8-19-2022

Advanced Triage Protocol: The Role of an Automated Lactate Order in Expediting Rapid Identification of Patients at Risk of Sepsis in the Emergency Department

Andrew Baum
US Acute Care Solutions

Brendan G Carr
Mount Sinai School of Medicine

Sarah M Perman
University of Colorado School of Medicine

Jennifer Barger
Perelman School of Medicine at the University of Pennsylvania

Munish Goyal
Georgetown University School of Medicine

See next page for additional authors

OPEN

Advanced Triage Protocol: The Role of an Automated Lactate Order in Expediting Rapid Identification of Patients at Risk of Sepsis in the Emergency Department

Andrew Baum, MD[1]
Brendan G. Carr, MD, MSCE[2]
Sarah M. Perman, MD[3]
Jennifer Barger, MS, BSN, RN[4]
Munish Goyal, MD[5]
David F. Gaieski, MD[6]

OBJECTIVES: We undertook a process improvement initiative to expedite rapid identification of potential sepsis patients based on triage chief complaint, vital signs, and initial lactate level.

DESIGN: Prospective cohort study.

SETTING: Seven hundred-bed tertiary care hospital with ≅65,000 patient visits/yr.

PATIENTS: Patients presenting to emergency department (ED) triage who met the following criteria: greater than or equal to two of the three systemic inflammatory response syndrome criteria assessable in triage, a chief complaint suggestive of infection, emergency severity index 2 or 3, and ambulatory to ED.

INTERVENTIONS: A computer-generated lactate order was created, staff education and resources increased, and point-of-care lactate testing was introduced.

MEASUREMENTS AND MAIN RESULTS: Primary endpoints include the following: percent of patients having a lactate level drawn, percent of lactate samples resulting before room placement, and time intervals from triage to lactate blood draw and to lactate result. Secondary endpoints were percentage of patients admitted to the hospital, percentage admitted to the ICU, and in-hospital mortality. Six thousand nine hundred six patients were included: 226 historic controls (HCs) and 6,680 intervention group patients. The mean serum lactate level was 1.77 ± 1.18 mmol/L. The percentage of patients having a lactate resulted increased from 27.4% in the HC period to 79.6%. The percentage of these lactate results available while the patient was still in the waiting room increased from 0.4% during the HC period to 33.7% during Phase 5 ($p < 0.0001$). In the intervention period, time from triage to lactate result decreased (78.1–63.4 min; $p < 0.0001$) and time to treatment room decreased (59.3–39.6 min; $p < 0.0001$).

CONCLUSIONS: Implementation of a computerized lactate order using readily available data obtained during ED triage, combined with point-of-care lactate testing, improves time to lactate blood draw and lactate result in patients at risk for severe sepsis. Initial lactate levels correlated with admission to the hospital, admission to the ICU, and in-hospital mortality.

KEY WORDS: assessment; early detection; lactic acid; risk; sepsis

Sepsis, the dysregulated immune response to infection, affects approximately 2 million in the United States annually (1, 2), has an overall mortality of 20–30%, and has a continually increasing incidence (3). Healthcare costs for sepsis care in the United States average $24,638 per case (4). Although sepsis develops across all settings in the hospital, the largest percentage have sepsis present at admission (POA) (5).

DOI: 10.1097/CCE.0000000000000736

A key aspect of treating sepsis is early recognition. Although a patient presenting with hypotension and a clear infectious source consistent with septic shock will be rapidly identified as requiring immediate resuscitation (6–8), the identification of more subtle sepsis cases requires a thoughtful approach to screening based on an understanding of the continuum between a regulated and dysregulated immune response to infection and the vital sign (VS) changes accompanying this transition (1, 9).

The systemic inflammatory response syndrome (SIRS), first described in 1992, is a nonspecific physiologic response to an inflammatory trigger (9). SIRS is the presence of two or more of the following: temperature less than 96.8°F or greater than 100.4°F, heart rate (HR) greater than 90 beats/min, respiratory rate (RR) greater than 20 breaths/min, and WBC count less than 4,000 or greater than 12,000 cells/cc or greater than 10% immature cells. When the SIRS criteria are present in combination with a presumed or confirmed infection, a patient is classified as having sepsis (9). The need for time-sensitive resuscitation centers on evidence of acute end-organ failure, which may be obvious (e.g., altered mental status) or subtle (e.g., elevated creatinine) and only recognized by laboratory testing.

Sepsis patients with an elevated lactate have increased risk of in-hospital mortality (IHM) independent of the presence of hypotension. Mikkelsen et al (10) demonstrated that normotensive sepsis patients had escalating IHM as initial lactate value increased from less than 2.0 mmol/L to 2.0–3.9 mmol/L to greater than or equal to 4.0 mmol/L (8.7% vs 16.4% vs 31.8%, respectively). Similar observations were incorporated into the 2002 revisions of the International Sepsis Guidelines in which a serum lactate greater than 3 mmol/L was considered a sign of tissue level hypoperfusion (11, 12).

Sepsis monitoring and screening became further complicated with the Third International Sepsis Definitions (2016), which eliminated SIRS as a screening tool and suggested that a quick Sequential Organ Failure Assessment (qSOFA) score could be rapidly applied at the bedside to identify patients at increased risk of mortality or prolonged ICU stay (1). The qSOFA score consists of a systolic blood pressure less than 100 mm Hg, a RR greater than or equal to 22 breaths/min, and a Glasgow Coma Scale score of less than 15. A score greater than or equal to 2 was considered positive. Subsequent research has demonstrated that qSOFA is not sensitive enough to capture a majority of patients presenting to emergency department (ED) triage at risk for sepsis (13, 14), and many EDs now use a combination of SIRS and qSOFA to expedite identification and risk stratification.

Further, given significant crowding and boarding in EDs, many patients' wait hours before they have definitive care initiated and subtle presentations of sepsis may be missed (15). Validated measures of ED crowding correlate with time to fluids and antibiotics in sepsis patients (16). Attempts have been made to overcome these challenges by using various early warning systems (EWS) (17, 18), which integrate a combinations of VSs, chief complaints (CCs), and laboratory values to expedite identification of and care for critically ill patients presenting to the ED (12, 15–18). Implementation of an EWS is associated with significant decreases in time to antibiotics, and scores correlate with ICU admission and mortality (18–26). In addition, triage point-of-care (POC) testing of various variables, including lactate, has demonstrated the potential for early identification of this patient cohort (27–29).

We undertook a bundle of process improvements to expedite rapid identification of potential sepsis patients in our ED using a combination of triage VS and presenting CC and then risk stratified the cohort based on a rapidly obtained lactate level. We hypothesized that these interventions would increase the percent of qualifying patients who had a lactate level resulted in the ED, increase the percent of lactate results available before room placement, and decrease the times from triage to lactate blood draw and to lactate result.

MATERIALS AND METHODS

Study Design

This was a prospective observational study of the stepwise implementation of a process improvement initiative. It was reviewed and approved by the Institutional Review Boards (IRBs) of the University of Pennsylvania and Thomas Jefferson University in expedited fashion with a waiver of informed consent (IAA no. 00004028; IRB no. 802726; approved 3/25/2015), and the study was conducted in accordance with institutional ethical standards on human experimentation and the Helsinki Declaration of 1975.

Study Setting and Population

The study was conducted in a 700-bed urban tertiary care hospital with a 56-bed ED, ≅65,000 annual adult patient visits, and a 24% admission rate.

All patients greater than or equal to 18 years old who presented to the ED between March 12, 2009, and March 31, 2014 and met the following criteria were included in the study:

- Presence of at least two of the three SIRS criteria assessable at triage (HR > 90; RR > 20; temperature > 100.4°F or < 96.8°F) during initial VS readings.
- One of 42 CCs suggestive of infection (derived from an institutional database, the 42 CCs were present in > 99% of sepsis patients admitted to the hospital [unpublished data]) (**Supplemental Table 1**, Supplemental Digital Content, http://links.lww.com/CCX/B42).
- Triaged as emergency severity index (ESI) class 2 or 3 (excludes most severe classification [ESI 1], who are immediately placed in a treatment room, and two classifications for nonurgent patients [ESI 4 and 5], who are seen in the fast track area of the ED).
- Patients who are classified as mode of arrival, self or private vehicle (all patients arriving by ambulance were excluded because ambulance patients were rarely taken to the waiting room and then triaged as an ESI 2 or 3). Rather, they went to an available room or a hallway bed where they were triaged and care was initiated by the treatment team. Their inclusion would have skewed the sample toward a subset of patients who had care (IV, laboratories) initiated immediately after arrival.

Study Protocol

To develop the advanced triage protocol (ATP), a task force was formed, including faculty, nurses, residents, emergency medical technicians (EMTs), medics, clerks, and the information technology director of emergency medicine. This task force met between September 2008 and March 2009 to develop the protocol and regularly during the study period to review preliminary data. The task force identified the main time points in patient flow from ED arrival to room placement and the time intervals between these time points (**Supplemental Fig.**, Supplemental Digital Content, http://links.lww.com/CCX/B42]. An algorithm was programmed into the electronic medical record (EMR) (Emergency Medicine Tracking System (EMTrac), University of Pennsylvania, Philadelphia, PA; replaced by Epic Systems Corporation (EPIC), Verona, WI, April 1, 2010), which identified all patients who met study inclusion criteria and automatically generated an order for a venous blood gas with lactate. After collecting baseline lactate utilization data during an historic control (HC) period from from January 19, 2009 to March 1, 2009, a five-phased protocol occurred between March 2, 2009, and March 31, 2014:

- Phase 1, March 02, 2009 to May 31, 2009: implementation of the computer-generated lactate order at triage and prioritization of patients with a lactate value greater than 3 mmol/L for immediate transfer to a treatment room.
- Phase 2, June 01, 2009 to April 30, 2010: education of ED EMTs about the importance of drawing blood immediately after order; the education was provided by email from the principle investigator (D.F.G.) and in-person education sessions by the department's lead EMT, repeated every 3 months; in addition, at the start of Phase 2, "sepsis guideline" pocket cards were redistributed by the investigators to all ED staff involved in direct patient care (**Supplementary Material**, Supplemental Digital Content, http://links.lww.com/CCX/B42).
- Phase 3, May 01, 2010 to May 13, 2011: assigned an EMT to triage/waiting room whose main tasks included rapidly drawing a serum lactate after the computer-generated order appeared and changed lactate value triggering immediate transfer to treatment room to greater than 2 mmol/L based on analysis of interim data.
- Phase 4, April 14, 2011 to June 12, 2013: ED EMT staffing reverted to Phase 2 staffing levels.
- Phase 5, June 13, 2013 to March 31, 2014: POC lactate analyzers were introduced in the ED to obtain triage lactate results immediately instead of sending to the hospital's main laboratory for processing and analysis.

Initial serum lactate levels were measured using a Radiometer ABL90Flex blood gas analyzer, a small footprint, 11 kg machine with automatic blood mixing capabilities, which can perform a lactate measurement on 65 microliters of blood in less than 60 seconds, accurately reporting a range of lactate values from 0.7 to 24.0 mmol/L, with internal calibrations and quality control performed once every 8 hours to ensure accuracy (Radiometer Medical ApS, Brønshøj, Denmark).

Measures

Primary outcome measures included the following: percent of lactates resulted while the patient was in the ED, the percent of lactates resulted while the patient was still in the waiting room, and the time intervals from triage to lactate blood draw and to lactate result. We also analyzed the time from lactate result to room placement, which could be negative (lactate resulted prior to room placement) or positive (lactate resulted after room placement). Secondary endpoints included

the following: the percentage of patients in each lactate category admitted to the hospital, admitted to the ICU, and IHM. Classification as a primary sepsis patient with POA was based on either the explicit *International Classification of Diseases,* 9th Edition (ICD-9) codes for severe sepsis (995.92) or septic shock (785.52) or the ICD-9 code for sepsis (995.91) or common infections combined with at least one ICD-9 code for acute organ dysfunction following the Angus method (3). Mortality data were not available for the HC period, so this cohort was excluded from the IHM analysis. We used the time period January 19, 2009, to December 31, 2009, from another institutional sepsis database, the details of which have been described elsewhere (30), to calculate the sensitivity of our screening technique.

Data Analysis

Data were compared between the different phases. All data were captured electronically from EMTrac or EPIC and stored in an Excel spreadsheet (Microsoft, Redmond, WA). During data cleaning, if physiologically implausible variables were present, they were imputed as the mean value for the variable. Data are presented as descriptive statistics. Categorical variables were reported as number and percent and compared with the chi-square test; continuous variables are presented as means with SDs when normally distributed, as medians with interquartile ranges (IQRs) when not normally distributed, and compared using analysis of variance or Student's *t* test. All analyses were performed using STATA: STATA Corp, LLC (Version 11, College Station, TX).

RESULTS

Demographics and Baseline VSs

A total of 6,906 patients were included in the study. Of these, 226 (3.3%) were part of the HC group; the remaining 6,680 patients (96.7%) received some form of intervention during Phases 1–5. The median age was 45.0; IQR 28.2-59 years; 4,184 (60.6%) were female (**Table 1**). The mean number of patients qualifying for the ATP daily was 3.6 patients/d (range, 0–16). The SIRS VS were as follows: mean HR, 113.8 ± 18.1 beats/min (mean ± SD); median RR, 22; IQR 18–24 breaths/min and median temperature of 100.5; IQR 98.2–101.9°F.

TABLE 1.
Demographics and Clinical Variables

Category	Values
Total patients, *n*	6,906
Age, mean ± SD	45.4 ± 18.1
Female, *n* (%)	4,184 (60.6)
ESI 2, *n* (%)	4,236 (61.3)
ESI 3, *n* (%)	2,670 (38.7)
Heart rate, mean ± SD	113.8 ± 18.1
Heart rate, > 90, *n* (%)	6,832 (98.9%)
Respiratory rate, median (IQR)	22 (18–24)
Respiratory rate > 20, *n* (%)	3,627 (52.5%)
Temperature, °F, median (IQR)	100.5 (98.2–101.9)
Temperature < 96.8°F, *n* (%)	66 (1.0)
Temperature > 100.4°F, *n* (%)	3,539 (51.2)
Lactic acid performed, *n* (%)	5,219 (75.0)
Lactic acid value (mmol/L), mean ± SD	1.77 ± 1.18
Lactic acid value by stratified levels, *n* (%)	
Lactic acid 0–1.0 mmol/L	1,205 (23.1)
Lactic acid 1.1–2.0 mmol/L	2,671 (51.2)
Lactic acid 2.1–3.0 mmol/L	897 (17.2)
Lactic acid 3.1–4.0 mmol/L	257 (4.9)
Lactic acid > 4.0 mmol/L	187 (3.6)
Lactic acid value (mmol/L), groupings, *n* (%)	
Lactic acid ≤ 2 mmol/L	3,876 (74.3)
Lactic acid > 2 mmol/L	1,343 (25.7)
Lactic acid > 3 mmol/L	444 (8.5)
Admit to hospital, *n* (%)	4,161 (60.2)
Admit to ICU, *n* (%)	343 (5.0)
In-hospital mortality, *n* (%)	275 (4.0)

IQR = interquartile range, ESI = emergency severity index.

Six thousand eight hundred thirty-two patients (98.9%) had a HR greater than 90 beats/min, 3,627 patients (52.5%) had a RR greater than 20 breaths/min, 3,539 patients (51.2%) had a temperature greater than 100.4°F, and 66 patients (1.0%) had a temperature less than 96.8°F.

Lactate Results

Five thousand two hundred nineteen patients (75%) had a lactate performed during their ED stay. The ATP lactate order shortened the time from triage to lactate order from 103.4 min (95% CI, 76.8–129.9 min) to 0.59 min (95% CI, 0.17–1.00 min; $p < 0.0001$).

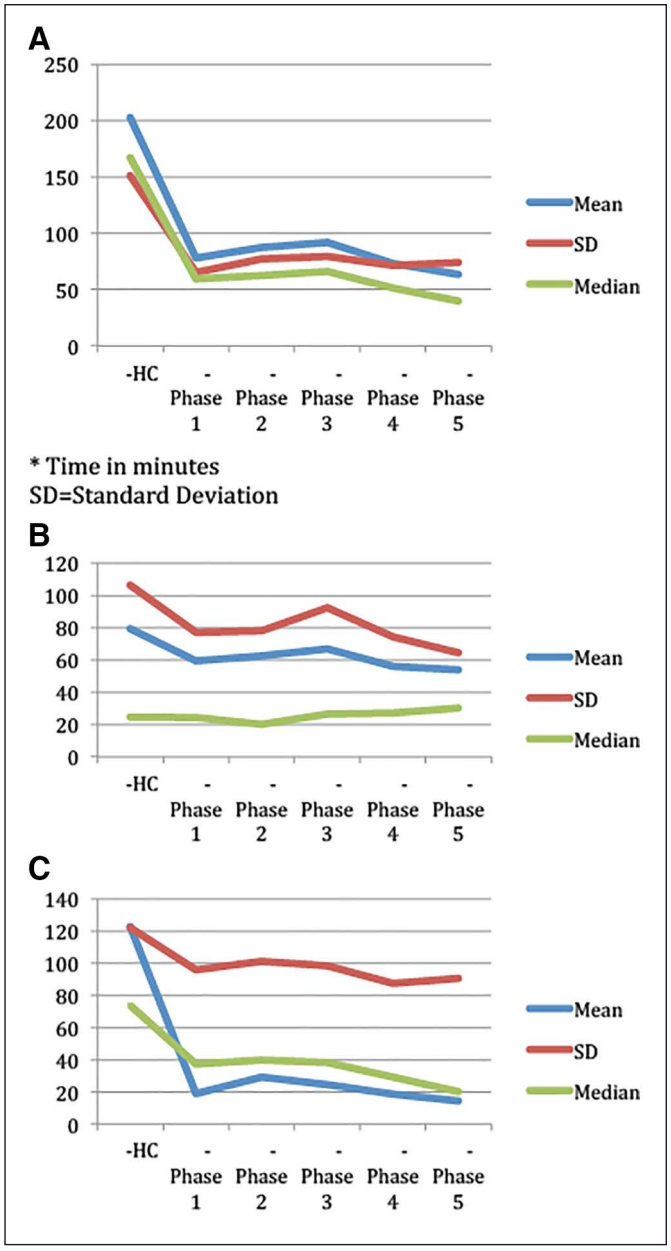

Figure 1. A–C, Statistical process control charts for performance improvement metrics.

The mean serum lactate level was 1.77 ± 1.18 mmol/L; 1,343 patients (25.7%) had an initial lactate level greater than 2 mmol/L; and 444 (8.5%) had a lactate greater than 3 mmol/L (Table 1 and **Fig. 1*A–C***].

Top 20 CCs

Ninety-four percent (6,471 patients) had one of 20 CCs, which could be readily consolidated into 12 main categories, for example, combining shortness of breath (SOB) and dyspnea on exertion (DOE) into one category. The most common category was fever/chills, assigned to 1,943 patients (28.1%); the second most common was SOB/DOE, in 1,644 patients (23.8%) (**Table 2**).

TABLE 2.
Top Chief Complaints

Top 20 Chief Complaints, Grouped Into 12 Categories, *n* (%)	6,471 (94.0)
1. Fever/chills	1,943 (28.1)
2. Shortness of breath/dyspnea on exertion	1,644 (23.8)
3. Pain, abdomen	666 (9.6)
4. Pain, chest	538 (7.8)
5. Cough/Upper Respiratory Infection signs, symptoms	413 (6.0)
6. Nausea, vomiting, diarrhea	383 (5.6)
7. Sore throat	210 (3.0)
8. Headache	191 (2.8)
9. Weakness/fatigue	184 (2.7)
10. Pain, flank	117 (1.7)
11. Change in Mental Status	101 (1.5)
12. Infection, any location, Upper Respiratory Infection, Urinary Tract Infection	101 (1.5)

Outcomes by Lactate Level Groups

As the screening lactate level increased from less than or equal to 2 mmol/L to greater than 2 mmol/L to greater than 3 mmol/L, an increasing percentage of patients were admitted to the hospital (66.5% vs 83.3% vs 89.4%), to the ICU (5.9% vs 15.9% vs 25.7%), and had IHM (3.8% vs 9.5% vs 14.9%) (**Table 3**).

ATP Implementation Process Impact by Phases

During the HC period, 27.4% of the patients meeting ATP inclusion criteria had a lactate value drawn and resulted during their ED care; this increased to 79.6% during Phase 5 of the study ($p < 0.0001$). The percentage of these lactate results that were available while the patient was still in the waiting room increased from 0.4% during the HC period to 33.7% during Phase 5 ($p < 0.0001$). Median time to lactate result decreased from 78.1 minutes (Phase 1) to 63.4 minutes (Phase 5) ($p < 0.0001$) and from triage to placement in a treatment room decreased from 59.2 minutes (Phase 1) to 39.6 minutes (Phase 5) ($p < 0.0001$) (**Table 4**). The median time from placement in a treatment room to lactate result decreased from 37.4 minutes (Phase 1)

TABLE 3.
Outcomes by Lactate Level Groups

Lactic Acid Value (mmol/L), Groupings	*n* (%)	*p*
Lactic acid performed, total	5,179	
Lactic acid ≤ 2 mmol/L	3,839 (74.1)	
Admit to hospital	2,552 (66.5)	
% of admitted patients to admitted to ICU	151/2,552 (5.9)	
In-hospital mortality, excluding HC period	96/2,521 (3.8)	
Lactic acid > 2 mmol/L	1,338 (25.9)	
Admit to hospital	1,101 (82.3)	< 0.00001
% of admitted patients to ICU	175/1,101 (15.9)	< 0.00001
In-hospital mortality, excluding HC period	103/1,080 (9.5)	< 0.00001
Lactic acid > 3 mmol/L	444 (8.6)	
Admit to hospital	397 (89.2)	0.3
% of admitted patients to ICU	102/397 (25.7)	0.0005
In-hospital mortality, excluding HC period	58/389 (14.9)	0.01

HC = historic control.

to 20.1 minutes (Phase 5) ($p < 0.0001$). The changes between each phase of the ATP implementation process are presented in Table 4 and Figure 1*A*–C.

Impact on Sepsis Quality Metrics

Overall, there was no change in time to antibiotics, time to IVF, or IHM during the study period (**Table 5**). There was a significant decrease in times to antibiotics and IVF when comparing Phases 1 and 2, but these improvements dissipated over the subsequent phases (Table 5). A trend toward improved IHM was seen between Phases 4 and 5, but the results were not statistically significant (Table 5).

Sepsis Versus No Sepsis in ICD-9 Codes Assigned to ED Visit

A sepsis-related ICD-9 code was assigned to 38.6% of the patients (2,665/6,906); no sepsis-related ICD-9 code was assigned to 61.3% (4,241/6,906) ($p < 0.0001$). When the sepsis-related ICD-9 group was compared with the no sepsis-related ICD-9 group, the time from triage to initial lactate result was similar (78.4 min vs 73.9 min; $p = 0.1142$). The sepsis-related ICD-9 patients were admitted to the hospital less frequently (56% vs 65.5%; $p = 0.0035$) but if admitted were more likely to be admitted to the ICU (10.5% vs 6.5%; $p < 0.0001$). Mortality between the two groups was similar (6.6% vs 7.1%; $p = 0.5891$). A similar percentage of both groups had an initial lactate level greater than 2 mmol/L (18.3% vs 20.2%; $p = 0.1069$) and, if the initial lactate was elevated, were admitted to the hospital (83.8% vs 81.2%; $p = 0.7109$); however, a higher percentage of sepsis-related ICD-9 code patients were admitted to the ICU (21.8% vs 9.2%; $p < 0.0001$); IHM was similar between the groups (10.8% vs 8.7%; $p = 0.3003$). Similar findings occurred when stratified by lactate greater than 3 and greater than 4 mmol/L (**Supplemental Table 2**, Supplemental Digital Content, http://links.lww.com/CCX/B42).

Sensitivity of Screening Protocol for Sepsis Patients Who Wait in the Waiting Room

Between January 19, 2009, and December 31, 2009, using data from another institutional sepsis database, 500 patients were admitted to the hospital; 73 ESI 1 and five ESI 4 or 5 patients were excluded leaving a cohort of 422 patients with an ESI 2 or 3 assigned when triaged. Two hundred thirty-five (55.7%) presented by "self" and were initially seen in the triage area; 187 (44.3%) presented by ambulance and were directly roomed, which was reflected in room times less than or equal to triage times. Thus, 235 of 500 severe sepsis patients (47%) during this period would potentially

TABLE 4.
Advanced Triage Protocol Implementation Process Impact

Lactate Resulted	Total Number	Percent of Patients With Lactate Resulted	No. of Patients With Lactate Resulted While Patient in Waiting Room	Percent Where Lactate Resulted While Patient in Waiting Room
HC	62	27.4	1	0.4
Phase 1	292	74.1	81	27.7
Phase 2	1131	71.5	266	23.5
Phase 3	915	75.9	208	22.7
Phase 4	1,990	77.7	574	28.8
Phase 5	743	79.6	250	33.7
Triage to Lactate Result		Mean (min)	*p*	
HC		167	NA	
Phase 1		78.1	HC-Phase 1, $p < 0.0001$	
Phase 2		87.3	Phase 1–2, $p = 0.0601$	
Phase 3		92	Phase 2–3, $p = 0.1{,}735$	
Phase 4		73.4	Phase 3–4, $p < 0.0001$	
Phase 5		63.4	Phase 4–5, $p = 0.0012$	HC-Phase 5, $p < 0.0001$
Triage to Treatment Room		Mean (min)	*p*	
HC		79	NA	
Phase 1		59.3	HC-Phase 1, $p = 0.2054$	
Phase 2		62.6	Phase 1–2, $p = 0.4166$.	
Phase 3		66.8	Phase 2–3, $p = 0.0002$	
Phase 4		56	Phase 3–4, $p = 0.0001$.	
Phase 5		53.9	Phase 4–5, $p = 0.2541$.	HC-Phase 5, $p < 0.0001$
Room to Lactate Result		Mean (min)	*p*	
HC		123.3	NA	
Phase 1		13.3	HC-Phase 1, $p < 0.0001$	
Phase 2		29.2	Phase 1–2, $p = 0.0712$	
Phase 3		24.5	Phase 2–3, $p = 0.3004$	
Phase 4		18.6	Phase 3-4, $p = 0.1063$.	
Phase 5		14.4	Phase 4-5, $p = 0.2665$.	HC-Phase 5, $p < 0.0001$

NA = not available.

benefit from the sepsis ATP protocol. However, 57 of 235 patients (24.3%) had less than 2 SIRS when triaged and waited in the waiting room but ultimately had sepsis with acute organ dysfunction POA; these patients would not be captured by the sepsis ATP at triage. Subtracting them yields a total of 178 patients. Thus, the sepsis ATP had a sensitivity of 75.8% (178/235) for identifying the ESI 2 or 3 patients with sepsis and acute organ dysfunction who were initially assessed in the triage area.

DISCUSSION

The results of this study demonstrate that interventions performed in ED triage can shorten the time interval between a potential sepsis patient's triage and initial

TABLE 5.
Sepsis Quality Metrics

Sepsis Quality Metrics				
Time[a] to Antibiotics				
Phase	***n***	**Mean ± SD**	**Median**	***p***
HC	24	199±138	175	NA
1	65	217±82	192	0.266
2	134	176±66	158	0.006
3	147	194±108	176	0.093
4	601	195±98	176	0.597
5	263	197±103	174	0.361
Time to IV Fluids				
Phase	***n***	**Mean ± SD**	**Median**	***p***
HC	24	126±123	95	NA
1	63	129±119	94	0.4515
2	129	84±70	65	0.0005
3	118	109±145	84	0.0391
4	476	113±85	92	0.3628
5	226	116±96	96	0.323
IHM				
Group	**Number in Group**	**Number with IHM***	**Mortality Rate**	***p***
1	65	4	9.2	NA
2	134	8	6	0.434
3	147	14	9.5	0.303
4	601	50	8.3	0.791
5	263	12	4.6	0.089

HC = historic control, IHM = in-hospital mortality, NA = not available.
[a]Time in minutes.

lactate order, blood draw, and lactate result while tripling the percentage of potential sepsis patients having a lactate drawn during their ED stay. Further, the percentage of lactate results available before the patient was placed in an ED evaluation room increased from 0.4% (HC period) to 33.7% (Phase 5). We accomplished this by implementing a computer-generated lactate order, which was triggered by triage variables concerning for severe sepsis.

This approach shortened the time from triage to lactate order for potential severe sepsis patients from 103.4 min (95% CI, 76.8–129.9 min) to an essentially instantaneous process (0.59 min; 95% CI, 0.17–1.00 min; $p < 0.0001$). This early notification of the need for a serum lactate translated into a shorter time to lactate result over the five phases of the study (78.1 vs 63.4 min; $p < 0.0001$). The greatest improvements in time to lactate result occurred after the incorporation of POC whole blood lactate devices during Phase 5. This has several implications for the management of potential sepsis patients. Prior research has demonstrated that lactate is a predictor of severe sepsis mortality independent of hypotension (10). Given problems with ED crowding, patients triaged

as ESI 2 or 3 are often exposed to delays to important metrics of sepsis resuscitation (16) and potential risk of decompensation.

When a lactate order is generated greater than or equal to 100 minutes sooner and the blood sample is drawn greater than or equal to 30 minutes sooner, objective data to further risk stratify these patients are obtained in an expedited fashion (28, 29). Further refinement of this protocol is needed to further shorten times from triage to lactate blood draw and result, identifying potential sepsis patients earlier in their ED course. In an optimized system, this should translate into decreased times to IVF infusion and antibiotic administration, which we did not observe. The goal for time from lactate order to lactate result should be less than or equal to 10 minutes, analogous to the time from triage to electrocardiogram analysis in patients with potential acute coronary syndromes. Use of finger stick POC lactate devices has the potential to overcome some of the barriers to specimen collection in triage (31, 32). Once a lactate value of greater than or equal to 2 mmol/L is obtained, patients should be immediately placed in a treatment room and fluids and antibiotics, if appropriate, expedited.

This study has several limitations. First, the sepsis ATP shortened the time from triage to lactate order by a much greater amount than the times from triage to lactate blood draw and lactate result. Second, during Phases 2 and 3 of our trial, increased ATP protocol education and waiting room EMT resources did not translate into the anticipated improvement in time to lactate result. Rather, the increased resources appeared to be used mostly to identify patients perceived as "at highest risk" for expedited examination room placement. Third, one of the goals of this study was to maximize the percentage of lactate values that were drawn and resulted while the patient was in the waiting room. Although we saw a significant increase in this metric, from 0.4% to 33.7%, we were not able to achieve our goal of the majority resulting under these conditions. This is partially explained by a significant decrease in the time from triage to room placement (from 59.3 to 39.6 min). We hypothesize that this occurred as a "work around" to barriers to obtaining a blood sample for lactate analysis. Fourth, this study was conducted prior to the third International Sepsis Definitions in 2016, which abandoned SIRS criteria for qSOFA, and this may limit the translatability to current sepsis quality improvement efforts. However, research has demonstrated the continued need for SIRS criteria in the initial detection of potential sepsis patients (13). Fifth, because the study period extended over 5 years, it is possible that other trends including patient demographics, staffing, hospital capacity, crowding, and alternative treatment sites influenced triage to treatment room time, and the outcomes seen were because of these factors and not because of the interventions undertaken. However, during the study period ED, boarding and crowding increased significantly, the percentage of patients admitted to the hospital and to the ICU remained stable, and ED volume increased at an average of 1.5% per/yr (unpublished data). Finally, there has been a significant delay from study end to submission for publication. This delay was multifactorial: 1) the senior author left the research institution in 2014, and IRB approvals had to be transferred; 2) statistical support at the study institution changed, and data analysis was delayed; and 3) analysis was almost complete when the COVID pandemic began, and the project went on hiatus. However, process metric changes have been sustained at the study institution, early lactate analysis remains a key component of sepsis screening, and The Severe Sepsis and Septic Shock Management Bundle compliance has remained significantly above the national average since the project was completed.

CONCLUSIONS

Implementation of a computerized lactate order using readily available data from ED triage, as well as POC lactate testing in triage, speeds times to lactate order, lactate blood draw, room placement, and lactate result in patients at risk for severe sepsis. In this cohort of 6,906 patients, elevated initial lactate levels correlated with admission to the hospital, the ICU, and IHM.

ACKNOWLEDGMENTS

We would like to acknowledge the invaluable contributions to this research made by Chris Boedec, the Department of Emergency Medicine's Information Technology Director, who programmed the advanced triage protocol automatic lactate order and provided interim data for analysis, and Jimmy Pisaturo, the lead emergency medical technician (EMT) in the department, who is a passionate advocate for improved sepsis

care and who led the education sessions for the department's EMTs. Without their contributions, this project would not have been possible.

1 *US Acute Care Solutions, Canton, OH.*

2 *Department of Emergency Medicine, Mount Sinai School of Medicine, New York, NY.*

3 *Department of Emergency Medicine, University of Colorado School of Medicine, Aurora, CO.*

4 *Department of Emergency Medicine, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA.*

5 *Department of Emergency Medicine, Georgetown University School of Medicine, Washington, DC.*

6 *Department of Emergency Medicine, Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, PA.*

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (http://journals.lww.com/ccejournal).

Address requests for reprints to: David F. Gaieski, MD, Sidney Kimmel Medical College at Thomas Jefferson University, Department of Emergency Medicine, 1025 Walnut Street, Suite 300, Philadelphia, PA 19107. E-mail: David.Gaieski@jefferson.edu

This work was performed at the Hospital of the University of Pennsylvania, part of the University of Pennsylvania Health System, Philadelphia, PA.

REFERENCES

1. Singer M, Deutschman CS, Seymour CW, et al: The third international consensus definitions for sepsis and septic shock (sepsis-3). *JAMA* 2016; 315:801–810
2. Dellinger RP, Levy MM, Rhodes A, et al; Surviving Sepsis Campaign Guidelines Committee including The Pediatric Subgroup: Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock, 2012. *Intensive Care Med* 2013; 39:165–228
3. Gaieski DF, Edwards JM, Kallan MJ, et al: Benchmarking the incidence and mortality of severe sepsis in the United States. *Crit Care Med* 2013; 41:1167–1174
4. Paoli CJ, Reynolds MA, Sinha M, et al: Epidemiology and costs of sepsis in the United States-An analysis based on timing of diagnosis and severity level. *Crit Care Med* 2018; 46:1889–1897
5. Wang HE, Shapiro NI, Angus DC, et al: National estimates of severe sepsis in United States emergency departments. *Crit Care Med* 2007; 35:1928–1936
6. Rivers E, Nguyen B, Havstad S, et al; Early Goal-Directed Therapy Collaborative Group: Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med* 2001; 345:1368–1377
7. Gaieski DF, Mikkelsen ME, Band RA, et al: Impact of time to antibiotics on survival in patients with severe sepsis or septic shock in whom early goal-directed therapy was initiated in the emergency department. *Crit Care Med* 2010; 38:1045–1053
8. Kumar A, Roberts D, Wood KE, et al: Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Crit Care Med* 2006; 34:1589–1596
9. Bone RC, Balk RA, Cerra FB, et al: Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. *Chest* 1992; 101:1644–1655
10. Mikkelsen ME, Miltiades AN, Gaieski DF, et al: Serum lactate is associated with mortality in severe sepsis independent of organ failure and shock. *Crit Care Med* 2009; 37:1670–1677
11. Shapiro NI, Howell MD, Talmor D, et al: Serum lactate as a predictor of mortality in emergency department patients with infection. *Ann Emerg Med* 2005; 45:524–528
12. Levy MM, Fink MP, Marshall JC, et al. 2001 SCCM/ESICM/ACCP/ATS/SIS international sepsis definitions conference. *Crit Care Med* 2003;31:1250–1256
13. Perman SM, Mikkelsen ME, Goyal M, et al: The sensitivity of qSOFA calculated at triage and during emergency department treatment to rapidly identify sepsis patients. *Sci Rep* 2020; 10:20395
14. Freund Y, Lemachatti W, Krastinova E, et al. For the french society of emergency medicine collaborators group: Prognostic accuracy of sepsis-3 criteria for inhospital mortality among patients with suspected infection presenting to the emergency department. *JAMA* 2017; 317:301–308
15. Pines JM, Localio AR, Hollander JE, et al: The impact of emergency department crowding measures on time to antibiotics for patients with community-acquired pneumonia. *Ann Emerg Med* 2007; 50:510–516
16. Gaieski DF, Agarwal AK, Mikkelsen ME, et al: The impact of ED crowding on early interventions and mortality in patients with severe sepsis. *Am J Emerg Med* 2017; 35:953–960
17. Subbe CP, Kruger M, Rutherford P, et al: Validation of a modified early warning score in medical admissions. *QJM* 2001; 94:521–526
18. Smith GB, Prytherch DR, Meredith P, et al: The ability of the national early warning score (NEWS) to discriminate patients at risk of early cardiac arrest, unanticipated intensive care unit admission, and death. *Resuscitation* 2013; 84:465–470
19. McGillicuddy DC, O'Connell FJ, Shapiro NI, et al: Emergency department abnormal vital sign "triggers" program improves time to therapy. *Acad Emerg Med* 2011; 18:483–487
20. Yamamoto S, Yamazaki S, Shimizu T, et al: Body temperature at the emergency department as a predictor of mortality in patients with bacterial infection. *Medicine (Baltimore)* 2016; 95:e3628
21. Kenzaka T, Okayama M, Kuroki S, et al: Importance of vital signs to the early diagnosis and severity of sepsis: Association between vital signs and sequential organ failure assessment score in patients with sepsis. *Intern Med* 2012; 51:871–876
22. Montassier E, Batard E, Segard J, et al: Base excess is an accurate predictor of elevated lactate in ED septic patients. *Am J Emerg Med* 2012; 30:184–187
23. Corfield AR, Lees F, Zealley I, et al; Scottish Trauma Audit Group Sepsis Steering Group: Utility of a single early warning score in patients with sepsis in the emergency department. *Emerg Med J* 2014; 31:482–487

24. Hong W, Earnest A, Sultana P, et al: How accurate are vital signs in predicting clinical outcomes in critically ill emergency department patients. *Eur J Emerg Med* 2013; 20:27–32
25. Berger T, Green J, Horeczko T, et al: Shock index and early recognition of sepsis in the emergency department: pilot study. *West J Emerg Med* 2013; 14:168–174
26. Barfod C, Lauritzen MM, Danker JK, et al: Abnormal vital signs are strong predictors for intensive care unit admission and in-hospital mortality in adults triaged in the emergency department - A prospective cohort study. *Scand J Trauma Resusc Emerg Med* 2012; 20:28
27. Soremekun OA, Datner EM, Banh S, et al: Utility of point-of-care testing in ED triage. *Am J Emerg Med* 2013; 31:291–296
28. Singer AJ, Taylor M, Domingo A, et al: Diagnostic characteristics of a clinical screening tool in combination with measuring bedside lactate level in emergency department patients with suspected sepsis. *Acad Emerg Med* 2014; 21:853–857
29. Gatewood MO, Wemple M, Greco S, et al: A quality improvement project to improve early sepsis care in the emergency department. *BMJ Qual Saf* 2015; 24:787–795
30. Drumheller BC, Agarwal A, Mikkelsen ME, et al: Risk factors for mortality despite early protocolized resuscitation for severe sepsis and septic shock in the emergency department. *J Crit Care* 2016; 31:13–20
31. Gaieski DF, Drumheller BC, Goyal M, et al: Accuracy of handheld point-of-care fingertip lactate measurement in the emergency department. *West J Emerg Med* 2013; 14:58–62
32. Goyal M, Pines JM, Drumheller BC, et al: Point-of-care testing at triage decreases time to lactate level in septic patients. *J Emerg Med* 2010; 38:578–581