department and has been strictly applied during daily rounds. However, how it influences the resuscitation of septic patients in the ICU has not been reported. We decided to retrospectively study the septic patients in this department and investigate what effect the target-and-endpoint protocol had on the treatment of these patients.

PATIENTS AND METHODS

Study population

We retrospectively reviewed the electronic medical database to identify septic patients with an acute onset of infection and being administered vasopressors on at least the first day in the ICU of the Peking Union Medical College Hospital. Patients were admitted to the ICU from May 1st, 2014 to May 1st, 2017.

Patients were excluded if they met the following criteria: clinical presentation not consistent with

the diagnosis of sepsis or septic shock, lack of central venous pressure (CVP) monitoring or invasive arterial pressure monitoring, ICU stay length shorter than 24 hours, refusal of active treatment, data missing or a state of sepsis lasting more than 24 hours before being transferred to the ICU. Finally, a total of 545 septic patients were included (Fig. 1).

The diagnosis of sepsis was made based on the new Sepsis-3 definition, which includes a suspected or confirmed infection and an acute change of ≥ 2 points in the patient's total sequential organ failure assessment score (SOFA) as a result of the infection. Septic shock patients were identified by the necessity of vasopressors to maintain a mean arterial pressure of 65 mm Hg (1 mm Hg=0.133 kPa) or greater and a serum lactate level greater than 2 mmol/L in the absence of hypovolemia.¹¹

Patients' data were collected from the hospital's electronic medical database. The data designated as 0-hour data were obtained at the exact time of admission. The data designated as 3-, 6- and 24-hour data were measured at 3, 6 and 24 hours after admission. Acute physiology and chronic health evaluation score II (APACHEII) and SOFA scores were calculated from the worst parameters within the first 24 hours, which were gathered from the electronic records. In-hospital mortality was defined as the proportion of patients who died during the period from ICU admission to discharge from the hospital.

The study was conducted according to the Declaration of Helsinki and was approved by the ethics committee of our institution. No informed consent was needed for this retrospective observational study.

“Target-and-endpoint” protocol

The “target-and-endpoint” protocol for resuscitation of the sepsis and septic shock patients is shown in Fig. 2. If the patient was diagnosed with sepsis or septic shock, the resuscitation protocol was indicated.

The ultimate goal (endpoint) of the treatment was the clearance of lactate, specifically, at least a 10% drop by 6 hours after admission. To accomplish the ultimate goal, we set three targets: mean arterial pressure (MAP), central venous pressure (CVP) and, if necessary, the cardiac output/velocity-time integral

Figure 1. Flow chart of the patient enrollment.

ICU: intensive care unit.

(VTI). A personalized value of each target was selected at 6 hours or even sooner while the patient's condition was monitored. At any given time, a specific value of each target was mandatory for each patient. The lactate level and saturation of central venous oxygen ($ScvO_2$) were to be measured regularly, and the target values were to be assessed and adjusted; most importantly, the actual values of those variables were to be maintained on target if such targets had been set.

If $ScvO_2$ was below 70% and CVP was below 8 mm Hg, volume expansion was recommended. If the CVP was equal or greater than 8 mm Hg, it was left to the doctors' discretion to monitor cardiac output. Volume responsiveness was to be assessed, whether through inferior vena cava (IVC) variability, VTI variability, stroke volume variation (SVV), pulse pressure variation (PPV), passive leg raising (PLR) or fluid challenge. If volume responsiveness was positive, fluid was to be administered. Otherwise, it was left to the doctors' discretion to decide whether to prescribe inotrope or take measures to decrease the oxygen consumption. Then norepinephrine would be given to maintain the MAP level according to the baseline blood pressure of each specific patient.

If $ScvO_2$ was above 70%, then the MAP goal was set and maintained. If the goal of CVP, MAP and cardiac output (if necessary) was reached, and lactate clearance still deteriorated, it was deemed acceptable

Figure 2. The "target-and-endpoint" protocol for resuscitation of the sepsis and septic shock patients.

▲Lactate level and lactate clearance rate were set as the "endpoint" parameter.

*CVP, MAP and CO/VTI were set as the "target" parameter. MAP: mean arterial pressure; $ScvO_2$: saturation of central venous oxygen; CVP: central venous pressure; NE: norepinephrine; CO: cardiac output; VTI: velocity-time-integral; SVV: stroke volume variation; IVC: inferior vena cava; PLR: passive leg raising; $\downarrow VO_2$: decreased oxygen consumption.

to tamper MAP level and turn again to source control and antibiotic adjustment. If the lactate clearance goal was reached, the clinicians need to assess whether the CVP could be lowered any further and whether the MAP or cardiac output/VTI needed to be adjusted.

If the patient was diagnosed with sepsis but the lactate level was below 2 mmol/L, but the $ScvO_2$ less than 60%, then there would be a high risk to develop hyperlactatemia, the resuscitation would still be proceeded. If the $ScvO_2$ was greater than 60%, then the clinicians need to assess whether the CVP could be lowered any further and whether the MAP or cardiac output/VTI needed to be adjusted.

Statistical analysis

Statistical analysis was performed using the statistical software package SPSS 13.0 (SPSS Inc., Chicago,

Illinois, USA). Continuous data were expressed as the mean $\pm$ standard deviation or as the median and the interquartile range (IQR). Categorical variables were presented as the number and percentage in each category. At admission patients were divided into the low-CVP group (CVP < 8 mm Hg) and the high-CVP group (CVP $\geq$ 8 mm Hg) according to CVP level, the low-MAP group (MAP < 75 mm Hg) and the high-MAP group (MAP $\geq$ 75 mm Hg) according to MAP level, and the low-ScvO₂ group (ScvO₂ < 70%) and the high-ScvO₂ group (ScvO₂ $\geq$ 70%) according to ScvO₂ level. Group comparisons of SOFA and APACHE II scores, lactate level and in-hospital mortality were performed by Student's *t*-test, Man-Whitney *U* test or the chi-squared test when appropriate. The variance analysis of repeated measurement data was used to compare the differences of each index within the groups and then least significant difference test was used to compare the difference between two groups. All *P* values were two tailed and were considered significant for *P* < 0.05.

RESULTS

General characteristics of all patients

Their mean age of the enrolled subjects was 60.6 $\pm$ 16.9 years old, and 59.2% (323/545) were men. The median APACHE II and SOFA scores were 22 (IQR, 17-29) and 11 (IQR, 9-14), respectively. The median maximum body temperature was 38°C. The median white blood cell count was 12.4 $\times 10^9$ /L (IQR, 7.6 $\times 10^9$ -18.3 $\times 10^9$ /L), and the median procalcitonin level was 4.0 (IQR, 0.9-21.1) ng/ml.

The sources of infection included pneumonia (60.0%), intraabdominal infection (28.6%), bacteremia (7.5%) and other infections (3.9%), such as urinary tract infection, dermal infection, and central nervous system infection etc. The comorbidities included hypertension (31.9%), coronary artery disease (4.6%), diabetes mellitus (7.2%) and chronic renal failure (10.1%).

The proportion of patients on ventilation was 87.2% (475/545). The mean positive end-expiratory pressure and plateau pressure were 7.1 $\pm$ 2.4 cmH₂O and 22.7 $\pm$ 6.3 cmH₂O respectively. The median norepinephrine dose was 0.15 (IQR, 0.10-0.42) μ g/kg·min. The median ICU stay length was 11 (IQR, 5-19) days, and in-hospital mortality was 9.4% (51/545).

Arterial blood lactate level and hemodynamics

The quantities of fluid administered at 3 hours and

24 hours were 965 (IQR, 615-1566) ml and 3207 (IQR, 2495-3950) ml, respectively. Only 19.8% (*n*=108) of patients were administered over 30 ml/kg of fluid at 3 hours. The rate of fluid loading was 250-500 ml/30 min or faster but with close monitoring. Among all the patients, 18.7% had a negative fluid balance during the first 24 hours and the median volume was 1444 (IQR, 489-2775) ml. The patients who were administered dobutamine accounted for 11% of all patients and the median dose was 3 (IQR, 2-5) μ g/kg·min.

The MAP level was much higher than the target in the EGDT protocol, with 89.7% (489/545) having MAP greater than 75 mm Hg at 6 hours. Only 68.8% (375/545) of patients had CVP greater than 8 mm Hg at 6 hours, and 70.6% (385/545) of patients had ScvO₂ greater than 70.0% at 6 hours. Among all the patients, 48.1% (262/545) had a lactate level above 2 mmol/L at admission. The 6-hour lactate clearance rate was 21.6% (IQR, 8.6%-39.0%). The arterial blood lactate level on admission and 6 hours of admission were 1.8 (IQR, 1.2-3.2) mmol/L and 1.6 (IQR, 1.1-2.6) mmol/L, respectively.

Subgroup comparison

The low-CVP group displayed lower SOFA and APACHE II scores than the high-CVP group (all *P* < 0.001). No significant difference was found in lactate level (*P* = 0.110) and in-hospital mortality between the two groups (*P* = 0.627). (Table 1)

In comparison with the high-MAP group, the low-MAP group displayed higher APACHE II scores (*P* = 0.019) and similar SOFA scores (*P* = 0.455). No difference was found on 0-hour lactate level (*P* = 0.111) and in-hospital mortality (*P* = 0.807) between the two groups. (Table 1)

No difference was found between the low-ScvO₂ group and high-ScvO₂ group in terms of SOFA (*P* = 0.614), APACHE II (*P* = 0.227), 0-hour lactate level (*P* = 0.628) and in-hospital mortality (*P* = 0.250). (Table 1)

Target of CVP, MAP and ScvO₂

For patients with CVP below 8 mm Hg at 0 h, the value at 0 h was significantly lower than that at 6 hours and 24 hours (*P* < 0.001). No difference was found between the values at 6 hours and 24 hours (*P* = 0.363). For patients with MAP below 75 mm Hg at 0 h, the value at 0 h was significantly lower than the value at 6 hours and 24 hours (*P* < 0.001). No difference was found be-

Table 1. Comparisons of SOFA and APACHE II scores, 0-hour lactate level and in-hospital mortality between subgroups

Groups	n	SOFA (score)	APACHE II (score)	0-hour lactate level (mmol/L)	In-hospital mortality (%)
Low-CVP group (CVP<8 mm Hg)	187	11	20	1.8	11.3
High-CVP group (CVP≥8 mm Hg)	358	12	23	1.9	9.5
P value		<0.001	<0.001	0.110	0.627
Low-MAP group (MAP<75 mm Hg)	148	11	24	1.7	8.8
High-MAP group (MAP≥75 mm Hg)	397	11	22	1.9	9.5
P value		0.455	0.019	0.111	0.807
Low-ScvO ₂ group (ScvO ₂ <70%)	185	12	23	1.8	11.4
High-ScvO ₂ group (ScvO ₂ ≥70%)	360	11	22	1.9	8.3
P value		0.614	0.227	0.628	0.250

SOFA: sequential organ failure assessment score; APACHE II: acute physiology and chronic health evaluation score II.

tween the values at 6 hours and 24 hours ($P=0.667$). For patients with ScvO₂ below 70% at 0 h, the value at 0 h was significantly lower than that at 6 hours and 24 hours ($P<0.001$). The value at 6 hours was slightly higher than the value at 24 hours, but the difference was not statistically significant ($P=0.063$). (Fig. 3)

For patients with CVP greater than or equal 8 mm Hg at 0 h, the value at 0 h was significantly higher than the value at 6 hours and 24 hours ($P<0.001$). No difference was found between the values at 6 hours and 24 hours ($P=0.452$). For patients with MAP greater than or equal 75 mm Hg at 0 h, the value at 0 h was significantly higher than the value at 6 hours and 24 hours ($P<0.001$). No difference was found between the values at 6 hours and 24 hours ($P=0.295$). For patients with ScvO₂ greater than or equal 70% at 0 h, the value at 0 h was significantly higher than the value at 6 hours and 24 hours ($P<0.001$). No difference was found between the values at 6 hours and 24 hours ($P=0.116$). (Fig. 3)

DISCUSSION

In this study, we found that the "target-and-end-point" protocol was effective, with most patients surviving. However, we did not administer as much fluid as the SSC guideline recommended. We also did not set the target CVP and MAP goals as the EGDT recommended.

The protocol had been established long before this study, and its implementation was discussed during morning and evening rounds, which guaranteed the quality of the protocol. The data were all objective data collected from our electronic database. The database has been existed for 5 years, and several papers based on its data have been published.¹²⁻¹³ The results

Figure 3. Comparisons of CVP (A), MAP (B) and ScvO₂ (C) values before and after resuscitation.

*In comparison with values at 6 hours and 24 hours after admission, the corresponding values at admission were significantly lower or higher ($P<0.001$). No difference was found between the values at 6 hours and the corresponding values at 24 hours.

of this study demonstrated that the patients had rather high APACHE II and SOFA scores comparable to those of patients from prior studies including EGDT, ProCESS, and ARIZE. Nonetheless, the mortality was not as high in the present study.^{5-7, 14}

The participants in this study were sepsis patients undergoing norepinephrine infusion. Previously, the SSC guidelines have defined septic shock as sepsis-induced hypotension persisting despite adequate fluid resuscitation.¹⁵ Hyperlactatemia and fluid-resistant hypotension requiring vasopressors are the prerequisites used to diagnose septic shock according to the new definition of Sepsis-3.¹⁶ Therefore, the study involved both sepsis and septic shock patients according to the new definition.

We chose arterial lactate level as the endpoint in our protocol as hyperlactatemia is a well-accepted marker of illness severity, with higher levels predictive of higher mortality.^{11, 17} The cause of hyperlactatemia might lie in altered microcirculation or disrupted mitochondrial dysfunction; the topic has attracted a great deal of interest, but there is still no adequate treatment method. Garrabou *et al*¹⁸ measured the mitochondrial activity of peripheral blood mononuclear cells in septic shock patients. Their study demonstrated that mitochondrial dysfunction may be responsible for cell damage in sepsis and may correlate with sepsis severity and outcome.

The SSC guidelines and their update clearly state that volume resuscitation should be performed within 3 hours.¹⁹ The notion of early resuscitation is thoroughly understood and widely accepted, and the fluid therapy or even more robust evaluation of volume status would be performed within 3 hours of admission. In our study, we found that only a small fraction of patients admitted to the ICU need more than 30 ml of fluid/kg within the first 3 hours. Because the protocol demanded that volume responsiveness should be evaluated if needed, we conclude that the reason for this is because more patients had been administered fluids in the emergency room, operating room or medical or surgical ward; therefore, they do not need as much volume at this time point. This also demonstrated an advantage of this protocol, namely, the ability to prevent volume overload and its related consequences.²⁰ We fully agree the SSC is very valuable for patients who have not been resuscitated. However, septic shock patients are often resuscitated to some extent before being transferred to ICU. Therefore, the volume status

assessment is crucial.

In this study, we found that the CVP value at 6 hours was much lower than that the EGDT protocol had suggested, meaning that much less fluid had been given, which is another indicator that the risk of volume overload is much lower.¹⁴⁻¹⁵ We found that high CVP at 6 hours did not mean that patients were resuscitated adequately; rather they were more severely ill, with higher APACHE II and SOFA scores and, eventually, higher mortality. Therefore, the CVP for each patient cannot be set at a fixed score; it is more reasonable to set a personalized goal. Prior research has found that increased CVP is associated with impaired renal function and all-cause mortality in a group of patients with cardiovascular diseases.²¹ Vellinga *et al*²² found that elevated CVP was associated with impairment of microcirculatory blood flow. Higher CVP means the impairment of microvascular perfusion through increases in venous pressure by venous congestion.

In our protocol, the CVP level is monitored and tapered to bring it as low as possible as long as tissue perfusion is sufficient. This is another reason the CVP level was kept slightly lower. The CVP is an indicator of the preload of the right heart; lowering it will benefit the function of the right heart, as well as kidney function and it is nevertheless useful when followed over time.²³⁻²⁴ Although we did not have access to the echocardiography results of these patients, the CVP value, which indicates the preload of the right heart, could be a result of cardiac dysfunction induced by septic shock. Septic cardiomyopathy, usually diagnosed through echocardiography, has a high incidence in septic shock patients, and both ventricles can be affected.²⁵⁻²⁶

A previous study noted that MAP combined with hyperlactatemia might be a strong predictor of worse prognosis.²⁷ In the present study, the value of target MAP was slightly higher than that the SSC guidelines recommended. As in a real clinical situation, the setting of a target blood pressure level takes baseline blood pressure, urine output and lactate clearance into consideration. Nearly a third of our patients had hypertension. Asfar *et al*²⁸ also concluded that septic patients with high blood pressure needed less renal replacement therapy. We found that when target blood pressure was set according to urine output in addition to lactate clearance rate, the MAP need to be higher than 65 mm Hg. Still, it is better for targets to be personalized. After admission, MAP decreased in some patients and increased in others. Higher MAP means the

afterload of the heart will be increased, which should be taken into consideration as the heart is often compromised in patients with septic cardiomyopathy.²⁹

ScvO₂ plays the important role of testing the final, crucial question of whether oxygen delivery is adequate.³⁰⁻³¹ However, the ARIZE and ProCESS study noted that mortality was not different in septic shock in a study of 300 patients when they were randomized to a target of ScvO₂ of 70% versus lactate clearance of at least 10%. Although we did not follow the exact values of the goals recommended by EGDT and did not even fulfill the need for a total fluid infusion of 30 ml/kg, we argue that it is inappropriate to conclude that no protocol is necessary in these patients. Instead, we believe it is necessary to use a “personalized” protocol. We can see that fluid was administered according to each patient’s need, and MAP was slightly higher, meaning that the resuscitation was even stricter. This was consistent with the idea of Head *et al.*⁹ In this study, the high-ScvO₂ group similarly showed no advantage over the low-ScvO₂ group, which means that personalized protocols are needed.

The present study has several limitations. First, it is a single-center retrospective study and, therefore, is not enough to provide a definite conclusion. Although the volume restoration was known to be completed by 6 hours after admission, we were not able to define the exact moment when the patients’ volume status was adequate. Therefore, a prospective study is still needed to confirm the results. Second, due to the various measurements of cardiac output, that variable was not statistically available. Third, in contrast to other studies, the patients were not included immediately after the sepsis erupted; instead, most of them were being given fluid or even vasopressors. We believe this to be a characteristic of ICU patients. As most sepsis and septic shock patients will be transferred to the ICU, a protocol suited for ICU treatment would be meaningful. When the patients were treated, they were far from stable, most of them because of deterioration, and they were still deeply in need of resuscitation. Finally, there was no control group to demonstrate the efficacy of the protocol. Despite these limitations, we have a homogenous hemodynamic treatment protocol for the management of septic shock patients, and this study provides the general characteristics of these patients.

In conclusion, this study suggested that in the resuscitation of sepsis and septic shock patients in the ICU, the target values did not have to be within

the “normal range” recommended by EGDT. The “target-and-endpoint” protocol, which aimed for personalized goals, deserves more consideration.

Conflicts of interest statement

The authors declare that they have no competing interests.

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应用“目标与目的”方案进行脓毒症患者的复苏：来自一个中国三级甲等医院 ICU 的回顾性研究

张宏民，王小亭，张青，刘大为

中国医学科学院 北京协和医学院 北京协和医院 重症医学科，北京 100730

关键词：脓毒症；感染性休克；乳酸；中心静脉压

目的 探讨“目标与目的”方案进行脓毒症复苏的效果。

方法 回顾性研究北京协和医院以脓毒症收入且应用去甲肾上腺素维持血压的患者 545 例。记录患者的一般资料，入室时、入室 6 及 24 h 动脉血乳酸水平，平均动脉压（MAP）、中心静脉压（CVP）、中心静脉血氧饱和度（ScvO₂）以及乳酸清除率、住院死亡率等。

结果 患者的 6h 乳酸清除率为 21.6%（四分位距，8.6%-39.0%），住院死亡率为 9.4%。入室时低 CVP（<8 mm Hg，1 mm Hg=0.133 kPa）患者，6h 后 CVP 显著上升（ 5.4 ± 1.6 mm Hg 比 7.7 ± 2.6 mm Hg， $P<0.001$ ）。入室时低 MAP（<75 mm Hg）患者，6h 后 MAP 显著升高（ 64.2 ± 7.1 mm Hg 比 82.2 ± 13.1 mm Hg， $P<0.001$ ）。入室时低 ScvO₂（<70%）患者，6h 后 ScvO₂ 显著升高（ $61.9\% \pm 7.0\%$ 比 $71.9\% \pm 7.8\%$ ， $P<0.001$ ）。各参数于 6h 和 24h 无明显变化。入室时高 CVP（ ≥ 8 mm Hg）患者，6h 后 CVP 显著下降（ 11.3 ± 4.0 mm Hg 比 10.3 ± 2.9 mm Hg， $P<0.001$ ）。入室时高 MAP（ ≥ 75 mm Hg）患者，6h 后 MAP 显著下降（ 94.2 ± 13.9 mm Hg 比 89.4 ± 11.4 mm Hg， $P<0.001$ ）。入室时高 ScvO₂（ $\geq 70\%$ ）患者，6h 后 ScvO₂ 显著下降（ $76.8\% \pm 4.2\%$ 比 $72.9\% \pm 7.3\%$ ， $P<0.001$ ）。各参数于 6h 和 24h 无明显变化。

结论 在对脓症患者进行复苏时，早期目标指导治疗提出的“目标正常值”并非适合于所有患者。“目标与目的”复苏方案能使治疗目标个体化，值得进一步研究。