

Lactate Testing in Suspected Sepsis: Trends and Predictors of Failure to Measure Levels

Chanu Rhee, MD^{1,2}; Michael V. Murphy, BA¹; Lingling Li, PhD¹; Richard Platt, MD, MSc¹; Michael Klompas, MD, MPH^{1,2}; for the Centers for Disease Control and Prevention Prevention Epicenters Program

Objectives: Serum lactate monitoring is central to risk stratification and management of sepsis and is now part of a potential quality measure. We examined 11-year trends in lactate testing and predictors of failure to measure lactates in patients with severe sepsis.

Design: Retrospective cohort study.

Setting: Two U.S. academic hospitals.

Patients: Adult patients admitted from 2003 to 2013.

Interventions: Annual rates of lactate measurement were assessed in patients who had blood cultures ordered and patients with severe sepsis, as defined by concomitant *International Classification of Diseases, Ninth Revision* codes for infection and organ dysfunction. The approximate time of suspected sepsis was determined by the first blood culture order with concurrent antibiotic initiation. Multivariate analysis was performed to identify predictors of failure to measure lactates in severe sepsis cases in 2013.

Measurements and Main Results: Among hospitalizations with blood culture orders, rates of lactate measurement increased from 11% in 2003 to 48% in 2013 ($p < 0.001$ for linear trend). Rates of repeat lactate measurement within 6 hours after lactate levels greater than or equal to 4.0 mmol/L increased from 23% to 69% ($p < 0.001$). Patients were progressively less likely to be on vasopressors at the time of first lactate measurement (49% in 2003 vs 21% in 2013; $p < 0.001$). Despite these trends, lactates were measured at the time of suspected sepsis in only 65% of patients with severe sepsis in 2013. On multivariate analysis, hospital-onset sepsis and hospitalization on a nonmedical service

were significant predictors of failure to measure lactates (adjusted odds ratio, 7.56; 95% CI, 6.31–9.06 and adjusted odds ratio, 2.08; 95% CI, 1.76–2.24, respectively).

Conclusions: Lactate testing has increased dramatically over time and is being extended to patients without overt shock. However, rates of serial lactate testing are still suboptimal, and lactates are not being measured in many patients with severe sepsis. Hospital-onset sepsis and nonmedical units may be high-yield targets for quality improvement initiatives. (*Crit Care Med* 2015; 43:1669–1676)

Key Words: quality monitoring; serum lactate; severe sepsis; trend analysis

Elevated serum lactate levels have long been known to identify patients with severe hypoperfusion and predict death (1–3). Measuring lactate levels can risk stratify patients with suspected sepsis, to prompt aggressive early treatment, and help monitor the impact of therapy (4–9). Implementation of bedside lactate measurement in the emergency department has also been associated with reduced time to administration of IV fluids in patients with suspected sepsis and decreased rates of ICU admission and mortality (10).

For these reasons, lactate testing in all patients with suspected severe sepsis has become increasingly emphasized and is now a key component of the Surviving Sepsis Campaign (SSC) Guidelines. In the most recent version of the guidelines, lactate measurement is a core component of the 3-hour bundle, whereas repeat lactate measurement for patients with hyperlactatemia is part of the 6-hour bundle (11). The National Quality Forum's adoption of the SSC guidelines means that lactate measurement in severe sepsis could be included in quality measures for public reporting and payment (12).

Participation in the SSC has been shown to improve compliance with the severe sepsis bundle, including increasing the frequency of lactate measurement within the first 6 hours of meeting screening criteria (13, 14). However, less is known about how lactate use has changed over time or how frequently clinicians are ordering this test in appropriate patients in

¹Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, MA.

²Division of Infectious Diseases, Brigham and Women's Hospital, Boston, MA.

Dr. Rhee received support for article research from the National Institutes of Health (NIH). Drs. Rhee, Platt, and Klompas' (Department of Population Medicine) institution received grant support from the Centers for Disease Control and Prevention (3U54CK00172-04S1) and the NIH (T32 AI007061). The remaining authors have disclosed that they do not have any potential conflicts of interest.

For information regarding this article, E-mail: crhee1@partners.org

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DOI: 10.1097/CCM.0000000000001087

hospitals that are not associated with the SSC. In addition, little is known about which clinical factors are associated with failure to measure a lactate in septic patients. Given the benefits associated with lactate testing, it is important to better understand how this test is being used, and gaps in its use, in order to identify potential areas for quality improvement.

We evaluated 11-year trends in serum lactate testing in patients with suspected sepsis and identified predictors of failure to appropriately measure lactates using a detailed clinical database at two academic medical centers that were not participating sites in the SSC.

MATERIALS AND METHODS

After obtaining approval from the Partners Healthcare Institutional Review Board, we identified all patients aged 18 and older admitted to Massachusetts General Hospital (MGH) and Brigham and Women's Hospital (BWH) between January 1, 2003, and December 31, 2013, who had a blood culture order during hospitalization. MGH (950 beds) and BWH (779 beds) are academic hospitals located in Boston, MA. We retrieved comprehensive clinical data including patients' demographics, *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes, medications, laboratory results, and dates of admission, discharge, and death from the

hospital's Research Patient Data Registry, a centralized clinical data warehouse (15). Any serum lactate test, whether from an arterial or venous sample, was included in our analysis. Blood culture data were obtained from the clinical microbiology laboratory database, and ventilator data were obtained from the Respiratory Therapy Departments of each hospital. Patients' comorbidities were derived from their ICD-9-CM and diagnosis-related group codes using the method of Elixhauser, and we used a validated summary scoring method to estimate total burden of comorbidities (16, 17). Patients who required ICU services were identified using the Current Procedural Terminology code 99291 (critical care, first 30–74 min). This approach for identifying critically ill patients has been previously validated in our administrative data source (18).

Patient Subgroups

We explored three different denominators to assess trends in lactate testing based on clinical markers and/or discharge diagnosis codes. We defined a broad subgroup of patients with suspected infection as any patient with a blood culture order (regardless of culture results) during hospitalization. We defined severe sepsis using the methods of Angus et al (19) as modified by Iwashyna et al (20). This widely cited claims definition uses 1,286 codes for infection and 13 codes

TABLE 1. Clinical Characteristics of Hospitalized Patients With Suspected Infection, Severe Sepsis, and Suspected Septic Shock, 2003–2013

Clinical Characteristic	Suspected Infection ^a (n = 230,620)	Severe Sepsis ^b (n = 41,275)	Suspected Septic Shock ^c (n = 24,330)
Median age (IQR)	61 (47–73)	65 (53–76)	63 (51–74)
Male sex, n (%)	119,892 (52.0)	23,453 (56.8)	14,073 (57.8)
White race, n (%)	177,398 (76.9)	32,761 (79.4)	19,120 (78.6)
Comorbidities			
Cancer, n (%)	50,532 (21.9)	8,215 (19.9)	4,095 (16.8)
Diabetes mellitus, n (%)	42,484 (18.4)	6,229 (15.1)	3,081 (12.7)
Heart failure, n (%)	35,346 (15.3)	9,183 (22.3)	5,685 (23.4)
Liver disease, n (%)	13,667 (5.9)	2,682 (6.5)	1,446 (5.9)
Lung disease, n (%)	36,925 (16.0)	6,115 (14.8)	3,391 (13.9)
Renal disease, n (%)	27,829 (12.1)	588 (14.3)	2,694 (11.1)
Median Elixhauser score (IQR)	6 (0–12)	9 (5–14)	8 (4–13)
Positive blood cultures, n (%)	22,389 (9.7)	9,637 (23.4)	5,381 (22.1)
Nonmedical service, n (%)	77,269 (33.5)	11,563 (28.0)	10,748 (44.2)
Required ICU care, n (%)	65,218 (28.3)	24,761 (60.0)	20,178 (82.9)
Median hospital length of stay (IQR)	7 (4–13)	13 (7–24)	15 (8–26)
Hospital mortality, n (%)	14,687 (6.4)	7,502 (18.2)	6,300 (25.9)

IQR = interquartile range.

^aPatients with a blood culture order anytime during hospitalization.

^bPatients with blood culture order with concurrent antibiotics and discharge diagnoses consistent with infection and organ dysfunction.

^cPatients with blood culture order with concurrent antibiotics and vasopressors.

for acute organ dysfunction; if a code from both categories is present, or an explicit code for severe sepsis (995.92) or septic shock (785.52) is present, the patient is labeled as having severe sepsis. In order to enable us to estimate the timing of suspected sepsis, we focused on the subset of patients who had at least one blood culture order with concurrent parenteral antibiotics started within ± 1 day of the blood culture, with any antibiotics continued for at least 3 days (or until death or hospital discharge if this occurred prior to 3 d). Finally, we defined “suspected septic shock” as a blood culture order and both vasopressors (norepinephrine, epinephrine, dopamine, vasopressin, or phenylephrine) and at least 3 days of antibiotics started within ± 1 day of blood culture order. We applied this denominator without regard to discharge diagnoses given that administrative coding for sepsis is of variable accuracy and possibly changing over time (20–22). Even though some of these patients likely ended up

having noninfectious diagnoses, we reasoned that clinicians’ decisions to order blood cultures and at least 3 days of new antibiotics were strong indicators that they initially suspected a possible infection and therefore lactate measurement was also indicated for these patients.

2003–2013 Trends. We examined the annual proportion of hospitalizations that had a serum lactate level measured at any point during hospitalization among patients with suspected infection. To examine trends in serial lactate testing, we assessed the annual proportion of hospitalizations with suspected infection and lactates greater than or equal to 4.0 mmol/L that had a repeat lactate checked within 6 and 24 hours, excluding patients that died within that time window. In hospitalizations where lactate testing was performed, we examined whether clinical thresholds for measuring lactates might be changing over time by examining the annual proportion of patients that required vasopressors before or at the time of lactate measurement. In order to estimate how well

clinicians are doing at ordering lactates at the time of suspected sepsis in patients with severe sepsis, we examined annual rates of lactate measurement within ± 1 day of the first blood culture order concurrent with antibiotic initiation. We also examined lactate measurements within ± 1 day of the first blood culture with concurrent antibiotics and vasopressors in patients with suspected septic shock.

Lactate Testing in Patients With Severe Sepsis in 2013. We examined factors that might be associated with the decision to measure a lactate at the time of suspected sepsis, defined as within ± 1 day of first blood culture order with antibiotics, in patients with severe sepsis. We focused on patients hospitalized in 2013 in order to assess most current practices. The following variables were considered: age (continuous variable), sex, race (white vs nonwhite), Elixhauser summary comorbidity score (continuous variable), mechanical ventilation at the time of suspected sepsis, ICU care or vasopressor before or at the time of suspected sepsis, and laboratory values indicative of organ dysfunction on the day of blood culture order (or the closest day if no laboratory drawn that day)—creatinine greater

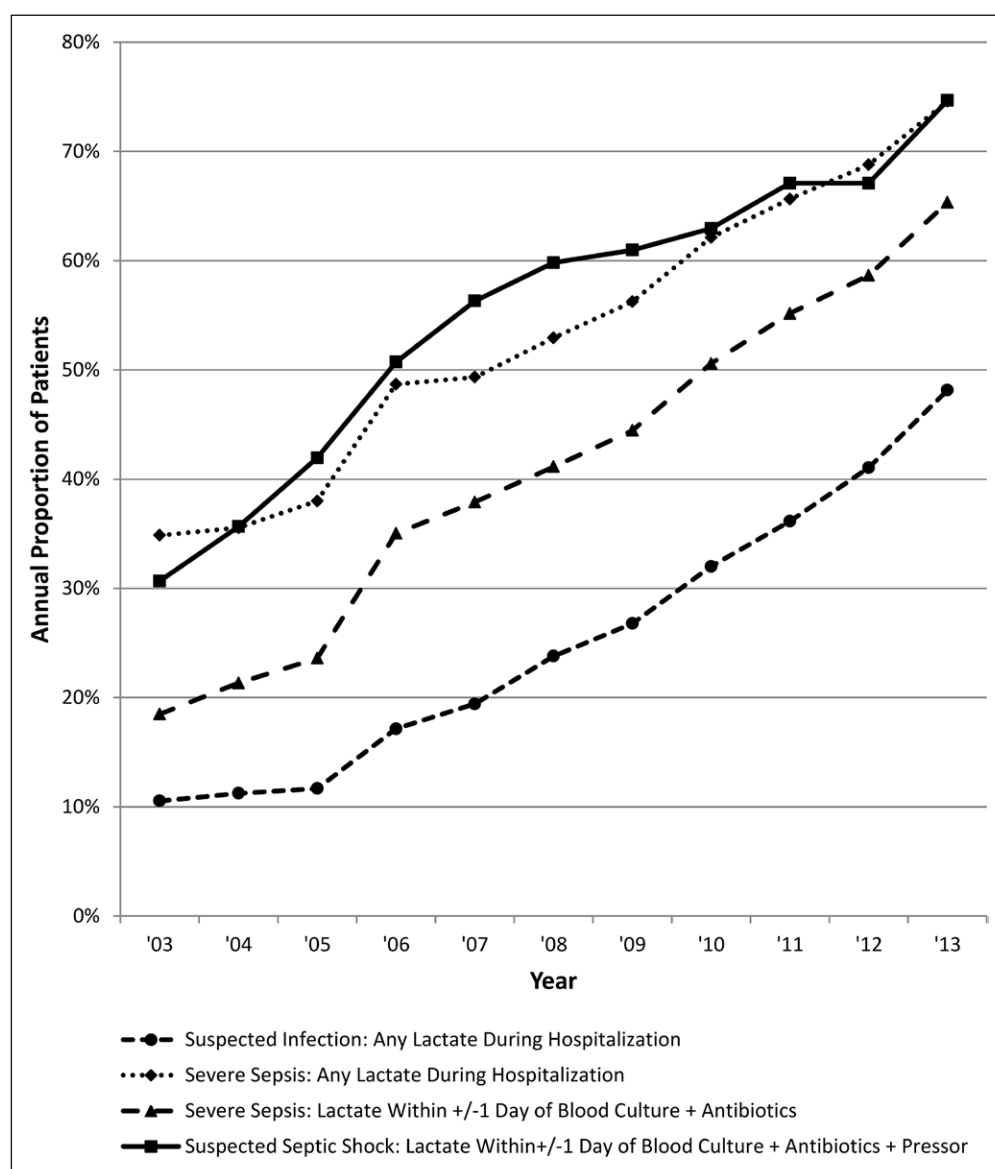


Figure 1. Rising annual proportion of patients with suspected and diagnosed sepsis that had serum lactates measured during hospitalization or at the time of suspected sepsis, 2003–2013.

than or equal to 2.0 mg/dL, total bilirubin greater than or equal to 2.0 mg/dL, international normalized ratio greater than 1.5, and platelet count less than 100,000/ μ L. We also included other key laboratories that might influence suspicion of infection or hypoperfusion: anion gap greater than 16 mEq/L, greater than or equal to 5% immature neutrophils (bands) on WBC count differential, maximum WBC count greater than 12,000/ μ L or minimum WBC count less than 4,000/ μ L, positive blood cultures before or at the time of suspected sepsis, hematocrit less than 21%, and albumin less than 2.5 g/dL. Lastly, we included hospital-onset sepsis, admission to a nonmedical service, and which hospital the patient was admitted to (with MGH as the reference hospital). We defined hospital-onset sepsis as the first blood culture order associated with initiation of parenteral antibiotics occurring on or after the 3rd calendar day of admission, with day of admission being day 1. The primary service was designated by the specialty of the attending of record at hospital discharge.

Statistical Analyses

Eleven-year trends were fitted using linear regression. All trends were analyzed in each hospital separately and in aggregate. In the cohort of severe sepsis patients hospitalized in 2013, we compared

differences in the above variables in patients who had lactates measured at the time of suspected sepsis versus those who did not have lactates measured. We used the Wilcoxon rank-sum test for continuous variables and the chi-square statistic for categorical variables. Variables that were statistically significant were included as potential predictors for failure to measure lactates at the time of suspected sepsis in the multivariate model. For all analyses, we considered p value less than 0.05 to be statistically significant and used two-tailed tests. The c-statistic was calculated to assess the discriminatory capability of the final multivariate model. All analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC).

RESULTS

There were 230,620 patients admitted from 2003 to 2013 who had blood cultures during their hospitalization. Clinical characteristics of these patients and the subgroups of severe sepsis and suspected septic shock are shown in **Table 1**.

Trends in Serum Lactate Testing

Lactate Measurements During Hospitalization and at the Time of Suspected Sepsis. In 2003, 2,024 out of 19,221 patients with

suspected infection (11%) had serum lactates measured during their hospitalization compared with 10,153 out of 21,090 patients (48%) in 2013 ($p < 0.001$ for linear trend over 11 yr) (**Fig. 1**). The trend was similar for the other subgroups. In 2003, 495 out of 2,677 patients (19%) with severe sepsis had a lactate measured within ± 1 day of first blood culture with concurrent antibiotics compared with 3,313 out of 5,071 patients (65%) in 2013 ($p < 0.001$ for linear trend). For suspected septic shock, patients with orders for blood cultures with concurrent antibiotics and vasopressors had lactates measured within ± 1 day of blood culture order in 542 of 1,225 cases (31%) in 2003 compared with 2,022 of 2,708 cases (75%) in 2013 ($p < 0.001$ for linear trend).

Serial Lactate Testing.

In 2003, patients with suspected infection and a lactate level greater than or equal to 4.0 mmol/L had a repeat lactate measured within 6 hours in 86 out of 367 cases (23%) and within 24 hours in 202 out of 340

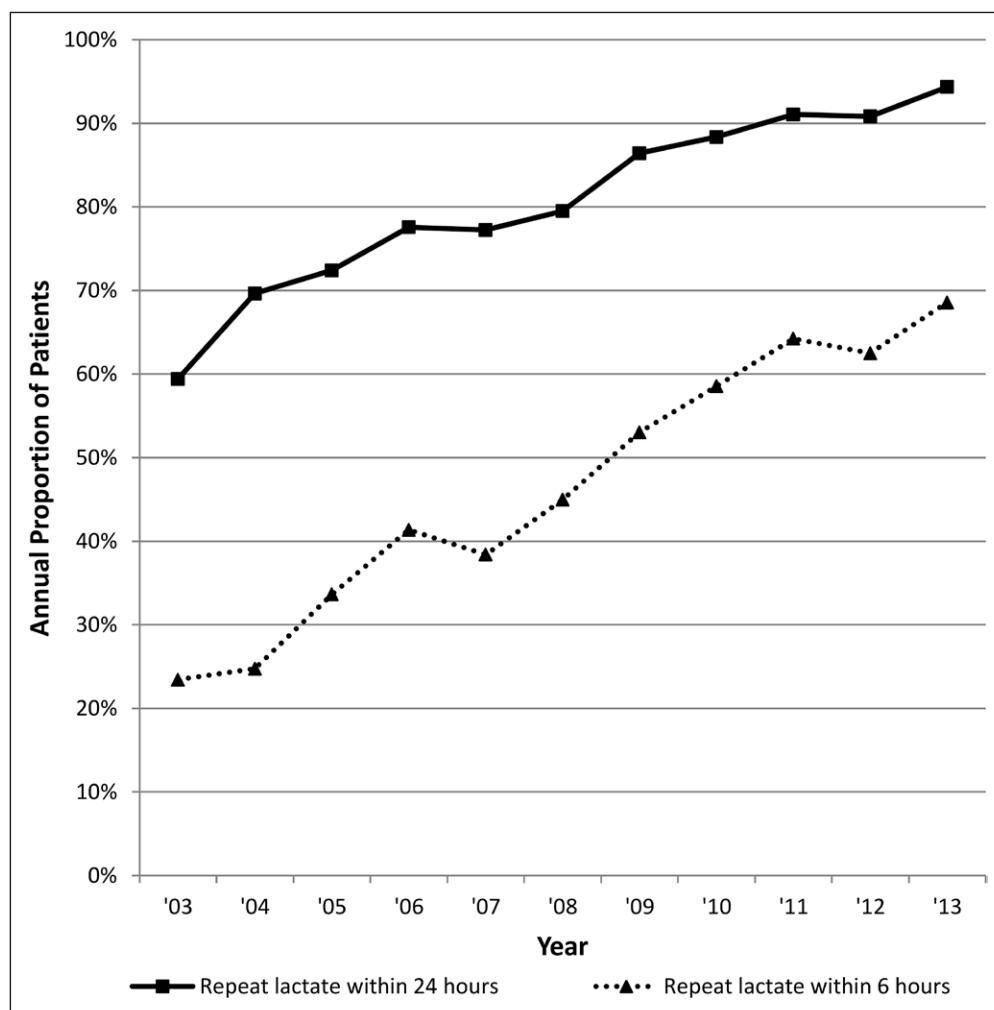


Figure 2. Rising annual rates of repeat lactate measurements within 6 and 24 hours after documented lactate levels ≥ 4.0 mmol/L in patients with suspected infection, 2003–2013.

cases (59%). In 2013, 951 out of 1,387 cases (69%) had a repeat lactate measured within 6 hours and 1,218 out of 1,291 cases (94%) had a repeat lactate measured within 24 hours ($p < 0.001$ for linear trend for both comparisons) (Fig. 2).

Clinical Threshold for Measuring Lactates. In patients with suspected infection, 998 out of 2,024 cases (49%) received vasopressors prior to or on the day of lactate measurement in 2003 compared with 2,139 of 10,153 cases (21%) in 2013 ($p < 0.001$ for linear trend) (Fig. 3).

All of the above trends were identical when examined in each hospital individually with p value less than 0.001.

Lactate Testing in 2013 in Patients With Severe Sepsis

Of the 5,071 patients with severe sepsis in 2013, 1,758 (35%) did not have a lactate measured at the time of suspected sepsis, and 1,288 (25%) did not have a lactate measured at any point during hospitalization. On bivariate analysis, patients who did not have a lactate measured at the time of suspected sepsis were more likely to be younger, have a lower burden of comorbidities, not require vasopressors or mechanical ventilation or ICU care, have hospital-onset sepsis, be admitted to a nonmedical service, and have fewer signs of organ dysfunction or infection compared with those who did have lactates measured (Table 2). Median hospital length of stay was longer in the no-lactate group (14 d vs 11 d; $p < 0.001$), although the hospital mortality rate was lower (10% vs 17%; $p < 0.001$).

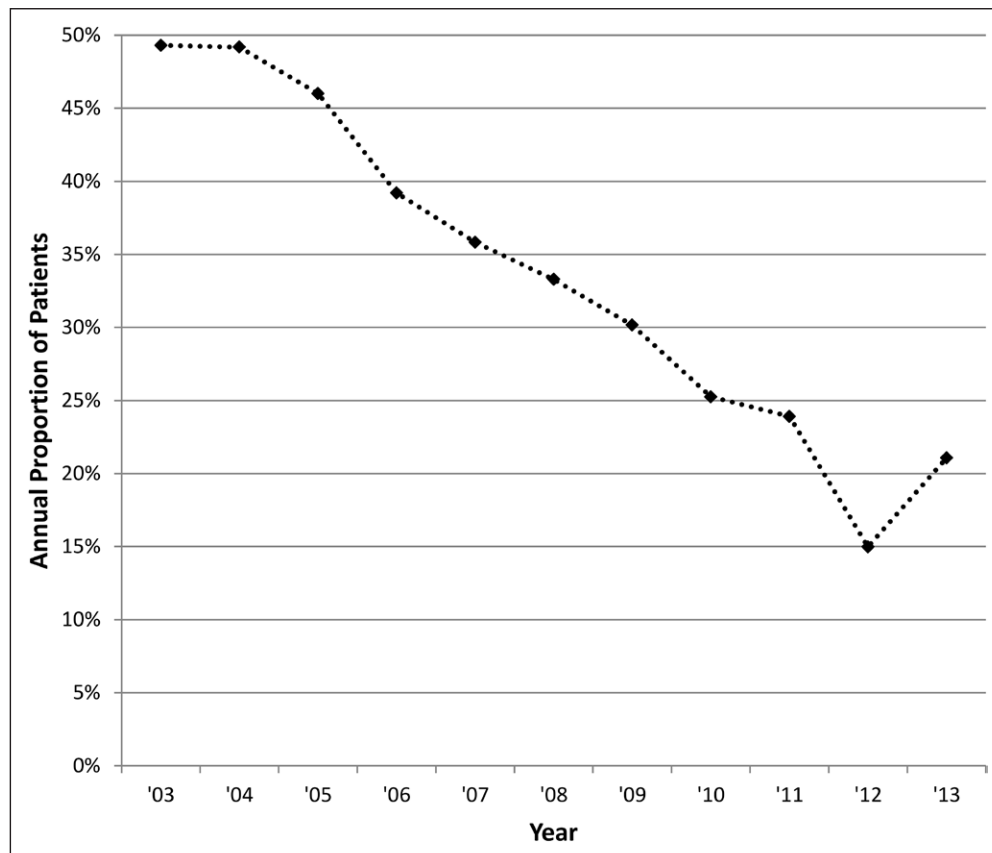


Figure 3. Decreasing proportion of patients with suspected infection who required vasopressors before or on the day of first lactate measurement, 2003–2013.

On multivariate analysis (Table 3), risk factors for failure to measure a lactate at the time of suspected sepsis included hospital-onset sepsis versus community-onset sepsis (adjusted odds ratio, 7.56; 95% CI, 6.31–9.06; $p < 0.001$) and admission to a nonmedical service (adjusted odds ratio, 2.08; 95% CI, 1.76–2.46; $p < 0.001$). Factors significantly associated with lactate measurement after adjustment included concurrent or preceding vasopressors, ICU care, older age, higher Elixhauser comorbidity score, positive blood cultures before or at the time of suspected sepsis, anion gap greater than 16 mEq/L, greater than or equal to 5% bands, total bilirubin greater than or equal to 2.0 mg/dL, and WBC count greater than 12,000/ μ L or less than 4,000/L. The c -statistic for the multivariate model was 0.816.

DISCUSSION

We found that the use of serum lactate testing in patients with suspected or diagnosed sepsis increased steadily every year since 2003. Rates of lactate measurement in patients who had blood cultures drawn during hospitalization increased more than four-fold in our study. In 2003, lactates were measured only a fraction of the time in patients with severe sepsis or those with evidence of suspected septic shock, but was performed in the majority of cases by 2013. The increase in lactate testing also included higher rates of serial lactate measurements in patients with elevated lactate levels, as almost all these patients had a repeat measurement within 24 hours. In addition, lactates were increasingly measured in patients who were not on vasopressors, suggesting that clinicians have lowered their thresholds for obtaining lactate levels by extending testing to patients without overt hypotension.

The marked increase in the use of lactate testing at our hospitals likely reflects multiple factors. There have been a plethora of publications over the past 2 decades, documenting the prognostic utility of lactate (6, 7, 23–25), its use as a therapeutic target for resuscitation (8, 9), its ability to alter provider behavior (26), and the potential for rapid testing to improve patient outcomes (10). Studies demonstrating the use of lactate as a severity marker in hemodynamically stable patients with suspected infection (7, 25) could also explain why clinicians are extending the test to patients who are not on vasopressors. In addition, the uptake of lactate testing we observed probably also reflects the increasing success and penetration of the

TABLE 2. Clinical Characteristics of Patients With Severe Sepsis in 2013 Who Did and Did Not Have Serum Lactates Measured at the Time of Suspected Sepsis

Clinical Characteristic	Lactate Measured (<i>n</i> = 3,313)	No Lactate Measured (<i>n</i> = 1,758)	<i>p</i> ^a
Median age (IQR)	67 (55–77)	65 (54–76)	0.012 ^b
Male sex, <i>n</i> (%)	1,913 (57.7)	1,015 (57.7)	0.997
White race, <i>n</i> (%)	2,636 (79.6)	1,442 (82.0)	0.036 ^b
Median Elixhauser score (IQR)	9 (5–14)	8 (4–13)	< 0.001 ^b
Vasopressor before or at the time of suspected sepsis, <i>n</i> (%)	1,411 (42.6)	375 (21.3)	< 0.001 ^b
Mechanical ventilation at the time of suspected sepsis, <i>n</i> (%)	921 (27.8)	264 (15.0)	< 0.001 ^b
ICU care before or at the time of suspected sepsis, <i>n</i> (%)	2,171 (65.5)	589 (33.5)	< 0.001 ^b
Positive blood cultures before or at the time of suspected sepsis, <i>n</i> (%)	510 (15.4)	177 (10.1)	< 0.001 ^b
Laboratory derangements (at the time of suspected sepsis)			
Albumin < 2.5 g/dL, <i>n</i> (%)	567 (17.1)	179 (10.2)	< 0.001 ^b
Anion gap > 16 mEq/L, <i>n</i> (%)	678 (20.5)	80 (4.6)	< 0.001 ^b
Bands ≥ 5%, <i>n</i> (%)	617 (18.6)	140 (8.0)	< 0.001 ^b
Creatinine ≥ 2.0 mg/dL, <i>n</i> (%)	861 (26.0)	268 (15.2)	< 0.001 ^b
Hematocrit < 21%, <i>n</i> (%)	390 (11.8)	175 (10.0)	0.050
International normalized ratio > 1.5, <i>n</i> (%)	731 (22.1)	231 (13.1)	< 0.001 ^b
Platelets < 100/μL, <i>n</i> (%)	905 (27.3)	494 (28.1)	0.553
Total bilirubin ≥ 2.0 mg/dL, <i>n</i> (%)	414 (12.5)	112 (6.4)	< 0.001 ^b
WBC > 12,000/μL, <i>n</i> (%)	1,724 (52.0)	624 (35.5)	< 0.001 ^b
WBC < 4,000/μL, <i>n</i> (%)	556 (16.8)	356 (20.3)	0.002 ^b
Hospital-onset sepsis, <i>n</i> (%)	436 (13.2)	704 (40.1)	< 0.001 ^b
Nonmedical service, <i>n</i> (%)	781 (23.6)	613 (34.9)	< 0.001 ^b
Hospital (Brigham and Women's Hospital vs Massachusetts General Hospital), <i>n</i> (%)	1,252 (37.8)	754 (42.9)	< 0.001 ^b

IQR = interquartile range.

^a*p* values obtained by Wilcoxon rank-sum test for continuous variables (age and Elixhauser score) and the chi-square statistic for categorical variables (all other variables).

^bStatistically significant variables.

SSC, which has emphasized the importance of spot and serial lactate testing, to clinicians and hospitals around world (11). Other hospitals have also noted improvements in lactate testing rates over time associated with sepsis quality initiatives (13, 14, 27). Our findings shed additional light on this important topic insofar as neither of our hospitals was explicitly enrolled in the SSC and, therefore, provide a window into the diffuse of lactate testing beyond the Campaign.

Although rates of lactate testing have increased significantly over time, our analysis of practice patterns in 2013 suggests that there is still significant room for improvement. The vast majority of patients who had lactate levels greater than or equal to 4.0 mmol/L had a repeat level measured

within 24 hours, but almost one third did not have a level rechecked within 6 hours. This suggests that the use of lactate clearance as a resuscitation target (8, 9) and the SSC recommendations of serial lactate testing for patients with hyperlactatemia have not become fully ingrained in clinicians yet. In addition, analysis of patients with severe sepsis in 2013 showed that more than one third did not have lactates measured around the time of suspected sepsis, and a quarter did not have lactates measured at any point during hospitalization. Closer examination of these patients showed a lower degree of organ dysfunction and proportion of patients in the ICU in the no-lactate group, indicating that clinicians are preferentially drawing lactates in more severely

TABLE 3. Multivariate Analysis of Risk Factors for Failure to Measure Serum Lactates at the Time of Suspected Sepsis in Patients With Severe Sepsis in 2013

Potential Predictor	Adjusted OR (95% CI)	p
Age (yr)	0.99 (0.99–1.00)	0.009 ^a
White race	1.22 (1.03–1.46)	0.026 ^a
Elixhauser comorbidity score	0.99 (0.98–1.00)	0.005 ^a
Vasopressor before or at the time of suspected sepsis	0.42 (0.34–0.52)	< 0.001 ^a
Mechanical ventilation at the time of suspected sepsis	0.98 (0.79–1.23)	0.898
ICU care before or at the time of suspected sepsis	0.28 (0.23–0.33)	< 0.001 ^a
Positive blood cultures before or on the day of suspected infection	0.68 (0.54–0.84)	< 0.001 ^a
Laboratory derangements (at the time of suspected sepsis)		
Albumin < 2.5 g/dL	0.83 (0.66–1.04)	0.104
Anion gap > 16 mEq/L	0.32 (0.24–0.42)	< 0.001 ^a
Bands ≥ 5%	0.52 (0.41–0.66)	< 0.001 ^a
Creatinine ≥ 2.0 mg/dL	0.90 (0.74–1.09)	0.270
International normalized ratio > 1.5	0.86 (0.71–1.05)	0.136
Total bilirubin ≥ 2.0 mg/dL	0.60 (0.47–0.79)	< 0.001 ^a
WBC > 12,000/μL	0.62 (0.53–0.72)	< 0.001 ^a
WBC < 4,000/μL	0.69 (0.57–0.84)	< 0.001 ^a
Hospital-onset sepsis	7.56 (6.31–9.06)	< 0.001 ^a
Nonmedical service	2.08 (1.76–2.46)	< 0.001 ^a
Hospital (Brigham and Women's Hospital vs Massachusetts General Hospital)	1.10 (0.95–1.26)	0.201

OR = odds ratio.

^aStatistically significant variables.

ill patients. However, the hospital length of stay and mortality rate in severe sepsis patients without lactates measured were high, suggesting that clinicians may underappreciate the utility of lactate testing to identify patients with occult hypoperfusion who are at increased risk for adverse outcomes. Interestingly, even overt hypotension is not always

triggering lactate tests, as a quarter of patients in 2013 who required vasopressors and had concurrent blood culture orders and antibiotics never had a lactate measured at the time of suspected infection.

We identified two clinical factors related to processes of care that predict failure to measure a lactate in patients with severe sepsis. For patients of roughly equivalent level of illness and organ dysfunction, a lactate was less likely to be measured if suspected sepsis occurred in the hospital rather than being present at admission and if the patient was admitted to a nonmedical service. Other studies have shown that sepsis that occurs on hospital ward units is associated with worse outcomes and that this may be due to delays in appropriate recognition and timely administration of fluids, vasoactive agents, and transfer to the ICU (13, 28). Another recent study using a nationally representative administrative database showed that risk-adjusted mortality was significantly worse for patients with a diagnosis of sepsis present-at-admission if they were directly admitted to the floor versus the emergency department (29). Delayed recognition of severe illness in hospitalized patients versus those presenting to the emergency department has also been documented for other conditions (30). All of this suggests that the current focus on lactate testing and early sepsis detection in emergency department settings should be extended to the inpatient setting as well. Targeting the implementation of automated triggers for lactate testing, sepsis protocols, and/or education initiatives to hospital ward units, particularly nonmedical units, might be a high yield area for quality improvement.

Our study has several limitations. First, our findings come only from two academic hospitals in one city. Hospitals around the world might vary significantly in the frequency of lactate testing, depending on resources and the presence or absence of specific protocols. In addition, both of our hospitals were participating sites for the Protocolized Care for Early Septic Shock trial from 2008 to 2013, which required that hospitals adhere to the SSC guidelines and use serum lactate levels to screen for hypoperfusion (31). This may have influenced trends in lactate ordering over the latter part of the time period we studied and may therefore limit generalizability. Second, our estimate of the population of patients with possible sepsis may have been incomplete, as underrecognition of sepsis is common and misclassification is possible when using discharge diagnoses (20, 32, 33). We chose the most widely used claims method, however, for retrospectively identifying patients with severe sepsis for purposes of quality monitoring. Furthermore, we addressed this limitation by considering three different methods to identify patients with suspected and diagnosed sepsis including two methods based solely on clinical data. Third, our assessment of risk factors for failure to measure a lactate level in patients with suspected sepsis was limited to data we could glean from electronic sources. Additional predictors such as vital signs, severity of illness scores, and evolving complications may also be important. Fourth, some degree of inaccuracy is possible when estimating the timing of suspected sepsis onset using the time stamps of blood culture orders. Lastly, it is possible that some patients who did not have lactates measured might have been

so overtly in shock and multiple organ failure that clinicians did not feel that lactates would add additional useful clinical information. However, the fact that overall level of illness was lower in the no-lactate group argues that this was not a major contributor.

In conclusion, the use of serum lactate testing in patients with suspected and diagnosed sepsis has increased dramatically since 2003, and clinicians appear to be progressively extending lactate testing to patients without overt signs of shock. However, even in 2013, serial lactate testing rates remained suboptimal, and a substantial proportion of patients with severe sepsis and those with clinical markers indicating suspected septic shock did not have serum lactate levels measured. Onset of suspected sepsis while hospitalized and admission to a nonmedical service were risk factors for failure to draw a lactate. Our findings have important implications for quality improvement and monitoring programs.

ACKNOWLEDGMENTS

We thank David Hooper, MD, Division of Infectious Diseases Infection Control Unit at Massachusetts General Hospital (MGH), for his assistance in obtaining the blood culture data needed for this study. We also thank Edwards Burns from the MGH Respiratory Care Department for providing ventilator data needed for this study.

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