Journal of Critical Care 33 (2016) 71–77

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.jccjournal.org

Lactate and combined parameters for triaging sepsis patients into intensive care facilities

Detajin Junhasavasdikul, MD [a], Pongdhep Theerawit, MD [a,*], Atiporn Ingsathit, MD, PhD [b], Sumalee Kiatboonsri, MD [a]

[a] Division of Pulmonary and Critical Care Medicine, Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, 270 Rama 6 Rd., Rajthevi, Bangkok, 10400, Thailand
[b] Section for Clinical Epidemiology and Biostatistics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, 270 Rama 6 Rd., Rajthevi, Bangkok, 10400, Thailand

ARTICLE INFO

Keywords:
Sepsis
Lactate
Scoring system
Intensive care
Triage
SOFA

ABSTRACT

Purpose: To find predictors of intensive care unit (ICU) requirement within the first 48 hours in newly diagnosed sepsis patients presenting at the emergency department.
Materials and methods: Analysis of a prospective observational cohort was performed. We recruited new sepsis patients at the emergency department, and collected baseline characteristics and parameters. Variables were compared between patients: those that required ICU within 48 hours and those that did not. Multivariate analysis was performed to identify independent predictors.
Results: Out of 719 patients enrolled, 275 were confirmed to have sepsis. There were 107 patients (39%) that required ICU admission within 48 hours. Independent predictors for ICU requirement were: lower body temperature ($P = .019$), initial lactate ($P = .02$), 2-hour lactate clearance ($P = .035$), and the Sequential Organ Failure Assessment (SOFA) score without cardiovascular component ($SOFA_{no\ CVS}$) ($P < .001$). The optimal cutoff values for the two strongest predictors were: $SOFA_{no\ CVS} \geq 5$ (adjusted OR, 5.3; 95% CI, 1.9-14.7) and initial lactate ≥1.9 mmol/L (adjusted OR, 3.3; 95% CI, 1.2-8.9). We also proposed a combined "LACTIC score" with higher predictive ability.
Conclusions: We suggested a way to predict ICU requirement in sepsis patients and proposed a combined score that might be better than individual parameters. Further validation should be performed before using them clinically.

1. Introduction

Cases with severe sepsis have high mortality rates [1–3] and usually require intensive care unit (ICU) admission for specialized care and continuous monitoring [4–7]. Unfortunately, the shortage of ICU beds has been problematic worldwide [5,8–11], and only 32% to 51% of severe sepsis patients are treated in the ICU [1,6,7].

ICU admission is usually based on predetermined criteria, namely shock state that requires a vasopressor, respiratory failure, and conditions demanding close monitoring [4,12,13]. In some patients, initial therapies could temporarily improve their conditions, especially in the early course of sepsis. These patients were usually admitted to general wards during ICU bed shortage and received less rigorous care, which might be inadequate for some of them. Levy et al demonstrated that 25% to 50% of sepsis patients initially admitted in general wards deteriorated and finally were transferred to the ICU [14].

To date, proposed triage systems have been mostly designed for a pandemic situation and have focused on prediction of mortality [2,13,15–17]. Diverting the mortality prediction to the prediction of the impending conditions requiring ICU admission (eg, vasopressor requirement or endotracheal intubation) may be more helpful for selecting an appropriate site of care, especially for patients with chances of looming deterioration. Triaging parameters focusing on early detection of organ dysfunction may be the most appropriate.

Lactate is universally used as a guide for sepsis treatment and monitoring [18–22]. Initial lactate level at the emergency department (ED) and the lactate clearance rate were able to predict mortality [23–27] and were associated with organ failure in terms of the Sequential Organ Failure Assessment (SOFA) score [28]. Nevertheless, information about using lactate as a triaging tool for ICU admission is still lacking.

The primary objective of this study was to investigate the parameters that can predict intensive care admission within the first 48 hours

Abbreviations: T, body temperature; RR, respiratory rate; $Paco_2$, partial pressure of carbon dioxide in arterial blood; HR, heart rate; WBC, white blood cell count; GCS, Glasgow Coma Score; L1, first arterial lactate; L2, delayed (second) arterial lactate; %LacCl2h, percentage of lactate clearance within 2 hours; $SOFA_{no\ CVS}$, SOFA score without cardiovascular component; P/F ratio, the ratio of arterial oxygen partial pressure to fractional inspired oxygen; Dx, diagnosis.

* Corresponding author at: Division of Pulmonary and Critical Care Medicine, Department of Medicine, Faculty of Medicine, Ramathibodi Hospital, 270 Rama 6 Rd., Rajthevi, Bangkok, 10400, Thailand. Tel.: +66 2 201 1629x17.
E-mail address: pongdhep@live.com (P. Theerawit).

http://dx.doi.org/10.1016/j.jcrc.2016.01.019
0883-9441/

in sepsis patients, with lactate as one of the factors of interest. Secondary objectives were to determine the parameters which can predict specific requirements of intensive care within the first 48 hours in sepsis patients, i.e. the requirements of vasopressor and invasive mechanical ventilation.

2. Materials and methods

2.1. Study design

We conducted a prospective observational cohort study at Ramathibodi Hospital, a tertiary care and university hospital in Bangkok, Thailand. All patients arrived at the ED between March and November 2012, and were prospectively screened by ED residents and staff. The inclusion criteria were: age ≥15 years and newly diagnosed with sepsis syndrome. The exclusion criteria were: presence of surgical conditions, refusal of intubation or vasopressor use, do not resuscitate order, prior parenteral antibiotics (ATB) use in this episode of illness, and patients who were discharged from the ED against advice, or who died at the ED, transferred to another hospital, or declined to participate. The study was approved by the Ethics Committee of Ramathibodi Hospital, Mahidol University.

2.2. Definition of sepsis

"Sepsis syndrome" consists of three different severities: sepsis, severe sepsis, and septic shock. Sepsis was defined according to the 1991 statement of the ACCP/SCCM Consensus Conference [29] as infection plus ≥2 systemic inflammatory response syndrome (SIRS) criteria: T >38°C or <36°C; RR >20/min, or $Paco_2$ <32 mmHg; HR >90 bpm; WBC >12,000 or <4,000 cells/μL or band count >10%. Severe sepsis was defined as sepsis plus at least one organ system dysfunction according to the SOFA score. A score of ≥2 in any organ category indicated organ dysfunction, except for cardiovascular dysfunction which was defined by the score 1, 3, or 4 in the cardiovascular system (CVS) component, and the Glasgow Coma Score which was omitted [30]. Septic shock was defined as sepsis plus persistent hypotension not responding to fluid and requiring inotropes or vasopressors. Hypotension was defined as: systolic blood pressure (SBP) <90 mmHg; mean arterial blood pressure <70 mmHg; or a reduction in SBP >40 mmHg from baseline [22].

2.3. Protocol and data collection

Medical students and residents practicing in the ED were comprehensively instructed in the study protocol. During the study period, the ED team consecutively enrolled eligible patients and registered them in the database.

Arterial blood gas and the first arterial lactate (L1) were collected within 24 hours after the diagnosis of sepsis, packed with ice, and sent for measurements in the central laboratory unit. Lactate collection was then repeated at 2 hours (called "delayed lactate" or L2), and this was used to calculate the percentage of lactate clearance within 2 hours ("%LacCl2h"). Since L2 might not be measured at a precise time point, the lactate clearance was adjusted by the equation: %LacCl2h = [100 × (L1 − L2) / L1] × [2 / duration between L1 and L2 (hours)]. A positive value meant a decrease of lactate, while a negative value signified an increase [27,31].

Completion of laboratory investigations was augmented by using pre-printed standing laboratory orders. Other data recorded into the hospital medical informatics system included: the time of each event (eg, ED arrival, first ATB use, ward admission, etc.), source of infection, dosage of vasopressor used, hemoculture results, etc. The worst values of body temperature and mean arterial pressure within 24 hours were used for analysis. The Fio_2 levels in patients prescribed an oxygen therapy device were estimated from the relationship between the device used and the flow rate. Moreover, we calculated the SOFA score without the cardiovascular component ($SOFA_{no\ CVS}$). Using the original SOFA score as a predictor for ICU admission would cause confusion during triage because it includes vasopressor use which is, by itself, an indicator for ICU admission regardless of total SOFA score. Omitting the cardiovascular component reduced the range of the original SOFA score from 0 to 24 to the new range of 0 to 20 for the $SOFA_{no\ CVS}$ score.

All patients then received routine care at the ED. Patients who developed a status that fulfilled the ICU admission criteria were then admitted to the 32-bed medical intensive care unit. This included: hemodynamic instability, requirement of invasive mechanical ventilatory support, and severe metabolic disturbances that required urgent treatment, eg, diabetic ketoacidosis and severe acidosis. The other patients were either treated at the ED or admitted to general wards, depending on the availability of hospital beds and their illness severity. Due to limitation of available beds, our ED has arranged an observation zone that can provide several days of treatment similar to those available on the general wards, eg, IV infusion of drugs, oxygen therapy, abdominal/thoracic paracentesis, etc. Some patients might be discharged home directly from the ED if their recovery was satisfactory, regardless of the severity at their presentation. For patients already admitted to general wards, development of ICU admission criteria at any time would also warrant transfer to the ICU.

After patients' discharge, electronic medical records were reviewed one-by-one by the investigators. Sepsis cases were confirmed by the presence of: (1) a final diagnosis of sepsis by the physicians in charge at the time of discharge, and (2) confirmation of sepsis from our chart review. Patients without a final diagnosis of sepsis were excluded.

2.4. Primary and secondary outcomes

The primary outcome was parameter(s) associated with all-cause admission and transfer to the ICU within 48 hours (primary endpoint), using the time of initial lactate measurement as a reference time point. The secondary outcomes were parameters associated with specific requirements of intensive care treatments, namely vasopressor use and invasive mechanical ventilation within 48 hours (secondary endpoints).

We used a 48-hour time frame since this was, according to our hospital registration, the period in which most transfers of sepsis patients from the wards to the ICU due to clinical deterioration occurred. On the contrary, ICU transfers after 48 hours should be regarded as the results of hospital-acquired complications. This cutoff value is generally accepted and traditionally used for the definition of nosocomial infection [32,33].

2.5. Data analysis

For primary outcome, we divided patients into two groups according to the primary endpoint. The first group was sepsis patients who did not require ICU admission within the first 48 hours, including patients who were discharged home from the ED (provided that they did not require ICU admission in their 48-hour ED revisit, if one occurred). The other group was sepsis patients who required ICU admission, defined as patients initially admitted to the ICU within 48 hours or patients who were transferred from the general wards to the ICU within 48 hours from the measurement of L1. Continuous parameters from each group were presented as mean (standard deviation) or median (interquartile range). Differences between the two groups were analyzed by unpaired *t*-test or Mann–Whitney U test. Categorical variables were presented in the form of percentage and analyzed by chi-square or Fisher's exact test. After univariate analysis, parameters with $P \le .10$ were included in logistic regression with backward stepwise method to identify independent parameters. $P \le .05$ was considered to be statistically significant.

Secondary outcomes were analyzed by comparing parameters between the group of patients who needed vasopressor use within 48 hours and those that did not, and also between the group of patients with invasive mechanical ventilator use within 48 hours and those without.