

Early lactate clearance is associated with improved outcome in severe sepsis and septic shock*

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Objective: Serial lactate concentrations can be used to examine disease severity in the intensive care unit. This study examines the clinical utility of the lactate clearance before intensive care unit admission (during the most proximal period of disease presentation) as an indicator of outcome in severe sepsis and septic shock. We hypothesize that a high lactate clearance in 6 hrs is associated with decreased mortality rate.

Design: Prospective observational study.

Setting: An urban emergency department and intensive care unit over a 1-yr period.

Patients: A convenience cohort of patients with severe sepsis or septic shock.

Interventions: Therapy was initiated in the emergency department and continued in the intensive care unit, including central venous and arterial catheterization, antibiotics, fluid resuscitation, mechanical ventilation, vasopressors, and inotropes when appropriate.

Measurements and Main Results: Vital signs, laboratory values, and Acute Physiology and Chronic Health Evaluation (APACHE) II score were obtained at hour 0 (emergency department presentation), hour 6, and over the first 72 hrs of hospitalization. Therapy given in the emergency department and intensive care unit was recorded. Lactate clearance was defined as the percent decrease in lactate from emergency department presen-

tation to hour 6. Logistic regression analysis was performed to determine independent variables associated with mortality. One hundred and eleven patients were enrolled with mean age 64.9 ± 16.7 yrs, emergency department length of stay 6.3 ± 3.2 hrs, and overall in-hospital mortality rate 42.3%. Baseline APACHE II score was 20.2 ± 6.8 and lactate 6.9 ± 4.6 mmol/L. Survivors compared with nonsurvivors had a lactate clearance of 38.1 ± 34.6 vs. $12.0 \pm 51.6\%$, respectively ($p = .005$). Multivariate logistic regression analysis of statistically significant univariate variables showed lactate clearance to have a significant inverse relationship with mortality ($p = .04$). There was an approximately 11% decrease likelihood of mortality for each 10% increase in lactate clearance. Patients with a lactate clearance $\geq 10\%$, relative to patients with a lactate clearance $< 10\%$, had a greater decrease in APACHE II score over the 72-hr study period and a lower 60-day mortality rate ($p = .007$).

Conclusions: Lactate clearance early in the hospital course may indicate a resolution of global tissue hypoxia and is associated with decreased mortality rate. Patients with higher lactate clearance after 6 hrs of emergency department intervention have improved outcome compared with those with lower lactate clearance. (Crit Care Med 2004; 32:1637-1642)

KEY WORDS: lactate clearance; severe sepsis; septic shock; global tissue hypoxia; resuscitation; outcome

When oxygen delivery fails to meet tissue oxygen demand in critical illness, there is a compensatory increase in oxygen extraction. If the imbalance between oxygen delivery and con-

sumption is uncorrected, the compensatory response is exhausted, resulting in an oxygen debt, global tissue hypoxia, anaerobic metabolism, and lactate production. Numerous studies have established the use of lactate as a diagnostic, therapeutic, and prognostic marker of global tissue hypoxia in circulatory shock (1-6). Blood lactate concentrations > 4 mmol/L are unusual in normal and noncritically ill hospitalized patients, regardless of their underlying comorbidities (7). Previous studies have shown that a lactate concentration > 4 mmol/L in the presence of the systemic inflammatory response syndrome (SIRS) criteria significantly increases intensive care unit (ICU) admission rates and mortality rate in normotensive patients (8-10).

Persistent elevations in lactate > 24 hrs are associated with mortality rate as

high as 89% (11). The sensitivity and specificity of single lactate concentrations as markers of tissue hypoperfusion have been debated (12-15); however, serial measurements or lactate clearance over time may be better prognosticators of organ failure and mortality (16-18). Persistent elevated lactate > 48 hrs in hemodynamically stable postoperative patients has been shown to be associated with an increased mortality rate (19).

The emergency department (ED) is a portal for > 108 million annual visits nationally, with 12% of ED visits resulting in hospital admission (20). Approximately 51% of hospital admissions for severe sepsis require intensive care (21). ED length of stay for the critically ill can range from 1 to 29 hrs before ICU admission, and recent trends in health care suggest that this duration is increasing

***See also p. 1785.**

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DOI: 10.1097/01.CCM.0000132904.35713.A7

(22–25). The unavoidable duration of stay frequently necessitates diagnostic and therapeutic interventions to attain hemodynamic stability that would otherwise be performed in the ICU. The ED is becoming an integral part of the chain of survival as it has been shown that the progression or resolution of organ dysfunction in critical illness is significant during the ED stay (26). Furthermore, early goal-directed therapy in the most proximal stages of disease presentation has been shown to significantly decrease mortality rate in severe sepsis and septic shock (27).

The purpose of this study was to examine the clinical utility of lactate clearance (or the percent decrease in lactate) as early as after 6 hrs as an indicator of multiple-system organ failure and death. We also define a lactate clearance cutoff that is associated with improved outcome after 6 hrs of ED intervention.

MATERIALS AND METHODS

Setting. The study was a prospective observational case series of adult patients enrolled over a 1-yr period and approved by the Institutional Review Board for Human Research at Henry Ford Hospital, Detroit. The study was conducted in an 850-bed urban tertiary care hospital with a 70-bed ED that provides care for approximately 86,000 patients per year. Critically ill patients are treated in a nine-bed intensive care area in the ED, equipped with hemodynamic monitoring and life support capabilities. This area is staffed by a board-certified emergency physician, two emergency medicine residents, and five nurses, 24 hrs a day. Patients requiring further critical care are admitted to an ICU (medical, cardiac, neurologic, or surgical ICU) from this area.

Inclusion and Exclusion Criteria. Adult patients presenting to the ED with severe sepsis or septic shock (28) from February 1, 1999, to February 1, 2000, were enrolled after written informed consent within 1 hr of arrival (29). Inclusion criteria consisted of a suspected sepsis source and the following: a) two of four SIRS (30) criteria (temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$, heart rate >90 beats/min, respiratory rate >20 breaths/min, or $\text{Paco}_2 <32$ mm Hg, or white blood cell count $>12,000$ cells per mm^3 , $<4,000$ cells per mm^3 , or $>10\%$ band cells) and a systolic blood pressure <90 mm Hg after a 20 mL/kg fluid challenge; or b) two of the SIRS criteria and an elevated lactate concentration (>4 mmol/L). Patients with an age <18 yrs, myocardial infarction, pulmonary edema, hemorrhagic shock, trauma, seizure, pregnancy, do-not-attempt-resuscitation orders, or requiring immediate surgery were excluded.

Patient Management. All patients received central venous and arterial catheterization in

the ED and were managed according to the Society of Critical Care Medicine practice parameters for hemodynamic support of sepsis (31). Volume resuscitation using crystalloids or colloids was initiated to achieve a central venous pressure of 8–12 mm Hg. Vasoactive agents were used to maintain a mean arterial pressure >65 mm Hg. Urine output >0.5 mL $\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$ also served as a target goal. Patients were intubated and mechanically ventilated as required. All patients received evaluation by an intensive care specialist and were admitted to the ICU as soon as a bed became available.

Data Collection. The primary outcome variable was in-hospital mortality. Patient demographic information, admission diagnoses, and ED and hospital length of stay were recorded. Baseline vital signs (temperature, heart rate, mean arterial pressure), central venous pressure, arterial lactate, and laboratory values were obtained in the ED. Additional variables required to calculate the Acute Physiology and Chronic Health Evaluation (APACHE) II score (32) as an indicator of organ dysfunction were obtained at ED presentation (hour 0), hour 6, and during 72 hrs while in the hospital. Therapy given in the ED and up to 72 hrs in the hospital was recorded. Data were recorded on data forms and then entered in a database software (Paradox, Corel). The clinicians caring for the patients in the ED and in the hospital were blinded to the data collection process, and the study investigators did not influence clinical decision making.

Lactate Clearance Definition. Lactate clearance (percent) was defined using the following formula: lactate at ED presentation (hour 0) minus lactate at hour 6, divided by lactate at ED presentation, then multiplied by 100. A positive value denotes a decrease or clearance of lactate, whereas a negative value denotes an increase in lactate after 6 hrs of ED intervention.

Lactate clearance

$$= \frac{(\text{Lactate}^{\text{ED Presentation}} - \text{Lactate}^{\text{Hour 6}}) \times 100}{\text{Lactate}^{\text{ED Presentation}}} \quad [1]$$

Statistical Analysis. The Statistical Analysis System software (SAS Institute, Cary, NC) was used for data analysis. In-hospital mortality rate was determined by dividing the total number of deaths occurring in the hospital by the total number of patients enrolled in the study. Unless otherwise noted, data are presented as mean \pm sd. Statistical significance was defined as $p < .05$. Univariate in-hospital mortality comparisons (survivors vs. nonsurvivors) were made using either two-sample Student's *t*-tests or Wilcoxon rank sum tests for the continuous variables and either chi-square tests or Fisher's exact tests for the categorical variables. The variables with univariate comparison $p < .05$ were then in-

cluded in a multivariate logistic regression analysis of in-hospital mortality rate. In addition, the sensitivity and specificity in predicting mortality of various lactate clearance cutoffs of -10 , 0 , 10 , 20 , 30 , 40 , and 50% were examined. Since there is no previous study defining lactate clearance as a percent decrease in lactate, we arbitrarily defined these cutoffs *a priori*. An optimal lactate clearance cutoff was defined as that lactate clearance with the maximum sum of sensitivity plus specificity for predicting in-hospital mortality. The various therapy and outcome measures of interest were then compared between the patients with lactate clearance below and above the cutoff. Kaplan-Meier estimation was used to obtain 60-day survival curves for lactate clearance below and above the cutoff, which were then compared using the log-rank test for survival data.

RESULTS

A total of 111 patients, 59 men and 52 women, were enrolled over a 1-yr period. The ED length of stay ranged from 1.5 to 17.6 hrs, which corresponded to 1.9% of the total hospital length of stay (range 6.8 hrs to 116.9 days). The predominant admission diagnoses were pneumonia and urosepsis, with 52.3% patients presenting in septic shock. Intubations were performed in the ED in 53.2% of patients requiring mechanical ventilation. Patients had a mean baseline APACHE II score of 20.2 ± 6.8 and lactate of 6.9 ± 4.6 mmol/L. The in-hospital mortality rate was 42.3% (Table 1). Survivors compared with nonsurvivors had a lactate clearance of 38.1 ± 34.6 vs. $12.0 \pm 51.6\%$, respectively ($p = .005$) (Table 2).

Univariate comparisons of age, sepsis category, APACHE II score, vital signs, laboratory values, therapy given in the ED, and lactate clearance between survivors and nonsurvivors were performed (Table 2). There was a statistically significant difference between survivors and nonsurvivors for septic shock, platelet, prothrombin time, albumin, total bilirubin, lactate, and lactate clearance (all $p < .05$). Multivariate logistic regression modeling was then performed using the statistically significant univariate variables. Only lactate clearance was significantly associated with decreased mortality rate in the multivariate comparison ($p = .04$) (Table 3). There was an approximately 11% decrease in likelihood of mortality for each 10% increase in lactate clearance. Septic shock was not significantly associated with mortality rate in the multivariate comparison ($p = .07$).

Table 1. Baseline characteristics and therapy given in the emergency department

No.	111
Age, yrs	64.9 ± 16.7
Male/female, %	53.2:46.8
ED length of stay, hrs	6.3 ± 3.2
Hospital length of stay, days	14.7 ± 18.6
In-hospital mortality rate, n (%)	47 (42.3)
Severe sepsis, n (%)	53 (47.7)
Septic shock, n (%)	58 (52.3)
APACHE II	20.2 ± 6.8
Diagnosis, %	
Pneumonia	47.7
Urosepsis	12.6
Pancreatitis	7.2
Peritonitis	5.4
Abdominal abscess	3.6
Endocarditis	2.7
Empyema	0.9
Cholecystitis	0.9
Other	19.0
Entry criteria	
Temperature, °C	36.8 ± 2.1
Heart rate, beats/min	116.9 ± 26.7
Systolic blood pressure, mm Hg	110.5 ± 35.2
Respiratory rate, breaths/min	30.6 ± 11.0
Pco ₂ , mm Hg	30.8 ± 15.3
WBC, per mm ³	14.5 ± 9.8
Lactate, mmol/L	6.9 ± 4.6
Baseline values	
MAP, mm Hg	77.0 ± 24.9
CVP, mm Hg	6.0 ± 7.8
Hematocrit, %	34.8 ± 8.0
Platelet, per mm ³	204,000 ± 112,000
Prothrombin time, secs	16.6 ± 6.3
D-Dimer, ng/mL	3347 ± 6876
Creatinine, mg/dL	2.6 ± 2.0
Albumin, g/dL	2.8 ± 0.7
Total bilirubin, mg/dL	2.1 ± 3.3
Base deficit, mmol/L	8.5 ± 7.6
pH	7.33 ± 0.18
Scvo ₂ , %	51.3 ± 13.2
Therapy in the ED	
Intravenous fluids, mL	3365 ± 2724
PRBC transfusion, %	18.0
Mechanical ventilation, %	53.2
Vasopressor, %	28.8
Dobutamine, %	2.7
Lactate clearance, %	27.1 ± 44.4

ED, emergency department; APACHE, Acute Physiology and Chronic Health Evaluation; WBC, white blood cell; MAP, mean arterial pressure; CVP, central venous pressure; Scvo₂, central venous oxygen saturation; PRBC, packed red blood cell.

Analysis of lactate clearance cutoffs showed that a lactate clearance cutoff of <10% had the maximum sum of sensitivity plus specificity for predicting in-hospital mortality. After 6 hrs of intervention, a lactate clearance of <10% had a sensitivity of 44.7%, specificity of 84.4%, and accuracy of 67.6% for predicting in-hospital mortality. Patients were then categorized as being in the low-clearance group (<10% clearance) or high-clearance group (≥10% clearance) (Table 4). Both groups had similar characteristics such as age, vital signs, and laboratory values. However, the high-clearance group had higher platelet counts and lower prothrombin times

compared with the low-clearance group ($p < .05$). The high-clearance group received significantly less vasopressor therapy in the first 6 hrs compared with the low-clearance group ($p = .02$) and continued to do so in the ICU ($p = .04$). Both low-clearance and high-clearance groups had similar baseline APACHE II scores; however, the high-clearance group had lower score at 6 hrs and throughout the 72-hr study period ($p < .05$ at hours 12, 24, and 36). The high-clearance group had a 52.0% relatively lower in-hospital mortality rate compared with the low-clearance group ($p < .001$), and this mortality difference was similarly observed up to 60 days (Table 4 and Fig. 1). The high-

clearance group received more fluid therapy and less blood transfusion in the ED compared with the low-clearance group; however, this was not statistically significant ($p = .44$ and $.18$, respectively).

There were significantly more severe sepsis patients with high lactate clearance compared with patients with low lactate clearance ($p = .01$; Table 4). In severe sepsis patients, those with high lactate clearance had significantly lower mortality rate than patients with low clearance ($p = .03$). There were significantly fewer septic shock patients with high lactate clearance; however, there was a trend toward decreased mortality rate in these patients compared with the septic shock patients with low lactate clearance ($p = .01$ and $.06$, respectively).

DISCUSSION

The pathogenic link between global tissue hypoxia, morbidity, and mortality in sepsis has been thoroughly documented. Although the mechanisms are complex, global tissue hypoxia that accompanies severe sepsis and septic shock independently contributes to the systemic inflammatory response leading to endothelial activation (33, 34), vasodilation (35), release of inflammatory mediators (36), and modulation of the coagulation system (37, 38), all resulting in the multiple organ dysfunction syndrome (39) and death. As a compensatory mechanism to the hemodynamic derangements in severe sepsis and septic shock, a surge in catecholamines and neural regulation maintains arterial pressure at the expense of decreased tissue perfusion. This renders vital signs poor resuscitation end points, prognosticators of outcome, and indicators of the degree of global tissue hypoxia in patients presenting with shock (40, 41). Lactate represents a useful and clinically obtainable surrogate marker of tissue hypoxia and disease severity, independent of blood pressure (42). Persistently elevated lactate has been shown to be better than oxygen transport variables (oxygen delivery, oxygen consumption, and oxygen extraction ratio) as an indicator of mortality rate. Among septic shock patients, only survivors had a significant decrease in lactate concentrations over the course of the disease. In contrast, nonsurvivors had significantly higher lactate concentrations during both the initial and final phases of shock (43).

Table 2. Univariate comparisons between survivors and nonsurvivors

Variable	Survivors (n = 64)	Nonsurvivors (n = 47)	p Value
Age	64.7 ± 17.6	65.1 ± 15.6	.89
Septic shock, %	39.1	70.2	.001 ^a
APACHE II	19.9 ± 6.8	20.6 ± 6.8	.58
Vital signs			
Temperature, °C	36.8 ± 2.3	36.9 ± 1.9	.78
Heart rate, beats/min	116.5 ± 29.6	117.5 ± 22.5	.85
MAP, mm Hg	74.3 ± 24.5	80.6 ± 25.1	.19
CVP, mm Hg	4.3 ± 5.5	7.2 ± 9.1	.24
Laboratory values			
WBC, per mm ³	15.5 ± 10.6	13.3 ± 8.5	.33
Hematocrit, %	36.0 ± 8.0	33.1 ± 7.9	.06
Platelet, per mm ³	224,000 ± 119,000	177,000 ± 97,000	.03 ^a
Prothrombin time, secs	14.7 ± 3.0	19.2 ± 8.3	<.001 ^a
D-Dimer, ng/mL	2751 ± 3849	4163 ± 9586	.11
Creatinine, mg/dL	2.3 ± 1.5	2.9 ± 2.5	.13
Albumin, g/dL	3.0 ± 0.7	2.6 ± 0.7	.004 ^a
Total bilirubin, mg/dL	1.3 ± 2.2	3.0 ± 4.1	.002 ^a
Base deficit, mmol/L	7.7 ± 8.1	9.5 ± 6.8	.06
pH	7.34 ± 0.17	7.31 ± 0.20	.57
Scvo ₂ , %	51.9 ± 15.2	50.6 ± 10.5	.79
Lactate, mmol/L	6.1 ± 4.4	8.0 ± 4.7	.01 ^a
Therapy in the ED			
Intravenous fluids, mL	3375 ± 2617	3351 ± 2892	.75
PRBC transfusion, %	12.5	25.5	.08
Mechanical ventilation, %	46.9	61.7	.12
Vasopressor, %	26.6	31.9	.54
Dobutamine, %	3.1	2.1	1.00
Lactate clearance, %	38.1 ± 34.6	12.0 ± 51.6	.005 ^a

APACHE, Acute Physiology and Chronic Health Evaluation; MAP, mean arterial pressure; CVP, central venous pressure; WBC, white blood cell; Scvo₂, central venous oxygen saturation; ED, emergency department; PRBC, packed red blood cells.

^aStatistically significant, *p* < .05.

Table 3. Multivariate logistic regression modeling using statistically significant univariate variables associated with mortality

Variable	OR (95% CI)	p Value
Septic shock	2.473 (0.927–6.600)	.07
Platelet	0.999 (0.994–1.004)	.69
Prothrombin time	1.140 (0.988–1.315)	.07
Albumin	0.569 (0.267–1.212)	.14
Total bilirubin	1.045 (0.855–1.276)	.67
Lactate	1.057 (0.945–1.182)	.34
Lactate clearance	0.989 (0.978–0.999)	.04 ^a

OR, odds ratio; CI, confidence interval.

^aStatistically significant, *p* < .05.

The interpretation of single lactate measurements has several limitations. First, blood lactate concentrations reflect the interaction between the production and elimination of lactate. For example, a sepsis patient with hepatic dysfunction may have a higher lactate compared with the patient without liver disease but may have a similar degree of stress. Second, an increased lactate concentration may indicate mechanisms other than cellular hypoxia, such as up-regulation in epinephrine-stimulated Na/K-adenosine triphosphatase activity in skeletal muscle

(12) and inhibition of pyruvate metabolism or an increase in its production (15, 44, 45). Given these limitations, serial lactate measurements are more important as an outcome prognosticator than a single lactate measurement (16–18, 46). Bakker et al. (16) defined “lactime” as the time during which lactate remains >2 mmol/L and observed that this duration of lactic acidosis was predictive of organ failure and survival. Trauma patients whose lactate normalized in 24 hrs (or lactime ≤24 hrs) were shown to have 100% survival (17), whereas persistent

Lactate clearance in the most proximal presentation of severe sepsis and septic shock is associated with improved morbidity and mortality rates.

lactate elevation >6 hrs is associated with increased mortality rate (47). Additionally, elevated lactate concentrations up to 48 hrs are associated with higher mortality rate in postoperative hemodynamically stable patients (19). A goal of resuscitation is then to minimize lactate.

The present study extends the concept of lactate normalization during early therapeutic intervention. Our findings suggest that lactate clearance, as defined by the percentage of lactate cleared over the first 6-hr period of disease presentation, is an independent variable associated with decreased mortality rate. Patients with high lactate clearance required less vasopressor therapy, had greater improvements in APACHE II scores, and had decreased mortality rates. During resuscitation, a lactate clearance of >10% from its baseline value in as brief a period as 6 hrs is achievable. When this clearance occurs during the most proximal stages of disease presentation such as the ED stay, it may be associated with improved organ function (decreased APACHE II score) and suggests decreased mortality rate up to 60 days. Our results also suggest that high lactate clearance is associated with decreased mortality rate in severe sepsis patients with elevated baseline lactate but without hypotension. This observation that organ hypoperfusion can exist in the presence of normotension further supports the notion that blood pressure is a poor indicator of disease severity.

Current methodologies using ICU-based physiologic scoring systems, such as APACHE II, have limited diagnostic and therapeutic application in the ED setting since those systems were designed to prognosticate outcome after the initial 24 hrs of ICU care (32, 48). In this study, we calculated APACHE II in a nontraditional

Table 4. Baseline characteristics, therapy, and outcome between high and low lactate clearance groups

	Low Lactate Clearance <10% (n = 31)	High Lactate Clearance ≥10% (n = 80)	p Value
Age, yrs	62.0 ± 15.7	66.0 ± 17.0	.25
Vital signs			
Temperature, °C	37.4 ± 1.4	36.6 ± 2.3	.07
Heart rate, beats/min	117.6 ± 20.9	116.6 ± 28.8	.87
MAP, mm Hg	82.5 ± 26.9	74.8 ± 23.8	.14
CVP, mm Hg	5.3 ± 5.9	6.4 ± 8.9	.96
Laboratory values			
WBC, per mm ³	13.1 ± 8.3	15.1 ± 10.3	.39
Hematocrit, %	33.6 ± 8.1	35.2 ± 8.0	.35
Platelet, per mm ³	164,000 ± 82,000	220,000 ± 119,000	.02 ^a
Prothrombin time, secs	18.2 ± 6.9	16.0 ± 5.9	.01 ^a
D-Dimer, ng/mL	4903 ± 1549	2728 ± 3604	.59
Creatinine, mg/dL	2.8 ± 2.8	2.5 ± 1.5	.59
Albumin, g/dL	2.6 ± 0.8	2.9 ± 0.7	.07
Total bilirubin, mg/dL	2.7 ± 3.3	1.8 ± 3.2	.06
Base deficit, mmol/L	7.6 ± 8.2	8.8 ± 7.4	.34
pH	7.32 ± 0.20	7.33 ± 0.18	.86
Scvo ₂ , %	50.8 ± 11.6	51.6 ± 14.3	.87
Lactate, mmol/L	7.0 ± 5.7	6.9 ± 4.2	.28
Therapy, hrs			
Intravenous fluids, mL			
0-6	2828 ± 1947	3572 ± 2956	.44
7-72	9200 ± 6629	10,246 ± 6550	.44
PRBC transfusion, %			
0-6	25.8	15.0	.18
7-72	41.9	35.4	.53
Mechanical ventilation, %			
0-6	58.1	51.3	.52
7-72	29.0	13.9	.07
Vasopressor, %			
0-6	45.2	22.5	.02 ^a
7-72	61.3	39.2	.04 ^a
Dobutamine, %			
0-6	0.0	3.8	.56
7-72	9.7	8.9	.99
Outcome			
APACHE II, hrs			
6	19.4 ± 5.8	20.5 ± 7.1	.46
12	19.3 ± 6.4	17.1 ± 6.3	.09
24	18.3 ± 6.4	14.9 ± 6.2	.02 ^a
36	17.2 ± 6.5	14.1 ± 6.1	.03 ^a
48	16.8 ± 6.8	13.1 ± 5.8	.01 ^a
60	14.3 ± 4.5	12.8 ± 6.2	.34
72	14.5 ± 5.3	12.6 ± 5.4	.18
72	14.7 ± 6.1	12.5 ± 5.4	.15
In-hospital mortality rate, %	67.7	32.5	<.001 ^a
30-day mortality rate, %	67.7	37.5	.004 ^a
60-day mortality rate, %	71.0	42.5	.007 ^a
Severe sepsis, %	29.0	55.0	.01 ^a
Lactate, mmol/L	4.8 ± 2.9	6.4 ± 3.8	.20
In-hospital mortality rate, %	55.6	20.5	.03 ^a
Septic shock, %	71.0	45.0	.01 ^a
Lactate, mmol/L	7.9 ± 6.4	7.5 ± 4.5	.41
In-hospital mortality rate, %	72.7	47.2	.06

MAP, mean arterial pressure; CVP, central venous pressure; WBC, white blood cell; Scvo₂, central venous oxygen saturation; PRBC, packed red blood cell; APACHE, Acute Physiology and Chronic Health Evaluation.

^aStatistically significant, *p* < .05.

manner at discrete time points over the first 72 hrs to serially follow the trend in scores as an indicator of the progression of disease (26). The addition of lactate clearance in assessing the patient's physiological reserve and as an indicator of outcome has further implications in understanding the progression of sepsis to

multiple organ failure and death in the pre-ICU period.

This study was limited to one urban ED setting with a high level of patient acuity and an ICU admission rate that nearly doubles the national average (49). Therefore, the stratification of patients into lactate clearance groups with the

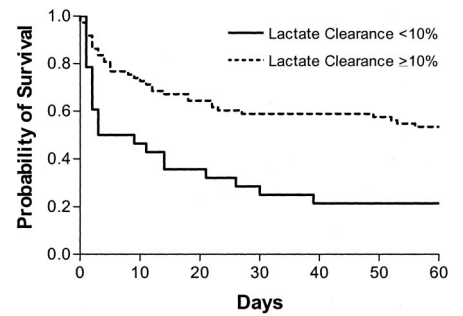


Figure 1. Kaplan-Meier survival analysis between patients with lactate clearance <10 vs. ≥10% at 6 hrs after emergency department presentation.

observed mortality rates should be generalized only with caution to other EDs. Traditional resuscitation end points such as vital signs fail to definitively address the severity of global tissue hypoxia and thus are a poor reflection of the resuscitation and the development of organ failure and death. Initial serial lactate measurements in the presence of SIRS alert the clinician to the severity of illness and may be associated with outcome.

CONCLUSIONS

Lactate clearance in the most proximal presentation of severe sepsis and septic shock is associated with improved morbidity and mortality rates. This is consistent with current efforts that emphasize the importance of identifying and treating tissue hypoperfusion during the first 6 hrs of resuscitation (50). Further clinical trials are needed to conclusively establish lactate clearance as a resuscitation end point and an outcome measure to be targeted during the most proximal phases of severe sepsis and septic shock.

ACKNOWLEDGMENTS

We thank the nurses and the technical and administrative support staff in the Department of Emergency Medicine at Henry Ford Hospital for their assistance in this study.

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