Sepsis Resuscitation Guideline Implementation in the Department of Emergency Medicine, Siriraj Hospital

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Background: *Sepsis management guidelines have been implemented in the Emergency Department, Siriraj Hospital since 2005.*
Objective: *Assess the impact of sepsis resuscitation guidelines on the mortality of patients after implementation.*
Material and Method: *A prospective cohort study was conducted in the Emergency Department, Siriraj Hospital between January 12 and October 2, 2011. Patients aged older than 18 years old were included. The baseline data and the extent of goal achievement were recorded. The primary outcome was the 30-day mortality rate.*
Results: *One hundred forty four patients (34% severe sepsis, 66% septic shock) were included. The overall 30-day mortality was 39.6%. Antibiotics were administered within 1 hour in 52.2% of the patients. At least 1 or at least 2 therapeutic goals were accomplished in 86.8% and 50.7% of patients, respectively, and the achievement of at least 2 goals was associated with lower mortality (adjusted OR 0.41, 95% CI 0.19-0.89). Two patients (1.4%) completely achieved goals within 6 hours. Respiratory failure requiring endotracheal tube insertion was associated with higher mortality (adjusted OR 3.12, 95% CI 1.32-7.38).*
Conclusion: *The 30-day mortality was 39.6%. The achievement of at least 2 goals was associated with lower mortality. Endotracheal tube insertion was associated with higher mortality.*

Keywords: *Sepsis, Implementation, Mortality, Emergency department, Siriraj Hospital*

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Severe sepsis/septic shock are critical conditions associated with high mortality. The incidence, in the United States, was reported to be approximately three cases per 1,000 population (around 751,000 cases), and the mortality rate was 28.6%[1]. Studies from other countries revealed mortality varying from 23.1% to 64%[2-4]. Data from Siriraj Hospital showed the mortalities of severe sepsis and septic shock in inpatient wards were 34.3% and 52.6%, respectively[5].

The successful management of sepsis requires prompt actions in both diagnosis and management. In 2001, Rivers et al reported on trial of early goal-directed therapy (EGDT) aimed toward prompt hemodynamic restoration and correction of tissue hypoxia. The mortality of the EGDT arm compared with the control treatment arm was significantly less (30.5% vs. 46.5%)[6]. Since then, a series of Surviving Sepsis Campaign International Guidelines consisting of early goal-directed hemodynamic resuscitation, organ support and source control have been announced[7,8]. This has led to worldwide implementation. Many publications have supported the benefit of these measures[9-11]. Although worldwide studies were conducted in various setting, in Thailand, most of studies were undertaken in intensive care units and inpatient wards[12-14].

The Siriraj Septic Shock Guidelines (Fig. 1) have been modified from the Surviving Sepsis Campaign International Guidelines and used in the Emergency Department, Siriraj Hospital since 2005. The purpose of the present study was to ascertain treatment outcomes after guidelines application.

Material and Method

This was a prospective observational study conducted in the Emergency Department, Siriraj Hospital between January 12 and October 2, 2011. Siriraj Hospital, a 2,500-bed tertiary university hospital, has two emergency rooms, the Trauma Unit and the Non-Trauma Unit. The study was undertaken in only the Non-Trauma Unit. Eligible patients were

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those over 18 years old and diagnosed of severe sepsis or septic shock according to the American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM) consensus conference committee definition[15]. The exclusion criteria were those who had do-not-resuscitate status, referred to other hospitals, and had incomplete data collection. Written informed consent was obtained before collecting data.

The patients were resuscitated according to the Siriraj Septic Shock Guidelines as shown in Fig. 1. Empirical antibiotics were given after blood samples and tissue specimens were collected. Fluid therapy starting with isotonic crystalloids given rapidly at the rate of 500 to 1,000 ml in 30 minutes was the initial step. This was repeated as necessary to restore mean arterial pressure (MAP) greater than or equal to 65 mmHg. A central venous catheter was placed in patients with uncertain volume status after initial fluid therapy to measure whether a goal central venous pressure (CVP) of 8 to 12 mmHg (10-15 cmH_2O) had been reached. If the patient was still hypotensive after optimal CVP, continuous intravenous norepinephrine (NE) was given. Tissue oxygenation, central venous oxygen saturation ($ScvO_2$), was assessed when the goal

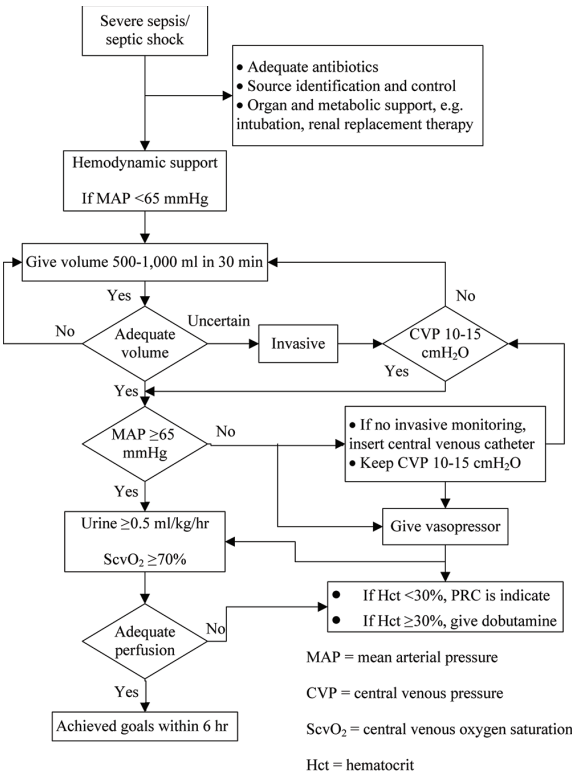

Fig. 1 Siriraj septic shock guidelines.

MAP and CVP were reached. The $ScvO_2$ goal was 70%. If the $ScvO_2$ was less than 70% and the patient was anemic (hematocrit <30%), red cells were transfused to correct the condition. If the hematocrit was above 30%, dobutamine was given to increase $ScvO_2$ by improving the cardiac output of the patient. The achievement of therapeutic goals during resuscitation was recorded at the following milestones: 1) CVP 8 to 12 mmHg (10-15 cmH_2O), 2) MAP greater than or equal to 65 mmHg, 3) urine output greater than or equal to 0.5 ml/kg/hour, and 4) $ScvO_2$ greater than 70%.

The difference between the Siriraj Septic Shock Guidelines and the Surviving Sepsis Campaign International Guidelines is that a central venous catheter was placed only in patients with uncertain volume status after initial fluid therapy.

The patients were followed for 30 days or until death. Data collection included demographic data, comorbidities, sites of infections, causative organisms, medications, and treatment outcomes.

Outcomes

The primary outcome was the 30-day mortality. The secondary outcomes were the factors associated with the mortality, the proportion of patients who achieved EGDT goals within six hours, and the rate of administration of appropriate antibiotics within the first hour after the diagnosis of severe sepsis or septic shock (appropriate antibiotics defined as antibiotics that had in vitro activity against the isolated causative pathogens[16]).

Statistical analysis

Sample size was calculated by estimating proportion of one group. Precision of estimates was 20% of mortality[6,10,14]. Mortality rate was 34.3%[5]. After adjusting for 20% of data loss, the sample size required was 141 patients.

Descriptive statistics were used to describe the characteristics of the patients. Chi-square or Fisher's exact test was used to compare categorical variables as appropriate. Student's t-test and Mann-Whitney U-test were used to compare normally distributed continuous variables and nonparametric data, respectively. A multivariate analysis of the predictive factors for mortality was performed by multiple logistic regression method. Variables with $p<0.2$ in the univariate analysis were included in multivariate analysis. A p-value <0.05 was considered to be statistically significant. The SPSS version 19.0 was used for statistical analysis.

Ethical considerations

The study protocol was reviewed and approved by the Siriraj Ethics Committee, using the Declaration of Helsinki.

Results

During the study period, 185 patients at the emergency department met the inclusion criteria for severe sepsis or septic shock. Of these, 41 (22%) were excluded because 1) do-not-resuscitate status (26 patients, 63.4%), 2) age below 18 years old (4 patients, 9.7%), 3) patient referred to another hospital (3 patients, 7.3%), 4) incomplete data collection (5 patients, 12.2%), and 5) having other diagnosis such as pancreatitis, adrenal shock and anaphylactic shock (3 patients, 7.3%). The data of the remaining 144 patients were analyzed. The mean age was 63.6±16.07 years and the male proportion was 50.7%. Forty-nine (34%) and 95 patients (66%) were diagnosed as severe sepsis and septic shock, respectively. Ninety-one percent of patients had co-morbid conditions. The most common was hypertension (37.5%), followed by malignancy (25.7%), and diabetes mellitus (29.2%). The patient characteristics between severe sepsis and septic shock groups were not significantly different except for systolic blood pressure, which was higher in sepsis group (81.71±13.45 vs. 76.46±11.75 mmHg,

Table 1. The characteristics of patients

	Severe sepsis (n = 49)	Septic shock (n = 95)	All patients (n = 144)
Age (years)	67.20±15.37	61.74±16.19	63.60±16.07
Sex			
Male	23 (46.9%)	50 (52.6%)	73 (50.7%)
Female	26 (53.1%)	45 (47.4%)	71 (49.3%)
Comorbidities	44 (89.8%)	87 (91.6%)	131 (91.0%)
Diabetes mellitus	18 (36.7%)	24 (25.3%)	42 (29.2%)
Hypertension	33 (34.7%)	21 (42.9%)	54 (37.5%)
Coronary artery disease	4 (8.2%)	6 (6.3%)	10 (6.9%)
Cirrhosis	8 (16.3%)	12 (12.6%)	20 (13.9%)
Dyslipidemia	5 (10.2%)	12 (12.6%)	17 (11.8%)
Chronic kidney disease	5 (10.2%)	9 (9.5%)	14 (9.7%)
COPD and asthma	1 (2.0%)	5 (5.3%)	6 (4.2%)
Stroke	3 (6.1%)	6 (6.3%)	9 (6.3%)
Malignancy	14 (28.6%)	23 (24.2%)	37 (25.7%)
Dementia and Parkinson's disease	4 (8.2%)	9 (9.5%)	13 (9.0%)
HIV infection	2 (4.1%)	5 (5.3%)	7 (4.9%)
SLE	0 (0%)	2 (2.1%)	2 (1.4%)
Others*	9 (18.4%)	15 (15.8%)	24 (16.7%)
Temperature (°C)	37.57±1.19	37.44±1.18	37.48±1.18
Pulse (beats/min)	100.39±23.76	101.56±24.09	101.16±23.90
Respiratory rate (breaths/min)	27.51±8.28	27.93±8.36	27.78±8.31
Systolic BP (mmHg)	81.71±13.45	76.46±11.75	78.25±12.56
Diastolic BP (mmHg)	47.78±11.76	46.96±11.57	47.24±11.60
Lactate (mmol/L)	3.8 (2.4-7.5)	5.0 (1.6-9.8)	4.2 (2.0-8.0)
Creatinine (mg/dL)	1.50 (1.0-2.2)	1.80 (0.9-3.0)	1.65 (1.0-2.7)
HCO_3 (mmol/L)	18.49±6.58	18.00±5.37	18.17±5.79

COPD = chronic obstructive pulmonary disease; HIV = human immunodeficiency virus; SLE = systemic lupus erythematosus; BP = blood pressure

Values are presented as mean ± SD or median (interquartile range)

One patient can have more than one comorbidities

* Others: thalassemia, valvular heart disease, chronic disseminated intravascular coagulation, benign prostate hypertrophy, gout, hypothyroid, obstructive sleep apnea, cervical spinal cord injury, traumatic head injury, multiple sclerosis, cauda equina syndrome

p = 0.017). The details of the characteristics of patients are shown in Table 1.

Pattern of infections

The most common site of infection was intraabdominal infection (36 patients, 25%) followed by urinary tract infection (33 patients, 22.9%), respiratory tract infection (26 patients, 18.1%), soft tissue infection (17 patients, 11.8%), bacteremia (10 patients, 6.9%), systemic infection (4 patients, 2.8%), endocarditis (2 patients, 1.4%), central nervous system (2 patients, 1.4%), catheter-related bloodstream infections (1 patients, 0.7%), and unknown sources (13 patients, 9%).

Hemocultures were positive in 60 patients (41.7%). Of these, 59 (95.1%) were bacteria, and three (4.8%) were other microorganisms. Gram-negative bacteria were the most identified pathogens (66.1%). The most common bacterial pathogen was ESBL-negative *E. coli* (46.4%). Antibiotic-resistant bacteria (ESBL-positive) were found in 8.6%. The details of hemoculture results are shown in Table 2.

Antibiotics and supportive treatment

Thirty-one patients (21.5%) had received antibiotics before transferring to the emergency department and were excluded from the analysis in this part. The median time from diagnosis to administration of antibiotics was 60 minutes (interquartile range (IQR), 30-107.5). Appropriate antibiotics were administered in 76.4% of 113 patients. Fifty-two point two percent of patients received appropriate antibiotics within one hour and 97.3% within 4 hours.

Of 144 patients, 36 (25%) were intubated and ventilated while 88 patients (61.1%) received vasopressors. Fifty-three patients (36.8%) received central venous access. The mean initial CVP was 14.16±6.12 cmH_2O. Norepinephrine was the most frequently used vasopressor (85.2%). The mean volume of fluid resuscitation in the emergency department was 2,782.51±1,405.47 ml and normal saline was the most frequently used (97.9%).

Of 144 patients, 22.9% achieved CVP goal, 76.4% achieved MAP goal, 46.5% achieved urine output goal, and 3.5% achieved $ScvO_2$ goal. Eighty-six point eight percent achieved at least one goal, 50.7% achieved at least two goals, 10.4% achieved at least three goals, and only 1.4% achieved all goals. The mean times taken to achieve CVP, MAP, urine, and $ScvO_2$ goals were 187.67±74.15, 182.19±95.49, 196.04±91.95, and 197±68.79 minutes, respectively.

Table 2. Details of positive hemoculture results

	n (%)
Positive hemoculture result	60 (41.7%)
Causative organism	
Bacteria	59 (95.1%)
Gram positive	12 (20.3%)
Gram negative	39 (66.1%)
Mixed organism	8 (13.6%)
Mycobacteria	1 (1.6%)
Fungus	1 (1.6%)
Virus	1 (1.6%)
Type of bacteria	
Streptococcus spp.*	11 (18.7%)
E. coli ESBL negative	22 (37.8%)
E. coli ESBL positive	5 (8.6%)
K. pneumoniae ESBL negative	8 (13.7%)
P. aeruginosa	2 (3.4%)
Other bacteria	
Proteus spp.**	2 (3.4%)
Salmonella gr C1	1 (1.7%)
S. marcescens	1 (1.7%)
V. cholera non 01/0139	1 (1.7%)
V. vulnificus	2 (3.4%)
Granulicatella spp.	1 (1.7%)
Coryneform bacteria	1 (1.7%)
Gram positive rod other than *L. monocytogenes*, *E. rhusiopathiae* and *Corynebacterium* spp.	1 (1.7%)

ESBL = extended spectrum beta-lactamase
* *Streptococcus* alpha hemolytic, *Streptococcus* beta hemolytic gr G, *S. agalactiae*, *S. pasteurianus*, *S. pneumonia*, *S. pyogenes*
** *P. mirabilis* ESBL negative, *Proteus* spp.

Treatment outcomes

The median length-of-stay time in the emergency department was 302.5 (IQR, 220-498.8) minutes (about 5 hours). One point four percent of patients died in emergency room. Thirty-six point six percent of patients were admitted to intensive care unit, and the others were admitted to general wards.

The overall 30-day mortality was 39.6%. The mortality in severe sepsis and septic shock were 30.6% and 44.2%, respectively without significant differences between these two groups (p = 0.11).

The univariate analysis of the factors associated with mortality is shown in Table 3. The patients who had bicarbonate level less than 15 mmol/L (crude OR 2.6, 95% CI 1.19-5.65), had respiratory failure requiring endotracheal intubation (crude OR

Table 3. Factors associated with 30-day mortality

Risk factors	Crude odds ratio	95% CI	*p*-value
Female	0.78	0.40-1.53	0.47
Lactate ≥4 mmol/L	1.96	0.77-4.99	0.16
Positive hemoculture results	1.66	0.84-3.27	0.14
HCO_3 <15 mmol/L	2.60	1.19-5.65	0.02
Central venous access	1.14	0.57-2.27	0.72
Vasopressor/inotropic drugs	1.68	0.84-3.39	0.15
Intubation	3.85	1.74-8.50	0.001
Corticosteroid	3.05	1.12-8.29	0.02
Antibiotics within 1 hour	0.93	0.47-1.84	0.83
Antibiotics within 4 hours	1.32	0.12-14.88	1.00
Septic shock	1.80	0.87-3.73	0.11
ICU admitted	1.27	0.63-2.54	0.50
Achieved goal			
CVP 8-12 mmHg	0.99	0.45-2.19	0.98
MAP ≥65 mmHg	0.49	0.22-1.06	0.07
Urine output ≥0.5 mL/kg/hour	0.26	0.12-0.54	0.00
$ScvO_2$ ≥70%	1.02	0.17-6.29	1.00
Number of goal achieved			
At least 1 goal	0.33	0.12-0.89	0.02
At least 2 goals	0.35	0.17-0.69	0.002
At least 3 goals	0.35	0.09-1.29	0.10
Achieved 4 goals	1.54	0.09-25.06	1.00

ICU = intensive care unit; CVP = central venous pressure; MAP = mean arterial pressure; $ScvO_2$ = central venous oxygen saturation

Table 4. Multivariate analysis of 30-day mortality

Factors	Adjusted odds ratio	95% CI	*p*-value
Intubation	3.12	1.32-7.38	0.01
Achieved at least 2 goals	0.41	0.19-0.89	0.025

3.85, 95% CI 1.74-8.50) or had received corticosteroids (crude OR 3.05, 95% CI 1.12-8.29) had a higher mortality rate. Patients who achieved urine output goal (crude OR 0.26, 95% CI 0.12-0.54), achieved at least one EGDT goal (crude OR 0.33, 95% CI 0.12-0.89) or achieved at least two EGDT goals (crude OR 0.35, 95% CI 0.17-0.69) had lower mortality rate.

Multivariate analysis is shown in Table 4. The factor independently associated with a higher 30-day mortality rate was endotracheal tube intubation (adjusted OR 3.12, 95% CI 1.32-7.38). Achievement of at least two EGDT goals was associated with lower mortality rate (adjusted OR 0.41, 95% CI 0.19-0.89).

Discussion

In the present study, compliance to the sepsis resuscitation guidelines was found to be moderately successful in the Emergency Department of Siriraj Hospital. More than half of patients received antibiotics within one hour after diagnosis. By using guidelines, early fluid therapy was given, as evidenced from crystalloids loading in almost all patients, followed by CVP placement, and vasopressor usage. A substantial proportion of patients had achieved at least one or two therapeutic goals at six-hour after diagnosis. This made the mortality of patients at the Emergency Department, Siriraj Hospital comparable to others[9,12-14,17]. However, venous oxygen saturation was assessed in very few patients. Most of the causative organisms were community-acquired bacteria, which responded to empirical antibiotics. The factor associated with high mortality was respiratory failure, which required endotracheal intubation, and the factor associated with survival was the achievement of at least two therapeutic goals.

Elimination of infection and source control are some of the most important parts of sepsis management. Several studies have demonstrated decreased mortality when appropriate antibiotics were administrated within one hour after diagnosis[16,18]. Recommendations were subsequently made in the Surviving Sepsis Guidelines[7,8]. However, in the present study, this practice was not associated with the mortality of patients. The sample size may have been too small because it was only calculated to find the overall mortality as the primary outcome.

The causative organisms reported here were important. They were gram-negative bacteria, which were consistent with the previous studies[5,12]. The present study showed only 8.6% antibiotic-resistant bacteria. This was lower than the study of Angkasekwinai[5], which reported a higher proportion of antibiotic resistant strains. This might have been because that study included patients in the inpatient wards, which could have had higher rates of hospital acquired infection.

The extent of guideline implementation measured by goal achievement was the achievement of at least one goal at six-hour in 86.8%, and at least two goals in 50.7%. This was less than previous studies. Nguyen et al reported their implementation of

the sepsis bundle in an emergency department. Fifty-three point seven percent achieved four EGDT goals and the mortality of this group was significantly lower compared with other groups that achieved fewer goals (p = 0.03)[11]. MacRedmon et al reported the achievement of all goals in 62.2% of their patients and the mortality in this group decreased from 51.4% to 27%[10]. Although the present study reported a lesser extent of achievement, the overall mortality was 39.6%. These different results might have been from the Emergency Department of Siriraj Hospital's guideline, which has differences with the EGDT protocol. Only the patients with uncertain volume status during fluid loading received central venous catheter placement. Those with blood pressure restored after fluid loading did not have a central venous catheter inserted, so did not have $ScvO_2$ analysis. Two patients (1.4%) achieved all goals, yet one of them died. The higher mortality rate in this group might have resulted from a few numbers and higher severity.

From multivariate analysis, patients with respiratory failure requiring endotracheal intubation had higher mortality rate. This reflected greater disease severity, which may have been from the underlying disease or the severity of the shock itself.

The limitations of the present study were incomplete data collections in some patients and absence of recording of the fluid given per hour. In addition, the present study aimed to assess the mortality, so the sample sizes may not have sufficient power to identify some factors associated with mortality such as achieving all EGDT goals or receiving appropriate antibiotics within one hour.

In conclusion, after implementation of sepsis/septic shock resuscitation guidelines, the compliance was moderately successful. More than half of patients achieved at least two therapeutic goals. Thirty-day mortality was 39.6%. Respiratory failure requiring intubation was associated with higher mortality. The achievement of at least two EGDT goals was associated with lower mortality.

What is already known on this topic?

A series of Surviving Sepsis Campaign International Guidelines consisting of early goal-directed hemodynamic resuscitation, organ support, and source control have been announced in 2004. This has led to worldwide implementation. Many publications have supported the benefit of these measures[1-8]. Although worldwide studies were conducted in various setting, in Thailand, most of studies were undertaken in intensive care units and inpatient wards[9-11].

What this study adds?

The Siriraj Septic Shock Guidelines have been modified from the Surviving Sepsis Campaign International Guidelines and used in the Emergency Department, Siriraj Hospital since 2005. The purpose of the study was to ascertain treatment outcomes after guidelines application.

Potential conflicts of interest

None.

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การศึกษาผลของการนำแนวทางการรักษาผู้ป่วยที่มีภาวะติดเชื้อในกระแสเลือดมาปรับใช้ในห้องฉุกเฉิน โรงพยาบาลศิริราช

ธันยพร นครชัย, อุษาพรรณ สุรเบญจวงศ์, อภิชญา มั่นสมบูรณ์, ณัฐกานต์ ประพฤติกิจ, ทิพา ชาคร

วัตถุประสงค์: ห้องฉุกเฉินของโรงพยาบาลศิริราชได้นำแนวทางการรักษาผู้ป่วยติดเชื้อในกระแสเลือดมาปรับใช้ตั้งแต่ พ.ศ. 2548 แต่ยังไม่เคยมีการเก็บข้อมูลผู้ป่วยหลังใช้แนวทางการรักษา การศึกษานี้จัดทำขึ้นเพื่อศึกษาหาผลลัพธ์การรักษาดังกล่าว

วัสดุและวิธีการ: เป็นการศึกษาแบบติดตามผลไปข้างหน้า โดยเก็บข้อมูลของผู้ป่วยที่อายุมากกว่า 18 ปี ที่ติดเชื้อในกระแสเลือดรุนแรง หรือ มีภาวะช็อกจากการติดเชื้อ (severe sepsis and septic shock) ที่เข้ามารับการรักษาที่ห้องฉุกเฉินของโรงพยาบาลศิริราช ตั้งแต่ วันที่ 12 มกราคม พ.ศ. 2554 ถึง 2 ตุลาคม พ.ศ. 2554 ข้อมูลพื้นฐาน และผลการรักษาของผู้ป่วยจะถูกบันทึกไว้ เพื่อศึกษาหาอัตราการเสียชีวิตใน 30 วัน

ผลการศึกษา: มีผู้ป่วยอยู่ในการศึกษาทั้งหมด 144 ราย (ผู้ป่วยติดเชื้อในกระแสเลือดรุนแรงร้อยละ 34 และผู้ป่วยที่มีภาวะช็อกจากการติดเชื้อในกระแสเลือดร้อยละ 66) อัตราการเสียชีวิตใน 30 วัน เท่ากับร้อยละ 39.6 ผู้ป่วยที่ได้ยาปฏิชีวนะภายใน 1 ชั่วโมง มีจำนวนร้อยละ 52.2 อัตราการรักษาจนบรรลุเป้าหมายตาม early goal-directed therapy อย่างน้อย 1 และ 2 ข้อ เท่ากับ ร้อยละ 86.8 และ ร้อยละ 50.7 ตามลำดับ การรักษาจนบรรลุเป้าหมายอย่างน้อย 2 ข้อ เป็นปัจจัยที่ช่วยลดอัตราการเสียชีวิต (adjusted OR 0.41, 95% CI 0.19-0.89) มีผู้ป่วย 2 ราย ที่ได้รับการรักษาจนบรรลุเป้าหมายครบทั้ง 4 ข้อ ภายใน 6 ชั่วโมง (ร้อยละ 1.4) ปัจจัยที่ทำให้อัตราการเสียชีวิตเพิ่มขึ้น คือ ระบบหายใจวายจนมีการใส่ท่อช่วยหายใจ (adjusted OR 3.12, 95% CI 1.32-7.38)

สรุป: อัตราการเสียชีวิตใน 30 วันของผู้ป่วยที่มีภาวะติดเชื้อในกระแสเลือดรุนแรงและผู้ป่วยที่มีภาวะช็อกจากการติดเชื้อที่ได้รับการรักษาในห้องฉุกเฉินของโรงพยาบาลศิริราช หลังจากเริ่มใช้แนวทางการรักษาเท่ากับร้อยละ 39.6 การรักษาจนบรรลุเป้าหมายอย่างน้อย 2 ข้อ เป็นปัจจัยที่ช่วยลดอัตราการเสียชีวิต และระบบหายใจวายจนมีการใส่ท่อช่วยหายใจเป็นปัจจัยที่ทำให้อัตราการเสียชีวิตเพิ่มขึ้น