

Factors Influencing Clinical Deterioration in Persons with Sepsis

Patiporn Bunyaphatkun, Siriorn Sindhu*, Patricia M Davidson, Ketsarin Utriyaprasit,
Chukiat Viwatwongkasem, Wittaya Chartbunchachai

Abstract: Sepsis is a common problem in patients in emergency rooms that need proper management within 72 hours to prevent clinical deterioration. The objective of this study was to determine factors influencing the clinical deterioration of persons with sepsis. A descriptive correlation study was conducted from September 2014 to February 2015 at 11 hospitals in central Thailand. Recruited into the study were 172 participants presenting with ≥ 2 criteria of systemic inflammatory response syndrome without white blood cell count and shock index ≥ 1 at triage, and diagnosed with infectious disease at the 11 emergency departments. Data were collected through interviews, physical examinations and reviewing patients' charts and were analyzed using descriptive statistics and binary logistic regression.

Results showed that symptoms of clinical deterioration manifested in 59.3% of participants. Over 40% demonstrated failure of the circulatory system occurred among 77.5% participants within 24 hours of emergency department arrival. Factors influencing clinical deterioration were higher severity of illness, incomplete triage practices and non-achieved performance of sepsis resuscitation bundle. These factors explained 22% of the variance of clinical deterioration. The implications for nursing practice in improving sepsis care are provision of triage training, development of sepsis fast track, and encouragement of compliances with triage assessment protocols and sepsis resuscitation bundle.

Pacific Rim Int J Nurs Res 2017; 21(2) 135-147

Keywords : Clinical deterioration, Emergency care, Influencing factors, Sepsis, Shock, Thailand

Introduction

Sepsis exerts a heavy burden on global healthcare systems, particularly in developing countries. The total mortality rate due to sepsis is about 60–80%.¹ In Thailand, sepsis complications are associated with mortality rates of over 50.0%,² in contrast to less than 20% in developed countries.³ Sepsis is a systemic response when pathogenic organisms spread into the bloodstream. Physiological derangements result in global tissue hypoxia from micro- and macro-circulatory dysfunction leading to hypoperfusion and organ dysfunction.⁴ Clinical deterioration manifests as

Patiporn Bunyaphatkun PhD candidate, Joint Program between Faculty of Nursing and Ramathibodi School of Nursing Faculty of Medicine Ramathibodi Hospital, Mahidol University, 2 Phrannok road, Bangkok 10700, Thailand **E-mail:** avajiraed@gmail.com

Siriorn Sindhu[†] PhD Nursing, Associate Professor., Faculty of Nursing, Mahidol University, 2 Phrannok road, Bangkok 10700, Thailand. **E-mail:** siriorn.sin@mahidol.ac.th

Patricia M Davidson PhD Nursing., Dean and Professor, Johns Hopkins University School of Nursing, 525 N. Wolfe street, Baltimore, MD, 21205, U.S. **E-mail:** pdavidson@jhu.edu

Ketsarin Utriyaprasit Associate Professor., Faculty of Nursing, Mahidol University, 2 Phrannok road, Bangkok 10700, Thailand **E-mail:** ketsarin.utr@mahidol.ac.th

Chukiat Viwatwongkasem Associate Professor., Department of Biostatistics, Faculty of Public Health, Mahidol University 420/1 Ratchawithi road, Bangkok 10400, Thailand. **E-mail:** chukiat.viw@mahidol.ac.th

Wittaya Chartbunchachai MD Dip.Thai Board of Surgery, Director of Trauma Center and Critical Care, Khon Kaen Hospital, 54 Srijan road, Khon Kaen 40000, Thailand. **E-mail:** buncha96@yahoo.com

hypotension, oliguria, and alteration of consciousness. Previous studies in other countries found that the clinical signs of persons with sepsis were sensitive, changing to clinical deterioration or improvement within 72 hours.^{5,6} Unfortunately, 17.8% of persons with sepsis progressed to shock⁷ and 38.6% exhibited respiratory compromised and/or alternation of consciousness within 48 hours after emergency department (ED) admission.⁸ Moreover, it was estimated that 30% of sepsis-related mortalities were preventable.⁹

To date, published studies have focused more on the factors affecting mortality than clinical deterioration in persons with sepsis. Severity of illness was also influenced by the access to appropriate care. Many patients with sepsis presented organ dysfunction and shock upon their first presentation to the ED.¹⁰ Higher sepsis acuity was correlated with an increased mortality rate,¹¹ especially when optimal care was delayed for persons with higher sepsis acuity.¹² Early access to definitive treatment was dependent on how triage nurses recognized sepsis as a time-sensitive illness. Triage practice is vital for initiating timely sepsis treatment, but it was generally accorded lower priority, which led to inferior health outcomes.¹³ Triage allocation could also be associated with adherence to the sepsis resuscitation bundle, leading to an increase in hospital mortality.¹⁴ All of these factors were risk factors associated with timely access and mortality in persons with sepsis; if they had timely access to ED and treatment including effective triage practice and compliance with practice guidelines, their clinical outcomes would be vastly improved.

In Thailand, many studies have revealed the impacts of limited resources and contradictory policies on patient outcomes. The early detection of sepsis with hypoperfusion by lactate measurement has been identified as rare, as well as the uptake of invasive monitoring.² Some hospitals initiated the sepsis resuscitation bundle when providers detected the clinical signs of sepsis with hypoperfusion or organ dysfunction by physical assessment,¹⁵ while others

started it when sepsis was diagnosed by laboratory results.² In medical ward settings, previous studies showed that 38.8% of persons diagnosed with sepsis deteriorated due to septic shock.¹⁶ Knowing the factors that contribute to clinical deterioration is necessary to reduce mortality rates, but limited studies have been conducted in this area. Thus this study explored factors in the clinical deterioration in persons with sepsis, particularly in emergency departments, where the nature of care is particularly crucial.

Review of Literature

Previous literature identified that the clinical outcomes of time-sensitive illness depended on three components related to emergency care: no delay in seeking care, timely access to care, and adequate and appropriate care.¹⁷ These have been defined as patient and emergency care factors. Health-seeking care depended on patient factors, including the time of perceived symptom onset and severity of illness.¹⁸ Factors in emergency care included triage practice for timely access to care¹⁹ and the performance of sepsis resuscitation bundle, following appropriate guidelines.²⁰

Sepsis manifests in systemic responses when the uncontrolled infection occurs in the systemic circulation by primarily stimulating the signs of systemic inflammatory response syndrome (SIRS). When sepsis affects the cardiovascular system, inadequate oxygen and tissue perfusion, as well as anaerobic metabolism occur. It leads to accumulated serum lactate level, known as sepsis with hypoperfusion.⁴ The severity of illness in sepsis is defined as the vulnerability of predisposition, infection, response, and organ dysfunction.²¹ Predisposing factors include increased age and comorbidity, which increase susceptibility and exaggerated response to infection due to decreased immune-competence and continued chronic inflammation. Organ dysfunction is associated with deteriorating function in the cardiovascular, respiratory, renal, neurologic, hepatic and hematologic

systems, when the onset of organ dysfunction is more than 48 hours prior to receiving necessary care, the risk of death increases 8.73 times.¹² There is limited data describing when persons with sepsis should seek emergency care relative to the onset of symptoms.²² In Thailand, many people with pneumonia had time to perceive symptom onset or a had a chief complaint of more than seven days in length. The majority required hospitalization because of the high severity of illness.²³

Triage practice is instituted to provide a quick and accurate assessment of a person's clinical condition and acuity level to streamline the subsequent consultation with a physician or another specialist health professional. It is particularly important for early sepsis recognition. Sepsis itself is difficult to identify,²⁴ with diagnosis being dependent on objective assessment. Persons are assigned a triage acuity level based on assessment and documentation of complete vital signs and clinical signs of organ dysfunctions, including alteration of conscious, hypotension and hypoxemia. When the SIRS criteria and clinical signs of organ dysfunction are used for early detection, the 28-day mortality and in-hospital mortality are lower than SIRS assessment alone.²⁵ The Emergency Severity Index (ESI) determines triage acuity level according to physiological changes in sepsis, whereby the criteria of level 1 includes clinical signs of hypoperfusion or organ dysfunctions, and level 2 is defined by the potential threat to life due to hypoperfusion.²⁶ When persons with sepsis are assigned a high severity of

triage acuity level according the severity of clinical signs, they are more than twice as likely to have faster access time to treatment.¹⁹

A sepsis resuscitation bundle is defined as the combination of evidence-based practices of medical treatment and monitoring, including fluid challenge, broad spectrum antibiotic administration, the achieved goals of urine output, mean arterial pressure (MAP), central venous pressure (CVP), and central venous oxygen saturation (ScvO₂).²⁰ Completing the performance of sepsis resuscitation bundle within six hours results in reduced mortality compared with standard care.²⁷ However, evidence shows that medical treatment and non-invasive monitoring only is associated with a decreased mortality rate in persons with sepsis.²⁸

When sepsis presents with hypoperfusion it is a poor prognostic marker because the clinical signs of vital organs are a high risk to deterioration within 72 hours of cardiovascular, renal, respiratory and neurological function.⁶ Clinical deterioration is defined as the worsening of vital signs and other clinical observations after a period of resuscitation or six hours of arrival. If the clinical signs deteriorate, patients are at an increased risk of death.⁸ Therefore, this study aimed to determine how much time is involved to perceive symptom onset, severity of illness, triage practice, and performance of sepsis resuscitation bundle influencing clinical deterioration in persons with sepsis, as shown in the research framework in Figure1.

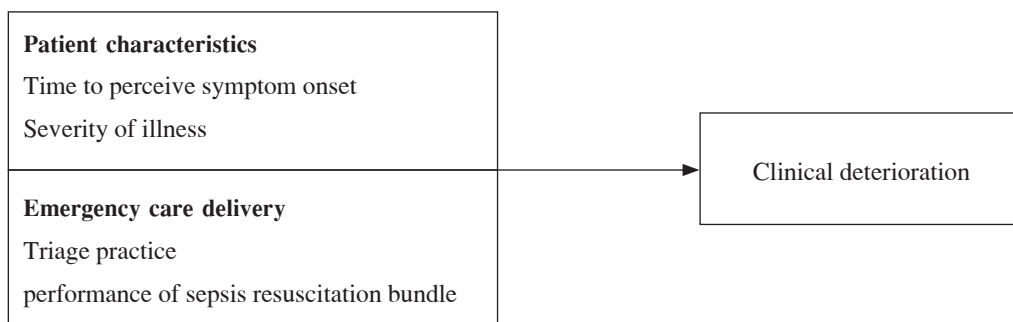


Figure 1 Research framework

Methods

Design: A descriptive correlational design was used for this study.

Sample and Setting: Purposive sampling was used. The potential participants were eligible when they presented to triage with signs of sepsis and hypoperfusion, including at least two SIRS criteria without white blood count (body temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$, pulse rate >90 beats/min and respiratory rate >20 breaths/min)²⁹ and shock index ≥ 1 ³⁰ (the ratio of heart rate per a minute to systolic blood pressure at more than or equal to one). The inclusion criteria were broad, limiting participation to those aged 18 years and older, diagnosed with an infectious disease. The exclusion criteria included: 1) need for immediate surgery; 2) diagnosis of dengue hemorrhagic fever or malaria; 3) referral from another hospital with fluid challenge and/or antibiotic in progress; 4) death within six hours following ED arrival; and 5) discharge within 72 hours since ED arrival.

The sample size of this study was 168 following the formula for logistic regression,³¹ calculated with a power of 0.80 and a 99.0% confidence level, the 3.10 odds ratio for clinical deterioration in persons with infection and SIRS,⁸ the 0.28 for the proportion of clinical deterioration⁸, and a 15.0% dropout rate. The study was conducted at the ED of five regional hospitals and six general hospitals in central Thailand. The research settings were selected with two-stage random sampling for the provinces and then the hospitals.

Ethical Considerations: The study was approved with ethical clearance and was considered risk-free for the participants through the process of Institutional Review Board (No.IRB-NS2O 141248.1908 Mahidol University). The principle investigator (PI) or research assistant (RA) approached the potential participants and/or family after six hours after ED admission and when the clinical signs of the potential participants

were stable. The participants were willing to participate in the study, and written informed consent was obtained before their recruitment. It was explained that they had the right to withdraw from the study at any time if they wished, without any effects on the treatment and care they would receive from the hospitals or their statutory rights.

Instruments:

There were six instruments used to obtain the data including patient characteristics, the time to perceive symptom onset, the severity of illness, the triage practice, performance of sepsis resuscitation bundle, and clinical deterioration. The overall of content validity index of all measures were judged 1.00 by a panel of five experts including one emergency physician, one chief nurse of ED, two head nurses of ED, and one lecturer in a school of nursing. Interrater reliability was assessed for 10 patients between the PI and research assistants (RAs) in all settings, identifying acceptable values of 0.89–1.00.

Patient characteristics comprised of demographic data about age, gender, comorbidity, chief complaint, diagnosis, and physiological parameters within six hours of arrival. It was collected by reviewing patients' charts.

The time to perceive symptom onset was the duration between the time of the perceived chief complaint and the time of ED arrival, counted in hours. It was obtained by interview the persons or their families if their consciousness altered after six hours of arrival at ED or any medical wards where the persons were admitted.

The severity of illness was measured with the Mortality in Emergency Department Sepsis (MEDS) score.¹¹ There are nine criteria. The scores of criteria are as following: **6** for metastatic cancer; **3** for age >65 years, band $>5\%$, platelet count $<150,000$ cell/mm³, tachypnea (respiratory rate >20 breaths/min) or hypoxemia (pulse oximetry saturation $<90\%$), and septic shock (systolic blood pressure <90 mmHg after an initial fluid challenge 30 ml/kg within three

hours); and 2 for lower respiratory infection (bronchitis or pneumonia), alteration of conscious, and nursing home resident. The aggregated score reflected the severity of illness ranging from 0 to 27 points. A higher score represents a higher severity. The risk groups of 28-day mortality were assigned as described: 0 – 7 points for low, 8 – 12 points for moderate, ≥ 13 points for high. The overall accuracy of MEDS score was 76% and 82% in the validation and derivation sets respectively for prediction of the 28-day mortality in infected patients. It was collected by reviewing patients' charts.

The triage practice was categorized as persons either receiving a complete or incomplete triage practice. The complete triage practice depends on 4 components: 1) complete vital signs assessment (blood pressure, pulse rate, respiratory rate, and body temperature); 2) one or more organ function assessment (oxygen saturation and level of consciousness); 3) an accuracy of the triage acuity level following the Emergency Severity Index (ESI),²⁶ which stated the criteria **level I** having clinical signs of organ dysfunction including oxygen saturation $<90.0\%$, acute mental status deterioration to pain stimuli or unresponsiveness, and/or SBP <90 mmHg, and **level II** having the potential threat to life with shock index ≥ 1 ³⁰ for this study; and 4) the access time to care was immediately and within 10 minutes for the triage acuity **level I and II** respectively. The completion of all components was scored 0 and the incomplete in any component was scored 1. It was collected by reviewing patients' charts.

Performance of sepsis resuscitation bundle was categorized as persons receiving either achieved or non-achieved of medical treatment and noninvasive monitoring following the Surviving Sepsis Campaign 2012.²⁰ There are 4 components: 1) fluid challenge at least 30 ml/kg within three hours, 2) broad spectrum antibiotic administration within one hour, 3) maintain MAP ≥ 65 mmHg and 4) maintain urine output ≥ 0.50 ml/kg/hr within six

hours. The achieved time was counted from the initial time of ED arrival. The achieved all components was scored 0 and the non-achieved in any component was scored 1. It was collected by reviewing patients' charts.

Clinical deterioration was collected by physical assessment for baseline of physiological parameters and then continued every four hours or when the persons were unstable until 72 hours at ED or any medical wards where the persons were admitted. It was measured with the single-parameter criteria of medical emergency team (MET).³² There are six physiological parameters in three systems as follows: 1) respiratory system consisting of respiratory rate and oxygen saturation; 2) circulatory system consisting of systolic blood pressure (SBP), pulse rate and urine output; and 3) neurological system was scored using the Glasgow Coma Scale (GCS). The clinical deterioration determined by the worsening of any parameter was compared at two time points: at six hours of ED arrival, and the first detected signs of clinical deterioration after 6–72 hours of ED arrival. The score was 1 when the value of any of the following parameters deteriorated from the baseline of six hours: 1) respiratory rate <8 or >30 breaths/min; 2) oxygen saturation $<90\%$ in the presence of oxygen supplementation; 3) SBP <90 mmHg; 4) pulse rate <40 or >130 beats/min; 5) urine output <50 ml per four hours; and 6) acute alteration of conscious with decreased GCS. If the clinical deterioration was not found in all parameters, the score was 0. This instrument is used with significant effect for the early detection of clinical deterioration in sepsis.³² The MET activation criteria (considering the parameters of respiratory rate, heart rate, systolic blood pressure, and level of consciousness) showed the overall accuracy was 71%–79% with the area under receiver operating characteristics.³³ The physiological parameters in severity of illness and clinical deterioration were not

the same; the former used the physiological data as weighted score at first time in ED while the latter compared data between six hours and after 6–72 hours.

Data Collection

After receiving permission from each hospital, the PI asked for a RA in each hospital with qualifications of professional nurse and nursing experience of at least one year. These RAs were trained comprehensively in data collection. When the informed consent was signed at six hours following ED arrival, the PI or RA started to collect the data. Data collection were from September 2014 to February 2015.

Data Analysis

The data were analyzed using descriptive statistics to analyze the factors of time to perceive symptom onset, severity of illness, triage practice, and performance of sepsis resuscitation bundle. These factors were used to examine the association with clinical deterioration using chi-square or Fisher's exact test. The univariate and multivariate analysis of the factors influencing clinical deterioration were performed by binary logistic regression to determine statistical significance with 95.0% confidence level. SPSS (version 18.0) was used for the analysis.

Results

Data were obtained from a total of 172 participants, more than half of whom were ≥ 65 years (58.1%), and male (54.7%) with an underlying comorbidity (79.1%), especially hypertension (36.0%) and diabetes (26.7%). Alteration of consciousness (50.0%) and dyspnea (29.1%) were the common chief complaints, while signs of tachypnea or hypoxia (86.6%) and alteration of conscious (58.1%) were usually found by first physical examination on ED arrival. The most common sites of infection were lower respiratory (47.1%), urinary tract (24.4%),

gastrointestinal (16.9%) and others (11.6%). In most instances the severity of illness presented as moderate (48.8%) to high (27.3%). Septic shock was found in 78 participants (45.3%) within three hours after ED admission, even though 32 of them had SBP ≥ 90 mmHg on arrival. A total of 50 participants deteriorated to SBP < 90 mmHg from the 110 who had SBP ≥ 90 mmHg on arrival.

Table 1 shows that the clinical deterioration was associated with the severity of illness, particularly in the components of lower respiratory infection and the signs of tachypnea or hypoxia, inaccuracy of triage acuity level, and non-achieved access time to care especially non-achieved MAP ≥ 65 mmHg within six hours.

Table 2 shows that 102 participants presented the clinical deterioration after six to 72 hours. Most of them deteriorated within 24 hours of ED arrival in the circulatory system. Next, the deterioration of circulatory system with the neurological system was frequently found. For univariate analysis, three out of four factors were significantly associated with this clinical deterioration, except time to perceived symptom onset ($p=0.17$). Table 3 presents multivariate analysis data for the three factors severity of illness, triage practice and performance of sepsis resuscitation bundle. They were all associated with clinical deterioration after 6–72 hours of ED arrival, with 22% variance. The results can be summarized as: 1) a one-unit increase in the severity of illness or MEDS score, whereby the probability of clinical deterioration increased by 22.0%; 2) the participants who did not achieved performance of sepsis resuscitation bundle increased the probability of clinical deterioration by 6.5 times than patients did; and 3) the incomplete triage practice increased the probability of clinical deterioration by 2.1 times compared to complete triage practice.

Table 1 The association between severity of illness, time to perceive symptom onset, triage practice, performance of sepsis resuscitation and clinical deterioration (n=172)

Factors	Clinical deterioration (n=102)		No clinical deterioration (n=70)		χ^2	p-value
	n	%	n	%		
Severity of illness					16.81	0.001 ^{bb}
Low (0-7)	14	13.7	27	38.6		
Moderate (8-12)	52	51.0	32	45.7		
High (≥ 13)	36	35.3	11	15.7		
$\bar{X} \pm SD$	10.80 \pm 3.75		8.49 \pm 3.40			
- Predisposition						
Age >65 years	59	57.8	41	58.6	0.01	0.927
Nursing home resident	3	2.9	2	2.9		0.974 ^a
Metastatic cancer	16	15.7	5	7.1	2.83	0.093
- Infection						
Lower respiratory infection	58	56.9	23	32.9	9.60	0.002 ^b
- Response						
Band >5%	18	17.6	8	11.4	1.25	0.263
- Organ dysfunction						
Tachypnea or hypoxemia	95	93.1	54	77.1	9.17	0.002 ^b
Septic shock	46	45.1	32	45.7	0.01	0.936
Platelet count <150,000/mm ³	32	31.4	15	21.4	2.07	0.151
Alteration of conscious	65	63.7	35	50.0	3.21	0.073
Time to perceive symptom onset					2.78	0.249
≤ 24 hours	36	35.3	31	44.3		
25 – 72 hours	38	37.3	27	38.6		
>72 hours	28	27.5	12	17.1		
$\bar{X} \pm SD$	74.47 \pm 77.12		57.97 \pm 72.83			
Triage practice					7.31	0.008 ^b
Complete	37	36.3	40	57.1		
Incomplete	65	63.7	30	42.9		
Incomplete initial vital signs	2	2.0	0	0		0.514 ^a
Incomplete organ function assessments	11	10.8	7	10.0	0.03	0.869
Inaccuracy of triage acuity level	49	48.0	22	31.4	4.73	0.030 ^b
Non-achieved access time to care	64	62.7	30	42.9	6.63	0.010 ^b
Performance of sepsis resuscitation bundle					7.65	0.006 ^b
Achieved	3	2.9	10	14.3		
Non-achieved	99	97.1	60	85.7		
Non-achieved fluid challenge	78	76.5	48	68.6	1.32	0.250
Non-achieved antibiotic administration	65	63.7	42	60.0	0.25	0.621
Non-achieved MAP	24	23.5	4	5.7	9.67	0.002 ^b
Non-achieved urine output	30	29.4	14	20.0	1.93	0.165

^a Fisher's Exact test

^b <0.05 ^{bb} <0.001

Table 2 Frequency and percentage of the characteristics of clinical deterioration (n=102)

Clinical deterioration	n	%
Clinical deterioration with one system		
Circulatory	41	40.2
Respiratory	3	2.9
Neurological	1	1.0
Clinical deterioration with two systems		
Circulatory and Neurological	26	25.5
Respiratory and Circulatory	13	12.7
Respiratory and Neurological	2	2.0
Clinical deterioration with three systems		
Respiratory, Circulatory and Neurological	16	15.7
Circulatory deterioration		
SBP <90 mmHg	43	42.2
Pulse rate ≥ 130 beats/min	9	8.8
Urine output <100ml/4hours	9	8.8
SBP < 90 and pulse rate ≥ 130 beats/min	7	6.9
SBP <90 and urine <100ml/4hours	17	16.7
Pulse rate ≥ 130 and urine <100ml/4 hours	1	1.0
SBP <90, Pulse rate ≥ 130 and urine <100ml/4 hours	10	9.8
Respiratory deterioration		
Respiratory rate ≥ 30 breaths/min	16	15.7
Oxygen saturation <90%	11	10.8
Respiratory rate ≥ 30 breaths/min and oxygen saturation <90%	7	6.9
Neurological deterioration		
Decreased GCS	45	44.1
Time to present clinical deterioration		
≤ 24 hours	79	77.5
25 – 48 hours	14	13.7
49 – 72 hours	9	8.8

Table 3 Multivariate logistic regression analysis of predictive model of the clinical deterioration in persons with sepsis (n=172)

Factors	b	S.E.	Wald	p	Exp (B)	95%CI
Severity of illness (MEDS score)	0.20	0.05	15.34	0.001**	1.22	1.10–1.35
Triage practice						
Complete						
Incomplete	0.72	0.35	4.33	0.037*	2.05	1.04–4.03
Performance of sepsis resuscitation bundle						
Achieved						
Non-achieved	1.88	0.77	6.01	0.014*	6.53	1.46–29.29
Constant	-3.66	0.96				

* $p < 0.05$, ** $p \leq 0.001$

-2LL = 201.61, Nagelkerke R Square = 0.22

Discussion

Higher severity of illness results in clinical deterioration

This study clearly demonstrated that clinical deterioration was closely related to higher severity of illness. Most participants (76.2%) showed moderate to high severity of illness. Although more than half were >65 years (57.6%), this older age was not associated with clinical deterioration, which has been a controversial subject in the literature.⁷ This might be explained by the fact that all adults and older adults came with an elevated shock index, indicating more severity with sustained inadequate oxygen delivery and left ventricular dysfunction.³⁴ Noticeably, many participants progressed to septic shock within three hours. Although 64% (n=110) arrived in ED with SBP \geq 90 mmHg, 50 participants deteriorated to SBP <90 mmHg and then 32 progressed to septic shock later. However, the condition of septic shock was not associated with clinical deterioration, which depended on keeping normal MAP within six hours. Persons who did not present septic shock on arrival had high probability to progress to septic shock within 72 hours.³⁵

The results revealed that participants identified with tachypnea or hypoxemia and diagnosed with lower respiratory infection most commonly experienced clinical deterioration, which could be due to particular issues involved in lower respiratory infection. Nearly 50% were diagnosed with lower respiratory infection while only 29.1% presented a chief complaint with dyspnea. Alteration of consciousness (50%) was a common chief complaint in the study. These data showed that the participants with lower respiratory infection presented higher severity with hypoxic symptoms on arrival. Hypoxia (failure of oxygenation) at tissue level resulted from hypoxemia (less than normal of arterial oxygen tension), leading to depressed organ function, such as neurological functions.⁴ Previous research showed that when persons with pneumonia decline to hypoxemia or confusion, the access time

for early antibiotic administration is not associated with mortality.³⁶

Inadequate emergency care delivery aggravating clinical deterioration

Clinical deterioration occurred significantly when the delivery of emergency care was inadequate. We demonstrated that when the triage nurse did not complete triage practice including alerting access time to care following the triage acuity level, the probability of clinical deterioration in participants with sepsis increased significantly. There are two possible reasons to explain this observation. First, the Emergency Severity Index criteria determined the triage acuity level II with generalized high risk situation, not to identify shock index \geq 1 as the potential treat of hypoperfusion in sepsis.^{26,30} Second, the Thai National Institute for Emergency Medicine prescribed the ESI criteria for nationwide use, but did not regulate time to care following triage acuity level.³⁷ The access time to care could be achieved from the agreement of clinical impression between triage nurses and physicians based on the policy of contemporary triage criteria for sepsis, and a concordance between the severity of sepsis and access time to care.³⁸

Moreover, only 7.6% of participants achieved performance of the sepsis resuscitation bundle in this study. It might be that the goals of access time to care were counted since triage in this study while it was determined by the time of medical diagnosis in most settings. Although the new definitions of sepsis are more dependent on laboratory testing,³⁹ the results support earlier detection by triage nurses using sepsis fast track guidelines. In previous studies the mortality rate of persons with sepsis was found to decrease when the triage nurse detected the clinical signs of sepsis and hypoperfusion, which led them to the sepsis guidelines.¹⁵ However, the results supported to control the achieved MAP to decrease a probability of clinical deterioration only. For this reason, the sepsis resuscitation bundle could be started considering the criteria shock of MAP²⁰ in patients with sepsis in

addition to the elevated shock index⁴⁰ to prevent clinical deterioration in the cardiovascular system and decrease mortality by improving the effectiveness of fluid resuscitation and early antibiotic administration.²⁰

Improvement of the fitted model

Since the factors identified in this study explained only about 22% of variance, any additional information or factors must be considered for further study to predict clinical deterioration in patients with sepsis. Existing strategies of sepsis policy included a protocol, an educational program, and a quality improvement program, which influenced the improvement of sepsis treatment.²⁵ Health workforce issues included competencies, specialist skill and workload, such the fulltime intensivist and a nurse-to-patient ratio of 1:2 being found to influence complete compliance with sepsis resuscitation bundle.¹⁴ Finally, the different locations of admission affect different outcomes, such as persons admitted to general wards having a prolonged duration of organ dysfunction without treatment compared to ICU admissions.¹² Furthermore, persons with infection displayed worse clinical signs within 48 hours compared to those without an infection in general wards.⁸

Limitations

The study design was limited by two potential types of bias pertaining to three factors in data collection. First, recall bias was likely to be greater among participants and relatives in their interviews concerning data on the time of perceived symptom onset. Logically, the data might be less reliable when participants had been asked for recall a short time after they had been seriously ill, especially from secondary sources such as relatives who did not have direct exposure. Second, there was potential for information bias due to the data collection regarding triage practice and the performance of sepsis resuscitation bundle retrospectively via chart review. Thus, the findings of this study must be interpreted with caution. For future

research, it is suggested to minimize recall bias and prevent information bias with the prospective cohort study. In addition, others variables need to be included in the model like sepsis policy, health workforce issues, and location of admission in order to improve the model validity and increase the ability to explain the variance.

Conclusions and Implications for Nursing Practice

Targeting factors of patient characteristics and emergency care delivery was essential to improve health outcomes in sepsis, emphasizing a need to improve both the pre-hospital and in-hospital phases. Delayed symptom recognition by persons and later presentation to the ED influences health outcomes. Moreover, low adherence with practice guidelines was noted. The implications for nursing practice most obviously pertain to implementation, particularly to promote public awareness of the signs and symptoms of organ compromise when infectious disease is suspected, especially in lower respiratory infection; implementation of robust triage processes with the completion of all components in triage practice; and implementation of evidence-based guidelines considering SIRS criteria and shock index ≥ 1 at triage to indicate sepsis fast track; and count the achieved time of performance of sepsis resuscitation at first time of ED admission, especially the achieved MAP.

The SIRS criteria used in this study to define sepsis have been abrogated in many health systems by new guidelines, particularly concerning sepsis-3, under the third international consensus,³⁹ regarding sepsis essentially as a life-threatening organ dysfunction instead of using SIRS criteria. However, the new model is based on laboratory confirmation of possible sepsis following Sequential Organ Failure Assessment (SOFA) score, which is not a feasible option in practice in many health services in Thailand due to limited resources.²

Acknowledgements

We would like to thank the Bangkok Metropolitan Administration for the scholarship and the National Institute for Emergency Medicine of Thailand for a research grant for this research.

References

1. World Sepsis Day. Fact Sheet Sepsis September 2013. [cited 2014 March 4]. Available from: http://www.world-sepsis-day.org/CONTENTPIC/2015_WSD_FactSheet_long_English.
2. Mahavanakul W, Nickerson EK, Srisomang P, Teparrukkul P, Lorvinitnun P, Wongyingsinn M, et al. Feasibility of modified surviving sepsis campaign guidelines in a resource-restricted setting based on a cohort study of severe *S. aureus* sepsis. *PLoS One*. 2012;7(2):e29858.
3. Kaukonen KM, Bailey M, Suzuki S, Pilcher D, Bellomo R. Mortality related to severe sepsis and septic shock among critically ill patients in Australia and New Zealand, 2000–2012. *JAMA*. 2014;311(13):1308–16.
4. Abraham E, Singer M. Mechanisms of sepsis-induced organ dysfunction. *Crit Care Med*. 2007;35(10):2408–16.
5. Levy MM, Macias WL, Vincent JL, Russell JA, Silva E, Trzaskoma B, et al. Early changes in organ function predict eventual survival in severe sepsis. *Crit Care Med*. 2005;33(10):2194–201.
6. Vosylius S, Sipylaite J, Ivaskевичius J. Sequential organ failure assessment score as the determinant of outcome for patients with severe sepsis. *Croat Med J*. 2004;45(6):715–20.
7. Glickman SW, Cairns CB, Otero RM, Woods CW, Tsalik EL, Langley RJ, et al. Disease progression in hemodynamically stable patients presenting to the emergency department with sepsis. *Acad Emerg Med*. 2010;17(4):383–90.
8. Tsai JC-H, Cheng C-W, Weng S-J, Huang C-Y, Yen DH-T, Chen H-L. Comparison of Risks Factors for Unplanned ICU Transfer after ED Admission in Patients with Infections and Those without Infections. *The Scientific World Journal*. 2014;2014:10.
9. Lu TC, Tsai CL, Lee CC, Ko PC, Yen ZS, Yuan A, et al. Preventable deaths in patients admitted from emergency department. *Emerg Med J*. 2006;23(6):452–5.
10. Wang HE, Weaver MD, Shapiro NI, Yealy DM. Opportunities for Emergency Medical Services care of sepsis. *Resuscitation*. 2010;81(2):193–7.
11. Shapiro NI, Wolfe RE, Moore RB, Smith E, Burdick E, Bates DW. Mortality in Emergency Department Sepsis (MEDS) score: a prospectively derived and validated clinical prediction rule. *Crit Care Med*. 2003;31(3):670–5.
12. Freitas FG, Salomao R, Tereran N, Mazza BF, Assuncao M, Jackiu M, et al. The impact of duration of organ dysfunction on the outcome of patients with severe sepsis and septic shock. *Clinics*. 2008;63(4):483–8.
13. Yurkova I, Wolf L. Under-triage as a significant factor affecting transfer time between the emergency department and the intensive care unit. *J Emerg Nurs*. 2011;37(5):491–6.
14. Kim JH, Hong SK, Kim KC, Lee MG, Lee KM, Jung SS, et al. Influence of full-time intensivist and the nurse-to-patient ratio on the implementation of severe sepsis bundles in Korean intensive care units. *J Crit Care*. 2012;27(4):414 e11–21.
15. Champunot R, Kamsawang, N., Tuandoung, P., & Tansuphaswasdikul, S. Saving 500 Lives Campaign: another way to improve the mortality rate of patients with severe sepsis and septic shock. Poster presented in sepsis 2012. *Critical Care*. 2012;16(Suppl 3):P105.
16. Angkasekwinai N, Rattanaumpawan P, Thamlikitkul V. Epidemiology of sepsis in Siriraj Hospital 2007. *J Med Assoc Thai*. 2009;92 Suppl 2:S68–78.
17. Razzak JA, Kellermann AL. Emergency medical care in developing countries: is it worthwhile? *Bull World Health Organ*. 2002;80(11):900–5.
18. Herlitz J, Wireklintsundstrom B, Bang A, Berglund A, Svensson L, Blomstrand C. Early identification and delay to treatment in myocardial infarction and stroke: differences and similarities. *Scand J Trauma Resusc Emerg Med*. 2010;18:48.
19. Larsen GY, Mecham N, Greenberg R. An Emergency Department Septic Shock Protocol and Care Guideline for Children Initiated at Triage. *Pediatrics*. 2011;127(6):e1585–e92.
20. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. *Intensive Care Med*. 2013;39(2):165–228.

21. Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, et al. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Intensive Care Med.* 2003;29(4):530-8.
22. Herlitz J, Bang A, Wireklint-Sundstrom B, Axelsson C, Bremer A, Hagiwara M, et al. Suspicion and treatment of severe sepsis. An overview of the prehospital chain of care. *Scand J Trauma Resusc Emerg Med.* 2012;20:42.
23. Jordan HT, Prapasiri P, Areerat P, Anand S, Clague B, Sutthirattana S, et al. A comparison of population-based pneumonia surveillance and health-seeking behavior in two provinces in rural Thailand. *Int J Infect Dis.* 2009;13(3):355-61.
24. Begier EM, Sockwell D, Branch LM, Davies-Cole JO, Jones LH, Edwards L, et al. The National Capitol Region's Emergency Department syndromic surveillance system: do chief complaint and discharge diagnosis yield different results? *Emerg Infect Dis.* 2003;9(3):393-6.
25. Westphal GA, Koenig A, Caldeira Filho M, Feijo J, de Oliveira LT, Nunes F, et al. Reduced mortality after the implementation of a protocol for the early detection of severe sepsis. *J Crit Care.* 2011;26(1):76-81.
26. Gilboy N, Tanabe P, Travers D, Rosenau AM. Emergency Severity Index (ESI) A Triage Tool for Emergency Department Care Version 4: Implementation Handbook 2012 [cited 2014 May 18]. Available from <http://www.ahrq.gov/professionals/systems/hospital/esi/esihandbk>.
27. Nguyen HB, Kuan WS, Batech M, Shrikhande P, Mahadevan M, Li CH, et al. Outcome effectiveness of the severe sepsis resuscitation bundle with addition of lactate clearance as a bundle item: a multi-national evaluation. *Crit Care.* 2011;15(5):R229.
28. Hanzelka KM, Yeung SC, Chisholm G, Merriman KW, Gaeta S, Malik I, et al. Implementation of modified early-goal directed therapy for sepsis in the emergency center of a comprehensive cancer center. *Support Care Cancer.* 2013;21(3):727-34.
29. Bone RC, Grodzin CJ, Balk RA. Sepsis: a new hypothesis for pathogenesis of the disease process. *Chest.* 1997;112(1):235-43.
30. Berger T, Green J, Horeczko T, Hagar Y, Garg N, Suarez A, et al. Shock index and early recognition of sepsis in the emergency department: pilot study. *West J Emerg Med.* 2013;14(2):168-74.
31. Hsieh FY. Sample size tables for logistic regression. *Stat Med.* 1989;8(7):795-802.
32. Bellomo R, Goldsmith D, Uchino S, Buckmaster J, Hart G, Opdam H, et al. Prospective controlled trial of effect of medical emergency team on postoperative morbidity and mortality rates. *Crit Care Med.* 2004;32(4):916-21.
33. Cretikos M, Chen J, Hillman K, Bellomo R, Finfer S, Flabouris A, et al. The objective medical emergency team activation criteria: a case-control study. *Resuscitation.* 2007;73(1):62-72.
34. Rady MY, Smithline HA, Blake H, Nowak R, Rivers E. A comparison of the shock index and conventional vital signs to identify acute, critical illness in the emergency department. *Ann Emerg Med.* 1994;24(4):685-90.
35. Wira CR, Francis MW, Bhat S, Ehrman R, Conner D, Siegel M. The shock index as a predictor of vasopressor use in emergency department patients with severe sepsis. *West J Emerg Med.* 2014;15(1):60-6.
36. Cheng AC, Buising KL. Delayed administration of antibiotics and mortality in patients with community-acquired pneumonia. *Ann Emerg Med.* 2009;53(5):618-24.
37. National Institute of Emergency Medicine. Guidelines to follow the rules, criteria and procedures to sort and prioritize emergency care at the emergency room, according to the Emergency Medical Board. Nonthaburi: National Institute of Emergency Medicine; 2015.
38. Vegt AE, Holman M, ter Maaten JC. The value of the clinical impression in recognizing and treating sepsis patients in the emergency department. *Eur J Emerg Med.* 2012;19(6):373-8.
39. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA.* 2016;315(8):801-10.
40. Power GS, Harrison DA, Mouncey PR, Osborn TM, Harvey SE, Rowan KM. The Protocolised Management in Sepsis (ProMiSe) trial statistical analysis plan. *Crit Care Resusc.* 2013;15(4):311-7.

ปัจจัยที่มีอิทธิพลต่ออาการทรุดลงทางคลินิกในผู้ป่วยที่มีภาวะพิษเหตุติดเชื้อ

ปฏิพร บุญยพัฒนกุล ศิริอร สินธุ* Patricia Davidson เกศรินทร์ อุทธิยะประสิทธิ์ ชูเกียรติ วิวัฒนวงศ์เกษม
วิทยา ชาติบัญชาชัย

บทคัดย่อ: อาการทางคลินิกของภาวะพิษเหตุติดเชื้อมีโอกาสทรุดลงหรือดีขึ้นภายใน 72 ชั่วโมง ในขณะที่อาการทรุดลงทางคลินิกถือว่าเป็นอาการไม่พึงประสงค์ที่ยังคงพบได้ทั่วไป รวมทั้งประเทศไทย การวิจัยครั้งนี้มีวัตถุประสงค์เพื่อศึกษาปัจจัยที่มีอิทธิพลต่ออาการทรุดลงทางคลินิกในผู้ป่วยที่มีภาวะพิษเหตุติดเชื้อในภาคกลางของประเทศไทย การวิจัยเป็นลักษณะเชิงบรรยาย ทำการศึกษาระหว่าง 1 กันยายน 2557 ถึง 10 กุมภาพันธ์ 2558 ในโรงพยาบาลภาคกลางของประเทศไทยจำนวน 11 โรงพยาบาล กลุ่มตัวอย่างในการศึกษาจำนวน 172 ราย กำหนดคุณลักษณะคือ ผู้ที่มีอาการมากกว่าหรือเท่ากับ 2 เกณฑ์ของ systemic inflammatory response syndrome ยกเว้นผลตรวจเม็ดเลือดขาว ร่วมกับค่าดัชนีภาวะช็อกมากกว่าหรือเท่ากับ 1 ที่จุดคัดแยกและได้รับการวินิจฉัยโรคติดเชื้อที่ห้องฉุกเฉิน การเก็บข้อมูลดำเนินการโดยการสัมภาษณ์ การตรวจร่างกาย และการทบทวนเวชระเบียน การวิเคราะห์ข้อมูลใช้สถิติเชิงบรรยายและวิเคราะห์การถดถอยโลจิสติก

ผลการวิจัย พบว่า 59.3% ของผู้ป่วยที่มีภาวะพิษเหตุติดเชื้อมีอาการทางคลินิกทรุดลง โดยมากกว่า 40% มีอาการทรุดลงของระบบไหลเวียนและ 77.5% มีอาการทรุดลงภายใน 24 ชั่วโมง ปัจจัยที่มีอิทธิพลต่ออาการทรุดลงทางคลินิก ได้แก่ ความรุนแรงของอาการ การปฏิบัติการคัดแยกและการได้รับแผนการรักษาของผู้ที่มีภาวะพิษเหตุติดเชื้อ โดยทั้งสามปัจจัยร่วมกันอธิบายโอกาสเกิดอาการทรุดลงทางคลินิกของผู้ที่มีภาวะพิษเหตุติดเชื้อได้ร้อยละ 22

การพัฒนาการดูแลผู้ป่วยที่มีภาวะพิษเหตุติดเชื้อ ได้แก่ กำหนดการฝึกอบรมเรื่องการคัดแยก การพัฒนาช่องทางเร่งด่วนสำหรับผู้ป่วยที่มีภาวะพิษเหตุติดเชื้อ การสนับสนุนและกระตุ้นเตือนเรื่องความครบถ้วนของการปฏิบัติการคัดแยกและการได้รับแผนการรักษาของผู้ที่มีภาวะพิษเหตุติดเชื้อ

Pacific Rim Int J Nurs Res 2017; 21(2) 135-147

คำสำคัญ : อาการทรุดลงทางคลินิก การดูแลฉุกเฉิน ปัจจัยที่มีอิทธิพล ภาวะพิษเหตุติดเชื้อ ภาวะช็อก

ปฏิพร บุญยพัฒนกุล RN, Ph.D. (Candidate) นักศึกษาปริญญาเอก หลักสูตร
ปรัชญาดุษฎีบัณฑิต สาขาวิชาการพยาบาล (หลักสูตรนานาชาติร่วมกับมหาวิทยาลัย
ในต่างประเทศ) บัณฑิตวิทยาลัย มหาวิทยาลัยมหิดล ประเทศไทย
E-mail: avajiraed@gmail.com; patiporn.ed@gmail.com
ติดต่อที่: ศิริอร สินธุ* PhD, RN รองศาสตราจารย์ คณะพยาบาลศาสตร์
มหาวิทยาลัยมหิดล ประเทศไทย E-mail: sirior.sin@mahidol.ac.th
Patricia Davidson PhD, RN, Professor, Johns Hopkins University School
of Nursing, USA
เกศรินทร์ อุทธิยะประสิทธิ์ PhD รองศาสตราจารย์ คณะพยาบาลศาสตร์
มหาวิทยาลัยมหิดล ประเทศไทย
ชูเกียรติ วิวัฒนวงศ์เกษม PhD รองศาสตราจารย์ ภาควิชาชีวสถิติ คณะ
สาธารณสุขศาสตร์ มหาวิทยาลัยมหิดล ประเทศไทย
วิทยา ชาติบัญชาชัย MD รองผู้อำนวยการอาวุโสและผู้อำนวยการ
ศูนย์อุบัติเหตุและวิกฤตบำบัด โรงพยาบาลขอนแก่น ประเทศไทย