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The impact of serial lactate monitoring on emergency department resuscitation interventions and clinical outcomes in severe sepsis and septic shock: an observational cohort study

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Abstract

Monitoring in the setting of critical illness must be linked to beneficial therapy in order to affect clinical outcome. Elevated serum lactate is associated with an increase in mortality in Emergency Department (ED) patients with severe sepsis and septic shock. The reduction of lactate levels towards normal during acute resuscitation is associated with improved clinical outcomes. The majority of data demonstrating the interventions used to achieve a reduction in lactate levels, and the associated clinical outcomes, have been obtained during protocolized randomized trials. We therefore conducted a retrospective observational cohort study of 243 adult patients with severe sepsis and septic shock to assess the interventions associated with non-protocolized serial lactate monitoring, and to assess clinical outcomes. A multivariable model was used to assess outcome differences between the serial lactate (SL) and no serial lactate (NL) cohorts. The SL group received more crystalloid resuscitation (3.6 vs. 2.5 liters, $p < 0.01$) central venous oxygen saturation monitoring (30% vs. 12%, $p < 0.01$), and central venous pressure monitoring (23.5% vs. 11.8%, $p = 0.02$). By day 28, a total of 31 patients in the SL group (23.5%) and 44 in the NL group (39.6%) had died. Multivariable logistic regression analysis demonstrated that the lack of serial lactate monitoring was independently associated with mortality (adjusted OR 2.09; 95% confidence interval [CI], 1.12 to 3.89; $p = 0.02$). The SL group also showed greater improvement in 24 hour SOFA scores (1.16 vs. 0.19, $p = 0.03$), decreased intensive care unit length of stay in days (4.6 vs 6.0, $p = 0.04$), more ventilator-free (19.9 vs. 16, $p = 0.05$) and vasopressor-free (21.6 vs. 17.9 $p = 0.02$) days. In the setting of routine clinical care, serial lactate monitoring is associated with an increase in crystalloid administration, resuscitation interventions, and improved clinical outcomes in ED patients with severe sepsis and septic shock. This suggests that serial lactate monitoring, targeting a reduction in lactate levels to normal, is a generalizable resuscitation target in the ED.

Keywords

sepsis; monitoring; lactate

INTRODUCTION

Quantitative resuscitation utilizes hemodynamic endpoints to guide interventions aimed at the reversal of early tissue hypoperfusion. In the setting of severe sepsis and septic shock, quantitative resuscitation utilizes surrogates of preload [central venous pressure (CVP)], cardiac output [central venous oxygen saturation ($S_{cv}O_2$)] and oxygen carrying capacity (hemoglobin and arterial oxygen saturation) to guide interventions aimed at the rapid correction of oxygen delivery (DO_2)/consumption (VO_2) mismatch.(1) While early implementation of this strategy has been shown to improve mortality in patients with severe sepsis and septic shock, the efficacy of its constituent components have been debated.(2–4) Specifically, the enthusiasm for using $S_{cv}O_2$ as a therapeutic endpoint has been limited by physiologic concerns, logistical concerns in implementing its use, and data showing a lack of benefit outside the setting of a randomized trial.(5–9) This suggests that a re-evaluation of the use of markers of end-organ perfusion outside the setting of highly protocolized care is needed.

Serum lactate is a marker of global tissue hypoperfusion and is used as a trigger for quantitative resuscitation for severe sepsis.(1) Lactate levels represent the balance between production and elimination; elevated levels are predictive of outcome in infection and are a valuable tool for risk stratification.(10) The reduction of an initially elevated lactate level toward normal, can serve as a surrogate for the reversal of global tissue hypoxia and response to therapy.(11, 12) Randomized trials targeting the normalization of elevated lactate levels as part of a comprehensive resuscitation strategy have shown improved survival in patients with shock and comparable outcomes when compared to an $S_{cv}O_2$ target in patients with severe sepsis.(13, 14) While these data provide robust evidence for the use of lactate monitoring as a therapeutic target in the setting of randomized trials, it is unknown if this target during non-protocolized, routine care is beneficial.

Monitoring in the setting of critical illness does not affect clinical outcomes unless tied to a specific therapeutic intervention.(8) The specific therapies used by clinicians to normalize elevated lactate levels during routine care are not well defined. As such, identifying emergency department (ED) resuscitation interventions employed during serial lactate monitoring could: 1) provide insight into the routine treatments aimed at normalizing lactate levels; and 2) allow assessment of the potential generalizability of lactate as a resuscitation target during routine care. If targeting lactate outside the auspice of a randomized trial is not only beneficial, but also associated with relatively simple interventions, serial lactate monitoring could serve as a useful strategy to guide resuscitation across multiple ED settings.

In this study of ED patients with severe sepsis and septic shock, our objectives were to: 1) identify the resuscitation interventions associated with the use of serial lactate monitoring; and 2) assess the clinical outcomes associated with this approach. We hypothesized that the

serial monitoring of lactate in ED patients with severe sepsis and septic shock would be associated with an increase in ED resuscitation interventions as well as an improvement in clinical outcomes when compared to patients resuscitated without the use of serial lactate monitoring.

MATERIALS AND METHODS

Study design

This was a retrospective observational cohort study. This observational study is reported in accordance with The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for Reporting Observational Studies (STROBE).(15) Financial support for this project was provided in part from the National Center for Research Resources (NCRR), and the National Center for Advancing Translational Sciences (NCATS), National Institutes of Health, through Grant KL2 TR000450. Additional funding comes from the Missouri College of Emergency Physicians Medical Student/Resident Research Grant. The funding organizations played no role in the study concept, design, data analysis, or writing of the manuscript. This study was approved by the Human Research Protection Office at the primary investigator's institution.

Study setting and population

This study was conducted at an urban academic ED with an annual census of >95,000 patients. The total study period was sixteen months. Over a one year period (January – December, 2011), adult patients with severe sepsis or septic shock and an initial ED lactate level ≥ 4 mmol/L were eligible for inclusion. Additional patients presenting from December 2012 – March 2013 were enrolled to ensure adequate sample size. During the study period, there were no systematic changes in interventions, resuscitation protocols, or other care delivery (e.g. antibiotics). Exclusion criteria included ED length of stay < 2 hours, documented do not resuscitate (DNR)/do not intubate (DNI) status, and patient transfer to a facility outside of hospital network.

Study protocol

Patients with severe sepsis or septic shock and lactate ≥ 4 mmol/L were identified by query of the electronic medical record and verified by record review. To insure uniform data collection and accuracy, all variables were defined prior to data extraction and placed in a standardized format during the data collection process. Regular meetings and monitoring of data collection were performed. Data was cross-checked for accuracy with the electronic medical record prior to final data entry. Demographic data were extracted from the ED chart, and comorbidities were defined as those listed in the "History of Present Illness" and "Past Medical History" of the ED record. Baseline patient characteristics included: age, gender, race, comorbidities, lactate level, sequential organ failure assessment (SOFA) score, time to initial lactate, suspected source of infection, and ED length of stay. ED resuscitation interventions included intravenous crystalloid volume administered, vasopressor and inotrope (i.e. dobutamine) use, packed red blood cell transfusion, central venous catheter placement, arterial catheter placement, and monitoring of $S_{cv}O_2$ and CVP. Other process of

care variables included time to antibiotics, need for mechanical ventilation, and corticosteroid administration.

Sepsis was defined as previously described.(16) To verify the diagnosis in the ED, suspected source of infection was extracted from hospital discharge summary or death summary for the hospital course after ED admission. The patients were dichotomized based on the use of serial lactate monitoring during the course of their resuscitation. The serial lactate cohort (SL) was defined as severe sepsis patients with an initial lactate ≥ 4 mmol/L that also had a second lactate drawn while in the ED. The no serial lactate cohort (NL) was defined as patients with an initial lactate ≥ 4 mmol/L that did not have a second lactate drawn while in the ED. Initial lactate was defined as the initial lactate value recorded in the ED with a value ≥ 4 mmol/L. The reduction in serial lactate levels was calculated as a percentage and defined as: initial lactate value minus second lactate value divided by initial lactate, then multiple by 100 $[(\text{lactate}^{\text{initial}} - \text{lactate}^{\text{second}})/\text{lactate}^{\text{initial}}] \times 100$. A significant reduction in lactate level was defined as a decrease in lactate of $\geq 20\%$ between the first and second measured lactate.

Mortality was defined as documented death within 28 days of ED presentation. SOFA score was assessed as previously described.(17) Due to the low inter-rater agreement for the Glasgow Coma Scale (GCS) component, a modified SOFA score was used, which omits the neurologic function component of the score.(18) When more than one value was present SOFA scores were calculated from the most abnormal value. For the calculation of initial SOFA score, if a value was not measured in the ED, then the first value after hospital admission was used to calculate initial SOFA score (only applicable to the bilirubin component of the score). If a component score was not assessed after hospital admission, the SOFA score for this value was assumed to have not changed between ED presentation and at 24 hours after hospital admission. 24-hour SOFA scores were calculated from the first data available after 24 hours from hospital admission. Delta (Δ)-SOFA score was defined as the difference between the initial SOFA score and the SOFA score at 24 hours, with a decrease in SOFA score reflecting an improvement in organ function. Ventilator-and vasopressor-free days were calculated as the number of calendar days the patient was alive and not receiving these therapies within 28 days of ED presentation. DNR/DNI was defined as documentation of “DNR,” “DNI,” or “comfort care” in the medical record.

Outcomes

The primary analysis of interest was to identify the specific ED resuscitation interventions employed during the monitoring of serial lactate. The primary clinical outcome of interest was 28-day mortality. Secondary outcomes included the change in organ failure, as reflected by Δ -SOFA score at 24 hours after hospital admission, intensive care unit (ICU) length of stay (LOS), ventilator-free days, and vasopressor-free days. An *a priori* subgroup analysis of the serial lactate cohort was performed to further assess the impact of the magnitude of lactate reduction on outcome.

Statistical analysis

Descriptive statistics, including mean $[\pm$ standard deviation (SD)] and frequency distributions were used to assess the characteristics of the patient cohort. Normality of the

data was assessed graphically with histograms and numerically by assessing skewness and kurtosis. Continuous and categorical data were compared using an unpaired t-test, chi-square test, or Fisher's exact test as appropriate. Multivariable models were used to assess outcome differences between the SL and NL cohorts. Logistic regression analysis was used to assess mortality difference between the two groups and analysis of covariance (ANCOVA) was used to assess differences in continuous outcomes. Variables statistically significant in univariable analysis were candidates for inclusion in multivariable analysis. Collinearity was assessed, and the model used variables that contributed information that was statistically independent of the other variables in the model. Adjusted odds ratios (aORs) and corresponding 95% confidence intervals are reported for variables in the multivariable model, adjusted for all variables in the model. To assess clinical outcomes based on magnitude of lactate reduction, chi-square, analysis of variance (ANOVA) using log-transformed data was used to compare groups. All tests were two-tailed and a p-value <0.05 was considered statistically significant. As relatively little was known on the expected effect size of non-protocolized lactate monitoring on clinical outcomes, we decided *a priori* to accrue our sample size by examining subjects during a predefined time period. However, as an assurance against inadequate power secondary to small sample size, a sample size calculation was performed to detect a change in SOFA score of 2 or more points from 0 to 24 hours, given the strong prognostic value of early change in organ failure on outcome.(19–22) A 2 point change was defined *a priori* as a significant change based on 1) 2 points was the approximate difference in SOFA score in our previous work examining risk factors for complications in severe sepsis and septic shock patients (i.e. development of acute respiratory distress syndrome [ARDS]); and 2) a full 2 point change is meaningful from a clinical perspective(23, 24). A two-tailed test, with 80% power and an alpha of 0.05, yielded a sample size of 66 patients in each group. With a total sample size of 243 patients, we were reasonably assured of an adequate sample to examine clinical outcome differences between the two groups. Analyses were performed in consultation with a biostatistician using SAS 9.3 (SAS Institute, Cary NC).

RESULTS

A total of 571 patients with a lactate of ≥ 4 mmol/L were screened for inclusion in the study (Figure 1). After exclusions, a total of 243 patients were included in the final analysis. Table 1 shows the baseline characteristics and ED interventions of the study population. Baseline characteristics were similar except for a higher rate of COPD (9% vs. 22%, $p<0.01$) and pulmonary source of infection (14% vs. 25%, $p=0.05$) in the NL group.

The ED resuscitation interventions are shown in Table 1 and Figure 2. The most common intervention performed was placement of a central venous catheter ($n=116$), followed by vasopressor use ($n=85$). By contrast, fewer patients received monitoring of the oxygen-derived variable $S_{cv}O_2$ ($n=52$) or therapies traditionally targeted at this value (transfusion, $n=44$; dobutamine, $n=13$). There were several differences in the ED interventions between the two groups. The SL group received more intravenous crystalloid (3.6 vs. 2.5 liters, $p<0.01$), and demonstrated a trend toward more central venous catheter placement (53% vs. 41%, $p=0.07$). With respect to monitoring, there was a higher prevalence of $S_{cv}O_2$

monitoring (30% vs. 12%, $p<0.01$) and CVP monitoring (24% vs. 12%, $p=0.02$) in the SL group.

By day 28, a total of 31 patients in the SL group (23.5%) and 44 in the NL group (39.6%) had died. Multivariable logistic regression analysis demonstrated that the lack of serial lactate monitoring was independently associated with mortality (adjusted OR 2.09; 95% confidence interval [CI], 1.12 to 3.89; $p=0.02$). The remainder of the multivariate analysis for clinical outcomes is also presented in Table 2. The NL group showed increased ICU LOS in days (6.0 vs 4.6, $p=0.04$), less ventilator-free days (16.0 vs. 19.9, $p=0.05$), and less vasopressor free days (17.9 vs. 21.6, $p=0.02$). The SL group had a reduction in 24-hour organ failure when compared to the NL group [SOFA 1.16 (2.6) vs. 0.19 (2.7), $p=0.03$]

Sub-group analysis comparing outcomes based on magnitude of lactate reduction are shown in Table 3. A greater reduction in lactate levels toward normal was associated with improved 28-day mortality ($p<0.001$) as well as increased numbers of ventilator-free ($p=0.03$) and vasopressor-free ($p<0.001$) days.

DISCUSSION

The quantitative resuscitation of patients with severe sepsis and septic shock improves outcome, yet has been viewed as difficult to implement and controversial.(4, 5) Recent data suggests that $S_{cv}O_2$ monitoring outside of a randomized trial (i.e. during routine, non-protocolized resuscitation) may not positively impact mortality.(7) The requirement for invasive monitoring to sample $S_{cv}O_2$, as well as non-inferiority data comparing $S_{cv}O_2$ versus lactate levels, has led to increased interest in lactate as an alternate, less-invasive resuscitation endpoint.(14) To date, much of the data regarding lactate has been restricted to prospectively collected data, either as part of a clinical trial or observational study at centers with established quantitative resuscitation protocols.(10, 11, 13, 14, 25–27) Outside of prospective research studies, little data exists regarding the outcomes and interventions associated with the adoption of serial lactate monitoring during the routine clinical care of septic shock patients in the ED. The results of the current study add significant information associated with this approach.

We first sought to characterize the ED resuscitation interventions associated with (and perhaps driven by) serial lactate monitoring. We found that the most common intervention associated with serial lactate monitoring was central venous catheter insertion, though not statistically different from the NL cohort. Central venous catheter use in the setting of severe sepsis and septic shock is typically used for safe vasopressor administration, transduction of CVP, or monitoring of $S_{cv}O_2$. However, a significant number of patients with central venous catheters placed had none of these other resuscitation interventions performed (Table 1, Figure 2). This suggests that a less-invasive approach could have likely achieved similar clinical outcome benefit. An interesting observation from our study is that the 53% central venous catheter insertion rate in the SL group is similar to the “usual-care” group (57.9%) from a recent multicenter trial examining protocolized care during early sepsis resuscitation (ProCESS).(28) This suggests that the usual practice for severe sepsis and septic shock resuscitation in an academic ED now involves insertion of a central venous catheter in the

slight majority of patients. The most significant resuscitation difference between the two groups was in the volume of intravenous fluids administered in the ED (1.1 liters; also similar to ProCESS data). Patients with early severe sepsis and septic shock are thought to be volume depleted and preload responsive.(1, 16) Our data, and biologic plausibility, suggest that early tissue hypoperfusion may have been improved with augmentation of recruitable preload. It also suggests that the primary clinical response in lactate-guided resuscitation is to expand intravascular volume. Our NL cohort received approximately the same amount of fluid as all of the cohorts in ProCESS prior to randomization.(28) This suggests that in routine practice, without a quantitative resuscitation goal, patients may receive insufficient intravenous resuscitation.

We also sought to describe the impact of lactate monitoring on clinical outcomes during routine resuscitation. Patients monitored with serial lactate in the ED had a reduction in mortality and organ failure, as well as ICU length of stay. Our data are congruent with clinical trials and prospective observational studies, and suggests that lactate-guided resuscitation is beneficial outside of a well-conducted randomized trial. This further promotes the generalizability of this monitoring strategy. Similar to all monitoring devices, unless tied to a therapy that improves outcome, simply collecting lactate levels should not improve outcome. The only therapeutic intervention differing between the two groups was in the volume of intravenous fluid administered in the ED, as detailed above. It would be difficult to ascribe an absolute risk reduction for mortality of 16.1% to 1.1 liters of fluid; though employed in a minority of patients, a statistically significant difference in S_{cVO_2} and CVP monitoring suggests that perhaps serial lactate monitoring was part of overall better care delivery in this group. Another interesting observation from this study is the very similar effect size for mortality between the two groups when compared to the original early goal-directed therapy trial (16.1% vs. 16.0%), as well as a similar mortality rate between our SL group and the protocol-based groups from the ProCESS trial (23.5% vs. 19.5%).(1, 28) While significant differences exist between these studies, these data provide further evidence that targeted resuscitation of severe sepsis and septic shock is accompanied by significant mortality reduction, perhaps irrespective of the exact target chosen. Previous data reveals improved organ failure and 60-day mortality in patients who achieved 10% reduction in lactate over 6 hours.(11) We demonstrated a congruent effect in our population, with a stepwise improvement in mortality as the percentage of lactate reduction increased.

Going forward, our study has several implications. By achieving a mortality rate similar to randomized trials, the results of this “usual practice” study further suggest that quantitative resuscitation targets play a role in the treatment of severe sepsis and septic shock. It suggests that in EDs where invasive monitoring may be logistically difficult to achieve, such as non-academic community hospitals, serial lactate monitoring can improve outcome in a real-world setting. Long-term observational studies should continue to compare the outcome of these patients. Our study also suggests that volume administration is the primary intervention given in the ED when serial lactates are assessed. Only half of critically ill ICU patients are preload responsive, suggesting that these hemodynamic studies are urgently needed in the ED, as it is possible that some patients are harmed by this approach.(29) It also draws further attention to the need to normalize lactate levels during early resuscitation.

Strategies that address persistently elevated lactate, including targets on the macrocirculatory, microcirculatory, or mitochondrial level are still needed.

There are limitations to our study. This is a retrospective study which limits causal inference. We cannot say if serial lactate monitoring is a driver of the difference in the resuscitation interventions employed and the mortality difference seen (cause-effect); it is also possible that serial lactate monitoring is part of a bundle of more appropriate care and is therefore only an association (effect-cause). However the consistent results between our study and previous clinical trials suggest cause-effect. Also due to the retrospective nature of the study, the time to first lactate measurement and the time interval between the first and the second lactate were not standardized. Therefore, it is difficult to identify the extent to which the second lactate measurement contributed to care decisions or impacted the outcome. However, doing so would have defeated one of the primary objectives of the study, which was the assessment of lactate clearance efficacy when employed during routine care, outside the setting of a highly protocolized trial. We believe that the applicability of our results in a real-world scenario is actually a strength of the study. An imbalance in the percentage of NL patients that were mechanically ventilated, and had COPD and a pulmonary source of infection, suggests that the NL group may have been sicker and more likely to have increased ventilator days, though other predictors of outcome (e.g. lactate, SOFA, time to antimicrobial therapy) were similar. The difference in ED mechanical ventilation rate may also reflect improved organ failure at any early stage in resuscitation, preventing the need for early intubation.⁽¹⁾ We restricted our analysis to a lactate level which should traditionally trigger quantitative resuscitation; therefore the study examined only those patients with a lactate ≥ 4 mmol/L. It is possible that our findings are not applicable to patients with a less significantly elevated lactate level.

In conclusion, serial lactate monitoring in the ED patients with severe sepsis and septic shock is associated with an increase in crystalloid administration, resuscitation interventions, and improved clinical outcomes. This supports the use of serial lactate values, aimed at normalization of lactate levels, as a less-invasive generalizable resuscitation target in the ED.

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Figure 1.

Flow diagram depicting the screening and exclusions of emergency department patients with an initial lactate ≥ 4 mmol/L

SL : serial lactate, NL: no serial lactate, DNR/DNI: do not resuscitate / do not intubate, LOS: length of stay

Figure 2.

Emergency Department resuscitation interventions between the two groups. PRBC: packed red blood cell; CVP: central venous pressure; $S_{cv}O_2$: central venous oxygen saturation; IV: intravenous

There were no differences in resuscitation interventions ($p > 0.05$ for all variables) when comparing the patients enrolled during the first twelve months of the study ($n = 179$) versus those enrolled during the last four months of the study ($n = 64$).

Table 1

Baseline characteristics of the study cohort

	Serial Lactates (SL, n=132)	No Serial Lactates (NL, n=111)	p-value
Baseline			
Age, yr	61.6 (15.8)	60.4 (17.8)	0.59
Female, n (%)	58 (44)	48 (43)	0.91
Race, n (%)			
– Caucasian	55 (42)	47 (42)	0.91
– Other	77 (58)	64 (58)	0.91
Comorbidities, n (%)			
– CHF	15 (11)	19 (17)	0.19
– Diabetes Mellitus	37 (28)	42 (38)	0.10
– COPD	12 (9)	25 (22)	0.004
– ESRD	8 (6)	10 (9)	0.38
– Liver Disease	17 (13)	15 (13)	0.88
– Malignancy	25 (19)	18 (16)	0.58
Temperature, C	36.7 (1.6)	36.7 (1.5)	1.0
sBP	81.5 (23.6)	85.2 (27.0)	0.26
CVP	13.9 (8.0)	11.5 (9.8)	0.40
P _a O ₂	220.5 (166.5)	187.9 (89.6)	0.52
Hemoglobin	11.6 (2.9)	11.5 (3.1)	0.80
Platelet	231.2 (164.6)	238.2 (151.4)	0.73
Bilirubin	1.3 (1.9)	1.6 (3.2)	0.38
Creatinine	2.1 (1.9)	1.8 (2.0)	0.23
Lactate, (mmol/L)	7.3 (3.8)	6.7 (2.9)	0.17
SOFA *	4.8 (3.2)	4.9 (3.5)	0.69
Time to initial lactate, min	82 (135)	136 (228)	0.02
Suspected Source of Infection			
– Pulmonary	18 (14)	26 (23)	0.05
– Urinary	28 (21)	19 (17)	0.42
– Intra-abdominal	11 (8.3)	6 (5.4)	0.37
– Skin/soft tissue	5 (3.8)	8 (7.2)	0.24
– Blood	13 (9.8)	9 (8.1)	0.64
ED LOS (min)	526 (289)	408 (289)	<0.001
Process-of-care variables			
Time to antibiotics, min	182 (138)	192 (147)	0.57
Mechanical ventilation, n (%)	41 (31)	51 (46)	0.02
Corticosteroids, n (%)	17 (13)	8 (7.4)	0.17
ED resuscitation interventions			

	Serial Lactates (SL, n=132)	No Serial Lactates (NL, n=111)	p-value
Intravenous crystalloid, mL	3552 (1693)	2478 (1791)	<0.001
Vasopressor use, n (%)	44 (33)	41 (37)	0.56
Dobutamine use, n (%)	8 (6)	5 (4.5)	0.59
pRBC transfusion, n(%)	24 (18)	20 (18)	0.97
Central line, n (%)	70 (53)	46 (41)	0.07
Arterial line, n (%)	25 (19)	23 (21)	0.73
S _{cv} O ₂ monitoring, n (%)	39 (30)	13 (12)	<0.001
CVP monitoring, n (%)	31 (23.5)	13 (12)	0.02

Continuous variables are reported as mean (SD)

There were no differences in baseline characteristics ($p > 0.05$ for all variables) when comparing the patients enrolled during the first twelve months of the study ($n = 179$) versus those enrolled during the last four months of the study ($n = 64$).

CHF=congestive heart failure, COPD=chronic obstructive pulmonary disease, ESRD=end stage renal disease, sBP: systolic blood pressure, CVP=central venous pressure, PaO₂: partial pressure of arterial oxygenation, SOFA=sequential organ failure assessment, ED=emergency department, LOS=length of stay, pRBC=packed red blood cell, S_{cv}O₂=central venous oxygen saturation

* Modified score, which excludes Glasgow Coma Score¹⁷

Table 2

Clinical outcomes by multivariable analysis

	Serial Lactates (n=132)	No Serial Lactates (n=111)	aOR	95% CI	p-value
28-day mortality, n(%)	31 (23.5)	44 (39.6)	2.09	1.12–3.89	0.02
ILOS, days	4.6 (9.5)	6.0 (8.2)	1.95	1.51–2.40	0.04
Ventilator-free days	19.9 (13)	16 (12.2)	3.14	0.07–6.21	0.05
Vasopressor-free days	21.6 (10.3)	17.9 (12)	4.13	0.50–7.22	0.02

Continuous variables are reported as mean (SD)

ILOS=intensive care unit length of stay; HLOS=hospital length of stay; aOR: adjusted odds ratio; CI: confidence interval

Table 3

Outcomes by magnitude of the decrease in lactate levels toward normal

	No decline in lactate (n=19)	Lactate reduction <20% (n=22)	Lactate reduction 20–40% (n=27)	Lactate reduction >40% (n=64)	p-value
28-day mortality, n (%)	10 (52.6)	8 (36.4)	8 (29.6)	4 (6.3)	<0.001
ILOS, days	3.5 (3.4)	4.3 (6.6)	4.1 (5.0)	5.2 (13)	0.58
Ventilator-free days	14 (12)	18 (12)	19 (11.5)	23 (13)	0.03
Vasopressor-free days	15 (13)	19 (11)	20 (11)	26 (6.4)	<0.001

Continuous variables are reported as mean (SD).

ILOS=intensive care unit length of stay