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The use of finger-stick blood to assess lactate in critically ill surgical patients☆

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HIGHLIGHTS

- Finger-stick capillary lactate correlates with blood gas and core lab values.
- Capillary lactate trends closely over time with arterial lactate.
- Rising or falling capillary lactate reflects the adequacy of global perfusion.
- Capillary lactate measurements require a fraction of the time and blood to process.
- Preliminary results imply capillary lactate may be used in lieu of invasive methods.

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ABSTRACT

Background: Using finger-stick capillary blood to assess lactate from the microcirculation may have utility in treating critically ill patients. Our goals were to determine how finger-stick capillary lactate correlates with arterial lactate levels in patients from the surgical intensive care unit, and to compare how capillary and arterial lactate trend over time in patients undergoing resuscitation for shock.

Methods: Capillary whole blood specimens were obtained from finger-sticks using a lancet, and assessed for lactate via a handheld point-of-care device as part of an “investigational use only” study. Comparison was made to arterial blood specimens that were assessed for lactate by standard laboratory reference methods.

Results: 40 patients (mean age 68, mean APACHEII 18, vasopressor use 62%) were included. The correlation between capillary and arterial lactate levels was 0.94 ($p < 0.001$). Capillary lactate measured slightly higher on average than paired arterial values, with a mean difference 0.99 mmol/L. In patients being resuscitated for septic and hemorrhagic shock, capillary and arterial lactate trended closely over time: rising, peaking, and falling in tandem. Clearance of capillary and arterial lactate mirrored clinical improvement, normalizing in all patients except two that expired.

Conclusion: Finger-stick capillary lactate both correlates and trends closely with arterial lactate in critically ill surgical patients, undergoing resuscitation for shock.

1. Introduction

Lactate is a principal biomarker used in the assessment and treatment of critically ill patients. Traditionally measured from arterial blood, lactate is generated in states of oxygen deprivation via reduction of pyruvate by lactate dehydrogenase. This lactate is cleared by the liver, kidneys, and heart. In the liver, lactate enters the Cori cycle to become glucose [1]. Under homeostatic conditions, lactate levels are usually below 2 mmol/L as clearance matches production. Under conditions of physiological stress and

Abbreviations used: ICU, intensive care unit; POC, point-of-care; BGA, blood gas analyzer; CL, core lab.

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pathological conditions, plasma lactate levels may rise above 2 mmol/L as production overwhelms clearance. As such, lactate rise secondary to inadequate oxygen delivery is an early sign of shock [1].

Initial lactate levels help risk-stratify patients for triage in the pre-hospital, emergency room, ward, and intensive care unit (ICU) environments [2–4]. Greater elevation and duration of lactic acidosis correlate with worse prognosis [1]. In contrast, clearance of lactate over time correlates with improved survival, and helps guide resuscitation protocols in shock [2,5–7].

Finger-stick capillary lactate is being evaluated as an alternative to arterial lactate testing in the care of critically ill patients. Growing interest in the application of capillary lactate has come with the development of handheld point-of-care (POC) devices that incorporate test strip technology similar to that of glucometers. These POC devices can process tiny microliter aliquots of capillary blood from patient finger-sticks, with rapid result turnaround time at the bedside.

The use of capillary lactate may have several advantages. Sampling of finger-stick capillary blood avoids the need for arterial and venous puncture, indwelling catheters, and large volume blood draws. Results are obtained within seconds and transport of specimens to the lab is eliminated, with demonstrated timesaving of greater than 1 h [8]. Using capillary lactate might enable the earlier identification and triage of patients with lactic acidosis. In addition, trending serial capillary lactate checks over time could help to guide resuscitation in a dynamic fashion.

Individual capillary lactate measurements have been shown to correlate with arterial lactate measurements in patients from both the emergency room and medical ICU populations [8,9]. However, further study is needed in surgical patients in whom the application of capillary lactate could be particularly beneficial, in such areas as triage, monitoring, and shock resuscitation. The correlation of capillary and arterial lactate levels in surgical patients has yet to be determined. In addition, the way in which capillary and arterial lactate levels together trend over time in a single patient, and the effect of vasopressors on capillary lactate in critically ill patients undergoing resuscitation has never been assessed. In this paper, we show for the first time that the trend of capillary and arterial lactate levels correlate over time, suggesting that capillary lactate can be used to monitor resuscitation and treatment for shock.

Table 1
Patient demographics.

Patient demographics	Number	Percent
Number of patients	40	
Male:Female	17:23	
Mean Age (years)	68	
Underlying Diseases		
Hypertension	23	58%
Diabetes	13	33%
Severity of Illness		
Mean APACHE II	18	
Vasopressors	25	63%
Types of Shock		
Septic	16	40%
Hypovolemic	8	20%
Cardiogenic	1	3%
Types of Cases		
General Surgery	29	72%
Vascular	4	10%
Urology	2	5%
Head Neck	2	5%
Neurosurgery	2	5%
Gynecology	1	3%

2. Methods

The study took place in the surgical intensive care unit of an 800 bed urban teaching hospital, from September 2013 until February 2014. The hospital's Institutional Review Board for human research approved the study protocol with waiver of consent (IRB #052-13). Patients were included if they were undergoing active resuscitation for shock. Most had either septic or hypovolemic shock as defined by standard criteria [7].

POC analysis was performed using a handheld POC lactate analyzer (StatStrip, Nova Biomedical Corporation, Waltham, MA), which has a 0.6 μl sample size, has a detection range 0.3 mmol/L to 20 mmol/L, and provides results in 13 s. This POC lactate analyzer is Clinical Laboratory Improvement Amendments approved for POC measurement of fresh venous and arterial whole blood specimens; assessment of capillary lactate was part of an "investigational use only" study. The analyzer uses single-use test strips containing an enzyme-coated electrode. Calibration was assessed every 24 h by using standard test strips with known lactate values.

Finger-stick capillary whole blood was collected every 4–6 h on average, from patients who were undergoing checks for finger-stick whole blood glucose as part of the ICU's glucose-control protocol. As part of this protocol, the fingertip was cleaned with 70% isopropyl alcohol and allowed to air dry. A drop of capillary blood was obtained by using a single-use disposable lancet (Roche Accu-Chek, Basel, Switzerland) to pierce the side of the fingertip. A small aliquot of this blood was transferred to the handheld POC lactate analyzer to assess capillary lactate level, with the remainder of the drop being transferred to the glucometer; consequently, no additional blood was required for the study, beyond that already being drawn as part of the ICU's standard operating procedure. Capillary lactate results were not reported to any physicians caring for the patients, nor used to guide clinical decisions.

Arterial blood specimens were drawn according to the clinical discretion of the ICU team, from indwelling arterial lines, and collected into either 3 ml heparinized-arterial blood sampling syringes (Smiths Medical, Keene, NH), or 4 ml grey-top Vacutainer tubes (BD, Franklin Lakes, NJ) placed on ice. The arterial blood was assessed for lactate by standard reference methods including a blood gas analyzer (BGA) (Premier 3500, Instrumentation Laboratory Co., Bedford, MA), and core lab (CL) (VITROS 5.1, Ortho-Clinical Diagnostics, Raritan, NJ). The BGA and CL were calibrated and maintained according to manufacturer standards.

Comparison was made retrospectively between capillary and arterial lactate results that had been drawn close in time, with values recorded within 10 min of each other. Correlation between capillary and arterial lactate was determined by simple linear regression using each value as a variable. The strength of association between the variables was measured by the Pearson correlation coefficient, with a p-value < 0.05 being considered statistically significant. Analysis of agreement was performed using the Bland-Altman method accounting for repeated measurements per individual [10]. Statistical data analysis was performed using Microsoft Excel for Mac 2011 (Redmond, WA), and MedCalc for Windows (MedCalc, Ostend, Belgium). Capillary and arterial lactate trending curves were created using Microsoft Excel for MAC 2011 (Redmond, WA).

3. Results

A convenience sample of 40 patients was included from June 2013 until February 2014. Patient demographics are shown in Table 1. The mean age was 68 years and the mean APACHE II score was 18. Sixty-two percent of patients were on vasopressors and in shock.

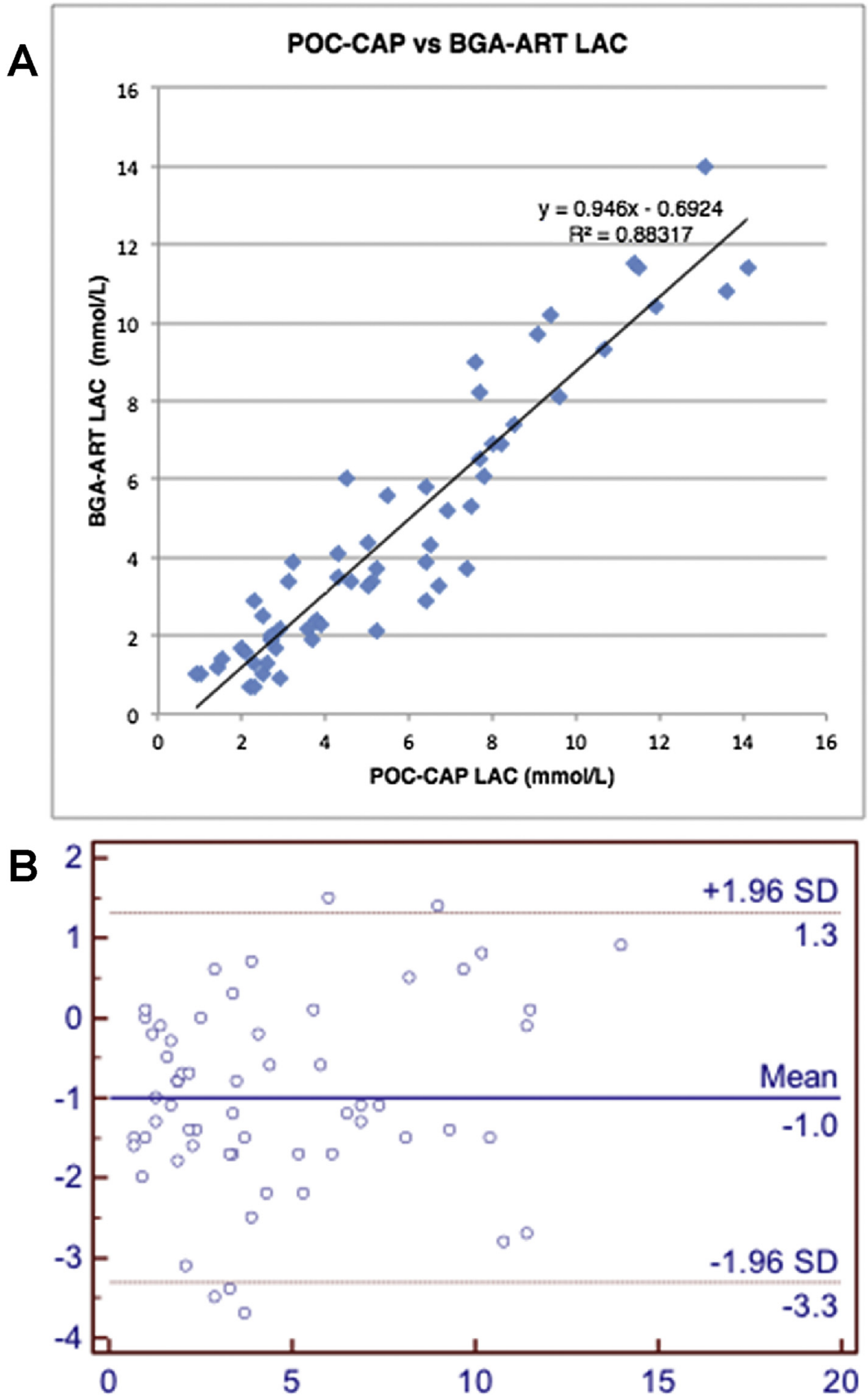

Fig. 1. a: The correlation between POC-Capillary and BGA-Arterial lactate levels. b: Bland-Altman Analysis. BGA-Arterial lactate (x-axis), BGA-Arterial lactate minus POC-Capillary lactate (y-axis).

The correlation between POC-capillary and BGA-arterial lactate levels was 0.94 ($p < 0.001$) (Fig. 1a). The mean POC-capillary and BGA-arterial lactate difference was 0.99 mmol/L, with limits of agreement between −3.3 and 1.3 mmol/L (Fig. 1b).

The correlation between POC-capillary and CL-arterial lactate levels was 0.94 ($p < 0.001$). The mean POC-capillary and CL-arterial lactate difference was 0.72 mmol/L, with limits of agreement between −2.66 and 1.21 mmol/L.

Subset analysis was performed on paired POC-capillary and BGA-arterial lactate samples, by examining values from patients who were either off or on vasopressors. *Off vasopressors*: correlation between POC-capillary and BGA-arterial lactate levels was 0.96 ($p < 0.001$). The mean POC-capillary and BGA-arterial lactate difference was 0.51 mmol/L, with limits of agreement between −2.00 and 0.98 mmol/L. *On vasopressors*: correlation between POC-capillary and BGA-arterial lactate levels was 0.93 ($p < 0.001$). The

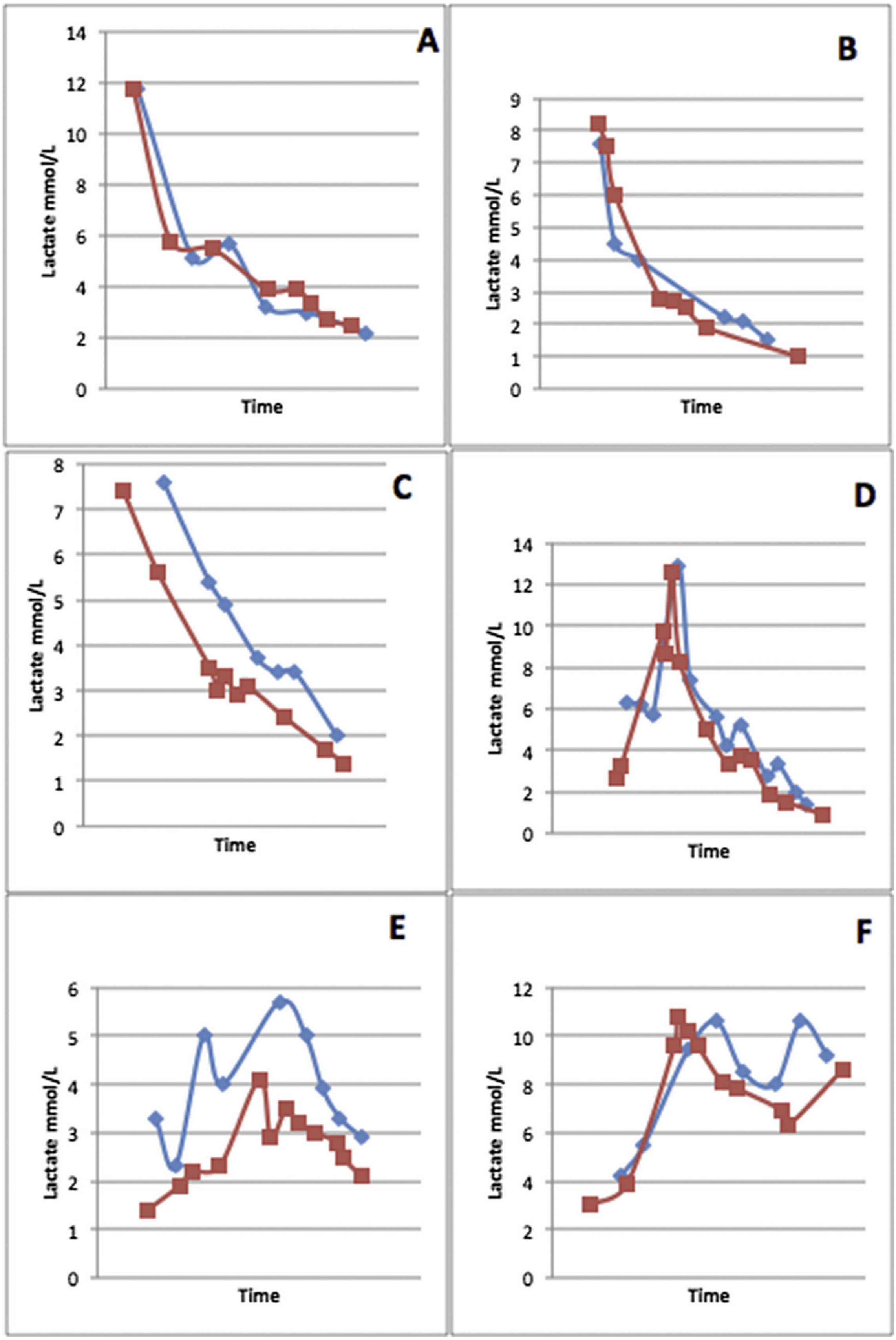

Fig. 2. Patients undergoing resuscitation for septic shock having: A) infectious colitis, B) peritoneal abscess s/p drainage, C) colonic perforation s/p Hartmann's, D) emphysematous pyelonephritis, E) postop aspiration pneumonia, F) anastomotic leak. Blue curve = Capillary lactate. Red curve = Arterial lactate. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

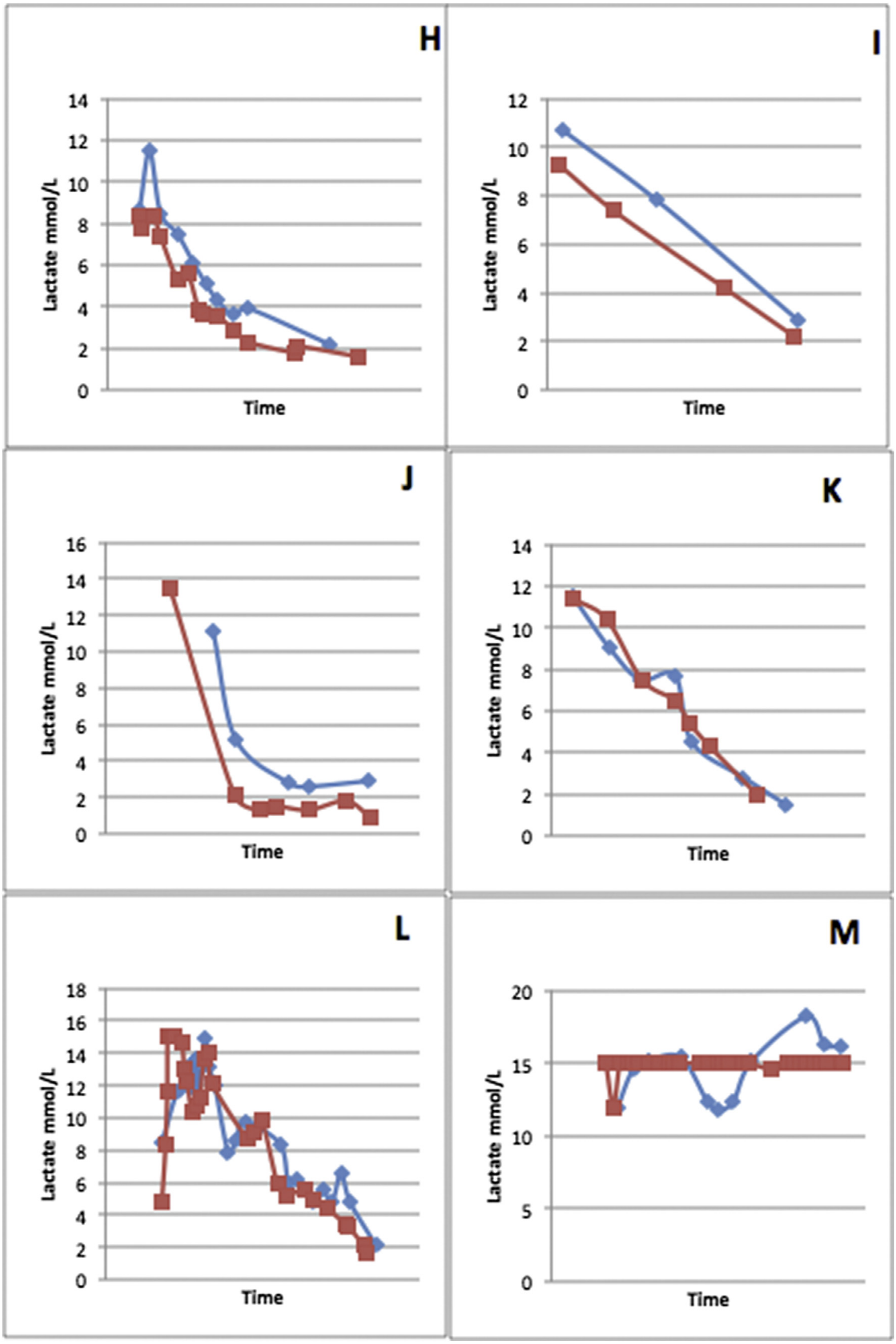

Fig. 3. Patients undergoing resuscitation for hemorrhagic shock, after the following operations complicated by bleeding: H) exploratory laparotomy, I) esophagectomy J) vascular bypass, K) hysterectomy, L) splenectomy, M) hepatectomy. Blue curve = Capillary lactate. Red curve = Arterial lactate. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

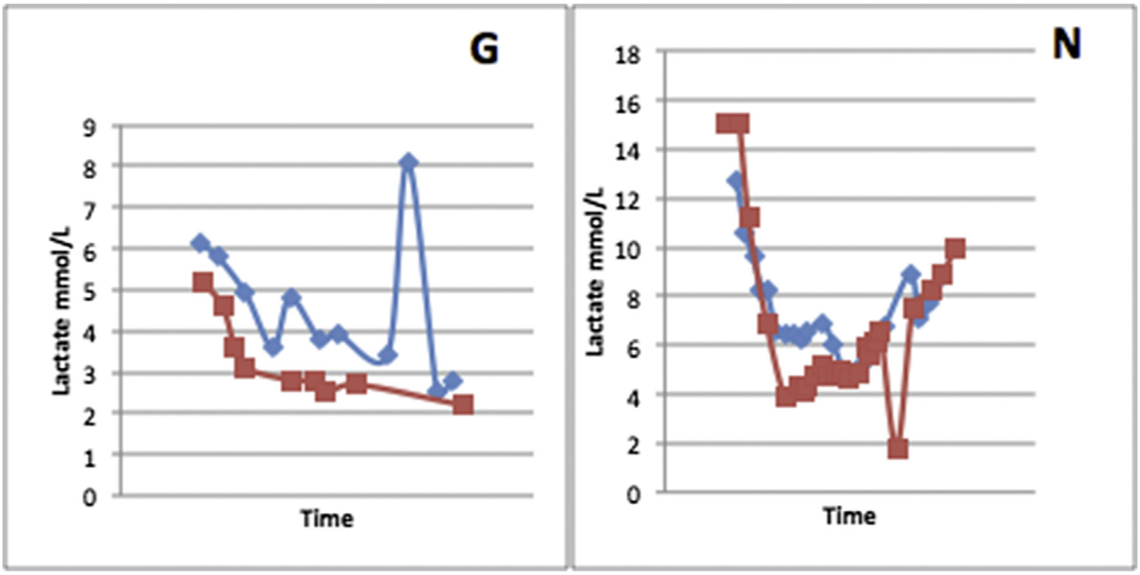

Fig. 4. Examples of random POC testing errors. G) septic shock from enterocutaneous fistula: likely error of a Capillary lactate reading with an upward spike, N) hemorrhagic shock s/p pancreatic necrosectomy complicated by bleeding: likely error of an Arterial lactate reading with a downward spike. Blue curve = Capillary lactate. Red curve = Arterial lactate. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

mean POC-capillary and BGA-arterial lactate difference was 1.28 mmol/L, with limits of agreement between −3.8 and 1.3 mmol/L.

Capillary and arterial lactate levels were also trended over time in individual patients undergoing resuscitation for shock. Patients with septic shock are shown in Fig. 2. Patients with hemorrhagic shock are shown in Fig. 3. Each subsection represents an individual patient. The curves demonstrate that capillary and arterial lactate levels trended closely over time: rising, peaking, and falling in tandem. Capillary and arterial lactate levels cleared in all cases, except for patients F and M, who did not recover. Significant deviations between capillary and arterial lactate were rare. Examples of suspected random POC testing errors of capillary lactate by the POC lactate analyzer, and of arterial lactate by the BGA are shown for patients G and N, respectively (Fig. 4).

The only data points excluded from the study included 3 arterial lactate samples that had values greater than the upper detection limit of the BGA (15 mmol/L), preventing their inclusion in calculating the correlation between POC-capillary and BGA-arterial lactate. No outliers of capillary lactate were dropped from analysis.

4. Discussion

Finger-stick capillary lactate measured by a handheld POC device correlated strongly with arterial lactate levels measured by standard laboratory reference methods, BGA (0.94, $p < 0.001$) and CL (0.94, $p < 0.001$). The study group included ICU patients from a variety of surgical subspecialties: general, vascular, urology, head and neck, neurosurgery, and obstetrics. These patients had a high severity of illness with mean APACHE II score of 18. Greater than 60% of patients were on vasopressors and in shock: septic (40%), hypovolemic (20%), and cardiogenic (3%). In addition, most had risk factors for peripheral vascular disease, including hypertension and diabetes.

As shown in prior studies [8,9], capillary lactate values measured slightly higher on average than paired arterial values. The mean difference between capillary and arterial lactate ranged from 0.51 mmol/L in patients not on vasopressors to 1.28 mmol/L in patients on vasopressors. Vasopressors may decrease perfusion to the capillary microcirculation, which could account for this difference. In addition, blood flow is shunted away from the capillary microcirculation to core vital organs in states of shock. Both processes could lead to a relative increase in capillary over arterial lactate – byproducts of the microcirculation and systemic circulation, respectively. Further understanding about these differences will come from work underway examining capillary lactate in patients with acute and chronic limb ischemia.

Our study is the first to demonstrate that changes in capillary lactate mirror those of arterial lactate over time: rising, peaking, and falling in tandem in critically ill patients undergoing resuscitation (Figs. 2–4). High lactate normalized in all cases except for two patients, who did not recover. Trending lactate and using targeted interventions to improve lactate clearance has been advocated as a resuscitation strategy for patients with septic shock [7], showing equivalent survival outcomes to targeting central venous oxygen saturation [6], and leading to decreased length of ICU stay and improved mortality [5]. More recently, lactate clearance has also been associated with improved mortality in trauma patients with hemorrhagic shock [11].

Using finger-stick capillary blood to track lactate may provide added benefit over using serum lactate alone, in helping to resuscitate critically ill patients. POC testing of capillary lactate can be performed and analyzed in real-time at the bedside, enabling rapid targeted intervention to improve lactate clearance. Tiny microliter sample size and fast result turnaround time help make the acquisition of serial lactate values extremely feasible, practical, and may conserve blood in patients with preexisting anemia. As shown in this study, lactate trending curves can be generated, providing a road map for directing ongoing resuscitation efforts.

In addition, tracking finger-stick capillary lactate may help in the surveillance of other patients at risk for clinical deterioration. Lactate is a proven screening tool [12–16] whose elevation can warn of occult tissue hypo-perfusion, even in the absence of hemodynamic instability [16]. Serial capillary lactate checks could be performed on select patients in intensive as well as resource-limited environments. A newly elevated capillary lactate level could alert staff of potential clinical deterioration, and trigger early intervention and potential escalation of care.

As has previously been suggested [8], capillary lactate could also be used to screen patients being triaged with sepsis. Here, progression to severe sepsis would be predicted by a capillary lactate increase to $\geq$6 mmol/L, correlating with an arterial lactate $\geq$4 mmol/L with 97.5% confidence. This calculation is based upon looking at the limits of agreement (−2.00 to +0.98 mmol/L) in the subgroup of patients not on vasopressors, who had a low bias (0.51) and high degree of correlation (0.96, $p < 0.001$) – suggesting that capillary lactate could be used in lieu of arterial lactate in this patient population.

Limitations of the study include the chance that capillary lactate results could have been contaminated by lactate contained in perspiration on the skin. Consideration in the future is being given to cleaning the fingertip with an antiperspirant in order to help eliminate this possibility. Random POC testing errors appeared rarely, and as shown in Fig. 3, affected both capillary and arterial lactate results. Continuing to trend lactate with repeat testing can help prove that these points are outliers.

5. Conclusions

Finger-stick capillary lactate measured by a handheld POC device correlated strongly with arterial lactate levels measured by standard laboratory reference methods in critically ill surgical patients. In addition, finger-stick capillary lactate trended closely over time with arterial lactate in patients undergoing resuscitation for septic and hemorrhagic shock, providing rapid feedback for ongoing resuscitation and early goal directed therapy.

This study helps validate finger-stick capillary lactate testing for use in surgical-critical care. Finger-stick capillary lactate testing may have clinical application to areas including triage, monitoring, and resuscitation. It's convenience and speed could decrease result turnaround time, with improved screening for shock and the care of critically-ill patients at the bedside. Furthermore, finger-stick capillary lactate testing could be performed by virtually any health care provider, in both intensive and resource-limited environments.

The use of capillary lactate as a triage marker in ED populations has already been studied and found to be predictive of patients at high risk of death [17]. Serum lactate is already known to be an important marker in critical care patients [12–16]. We have shown that capillary lactate has similar kinetics and levels as serum lactate; by extension, capillary lactate will give clinicians the same data more quickly and with a smaller blood sample in this population of critically ill patients undergoing resuscitation. We are currently assessing its role as a biomarker for determining adequacy of peripheral perfusion in patients undergoing revascularization for limb ischemia.

Ethical approval

This study was approved by the Mount Sinai Beth Israel (MSBI) IRB (study number 052-13).

Sources of funding

The measurement strips and the point of care device were provided free of charge to the department.

Author contributions

Simon D. Eiref – Concept and study design, data collection, manuscript and figure preparation, final approval.

Scott Gould, Ezra Gillego, Anita Hariprashad, Christine Wiest, Shailyn Almonte – Data collection, final approval.

Asaf Gave, Joseph Sabat, and I. Michael Leitman – Manuscript preparation, final approval.

David Lucido – Data analysis, final approval.

Conflicts of interest

The authors have no conflicts of interest to report. None of the authors had a financial relationship with Nova Biomedical Corporation, the maker of the StatStrip lactate analyzer used in this study.

Trial registry number

researchregistry703.

Guarantor

Joseph Sabat and Simon D. Eiref.

Consent

No identifying details have been included in the manuscript. The MSBI IRB approved the research study as minimal risk with waiver of consent.

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