Therapeutic Goal Achievements during Severe Sepsis and Septic Shock Resuscitation and Their Association with Patients' Outcomes

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Background: *Severe sepsis and septic shock are associated with high mortality. "Early goal-directed therapy" (EGDT) has been shown to improve survival. The authors report here the goal achievements in the protocol and their association with patients' outcomes.*

Material and Method: *A prospective cohort study of patients with severe sepsis and septic shock who were admitted from the Emergency Department from April 2011 to September 2012. All underwent the resuscitation protocol aimed to achieve hemodynamic goals within 6 hours after diagnosis. These goals included: 1) mean arterial >65 mmHg, 2) urine output >0.5 ml/kg/hour and 3) superior vena cava O_2 saturation >70% or serum lactate clearance >10%. The primary outcome was 28-day mortality.*

Results: *Of the 175 enrolled patients, 23 (13.1%) achieved all 3 goals at 6 hour while 75 (42.8%) achieved 2 goals and 52 (29.8%) achieved only 1 goal. The 28-day mortality of these patients was 8.7%, 16% and 35.5%, respectively while 44% of those who did not achieve any goal died. A central venous catheter was placed in 79 patients, 46 of whom had it inserted during the first 6 hours, and 42 of whom had a CVP of 8-12 mmHg. Only 13 patients had their $ScvO_2$ measured. Mean arterial pressure target was achieved in 129 patients, who had lower initial APACHE II score, lower initial lactate level and higher initial blood pressures than those who did not. These patients received less fluid at 6 hours, at 24 hours and at 3 days, respectively; they also received less norepinephrine. This group had lower mortality (28-day mortality 19.4% vs. 34.86%, p = 0.043). Of 119 patients who had achieved the urine output goal, 21 reached this goal alone and their survival was better than those who did not achieve any target goal. Serum lactate was monitored in 51 patients and a clearance of >10% was noted in 23 of them. These patients were divided into 3 groups: group 1 consisted of patients with initial lactate <2; group 2 were patients with initial lactate >2, which decreased during resuscitation; group 3 consisted of patients with initial lactate >2, which increased after wards. The mortalities were 7.7%, 14.3% and 43.6%, respectively, p = 0.011.*

Conclusion: *The achievement of therapeutic targets at 6 hours after sepsis/septic shock resuscitation was associated with improved survival, especially when more goals were reached. Although the achievement of adequate tissue oxygenation was proved beneficial, only one-third of the patients were monitored.*

Keywords: *Severe sepsis, Septic shock, Early goal-directed therapy, Goal achievement, Mortality rate*

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Sepsis and septic shock are the major causes of intensive care mortality all over the world[1,2]. Bundles of evidence-based information, namely Surviving Sepsis Guidelines, have proved to improve outcomes[3,5]. The main concepts of these remedies, apart from early appropriate antibiotics and effective source control, include early restoration of patients' tissue oxygenation by prompt and effective management of shock. This includes initial rapid volume replacement, appropriate uses of vasopressors and correction of microcirculation perfusion deficit, if present. The major milestones to be achieved at 6 hours consist of 1) central venous pressure (CVP) 8-12 mmHg, 2) mean arterial pressure (MAP) ≥65 mmHg, 3) urine output ≥0.5 ml/kg/hr and 4). central venous oxygen saturation ($ScvO_2$) >70% or lactate clearance >10%. However, the adherence to each step of the protocol varies from one institution to another[6-8] and the extent of goal accomplishment during treatment and its association with outcomes have not yet been examined. In addition, the significance

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of each target in the management flow needs to be established. For example, it has yet to be discovered whether central venous pressure assessment is beneficial or whether tissue perfusion optimization is a necessity. The authors, therefore, conducted a prospective study in sepsis/septic shock patients who underwent sepsis and septic shock resuscitation in our institution.

Material and Method

Patients

This prospective cohort study was conducted in Department of Emergency Medicine and Department of Medicine, Siriraj Hospital from April 2011 to September 2012. A consecutive sampling method was applied to all patients aged over 18 who presented at the Emergency Room with severe sepsis/septic shock as defined by the ACCP/SCCM consensus conference definition[9]. Informed consent was obtained from the patients or their relatives, as the patients were mostly incapacitated during admission. Patients were excluded if they met any of the following criteria: 1) had standing order "Do-not-resuscitate", 2) pregnancy, 3) acute stroke, 4) acute coronary syndrome, 5) acute pulmonary edema, 6) status asthmaticus, 7) active gastrointestinal bleeding, 8) status epilepticus, 9) severe burn, 10) severe trauma, 11) fatal drug overdose, 12) requirement for immediate surgery, 13) hepatic failure (PT >15 sec, INR >1.5)[12], 14) Grand mal seizure in previous 24 hours or during admission, and 15) end stage malignancy.

Data collection

After the patients were enrolled, they underwent treatment according to the institute's sepsis/septic shock management guidelines. Briefly, isotonic crystalloid was rapidly transfused at the rate of 10-20 ml/kg during the first half hour and additional bolus was given in order to raise mean arterial pressure toward 65 mmHg. Central venous catheterization (CVC) was recommended if patients remained hypotensive after 1,000-2,000 ml intravenous fluid to monitor central venous pressure (CVP) and to guide fluid challenge. Norepinephrine was administered when adequate intravascular volume was achieved as noted by a CVP of 8-12 mmHg. When the target blood pressure was reached, central venous blood was sent for $ScvO_2$ determination. Serum lactate was determined upon initiation of treatment and after blood pressure goal was reached. Tissue perfusion achievement was denoted by $ScvO_2$ >70% or lactate clearance >10%. Dobutamine was infused in patients who failed to reach this goal and had a hematocrit of more than 30%. For those who had a hematocrit of less than 30%, red blood cell transfusion was recommended. Empirical antibiotics were given in all patients, and later, they were adjusted according to the culture results.

The achievement of the therapeutic milestones in each patient was recorded. This included 1) central venous pressure (CVP) 8-12 mmHg, 2) mean arterial pressure (MAP) $\geq$65 mmHg, 3) urine output $\geq$0.5 ml/kg/hr and 4) central venous oxygen saturation ($ScvO_2$) $\geq$70% or lactate clearance $\geq$10%.

Patients' demographic data together with initial Acute Physiology and Chronic Health Evaluation II (APACHE II) score on admission were collected. Parameters to determine success of EGDT including time taken to establish diagnosis and time to reach each hemodynamic end point were also documented. Outcome measures were determined by 28-day mortality, duration of stay in intensive care unit and hospital length of stay.

Ethical considerations

The present study was reviewed and approved by the Siriraj ethics committee, using the Declaration of Helsinki.

Statistical analysis

Subjects' characteristics were presented by descriptive analysis. Differences between the two groups-(1) the group that survived and the group that did not, and (2) the group who had blood pressure achieved and the group who did not-were tested with the use of Student's t-test, the Chi-square test, or Wilcoxon's rank-sum test. p-value of less than 0.05 was considered to indicate statistical significance. For the comparison of outcomes in patients who achieved different resuscitation goals, one-way ANOVA was used to compare the continuous variables and Chi-square test was used to compare the categorical variables.

Results

One hundred seventy-five patients with severe sepsis/septic shock who presented at the Emergency Department were admitted to the Medical ICU and the Medical wards during the study period. As summarized in Table 1, patients' average age was 63.9$\pm$16.8 years and 49.1% were male. Mean APACHE II score was 21.5$\pm$7.6. Most patients had co-morbid diseases including hypertension (41.1%), diabetes mellitus (34.3%), malignancy (18.9%), cerebrovascular

Table 1. Patients' demographic data

Baseline data	n = 175
Age (year)	63.9±16.8
Male sex (%)	49.1
Body weight (kg)	57.5±17.7
Height (cm)	160.1±10.3
APACHE II score	21.5±7.6
Underlying conditions (%)	
Hypertension	41.1
Diabetes mellitus	34.3
Malignancy	18.9
Previous cerebrovascular disease	14.5
Coronary artery disease	10.3
Cirrhosis	10.3
Chronic renal failure	9.7
HIV infection	2.3
Source of infection (%)	
Upper urinary tract infection	26.9
Lower respiratory tract infection	25.7
Intra-abdominal infection	17.1
Skin and soft tissue infection	8.6
Septicemia	22.9
Organ dysfunction (%)	73.7
Hypotension	84
:Hypotension response to fluid resuscitation	13.1
:Hypotension persist despite fluid resuscitation	70.9
Acute kidney injury	48.6
Acute respiratory distress syndrome (PaO_2/FiO_2 <200)	24.6

disease (14.5%), coronary artery disease (10.3%), chronic renal failure (9.7%) and cirrhosis (10.3%). Of the organs involved, urinary tract infection was the most common (26.9%), followed by lower respiratory tract infection (25.7%), intra-abdominal infection (17.1%) and skin/soft tissue infection (8.6%). Twenty-nine percent of these patients had septicemia. Gram-negative bacilli were the most common causative organism (44.8%), which mostly consisted of Escherichia coli, Klebsiella pneumonia, Acinetobacter Baumanii and Pseudomonas Aeruginosa. Gram-positive cocci, specifically both methicillin sensitive and methicillin resistant Staphylococcus aureus and Streptococci, accounted for 24.8% of the organisms.

At 6 hours after the initiation of resuscitation, 45 patients (25.7%) had central venous catheter placed and 36 of these (24%) reached the CVP goal. Thirty-four patients had CVC inserted later during treatment and 96 patients did not have CVC placed. The 28-day mortality in patients who achieved CVP goal at 6 hours, those who had CVP inserted without CVP goal at 6 hours and those in whom CVP was placed after 6 hours were 33.3%, 44.4% and 20.6%, respectively. The mortality in patients who did not have CVC placed was 18.8%.

Blood pressure goal was reached in 129 patients (73.7%). Of these, only 31 achieved this goal; 75 had urine output goal reached; and 23 had urine output and lactate clearance targets reached in addition. As shown in Table 2, patients were categorized into those who achieved the blood pressure goal (achievement group) and those who did not (no achievement group). The achievement group had lower APACHE II score (20.6±7.2 vs. 23.9±8.2), and had higher initial blood pressures (systolic blood pressure 85.2±25.2 vs. 77.2±13.1, p = 0.007; diastolic blood pressure 50.8±15.3 vs. 45.1±8.3, p = 0.017 and mean arterial pressures 61.9±18.1 vs. 58.5±8.8, p = 0.024). Initial serum lactate level was lower in achievement group (3.9±4.4 vs. 7.7±6.2 mmol/L). In addition, this group had lower proportion of oliguria (43.4 vs. 63%, p = 0.030). The proportion of those who achieved urine output goal (urine >0.5 ml/kg/hour) and those who achieved lactate clearance were higher in the achievement group (urine output goal 75.8 vs. 46.7%, p<0.001, lactate clearance goal 55.9 vs. 0%, p<0.001). The 28 day mortality and the hospital mortality were lower in the achievement group (28 day mortality 19.4 vs. 34.8, p = 0.043; hospital mortality 22.5 vs. 39.1, p = 0.034). However, ICU length of stay was higher in the achievement group (34.5±12.7 vs. 29.1±34.5 days).

Urine output goal was achieved in 119 patients. Of these, 21 reached this goal alone while 75 and 23 also reached blood pressure target and blood pressure together with lactate clearance, respectively, as mentioned above. The patients who had urine output goal reached alone had somewhat better 28-day survival than those who did not achieve any goal (23.8% vs. 44%, p = 0.22). Tissue oxygenation was determined in 64 patients (36.6%). Of these, 13 had central venous oxygen saturation ($ScvO_2$) measurement and 51 underwent sequential serum lactate monitoring. Eight patients achieved $ScvO_2$ goal at 6 hours and two of them died. Among 51 patients who underwent sequential lactate assessment, 23 achieved the clearance goal within 6 hours. The mortality of those who achieved this goal is much lower than those who did not (5.2% vs. 43.7%, p<0.001).

Since the rate of CVC insertion was low, we moved to focus the milestones of our sepsis management on 1) blood pressure, 2) urine output and

Table 2. Characteristics and resuscitation details in patient groups according to blood pressure achievement at 6 hour

	Mean arterial pressure goal achievement		p-value
	No achievement (n = 46)	Achievement (n = 129)	
APACHE II score	23.9±8.2	20.6±7.2	0.020
Initial blood pressures (mmHg)			
Systolic blood pressure	77.2±13.1	85.2±25.2	0.007
Diastolic blood pressure	45.1±8.3	50.8±15.3	0.017
Mean arterial pressure	58.5±8.8	61.9±18.1	0.024
Initial organ function (%)			
Organ dysfunction	82.6	70.5	0.123
Acute renal failure (urine <0.5 ml/kg/hr)	63.0	43.4	0.030
ARDS (P/F ratio <200)	32.6	21.7	0.160
DIC	17.4	24.8	0.320
Metabolic acidosis	50.0	38.0	0.170
Initial lactate	7.7±6.2	3.9±4.4	0.004
Fluid therapy (ml)			
Total fluid in 1st hour	726.1±305.2	635.0±385.1	0.150
Total fluid in 6 hours	2,724.2±1,010.2	2,330.0±1,147.4	0.030
Total fluid in 24 hours	5,765.5±1,730.9	5,012.7±1,865.8	0.020
Total fluid on day 2	2,016.5±1,272.0	1,736.4±1,000.0	0.190
Total fluid on day 3	1,557.0±1,443.3	992.9±953.1	0.023
Vasopressors			
Norepinephrine (%)	84.8	69.8	0.052
Mean dose (mcg/kg/min)	0.24±0.32	0.14±0.14	0.020
Dopamine (%)	23.9	10.1	0.025
Mean dose (mcg/kg/min)	12.3±6.9	11.2±6.1	0.680
Adrenaline (%)	4.3	3.1	1.000
Mean dose (mcg/kg/min)	0.52±0.68	0.81±0.61	0.670
Dobutamine	6.6	10.1	1.000
Mean dose (mcg/kg/min)	5.7±1.3	5.6±4.5	0.570

3) tissue perfusion (mean arterial pressure >65 mmHg, urine output >0.5 ml/kg/hour and $ScvO_2$ >70% or lactate clearance >10%). Twenty-three total patients (13.1%) achieved these three goals; 75 patients (42.9%) achieved two goals; 52 (29.8%) patients achieved one goal; and 25 (14.3%) patients did not achieve any goals. Table 3 shows the outcomes of patients with different achievements. As noted, the hospital mortality in patients who failed to accomplish any treatment goal was the highest (48%, p = 0.008). Patients who achieved only blood pressure goal had a 41.9% mortality while the mortality of those who reached blood pressure and urine output goal was 19%, patients who achieved blood pressure, urine output and lactate clearance goal had only 8.7% mortality.

Fig. 1 demonstrates the effect of goal accomplishment on patients' survival. As noted in Fig. 1a), patients' survival improved as blood pressure increased. Although no significant difference was noted, the survival reached plateau at MAP 60-65 mmHg ranges. This was identical for hourly urine output. Fig. 1b) disclosed increased survival when hourly urine output reached 0.5-0.75 ml/Kg.

When focusing on serum lactate, it was found that the initial levels and the changes during treatment conveyed patients' prognosis. As demonstrated in Fig. 2, patients were classified to 3 groups according to initial lactate level: group 1) patients with initial serum lactate <2 mmol/L, group; 2) patients with initial serum lactate >2 mmol/L in whom the level declined during treatment; and group 3) patients with initial serum lactate >2 mmol/L in whom the level increased thereafter. Patients in group 1 had the highest survival rate, followed by groups 2 and 3 respectively.

Discussion

Our findings can be summarized as follows: at 6 hours after the initiation of resuscitation, a significant

Table 3. Resuscitation goals at 6 hours and outcomes

Outcomes/ goal achievement	No goal (n = 25)	Blood pressure (n = 31)	Blood pressure and urine output (n = 75)	Blood pressure and urine output and lactate(n = 23)	Urine output (n= 21)	p-value
28 days mortality (%)	44	35.5	16	8.7	23.8	0.008
Hospital mortality (%)	48	41.9	18.7	8.7	28.6	0.003
ICU LOS only 48 pts (days)	16.2±13.9	20.1±25.0	5.7±4.7	5.8±5.0	61.5±58.7	<0.001
Hospital LOS (days)	24.5±21.9	31.0±30.0	19.0±16.5	23.5±30.7	28.6±22.1	0.34
Survival days without ventilator in the 1st 28 days	11.9±13.4	14.7±12.8	21.9±9.6	22.1±9.7	17.8±13.1	<0.001
Survival days without vasopressor in the 1st 28 days	16.0±12.1	18.0±11.8	23.4±7.5	23.1±7.8	19.1±10.5	0.006

Treatment outcomes from patients who achieved treatment goal at 6 hours were evaluated. One-way ANOVA was used to compare the continuous variables and Chi-square test was used to compare the categorical variables of 5 groups

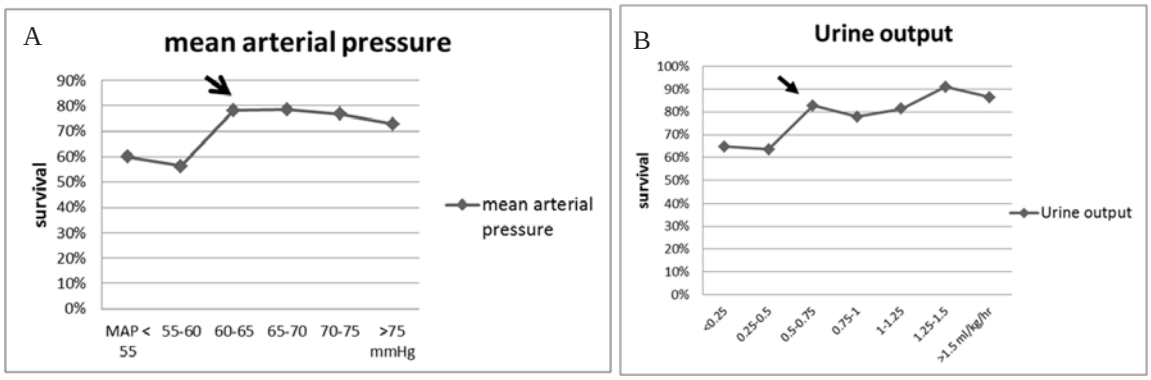

Fig. 1 Patients' survival according to therapeutic milestones at 6 hours. A) denoted that the survival reached plateau at a mean arterial pressure of 60-65 mmHg. B) demonstrated a hourly urine output of 0.5-0.75 ml/kg where patients' survival improved.

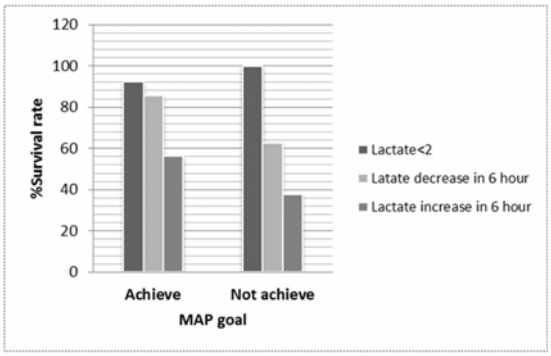

Fig. 2 Survivals in patient groups with and without blood pressure achievement with different pattern of lactate clearance.

number of sepsis/septic shock patients achieved the resuscitation target. Approximately three quarters reached target blood pressure. These patients were initially less sick and had better outcomes. Urine output goal and lactate clearance goal were accomplished in 68% and 15%, respectively, and also, these patients had lower mortality. The outcomes were much improved if more goals were reached. Low central venous catheterization rate was noted in our series. Although the achievement of adequate tissue oxygenation was proved beneficial, only one-third of the patients were monitored.

The basis for sepsis and septic shock resuscitation includes early restoration of perfusion deficit by rapid fluid replacement and appropriate uses of vasopressors followed by optimizing tissue oxygenation. The first aim is characterized by optimal blood pressure, namely MAP >65 mmHg in previously normotensive patients. Fluid bolus is recommended at the beginning

to correct volume deficit and central venous pressure or dynamic volume responsive tests are later recommended to monitor volume adequacy. Vasopressors are indicated if patients are still hypotensive despite optimal preload. In the present study, however, only a quarter of the patients had CVC placed. This was parallel to many studies[10,11]. A part from low adherence to the guidelines, this finding may be explained by some other reasons. First, in certain patients, blood pressure was restored after early fluid resuscitation and CVC was, therefore, considered unnecessary in this setting. This was supported by the fact that only 18.8% of those who did not have CVC placed died. In addition, certain patients had contraindications for central venous cannulation. This finding gave rise to a significant question as to whether CVC or even the volume responsive test was needed in every patient as recommended in the guidelines, or only in specific patients in whom blood pressure was not restored after fluid loading.

The achievement of blood pressure target was noted in 73.7% of the patients at 6 hours. The achievement group had milder disease severity as judged by higher initial blood pressures, less proportion of oliguric patients, lower mean lactate level and lower APACHE II score. Moreover, treatment outcomes, namely mortality, amount of fluid therapy and norepinephrine, were better in this group. This supports the study of Alberti[12] that treatment outcomes of earlier stages of sepsis were much better than in later stages. Thus, early recognition of sepsis together with prompt and appropriate treatment results in good outcomes. Further, the target blood pressure of 65 mmHg was a matter of debate, the finding in Fig. 1a) that patients' survival reached a plateau at 60-65 mmHg gave rise to the hypothesis that, in certain patients, the target mean arterial pressure may be lower or higher. This was reviewed elsewhere[13] and the concept of individual targets should be considered in patient management.

Urine output, target achievement is another milestone that indicates adequate organ blood flow. Theoretically, this target is reached after perfusion pressure has been achieved. As noted, the accomplishment of this goal, in addition to blood pressure target achievement rendered better survival. Additionally, we found that some patients reached target urine flow without blood pressure achievement and these patients had lower mortality rates than those who did not achieve any target. This supports the hypothesis above that perfusion pressure target of >65 mmHg as described in guidelines may be higher than the real perfusion threshold in specific patients.

As for tissue oxygenation, our data demonstrated that, after perfusion goals had been reached, achievement of this milestone enhanced survival. This finding paralleled with others[14-16]. In addition, we showed in Fig. 2 the initial lactate level and its changes during treatment signified prognosis. Patients who achieved the perfusion target alone, especially those to whom norepinephrine was given, might have tissue hypoxia despite reaching the blood pressure goal[17]. All results supported the benefit of monitoring tissue oxygenation. However, such monitoring was utilized in only one-third of the patients (13 and 51 respectively). Thus, the conclusion that tissue perfusion monitoring is needed in every patient cannot be made here and more work is needed to clarify this issue. At present, a multicenter randomized control trial of early goal directed therapy in patients with severe sepsis and septic shock is in progress[18]. The present study, after completion, should support more reliable answers regarding efficacy and benefits of each goal achievement during the resuscitation pathway.

In conclusion, the present study disclosed the practices and outcomes after implementation of sepsis resuscitation guidelines in our institution. At 6 hours, approximately three-quarters of the patients reached target blood pressure. These patients were initially less sick and had better outcomes. Urine output goal and lactate clearance goals were accomplished in 68% and 15%, respectively, and additionally, these patients had lower mortality. The outcomes were much improved if more goals were reached. CVC was placed in only a quarter of the patients. Tissue perfusion, mostly lactate clearance, was monitored in only one-third of them. Although EGDT proved beneficial, more work is needed to clarify the necessity of each goal in specific patients.

Potential conflicts of interest

None.

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การบรรลุเป้าหมายย่อยในขั้นตอนของการรักษาระหว่างการรักษาภาวะช็อกจากการติดเชื้อ และความสัมพันธ์ต่อผลลัพธ์การรักษา

ไชยรัตน์ เพิ่มพิกุล, พีรวัฒน์ ศรีงาม, สุรัตน์ ทองอยู่

วัตถุประสงค์: การรักษาภาวะช็อกจากการติดเชื้อ นอกเหนือจากการให้ยาปฏิชีวนะและการกำจัดแหล่งติดเชื้อแล้ว ยังประกอบด้วยการให้สารน้ำในระยะเริ่มต้นอย่างรวดเร็ว การให้ยาบีบหลอดเลือดถ้าผู้ป่วยยังคงมีภาวะช็อก เมื่อได้สารน้ำเพียงพอ และการประเมิน tissue oxygenation โดยมุ่งให้ระดับ central venous oxygen saturation, $ScvO_2$ กลับเข้าสู่ระดับ 70 มม.ปรอท หรือ lactate clearance มากกว่า 10% สรุปเป้าหมายการรักษาคือ 1. ความดันเลือด เฉลี่ย 65 มม.ปรอท, 2. ปริมาณปัสสาวะต่อชั่วโมงมากกว่า 0.5 มล./กก./ชั่วโมง และ 3. tissue oxygenation เข้าสู่เป้าหมายข้างต้น การศึกษานี้มีวัตถุประสงค์เพื่อตรวจสอบการบรรลุถึงเป้าหมายต่าง ๆ ดังกล่าวและผลต่อผลลัพธ์การรักษา

วัสดุและวิธีการ: เป็นการศึกษาไปข้างหน้าในผู้ป่วยที่ติดเชื้อในกระแสเลือดรุนแรงหรือภาวะช็อกจากการติดเชื้อ ที่มาห้องฉุกเฉินและรับไว้ในหอผู้ป่วยวิกฤตอายุรศาสตร์ ข้อมูลที่นำมาศึกษาคือการบรรลุเป้าหมายการรักษาทั้ง 3 ขั้นตอนข้างต้นหลังจากการรักษาได้ 6 ชั่วโมงและผลลัพธ์การรักษาที่สำคัญคือ อัตราตายที่ 28 วัน (28 day mortality)

ผลการศึกษา: ผู้ป่วยทั้งหมด 175 ราย มีผู้บรรลุผลการรักษาหลังจากการรักษาได้ 6 ชั่วโมง 1 ขั้นตอน 52 ราย (29.8%), 2 ขั้นตอน 75 ราย (42.8%) และ 3 ขั้นตอน 23 ราย (13.1%) โดยอัตราตายของทั้ง 3 กลุ่มเป็น 35.5%,16%,และ 8.7% ตามลำดับ โดยกลุ่มที่ไม่ได้บรรลุเป้าหมายการรักษามีอัตราตาย 44% ผู้ป่วย 45 รายได้รับการใส่สายสวนหลอดเลือดดำและ 36 รายมีค่า CVP 8-12 มม.ปรอทเมื่อ 6 ชั่วโมงหลังการรักษา มีผู้ป่วยเพียง 13 รายได้รับการตรวจ $ScvO_2$ ผู้ป่วย 129 รายมีระดับความดันเลือดกลับเข้าสู่เป้าหมาย ผู้ป่วยกลุ่มนี้มีค่าความดันเลือดเริ่มต้นสูงกว่ากลุ่มที่ ความดันเลือดไม่กลับเข้าสู่เป้าหมาย มีค่า APACHE II score มากกว่า ได้รับสารน้ำและยาบีบหลอดเลือด (norepinephrine) น้อยกว่าและมีอัตราตายน้อยกว่า (อัตราตายที่ 28 วัน 19.4% vs. 34.86%, p = 0.043) ผู้ป่วย 119 ราย บรรลุเป้าหมายของปริมาณปัสสาวะต่อชั่วโมง ในจำนวนนี้มี 21 ราย ที่บรรลุเป้าหมายนี้เพียงอย่างเดียวทั้งที่ความดันเลือดยังไม่กลับเข้าตามเกณฑ์ ในจำนวนผู้ป่วย 51 ราย ที่ได้รับการตรวจ lactate level, 23 รายมี lactate clearance กลับเข้าตามเกณฑ์ ผู้ป่วยกลุ่มนี้มีอัตราตายน้อยกว่ากลุ่มอื่น ๆ อย่างชัดเจน และเมื่อพิจารณาระดับ lactate เริ่มต้นและการเปลี่ยนแปลงในช่วง 6 ชั่วโมง พบว่าสามารถแบ่งผู้ป่วยเป็น 3 กลุ่ม คือ 1) กลุ่มที่มีระดับ lactate เริ่มต้นน้อยกว่า 2 mmol/L, 2) กลุ่มที่มีระดับ lactate เริ่มต้นมากกว่า 2 mmol/L และระดับลดลงเมื่อติดตามภายใน 6 ชั่วโมง, 3) กลุ่มที่มีระดับ lactate เริ่มต้นมากกว่า 2 mmol/L และระดับเพิ่มขึ้นเมื่อติดตามภายใน 6 ชั่วโมง พบว่าอัตราตายในกลุ่มที่ 1 กลุ่มที่ 2 และกลุ่มที่ 3 เป็น 7.7%, 14.3% และ 43.6% ตามลำดับ, p = 0.011.

สรุป: การศึกษานี้ได้แสดงประโยชน์ของการบรรลุผลการรักษาตามเป้าหมายที่สำคัญหลังการรักษา 6 ชั่วโมง และแสดงว่าประโยชน์ที่ได้รับมีมากขึ้นเมื่อมีการบรรลุเป้าหมายการรักษามากขึ้น การประเมิน tissue oxygenation ยังมีน้อยทั้งที่ได้รับการพิสูจน์ว่ามีประโยชน์