Received: 27 August 2023 | Revised: 19 June 2024 | Accepted: 18 July 2024

DOI: 10.1002/emp2.13281

JACEP OPEN
JOURNAL OF THE AMERICAN COLLEGE OF EMERGENCY PHYSICIANS OPEN
A GLOBAL JOURNAL OF EMERGENCY MEDICINE
WILEY

ORIGINAL RESEARCH

General Medicine

Association between measures of resuscitation in the critical care resuscitation unit and in-hospital mortality among patients with sepsis

Nikki Emamian BS[1] | Taylor Miller MD[2] | Zoe Glick MD[2] | Lauren Day MD[2] | Lauren Becker MD[3] | Aditi Singh BS[1] | Tesia Shi[1] | Jeffrey Rea MD[4] | Kimberly Boswell MD[4] | Quincy K. Tran MD, PhD[1,2,4]

[1]Emergency Medicine and Critical Care, Department of Emergency Medicine, University of Maryland School of Medicine, Baltimore, Maryland, USA

[2]Department of Emergency Medicine, University of Maryland School of Medicine, Baltimore, Maryland, USA

[3]Departments of Pulmonary and Critical Care Medicine, University of Maryland School of Medicine, Baltimore, Maryland, USA

[4]Program in Trauma, University of Maryland School of Medicine, Baltimore, Maryland, USA

Correspondence
Nikki Emamian, BS, Emergency Medicine and Critical Care, Department of Emergency Medicine, University of Maryland School of Medicine, Baltimore, Maryland, USA.
Email: nikki.emamian@umm.edu

Data from this manuscript was presented in part at the National Congress, Society of Critical Care Medicine, San Francisco, USA in January 2023.

Supervising Editor: Robert Levine, MD

Funding and support: By *JACEP Open* policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article as per ICMJE conflict of interest guidelines (see www.icmje.org). The authors have stated that no such relationships exist.

Abstract

Objectives: We hypothesized that lactate clearance and reduction of the Sequential Organ Failure Assessment (SOFA) score during patients' critical care resuscitation unit (CCRU) stay would be associated with lower in-hospital mortality.

Methods: This was a retrospective study of adult patients who had sepsis diagnoses and were admitted to the CCRU in 2018. Multivariable logistic regression analysis was performed to assess the association of clinical factors, lactate clearance, and SOFA reduction with hospital mortality.

Results: A total of 401 patients with lactate clearance data and 455 patients with SOFA score data were included in the study. The mean (SD) lactate and SOFA score on admission were 2.2 (1.8) mmol/L and 4.4 (4.3), respectively. Average lactate clearance was 0.1 (2.6) mmol/L, and average SOFA score reduction was 0.65 (5.9). Patients with a one point reduction in SOFA score during their CCRU stay had a 31% reduction of mortality (odds ratio [OR] 0.69, 95% confidence interval [CI] 0.62–0.77, $p < 0.001$). SOFA score reduction was associated with lower hospital mortality for both surgical patients (OR 0.69, 95% CI 0.58–0.81, $p < 0.001$) and non-surgical patients (OR 0.71 95% CI 0.06–0.83, $p < 0.001$).

Conclusion: SOFA score reduction, but not lactate clearance during the CCRU stay, was associated with lower odds of in-hospital mortality. These findings suggest that resuscitative efforts leading to an early improvement in SOFA score may benefit patients with sepsis.

KEYWORDS
critical care, resuscitation, sepsis, shock, SOFA

1 | INTRODUCTION

1.1 | Background

Sepsis continues to be a large driver of mortality in US hospitals, with mortality rates on hospital admission reported to be as high as 34.9%.[1] Mortality among critically ill patients with sepsis has been shown to be associated with severity of organ dysfunction and biomarkers, such as lactate. A major focus of modern sepsis treatment is the early recognition and implementation of intensive resuscitation of septic patients to reduce mortality.[2]

1.2 | Importance

Lactate and lactate clearance have been demonstrated to be predictors of mortality in critically ill patients in various settings.[3–6] The correlation between disease severity, as measured by in-hospital mortality, and elevated lactate has been particularly evident in sepsis, even in the absence of significant hypotension.[7,8] In particular, lactate clearance in intensive care unit (ICU) settings has been linked to decreased mortality in patients with septic shock.[9–11]

Besides lactate, Sequential Organ Failure Assessment (SOFA) scores have also demonstrated an association with mortality in critical illness.[12] This scoring system was designed to standardize levels of organ dysfunction and has been demonstrated to be more accurate at predicting mortality in patients with septic shock than Systemic Inflammatory Response Syndrome (SIRS) criteria.[13] SOFA scores have provided clinicians with valuable data for patient prognosis both in the ICU and in the emergency department (ED).[14]

1.3 | Goals of this investigation

The impact of ED interventions on organ failure has been well documented with the greatest decrease in organ dysfunction scores, such as SOFA scores, occurring during a patient's ED stay.[15] In addition, a previous study from the Critical Care Resuscitation Unit (CCRU) at the University of Maryland Medical Center (UMMC) found that transferring outside patients directly to the CCRU rather than to a traditional ICU was associated with decreased transfer times and decreased mortality rates.[16]

A recent analysis of a heterogenous group of patients including critical vascular and neurologic patients with elevated serum lactate levels found that resuscitative interventions in the CCRU decreased lactate and SOFA scores. In this group, a decrease in SOFA score was associated with decreased in-hospital mortality.[17] However, this patient population included patients whose outcomes are not generally expected to be as closely related to markers of resuscitation such as lactate and SOFA score. Given the known association between these variables and mortality in sepsis, we hypothesized that early lactate clearance and SOFA score reduction during patients' CCRU stay would be associated with decreased risk of in-hospital mortality among critically ill sepsis patients.

The Bottom Line

Early recognition and treatment are key for improving sepsis outcomes. In this study of over 400 sepsis patients treated in a critical care resuscitation unit, Sequential Organ Failure Assessment (SOFA) reduction, but not lactate clearance, was associated with lower odds of death. SOFA change may have utility as a gauge of successful sepsis resuscitation.

2 | METHODS

2.1 | Study settings

The CCRU is a six-bed resuscitation ICU located in the R. Adams Cowley Shock Trauma Center at UMMC and is physically separated from the ED at our institution. The CCRU accepts nontraumatic critically ill transfers to expedite access to care only available at a quaternary medical center.[18] Patients from any EDs, any non-acute inpatient units (medical or surgical wards), or any ICUs can be transferred to the CCRU. This function distinguishes the CCRU from other ED-based resuscitation units, which cannot accept transfer from other ICUs. Prior to transfer, these patients received initial resuscitative measures including early fluids, antibiotics, and bundled sepsis measures. Through an expert critical care team, the CCRU provides early, aggressive resuscitation to critically ill patients. The CCRU is composed of and staffed continuously by a dual boarded emergency medicine–critical care attending physician, an advanced practice provider (APP), three nurses, and a charge nurse. Nursing staff are required to have at least 2 years of prior ICU experience before working in the CCRU. Flexible staffing provides up to two nurses for clinical management at the bedside during the acute phase, facilitating early, aggressive resuscitative measures. There are no specific protocols or policies guiding resuscitation in the CCRU. Rather, interventions are guided by the ED-Intensivist, in collaboration with the subspecialty teams for each patient's disease state, providing additional resuscitation, early provision of invasive procedures, or referral for surgical source control if necessary. Following CCRU stabilization, patients are transferred to the appropriate inpatient units for further longitudinal care.

2.2 | Study design, patient selection, and physiologic measures

We conducted a retrospective analysis of all adult patients diagnosed as septic at the time of admission to the CCRU in the full calendar year of 2018. Exclusion criteria included trauma, death in the CCRU, change in resuscitation status in the CCRU, and incomplete data. Two specific variables, lactate clearance and SOFA score reduction, were evaluated as markers for patients' clinical course in the CCRU. This study was approved by the University of Maryland Baltimore's IRB (HP-00084554). For this type of study, formal consent is not required.

2.3 | Outcome measures

The primary outcome was in-hospital mortality. We hypothesized that improvement in resuscitation measures, reflected in lactate clearance and reduction in SOFA score in the CCRU, would be associated with decreased risk of subsequent in-hospital mortality for septic patients. Lactate clearance was calculated by subtracting the lactate level upon departure from the CCRU from the patients lactate level on arrival. SOFA score reduction was similarly calculated as SOFA score on arrival minus SOFA score on departure from the unit. A secondary analysis of the association between SOFA score reduction and lactate clearance and in-hospital mortality was performed among the pre-specified subgroups of surgical or non-surgical CCRU patients. Surgical patients were defined as patients who had emergent surgical infections and required any surgical intervention in an operating room either during their CCRU stay or immediately afterwards. Patients undergoing a bedside procedure or a procedure performed by interventional radiology were considered non-surgical.

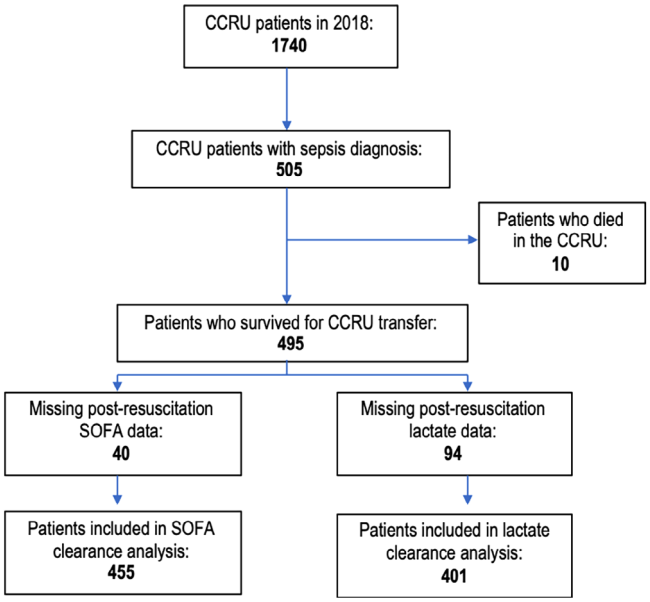

FIGURE 1 Patient selection diagram.

2.4 | Data collection

The UMMC's electronic medical records were used for data collection. Members of the research team were trained by the principal investigator to collect data using sets of five study patients' charts. Training continued until junior investigator accuracy reached 90% of the senior investigators. Up to 10% of SOFA score data were also randomly checked for accuracy. Any discrepancies were corrected by senior investigators. Collected data included patient age, gender, past medical history, hospital mortality, hospital length of stay, hospital discharge, serum lactate levels, and components of the SOFA score. A Microsoft Excel spreadsheet was used for data collection (Microsoft Corp). Patients in which it was still possible to calculate a SOFA score despite missing one component of the SOFA score were included in analysis. Patients missing more than one component of the SOFA score were excluded from analysis as were those missing data that made it impossible to calculate accurate SOFA score.

2.5 | Statistical analysis

Demographic and clinical information are presented using descriptive analyses with mean (± standard deviation [SD]) or median (interquartile range [IQR]) as appropriate. Comparisons between independent variables are expressed with differences between groups (hospital survivors vs. non-survivors) and their associated 95% confidence intervals (95% CI).

Multivariate logistic regression analyses are conducted to determine the association between lactate clearance and SOFA score reduction and in-hospital mortality. The effect of SOFA score reduction is further examined in surgical and non-surgical patients. Independent variables, considered important factors for in-hospital mortality, were selected a priori according to previous literature and entered into the models.[17] Results from multivariable logistic regression analyses are expressed as odd ratio (OR), 95% CI, and *p*-value. Multicollinearity is assessed using the variance inflation factor (VIF). Factors with VIF > 5 were considered to have high collinearity and are eliminated from the models. The goodness-of-fit of the models is assessed with the Hosmer–Lemeshow analysis, of which *p*-value > 0.05 indicates good fit of the data. Performance of the models is evaluated with the area under the receiver operating curve (AUROC). A model with AUROC approaching 1.0 would indicate excellent discriminatory capability between dichotomous outcomes (survivor vs. non-survivor).

All descriptive analyses and multivariable logistic regression analyses are performed with Minitab version 20 (www.minitab.com). All statistical analyses with *p*-value < 0.05, except the Hosmer–Lemeshow test, are considered statistically significant.

3 | RESULTS

3.1 | Patient characteristics

A total of 1740 patients were admitted to the CCRU in 2018, 505 (29%) of whom had a sepsis diagnosis (Figure 1). Ten (2%) patients died during their CCRU stay and were excluded from analysis. Of these 10 patients, decision makers withdrew life support from eight patients prior to their death. Primary analysis included 401 patients with lactate clearance data and 455 patients with SOFA score data. Patients' average (SD) age was 53.9 (16.0) years, with a median length of stay in the CCRU of 6 h and 24 min (IQR 3:12–17:36). The average lactate and SOFA score on admission were 2.2 (1.8) mmol/L and 4.4 (4.3), respectively. Average lactate clearance was 0.1 (2.6), and average SOFA score

TABLE 1 Patient characteristics.

	All patients	Survivors	Non-survivors
Number of patients	495	445	50
Age, mean (SD)	53.9 (16.0)	54.0 (16.0)	53.1 (15.8)
Female, *n* (%)	6.4 (3.2, 17.6)191 (42.9)		23 (46.0)
Past medical history, *n* (%)			
Hypertension	213 (43.0)	179 (40.2)	16 (32.0)
Diabetes	164 (33.1)	144 (32.4)	20 (40.0)
Liver disease	47 (9.5)	45 (10.1)	2 (4.0)
Kidney disease	97 (19.6)	86 (19.3)	11 (22.0)
Cardiac disease	99 (20.0)	90 (20.2)	9 (18.0)
Shock index, mean (SD)	0.8 (0.2)	0.8 (0.2)	0.8 (0.2)
White blood cell count (counts/μL), mean (SD)	17.5 (23.4)	17.5 (24.5)	17.5 (9.2)
Hemoglobin (g/dL), mean (SD)	10.6 (3.7)	10.6 (3.8)	9.9 (1.9)
Arrival lactate (mmol/L), mean (SD)	2.2 (1.8)	2.1 (1.6)	2.5 (3.1)
Lactate change in CCRU, mean (SD)	0.1 (2.6)	0.1 (2.4)	−0.1 (4.0)
Arrival SOFA score, mean (SD)	4.4 (4.3)	4.3 (4.2)	5.4 (5.0)
SOFA change in CCRU, mean (SD)	−0.65 (5.9)	−0.2 (5.6)	−4.6 (6.8)
CCRU length of stay, h (IQR)	6.4 (3.2, 17.6	6.1 (3.2, 17.8)	11.1 (3.6, 17.2)
Invasive ventilation, *n* (%)	140 (28.3)	123 (27.6)	17 (34.0)
Requiring vasopressors, *n* (%)	110 (22.2)	94 (21.1)	16 (32.0)
Diagnoses[a], *n* (%)			
Soft tissue	259 (52.3)	233 (52.4)	26 (52.0)
Intra-abdominal	86 (17.4)	80 (18.0)	6 (12.0)
Respiratory	43 (8.7)	38 (8.5)	5 (10.0)
Medical other	42 (8.5)	36 (8.1)	6 (12.0)
Surgical other	36 (7.3)	33 (7.0)	3 (6.0)

Abbreviations: CCRU, critical care resuscitation unit; CI, confidence interval; IQR, interquartile range; SD, standard deviation; SOFA, Sequential Organ Failure Assessment.
[a]Top five diagnosis categories indicated here.

reduction was 0.65 (5.9) during CCRU stay (Table 1). Further characteristics between hospital survivors and non-survivors are presented in Table 1.

A significant proportion of these patients received major interventions during their CCRU stay (65.9%, 326/495) (Table 2). The most common interventions were emergent surgical intervention (53.3%, 264/495 patients), intubation (8.7%, 43/495 patients), continuous renal replacement therapy (5.5%, 27/495 patients), and hyperbaric oxygenation therapy (4.0%, 20/495 patients).

TABLE 2 Interventions done in the critical care resuscitation unit (CCRU) separated by survival.

Intervention, *N* (%)	All patients	Survivors	Non-survivors
VV ECMO	13 (2.6)	13 (2.9)	0 (0.0)
VA ECMO	1 (0.2)	1 (0.2)	0 (0.0)
Continuous renal replacement therapy (CRRT)	27 (5.5)	22 (4.9)	5 (10.0)
Intra-aortic balloon pump (IABP)	3 (0.6)	2 (0.4)	1 (2.0)
Intubation	43 (8.7)	38 (8.5)	5 (1.0)
Interventional radiology	10 (2.0)	10 (2.2)	0 (0.0)
Operating room	264 (53.3)	236 (53.0)	28 (56.0)
Hyperbaric therapy	20 (4.0)	18 (4.0)	2 (4.0)
Intermittent hemodialysis	12 (2.4)	9 (2.0)	3 (6.0)
Cardiac cath	1 (0.2)	1 (0.2)	0 (0.0)
EGD	2 (0.4)	2 (0.4)	0 (0.0)

Abbreviations: EGD, esophagogastroduodenoscopy; EVD, external ventricular drainage; VA ECMO, veno-atrial extracorporeal membrane oxygenation; VV ECMO, veno-venous extracorporeal membrane oxygenation.

TABLE 3 Multivariate logistic regression results of association between physiological measures, including both lactate level plus Sequential Organ Failure Assessment (SOFA) score and in-hospital mortality.

	Odds ratio	95% CI	*p*	VIF
Age	1.00	(0.97, 1.03)	0.97	1.22
White blood cell	0.99	(0.98, 1.01)	0.46	1.15
Hemoglobin	0.80	(0.67, 0.96)	0.02*	1.15
Lactate at CCRU admission[a]	0.98	(0.75, 1.27)	0.87	2.33
Lactate clearance[a]	1.11	(0.91, 1.36)	0.30	2.66
SOFA at CCRU admission[b]	1.61	(1.35, 1.92)	0.001*	4.29
SOFA clearance[b]	0.69	(0.62, 0.77)	0.001*	3.96
Hypertension	0.75	(0.30, 1.86)	0.53	1.39
Diabetes	1.52	(0.64, 3.63)	0.34	1.28
Liver disease	0.18	(0.03, 0.97)	0.046*	1.10
Kidney disease	1.12	(0.40, 3.15)	0.84	1.25
Heart disease	1.72	(0.53, 5.53)	0.37	1.39

Note: Hosmer–Lemeshow test chi-square $p = 0.29$; AUROC = 0.88.
Abbreviations: AUROC, area under the receiving operating characteristic curve; CI, confidence interval; VIF, variance inflation factor.
[a]Pearson correlation between SOFA at CCRU admission and SOFA clearance, $r = 0.67$, $p = 0.001$.
[b]Pearson correlation between lactate at CCRU admission and lactate clearance, $r = 0.66$, $p = 0.001$.
*The indicates statistically significant value.

3.2 | Main results

In a multivariate logistic regression analysis that included lactate, lactate clearance, SOFA, and SOFA reduction, each unit of higher SOFA score at arrival to the CCRU was associated with 61% higher odds

TABLE 4 Results of two separate regressions for surgical and non-surgical populations showing association between Sequential Organ Failure Assessment (SOFA) score reduction and lactate clearance and in-hospital mortality. Only primary variables of interest were reported in the model.

	Surgical (196 patients)[a]				Non-surgical (172 patients)[b]			
	Odds ratios	95% CI	*p*-value	VIF	Odds ratio	95% CI	*p*-value	VIF
Lactate at CCRU admission	0.37	(0.16, 0.85)	0.02	1.76	0.92	(0.51, 1.67)	0.79	3.41
Lactate clearance	1.18	(0.94, 1.49)	0.16	1.51	1.19	(0.76, 1.88)	0.45	3.37
SOFA at CCRU admission	1.61	(1.28, 2.02)	0.001	4.16	1.15	(0.90, 1.48)	0.27	2.23
SOFA reduction	0.69	(0.58, 0.81)	0.001	3.27	0.71	(0.60, 0.83)	0.001	2.25

Abbreviations: CCRU, critical care resuscitation unit; CI, confidence interval; VIF, variance inflation factor.
[a]Hosmer–Lemeshow $p = 0.69$, AUROC = 0.89.
[b]Hosmer–Lemeshow $p = 0.93$, AUROC = 0.90.

of in-hospital mortality (OR 1.61, 95% CI 1.35–1.92). For every point of SOFA score reduction achieved during resuscitation in the CCRU, patients had an associated 31% reduced odds of in-hospital mortality (OR 0.69, 95% CI 0.62–0.77). Lactate at arrival to the CCRU and lactate clearance did not show a statistically significant relationship with mortality in this model. The model had an AUROC of 0.88, indicating very good discriminatory capability. A high VIF was not seen for independent variables in the model, indicating a low likelihood of multicollinearity among the variables (Table 3). Lactate values and SOFA scores on admission to the CCRU were not strongly associated with lactate clearance or SOFA score reduction (Pearson $r = 0.66$ and 0.67, respectively) (Table 3).

SOFA score and serum lactate levels at CCRU admission were associated with increased odds of in-hospital mortality for surgical patients (Table 4). This association was not found for non-surgical patients. In contrast, SOFA score reduction was associated with lower odds of subsequent in-hospital mortality for both surgical patients (OR 0.69, 95% CI 0.58–0.81) and non-surgical patients (OR 0.71, 95% CI 0.60–0.83) (Table 4).

4 | LIMITATIONS

This study has several limitations. First, the generalizability of these findings is limited by the unique clinical setting and the practice of the CCRU. Unlike most ED patients, CCRU patients have already received early sepsis bundled resuscitation, whereas unlike most ICU patients, CCRU patients benefit from expedited transfer from outside hospitals allowing resuscitation earlier in the hospital course. Second, excluding patients with incomplete data may introduce selection bias. Patients for whom complete data were not obtained by the treating team may have had a lower expected mortality than those included in the analysis. Similarly, patients who were taken directly for surgical intervention and thus did not have serial lactate and SOFA scores to calculate may have a higher expected mortality than included patients. Our analysis studied in-hospital mortality but no other outcomes such as hospital length of stay. Additionally, just over half of the patients treated for sepsis in the CCRU had soft tissue infection or necrotizing fasciitis as a source of infection, which is a unique patient population. Patients with necrotizing soft tissue infections may respond differently to resuscitative efforts than patients with other sources of sepsis. Finally, though SOFA score reduction is generally considered to be a marker of successful resuscitation, some patients in our study had an increase in their SOFA score due to appropriate resuscitation efforts (e.g., intubation and initiation of vasopressors) and this patient population was not studied separately.[19,20]

5 | DISCUSSION

This study demonstrates an association between reduction in SOFA score, a marker of successful reduction of risk for multiorgan dysfunction, and in-hospital mortality among septic patients. Each point of reduction in SOFA in the CCRU was associated with a 31% reduction of in-hospital mortality. Lactate clearance, a commonly used measurement for resuscitation, was not found to be associated with mortality.

This study supports prior literature focusing on patients with septic shock that suggests early and effective resuscitation as measured by improvement in clinical and laboratory markers is associated with improved patient outcomes. A prior study by Nguyen et al. demonstrated that early resuscitation of septic shock in the ED, as measured by improved physiologic scores during the first 24 h, was associated with lower mortality.[10] Another prior study of CCRU patients found a relationship between improvement in physiologic score and mortality in patients with severe shock.[17]

Unlike other studies investigating lactate clearance, this study did not find a relationship between lactate clearance and mortality. This may be because patients had already received the standard sepsis bundle of care prior to being included in this study. This study also included patients with a diagnosis of sepsis with and without shock and accordingly had a patient population with a relatively low initial lactate value (median lactate at CCRU admission of 2.2 mmol/L) and small lactate clearance during CCRU stay. The small level of lactate clearance after initial sepsis bundled care was not enough to demonstrate improved outcomes.

Patients in this study had a mean SOFA score reduction of 0.65 points, and each point of SOFA score reduction was associated with

31% lower likelihood of in-hospital mortality. These findings suggest that even in the absence of a highly elevated serum lactate level, reversing organ dysfunction, as reflected by the SOFA score, is associated with reduced in-hospital mortality. This study demonstrates a greater reduction of mortality for each point reduction in SOFA score than a previous study of patients with elevated serum lactate due to severe shock. Thus, this study may suggest a stronger association between SOFA score reduction and mortality in patients who have not yet developed severe shock. The fact that patients in this study already received the standard sepsis bundle such as early fluids and antibiotics prior to being transferred to the CCRU suggests benefits to further resuscitative efforts even after the standard sepsis bundle has been completed. If lactate clearance at this stage of resuscitation is not associated with mortality, the use of detailed physiologic parameters included in the SOFA score may be a good alternative measure of patients' clinical progress. These findings appeared to apply to both surgical and non-surgical patients within the study population.

Each point of SOFA score reduction during CCRU stay was associated with 31% reduced odds of in-hospital mortality, but lactate clearance was not associated with mortality. This study suggests that early and successful prevention of further organ failure, as measured by SOFA score, improves outcomes in patients with sepsis. Further studies are needed to confirm this observation (Supporting Information).

AUTHOR CONTRIBUTIONS

Data collection, data analysis, visualization, and writing—original draft: Nikki Emamian. Conceptualization, data analysis, validation, writing—original draft, and writing—review and editing: Taylor Miller. Data collection and validation: Zoe Glick. Writing—original draft: Lauren Day. Writing—original draft: Lauren Becker. Data collection and validation: Aditi Singh. Data collection and validation: Tesia Shi. Conceptualization and writing—reviewing and editing: Jeffrey Rea. Conceptualization and writing—reviewing and editing: Kimberly Boswell. Conceptualization, data analysis, writing—original draft, and writing—review and editing: Quincy K. Tran.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

ORCID

Nikki Emamian BS https://orcid.org/0009-0006-9201-4478

REFERENCES

1. Rhee C, Jones TM, Hamad Y, et al. Prevalence, underlying causes, and preventability of sepsis-associated mortality in US acute care hospitals. *JAMA Netw Open*. 2019;2(2):e187571. doi:10.1001/jamanetworkopen.2018.7571
2. Evans L, Rhodes A, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. *Intensive Care Med*. 2021;47(11):1181-1247. doi:10.1007/s00134-021-06506-y
3. Vincent J, Silva AQE, Couto L, et al. The value of blood lactate kinetics in critically ill patients: a systematic review. *Critical Care*. 2016;20(1):257. doi:10.1186/s13054-016-1403-5
4. Mungan İ, Kazancı D, Bektaş Ş, et al. Does lactate clearance prognosticates outcomes in ECMO therapy: a retrospective observational study. *BMC Anesthesiol*. 2018;18(1):152. doi:10.1186/s12871-018-0618-1
5. Zhang Z, Xu X. Lactate clearance is a useful biomarker for the prediction of All-Cause mortality in critically ill patients. *Crit Care Med*. 2014;42(9):2118-2125. doi:10.1097/ccm.0000000000000405
6. Scolari FL, Schneider D, Fogazzi DV, et al. Association between serum lactate levels and mortality in patients with cardiogenic shock receiving mechanical circulatory support: a multicenter retrospective cohort study. *BMC Cardiovascular Disorders*. 2020;20(1):496. doi:10.1186/s12872-020-01785-7
7. Lokhandwala S, Moskowitz A, Lawniczak R, et al. Disease heterogeneity and risk stratification in sepsis-related occult hypoperfusion: a retrospective cohort study. *J Crit Care*. 2015;30(3):531-536. doi:10.1016/j.jcrc.2015.01.009
8. Casserly B, Phillips G, Schorr C, et al. Lactate measurements in sepsis-induced tissue hypoperfusion. *Crit Care Med*. 2015;43(3):567-573. doi:10.1097/ccm.0000000000000742
9. Shadvar K, Nader ND, Vahed N, et al. Comparison of lactate/albumin ratio to lactate and lactate clearance for predicting outcomes in patients with septic shock admitted to intensive care unit: an observational study. *Sci Rep*. 2022;12(1):13047. doi:10.1038/s41598-022-14764-z
10. Nguyen HB, Rivers EP, Knoblich B, et al. Early lactate clearance is associated with improved outcome in severe sepsis and septic shock. *Crit Care Med*. 2004;32(8):1637-1642. doi:10.1097/01.ccm.0000132904.35713.a7
11. Jansen TC, Van Bommel J, Schoonderbeek FJ, et al. Early lactate-guided therapy in intensive care unit patients. *Am J Respir Crit Care Med*. 2010;182(6):752-761. doi:10.1164/rccm.200912-1918oc
12. Vincent JL, de Mendonca A, Cantraine F, et al. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. *Crit Care Med*. 1998;26(11):1793-1800.
13. Seymour CW, Liu VX, Iwashyna TJ, et al. Assessment of clinical criteria for sepsis: for the third international consensus definitions for sepsis and septic shock (sepsis-3). *JAMA*. 2016;315(8):762-774. doi:10.1001/jama.2016.0288
14. Jones AE, Trzeciak S, Kline JA. The sequential organ failure assessment score for predicting outcome in patients with severe sepsis and evidence of hypoperfusion at the time of emergency department presentation. *Crit Care Med*. 2009;37(5):1649-1654. doi:10.1097/CCM.0b013e31819def97
15. Nguyen HB, Rivers EP, Havstad S, et al. Critical care in the emergency department a physiologic assessment and outcome evaluation. *Acad Emerg Med*. 2000;7(12):1354-1361. doi:10.1111/j.1553-2712.2000.tb00492.x
16. Tran QK, O'Connor J, Vesselinov R, et al. The critical care resuscitation unit transfers more patients from emergency departments faster and is associated with improved outcomes. *J Emerg Med*. 2020;58(2):280-289. doi:10.1016/j.jemermed.2019.09.041
17. Miller T, Emamian N, Glick Z, et al. Association between resuscitation in the critical care resuscitation unit and in-hospital mortality. *Am J Emerg Med*. 2022;60:96-100. doi:10.1016/j.ajem.2022.07.042
18. Scalea TM, Rubinson L, Tran QK, et al. Critical care resuscitation unit: an innovative solution to expedite transfer of patients with time-sensitive critical illness. *J Am Coll Surg*. 2016;222(4):614-621. doi:10.1016/j.jamcollsurg.2015.12.060
19. Xixi NA, Kremmydas P, Xourgia E, et al. Association between timing of intubation and clinical outcomes of critically ill patients: a meta-analysis. *J Crit Care*. 2022;71:154062. doi:10.1016/j.jcrc.2022.154062

20. Li Y, Li H, Zhang D. Timing of norepinephrine initiation in patients with septic shock: a systematic review and meta-analysis. *Crit Care*. 2020;24(1):488. doi:10.1186/s13054-020-03204-x

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Emamian N, Miller T, Glick Z, et al. Association between measures of resuscitation in the critical care resuscitation unit and in-hospital mortality among patients with sepsis. *JACEP Open*. 2024;5:e13281. https://doi.org/10.1002/emp2.13281

AUTHOR BIOGRAPHY

Nikki Emamian is a Clinical Research Associate at the University of Maryland Medical Center in Baltimore, MD.