A Point-of-Care Serum Lactate Level and Mortality in Adult Sepsis Patients: A Community Hospital Setting

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Abstract

Introduction: Sepsis is a serious and emergency condition that may lead to acute circulatory failure associated with infection. Serum lactate level of over 4 mmol/L is associated with sepsis mortality. However, there is limited data on using a point of care (POC) for fingertip lactate level on sepsis mortality in community hospital setting. This study aimed to evaluate roles of POC for serum lactate with combination of clinical factors on mortality prediction in sepsis patients. **Methods:** This was a retrospective cohort study conducted at 7 community hospitals. The inclusion criteria were adult patients with diagnosis of sepsis who were tested for POC lactate level. Electronic chart reviews of eligible patients were performed. Predictors for mortality were computed using clinical factors and POC lactate level. **Results:** There were 1641 patients met the study criteria. The mortality rate was 8.96% (147 patients). There were 3 independent factors associated with mortality: age, co-morbid diseases, and POC lactate level. The adjusted odds ratio (95% CI) of POC lactate level was 1.025 (1.002, 1.048). The cut point of serum lactate was 1.6 mmol/L gave sensitivity of 79.59% and specificity of 32.10%. **Conclusion:** POC serum lactate level may be associated with mortality in sepsis patients at community hospitals. Lactate level of 1.6 mmol/L may be an indicator for mortality with good sensitivity. Physicians may consider more aggressive and prompt management in individuals with sepsis and POC serum lactate of 1.6 mmol/L or over.

Keywords

serum lactate, community hospital, sepsis

Introduction

Sepsis, defined as life-threatening organ dysfunction caused by a dysregulated host response to infection, is a serious and emergency condition that may lead to acute circulatory failure associated with infection.[1] An in-hospital mortality rate may be more than 10% in sepsis patients.[1] The incidence of sepsis in 2017 was 48.9 million cases worldwide with a mortality rate of 19.7%.[2] Early detection and treatment of sepsis is one of key treatment to prevent deaths. A new definition of septic shock was proposed to facilitate sepsis care by adding serum lactate level.[1]

Serum lactate level is an indicator of sepsis mortality and should be measured within 1 h.[3,4] Sepsis patients with a serum lactate of ≥4 mmol/L should be administered rapid crystalloid therapy.[4] Repeated serum lactate measurement is also recommended if initial serum lactate level of ≥2 mmol/L.[4] Even though serum lactate is not an indicator

of tissue perfusion, 5 randomized controlled trials showed that lactate-guided resuscitation significantly reduced mortality compared with no lactate monitoring by 23%.[5] Additionally, serum lactate is associated with tissue hypoxia, aerobic glycolysis, and liver or renal failure. These factors are related with sepsis severity, septic shock, or mortality.[5-8] Serum lactate level can be measured by a standard, conventional, central laboratory method using whole blood.[8]

As detection of conventional serum lactate may be a time consuming method, a point of care (POC) device to detect a fingertip lactate level is another feasible test at the

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Emergency Department with good correlation with laboratory measurement (*r* 0.97).[5,9] The POC measurement had shorter time to reveal lactate level by 151 min than conventional whole blood lactate measurement (21 vs 172 min).[9] The POC lactate test also reduced time to intravenous fluid treatment and mortality significantly compared with traditional lactate test (55 vs 71 min, *P* .03).[10] The mortality rate was lower by 13% in the POC group (6% vs 19%; *P* .02).[10] Combining clinical factors with POC serum lactate level was shown to have good specificity (82%) but low sensitivity (34%) for sepsis detection.[11] However, there is limited data of on POC serum lactate level and mortality in sepsis patients in a community hospital setting. This study aimed to evaluate roles of POC for serum lactate with combination of clinical factors on mortality prediction in sepsis patients.

Methods

This was a retrospective cohort study conducted at 7 community hospitals in Khon Kaen province, Thailand. The study sites included Kranuan Hospital, Nampong Hospital, Manjakiri Hospital, Phol Hospital, Samsung Hospital, Nong Song Hong Hospital, and Phuviang Hospital. The inclusion criteria were adult patients with diagnosis of sepsis who were tested for POC lactate level. Pregnant women or those with 18 years of age or under were excluded due to interfering of serum lactate measurement from pregnancy and ethical approval of the research project only in adult patients. The diagnosis of sepsis was made according to the previous report: presence of 2 of the following: body temperature of over than 38°C or lower than 36°C or lower, heart rate of 90 beats/min or over, respiratory rate of 20 breaths/min or over, or altered mental status.[11] The study period was between January and December 2019.

Electronic chart reviews of eligible patients were performed. Socio-demographic data, co-morbid diseases, site of infection, serum lactate level by POC, and mortality data were recorded. Co-morbid diseases were present if 1 of the following diagnostic conditions: cancer, cirrhosis, chronic kidney disease, diabetes, hypertension, chronic obstructive airway disease, tuberculosis, asthma, hepatitis viral infection, HIV infection, coronary artery disease, or stroke. The site of infection was based on clinical diagnosis of an attending physician and categorized as respiratory tract (RS), gastrointestinal (GI), central nervous system (CNS), urinary tract infection (UTI), systemic infection, or unknown. Systemic infection comprised of viral infection, leptospirosis, or rickettsia infection. Co-morbid diseases were retrieved from medical records at admission. The POC lactate level was measured by the fingertip device (StatStrip® Lactate, Nova Biomedical Corporation, Waltham, MA, USA) and reported as mmol/L. The primary outcome was the in-hospital mortality. This device provided high correlation with the ABL blood gas analyzer ($R^2 = 0.994$).[12]

Sample size calculation. Based on the previous study, mortality rate of sepsis patients using the POC was 6%,[11] we estimated a mortality rate of 10% in this study. With a power of 90% and confidence of 99%, the required study population was 1357 patients.

Statistical analyses: Patients were divided into 2 groups according to survival at the end of hospital course; death or survived. The in-hospital mortality rate was also executed. Descriptive statistics were used to calculate means (SD) or proportions of studied variables when appropriated. Factors associated with mortality were executed by logistic regression analysis. Those factors with a *P* value of less than .20 by univariate logistic regression analysis were put into multivariate logistic regression analysis. Results were reported as unadjusted, adjusted odds ratio with their 95% confidence interval (CI). The final model predictive of mortality was tested for goodness of fit by Hosmer-Lemeshow method. A numerical predictor for mortality was calculated for appropriate cut point with an area of a receiver operating characteristic curve (ROC curve). Sensitivity and specificity of the cut point were computed. Statistical analyses were calculated by STATA software (College Station, TX, USA). The study protocol was approved by the institutional board review (KEXP63036) and complied with the Helsinki Declaration.

Results

There were 1695 patients presenting with sepsis. Of those, 54 patients were excluded due to age of under 18 years. In total, 1641 patients met the study criteria. The average length of hospitalization was 6.26 days (SD 7.34). The in-hospital mortality rate was 8.96% (147 patients). There were 3 significant factors between those who were alive and dead including age, RS infection, and UTI infection as shown in Table 1. The dead group had significantly older age than the alive group (64.72 vs 61.36 years; *P* .024). The proportions of RS infection and UTI were higher and lower in the dead group than the alive group significantly (*P* value .020 and .034) as well as presence of any co-morbid diseases (44.22% vs 12.78%; *P* .001). The serum lactate level was also significantly higher in the dead group than the alive group (4.56 vs 2.85 mmol/L; *P* .029).

There were 3 independent factors associated with mortality by multivariate logistic regression analysis (Table 2): age, serum lactate level, and comorbid diseases. The Hosmer-Lemeshow Chi square of the final model was 11.88 (*P* .156). The cut point of serum lactate was 1.6 mmol/L gave sensitivity of 79.59% and specificity of 32.10%. The area under ROC curve was 65.60% (95% CI 60.46, 70.73) as shown in Figure 1. Age of over 53 years had sensitivity and specificity of 80.95% and 29.02% with the area of ROC curve of 54.74% (95% CI 20.23%, 59.24%).

Table 1. Clinical Features and Serum Lactate by Point of Care Method in Patients Presenting with Sepsis at Community Hospitals and Categorized by Mortality.

Clinical factors	Survived (n = 1494)	Death (n = 147)
Mean (SD) age, years	61.36 (17.45)	64.72 (14.18)
Male sex	813 (54.42)	86 (58.50)
Sites of infection		
RS infection	450 (30.12)	58 (39.46)
GI infection	187 (12.52)	20 (13.61)
Urinary tract infection	206 (13.79)	11 (7.48)
Skin infection	71 (4.75)	6 (4.08)
CNS infection	16 (1.06)	4 (2.72)
Systemic infection	83 (5.56)	5 (3.40)
Unknown site of infection	481 (32.20)	43 (29.25)
Co-morbid diseases	191 (12.78)	65 (44.22)
Cancer	19 (1.27)	3 (2.04)
Cirrhosis	20 (1.34)	8 (5.44)
Chronic kidney disease	48 (3.21)	20 (13.61)
Diabetes	86 (5.76)	32 (21.77)
Hypertension	2 (0.13)	0
Chronic obstructive airway disease	14 (0.94)	1 (0.68)
Tuberculosis	18 (1.20)	5 (3.40)
Asthma	1 (0.07)	1 (0.68)
Hepatitis	19 (1.27)	4 (2.72)
HIV infection	14 (0.94)	5 (3.40)
Coronary artery disease	0	0
Stroke	5 (0.33)	4 (2.72)
Mean (SD) serum lactate, mmol/L	2.85 (5.87)	4.56 (3.99)

Data presented as number (percentage calculated per column) unless indicated otherwise.
Abbreviations: CNS, central nervous system; systemic infection indicated viral infection, leptospirosis, or rickettsia infection; GI, gastrointestinal tract; RS, respiratory tract.

Table 2. Factors Associated with Mortality in Patients Presenting with Sepsis at Community Hospitals.

| Factors	Unadjusted odds ratio (95% CI); *P* value	Adjusted odds ratio (95% CI); *P* value
Age	1.011 (1.001, 1.022); .024	1.013 (1.002, 1.024); .021
Male sex	1.118 (0.873, 1.665); .343	1.110 (0.772, 1.596); .571
Respiratory tract infection	1.511 (1.066, 2.142); .020	1.323 (0.908, 1.928); .144
Urinary tract infection	0.505 (0.268, 0.952); .034	0.602 (0.309, 1.172); .136
Comorbid diseases	5.407 (3.775, 7.744); .001	5.469 (3.797, 7.876); .001
Serum lactate	1.027 (1.003, 1.051); .029	1.019 (1.001, 1.040); .044

Discussion

This study showed that serum lactate level by the POC was related with mortality in community hospital setting.

A global report in 2017 showed that sepsis deaths were 11.0 million or accounted for 19.7% of total deaths.[2] While, the global mortality of sepsis was 20.1%.[2] The mortality rate in this study or community setting was comparable with the previous study conducted at the Emergency Department (8.96% in this study vs 6.08%).[11] These results may confirm the benefits of POC lactate level on mortality reduction regardless of hospital setting. Rapid detection of

serum lactate level may facilitate clinical care of sepsis patients and result in improving survival outcome.

This study also showed that serum lactate level by the POC was shown to be associated with in-hospital mortality in community hospital setting. Among clinical factors, age and serum lactate were independently associated with sepsis mortality in this setting. A previous study in African children admitted due to fever was also found that POC serum lactate was associated with mortality.[13] Note that over half of patients had falciparum malaria (1894/3211; 58.98%). This study provided a correlation data of POC serum lactate in adult sepsis patients.
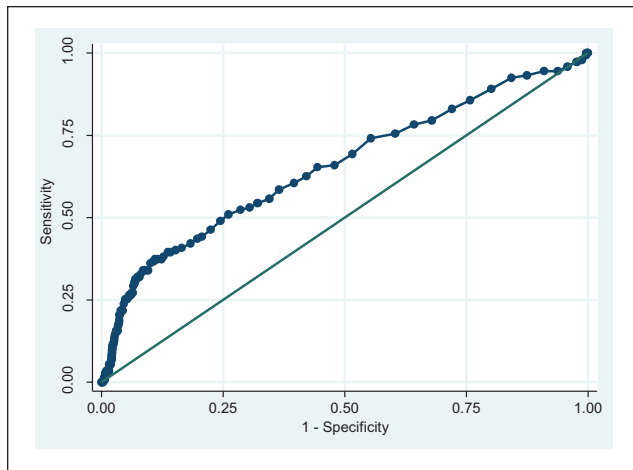
Figure 1. A receiver operating characteristic curve of serum lactate level by point of care on mortality of patients presenting with sepsis at community hospitals.

The third consensus on sepsis and septic shock stated that serum lactate level of 2 mmol/L or over is suggestive for septic shock.[11] The study in children found that POC serum lactate over 8 mmol/L was associated with mortality significantly (adjusted odds ratio of 5.65; 95% CI 1.96, 16.26).[13] In this study, we found that POC serum lactate of over 1.6 mmol/L had good sensitivity for mortality prediction. Even though the cut point of serum lactate of 4 mmol/L was proposed to be associated with sepsis mortality,[3] it was the highest serum lactate level by conventional method. This study showed that the first time POC serum lactate of lower level was associated with mortality. The results may imply that rigorous sepsis interventions may be required with lower cut point of POC serum lactate level.

An increasing age was another independent factor for higher mortality in this study. As previously reported, sepsis is increasing by age as well as mortality.[14-16] The elderly patients may have more co-morbid diseases and poor immune system.[16] Increasing age is related with poor both innate and adaptive immune responses resulting in increasing risk of infection and sepsis mortality. For innate immune system, functions of neutrophils and macrophages are reduced leading to impaired phagocytosis, antibacterial defense, and chemotaxis.[17,18] While, adaptive immune system may be poor as B and T cells have decreasing numbers by aging resulting in poor adaptive immune system particularly to new pathogens.[18,19]

Both age and serum lactate level had comparable adjusted odds ratio (Table 2). Increasing of age and serum lactate by 1 unit, the risk of in-hospital death was increasing by 1.1% and 2.3%, respectively after adjusted by factors shown in Table 2. The adjusted odds ratio of age and serum lactate in this study were slightly lower than other studies (1.01 vs 1.05 for age and 1.02 vs 1.09).[20,21] These may be

explained by less severity of sepsis in community hospital setting which had fewer co-morbid diseases. The final predictor for sepsis mortality in this study was presence of co-morbid diseases which was similar as previous reports.[22-25]

As previously reported, POC lactate may facilitate sepsis treatment at the ED.[9,10] The fingertip POC lactate meter was highly accurate as it has interclass correlation of over 90% at both ED arrival and 6 h after ED arrival.[26] Even though there are several available POC lactate meters, they are comparable and reliable.[27]

In conclusion, POC serum lactate level may be associated with mortality in sepsis patients at community hospitals. Lactate level of 1.6 mmol/L may be an indicator for mortality with good sensitivity. POC lactate can be used in sepsis patients presenting at the community hospitals to facilitate prompt management. Physicians may consider more aggressive and prompt management in individuals with sepsis and POC serum lactate of 1.6 mmol/L or over.

Author Contributions

Declaration of Conflicting Interests

Funding

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