Effectiveness of arterial, venous, and capillary blood lactate as a sepsis triage tool in ED patients

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Abstract

Objective: We evaluate the capacity of arterial (ABL), peripheral venous (VBL), and capillary (CBL) blood lactate concentration to early detect the presence of severe sepsis in patients admitted to the emergency department for a septic syndrome.

Methods: Patients with signs of sepsis presenting to the emergency department were prospectively enrolled. Blood lactate was measured using a handheld point-of-care analyzer on microsamples of arterial, peripheral venous, and capillary blood. An arterial blood sample was dispatched to the central laboratory as a reference measurement.

Results: A total of 103 patients were enrolled in the study, with 63 patients presenting with a severe sepsis. There was a strong correlation between the point of care and the reference blood lactate measurement. The CBL, VBL, and ABL were all significantly different (3.01 ± 0.29, 2.51 ± 0.21, and 2.03 ± 0.18 mmol/L, respectively; \( P < .001 \)). The VBL value was the most efficient to detect early the presence of severe sepsis (areas under the receiver operating characteristic curves were 0.85 ± 0.04, 0.76 ± 0.05, and 0.75 ± 0.05 for VBL, ABL, and CBL, respectively; \( P < .01 \)). Mortality at 28 days was related to the severity of sepsis (28.6% vs 7.5%) and to the number or organ dysfunctions (\( P < .01 \)). Arterial blood lactate, VBL, and CBL were all significantly associated with the 28th-day mortality.

Conclusions: Initial VBL may be used efficiently to assess the severity of sepsis, and it could even be more effective than ABL and CBL to early detect the presence of severe sepsis.
results regarding agreement between peripheral venous and arterial blood lactate values [17–22], and only few works have evaluated the interest of capillary blood lactate in this setting [23,24].

To date, there is no available prospective study evaluating the reliability of blood lactate sampled at different sites to assess the presence of severe sepsis in ED patients.

1.2. Goals of this investigation

This study aimed to compare the ability of arterial, venous, and capillary blood lactate (measured with a POC method) to detect the presence of severe sepsis in ED patients admitted for a septic syndrome.

2. Methods

2.1. Setting and selection of participants

This study was a prospective cohort design, observational, and monocentric. It took place from December 2013 to March 2014, in the ED of a French university hospital with an annual census of about 80,000. The research protocol was approved by our institutional review board, and the subjects signed a written informed consent.

Patients who were assessed for inclusion required to be older than 18 years, to have 2 or more systemic inflammatory response criteria (fever ≥ 38.3°C or hypothermia < 36°C, heart rate ≥ 90 beats/min, tachypnea ≥ 20/min, altered mental status), and to have a suspected infection.

2.2. Methods of measurement

Point-of-care analysis was performed with a Lactate Scout analyzer (EKF Diagnostics, Wales, UK) which uses a 5-μL blood sample and provides results in 10 seconds.

For each patient included, capillary, venous, and arterial blood samples were drawn in order to measure the lactate concentration with the POC device. Ear lobe was preferred to fingers for the assessment of capillary lactate value in order to avoid peripheral vasoconstriction potential effects. Capillary sample was performed within triage zone and patients were installed immediately thereafter in a dedicated ED room. Venous blood was sampled through a venous catheter placed in the forearm that was then used for the intravenous line. An arterial blood sample was taken immediately thereafter at the radial site. Measurements of venous and arterial blood lactate using the POC device were done with the blood remaining within the needles, which were used for venous catheterization and arterial sampling. Blood test tubes were dispatched thereafter to hospital's central laboratory for blood measurements, and among these laboratory tests, arterial lactate was used as the reference value for arterial blood lactate (Modular; Roche Diagnostics, Meylan, France). Time between blood sampling and results was noted for each study patient.

2.3. Outcome measures

Patients were managed thereafter according to standard protocols, based on the recommendations published in the last Surviving Sepsis Campaign [2]. Severe sepsis was defined as sepsis associated with at least one organ dysfunction using the 8 following criteria:

- systolic blood pressure < 90 mm Hg
- arterial blood lactate (reference method) > 2 mmol/L
- serum creatinine > 177 μmol/L
- thrombocytopenia (platelets count < 150,000 μL/L)
- plasma total bilirubin > 34 μmol/L
- pulse oximetry < 90% without oxygen
- acute alteration of mental status (Glasgow Coma Scale score < 14)
- prothrombin time < 50%

The primary outcome was to evaluate the effectiveness of capillary, venous, and arterial lactate measured with the POC device, to early detect the presence of severe sepsis in patients admitted in the ED with a septic syndrome.

The secondary clinical outcomes were as follows:

- to evaluate the POC system accuracy by comparing arterial lactate measurement obtained with the POC analysis and that used as the reference value
- to analyze correlations between venous, arterial, and capillary blood lactate
- to evaluate the prognostic value of blood lactate sampled at different sites

We calculated the sample size assuming that the area under the receiver operating characteristic curve (AUC ROC) representing the capacity of arterial blood lactate to detect the presence of severe sepsis was 0.65 [25,26]. If we assume that a difference in the AUC ROC of at least 0.10 is clinically significant and that we accept a type I error of 5% and a type II error of 10%, we calculated that it was necessary to include at least 100 patients.

2.4. Data analysis

All analyses were performed using MedCalc Statistical Software version 13.3 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2014). Data are presented as means ± SD. The measurement of arterial blood lactate using the POC device was compared with the reference method by constructing the Bland & Altman plot and calculating the correlation between the 2 variables using the least squares method. Bias was evaluated using Student t test for paired measurements. Comparison between arterial, capillary, and venous blood lactate values was made by using an analysis of variance for repeated measurements. Ability of blood lactate sampled at each site for detecting the presence of severe sepsis was evaluated by comparing AUC ROCs using the method described by DeLong et al [27]. In order to avoid bias linked to the weight of arterial blood lactate, severe sepsis was defined in 2 different ways, depending on whether or not the arterial blood lactate concentration was taken into account. The comparison between categorical data was performed using a χ² test or a McNemar test for paired data. A P value less than .05 was considered as significant.

3. Results

3.1. Characteristics of study subjects

One hundred seventeen patients were enrolled in this study. Fourteen patients were excluded because the arterial blood gas was not performed. Demographic and diagnostic population's characteristics of the 103 remaining patients are shown in Table 1. Fourteen patients were transferred to an intensive care unit after their initial management in the ED, and 12 patients were discharged home. Severe sepsis was present in 63 patients (61.2%) when taking into account the arterial blood lactate and in 52 patients (50.5%) when ignoring the arterial blood lactate concentration. Among the 63 patients with severe sepsis, 36 patients had only 1 criterion present on all 8 to categorize the patient as severe, 14 patients had 2 criteria, 8 patients had 3 criteria, and 5 patients had 4 criteria. Mortality at 28 days was greater in patients with severe sepsis (28.6% vs 7.5%, P < .05), and it was related to the number of criteria to categorize the patients as severe (16.7% for 1 criterion, 21.4% for 2 criteria, 62.5% for 3 criteria, and 80% for 4 criteria; P < .001). Among the 63 patients with a severe sepsis, 27 (42.9%) had clinical criteria that were detected in the triage zone (Glasgow Coma Scale score < 14 or systolic blood pressure < 90 mm Hg or pulse oximetry < 90%), whereas the 36 other patients (57.1%) were classified as severely septic once their blood tests checked (Table 2).
3.2. Measurements of blood lactate

Average time between capillary and venous samples was 11 ± 3 minutes and 8 ± 2 minutes between venous and arterial samples. The results of blood lactate were obtained in 10 seconds after sampling with the POC device and in about 60 minutes with the reference method. Point-of-care arterial lactate measurement was highly correlated with the reference method ($r = 0.96$, Fig. 1), and there was a significant ($P < .05$) average bias for POC lactate of −0.2 mmol/L (Fig. 2).

Mean capillary blood lactate was higher than the venous one, which was itself higher than mean arterial value ($3.01 ± 0.29$ mmol/L vs $2.51 ± 0.21$ mmol/L vs $2.03 ± 0.18$ mmol/L, respectively; $P < .001$). There was a strong correlation between arterial and venous blood lactate values ($r = 0.96$, $P < .0001$; Fig. 3), whereas the correlation was lower for arterial and capillary blood lactate values ($r = 0.82$, $P < .001$; Fig. 4).

3.3. Effectiveness of blood lactate to detect the presence of severe sepsis

Areas under ROC curves for arterial, capillary, and venous blood lactate in the early detection of severe septic patients were $0.759 ± 0.047$, $0.747 ± 0.048$, and $0.853 ± 0.039$, respectively ($P < .01$, Fig. 5). Venous blood lactate value was still more effective to early detect the presence of severe sepsis when arterial lactate value was ignored in the definition of severe sepsis (AUC ROC for venous lactate value $0.846 ± 0.042$ vs $0.751 ± 0.050$ for arterial lactate and $0.727 ± 0.051$ for capillary, $P < .01$).

A venous blood lactate value of more than $1.6$ mmol/L was associated with severe sepsis with a sensitivity of $81%$ (95% confidence interval [CI], 69-90) and a specificity of $80%$ (95% CI, 64-91), whereas an arterial blood lactate value of more than $1$ mmol/L had a similar sensitivity but a specificity of only $42%$ (95% CI, 27-59). Among the 36 severe septic patients without early clinical signs of organ failure, 29 patients would be detected using an arterial blood lactate threshold value of $1$ mmol/L and 30 patients using a venous blood lactate threshold value of $1.6$ mmol/L. However, using such threshold values, among the 40 nonsevere septic patients, 23 patients would be falsely declared severe using the arterial blood lactate, whereas only 8 patients would be overclassified using the venous lactate value ($P < .01$).

3.4. Association between blood lactate and mortality at 28 days

Overall mortality at 28 days was near $20%$ ($n = 21$). Arterial, venous, and capillary initial blood lactate were all significantly different ($P < .05$) between the patients who survived and those who died ($1.8 ± 1.7$ vs $2.9 ± 2.0$ mmol/L, $2.3 ± 2.1$ vs $3.4 ± 2.2$ mmol/L, and $2.7 ± 2.5$ vs $3.3 ± 2.0$ mmol/L, respectively; $P < .01$).

### Table 1
Demographics of the study population

<table>
<thead>
<tr>
<th></th>
<th>All subjects (n = 103)</th>
<th>Sepsis (n = 40)</th>
<th>Severe sepsis (n = 63)</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td>Age (y), mean ± SD</td>
<td>70 ± 20</td>
<td>65 ± 24</td>
<td>73 ± 17</td>
<td>.03</td>
</tr>
<tr>
<td>Sex, % female</td>
<td>55 (53.4%)</td>
<td>17 (42.5%)</td>
<td>38 (60.3%)</td>
<td>.12</td>
</tr>
<tr>
<td>Comorbidities, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>49 (47.6)</td>
<td>23 (57.5)</td>
<td>26 (41.3)</td>
<td>.16</td>
</tr>
<tr>
<td>Hypertension</td>
<td>30 (29.1)</td>
<td>8 (20)</td>
<td>22 (34.9)</td>
<td>.16</td>
</tr>
<tr>
<td>Diabetes</td>
<td>11 (10.7)</td>
<td>4 (10)</td>
<td>10 (16.3)</td>
<td>.88</td>
</tr>
<tr>
<td>Cancer</td>
<td>13 (12.6)</td>
<td>5 (12.5)</td>
<td>8 (12.7)</td>
<td>.78</td>
</tr>
<tr>
<td>Dementia</td>
<td>15 (14.6)</td>
<td>3 (7.5)</td>
<td>12 (19)</td>
<td>.18</td>
</tr>
<tr>
<td>Inclusion criteria, n (%)</td>
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<tr>
<td>Fever &lt; 38.3°C</td>
<td>84 (81.6)</td>
<td>32 (80)</td>
<td>52 (82.5)</td>
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<tr>
<td>Hypothermia &lt; 36°C</td>
<td>2 (1.9)</td>
<td>0 (0)</td>
<td>2 (3.2)</td>
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<td>Respiratory rate &gt; 20 c/min</td>
<td>50 (48.5)</td>
<td>18 (45)</td>
<td>32 (50.8)</td>
<td>.71</td>
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<tr>
<td>Heart rate &gt; 90 beats/min</td>
<td>92 (89.3)</td>
<td>34 (85)</td>
<td>58 (92.1)</td>
<td>.42</td>
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<td>Origin of sepsis, n (%)</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Pulmonary</td>
<td>47 (45.6)</td>
<td>20 (50)</td>
<td>27 (42.9)</td>
<td>.62</td>
</tr>
<tr>
<td>Digestive</td>
<td>13 (12.6)</td>
<td>2 (5)</td>
<td>11 (17.5)</td>
<td>.12</td>
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<tr>
<td>Urinary</td>
<td>19 (18.4)</td>
<td>8 (20)</td>
<td>11 (17.5)</td>
<td>.95</td>
</tr>
<tr>
<td>Skin and soft tissues</td>
<td>11 (10.7)</td>
<td>5 (12.5)</td>
<td>6 (9.5)</td>
<td>.88</td>
</tr>
<tr>
<td>Other</td>
<td>13 (12.6)</td>
<td>5 (12.5)</td>
<td>8 (12.7)</td>
<td>.78</td>
</tr>
</tbody>
</table>

### Table 2
Distribution of organ failures among the patients with severe sepsis

<table>
<thead>
<tr>
<th>Type of organ failure</th>
<th>Severe sepsis detectable with clinical signs (n = 27)</th>
<th>Severe sepsis detectable with blood tests only (n = 36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
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<td>0</td>
</tr>
<tr>
<td>Hypoxemia</td>
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<td>0</td>
</tr>
<tr>
<td>Confusion</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>3</td>
<td>11</td>
</tr>
<tr>
<td>Hyperlactatemia</td>
<td>13</td>
<td>20</td>
</tr>
<tr>
<td>Renal failure</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Cholestasis</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Low prothrombin time</td>
<td>2</td>
<td>7</td>
</tr>
</tbody>
</table>

Fig. 1. Regression line between the 2 methods of measurement of arterial blood lactate concentration using the reference method (ABL ref) and the POC one (ABL POC).

Fig. 2. Bland & Altman plot showing the comparison of arterial blood lactate concentration measured with the reference method (ABL ref) and the POC (ABL POC) performed on a microsample of whole blood.
4.4 ± 4.1 mmol/L, respectively), but their ability to discriminate the patients with a bad prognosis was similar (AUC ROC between 0.69 and 0.74, $P > .20$).

4. Discussion

Lactate is an end-product of glycolysis and is reputed to increase in case of tissue dysxia or metabolic activation. Blood lactate has been measured for a long time in critically ill patients and is usually associated with the measurement of other oxygenation parameters, such as blood gases, that require an arterial puncture [28]. Arterial blood lactate is therefore the reference sampling site for the assessment of tissue oxygenation [28].

The last Surviving Sepsis Campaign [2] emphasizes the need to early recognize severely septic patients, and blood lactate measurement is strongly recommended in this setting [29,30]. An elevated blood lactate should lead to treatment intensification. Blood lactate measurement should therefore be a routine part of initial assessment of septic patients admitted in ED triage zone, but an arterial puncture is painful, can be harmful, and takes an unaffordable time in an overcrowded ED. Several works have therefore tried to evaluate correlation between arterial and peripheral venous or capillary blood lactate values, but these studies have shown conflicting results [17–22]. We report in this study that peripheral venous blood lactate concentration during sepsis is slightly higher than the arterial one, but interestingly, peripheral venous blood lactate appears to be more effective in assessing initial severity of sepsis than arterial lactate. A venous blood lactate value of more than 1.6 mmol/L was associated with severe sepsis with a 80% specificity and a 80% sensitivity, whereas arterial blood lactate value had a poorer reliability. These results challenge the interpretation of venous blood lactate during sepsis and suggest that venous blood content could be a better witness of sepsis-induced tissue damages than arterial blood.

Capillary blood lactate concentration was also higher in severe septic patients. However, correlation between capillary and arterial blood lactate was relatively weak and its capacity to early detect these patients was poor. Moreover, the specificity of capillary lactate to detect a high
venous blood lactate value was low, which may underestimate the severity of sepsis and therefore delay treatment. Hence, capillary lactate value does not seem to be a good indicator of the presence of severe sepsis in patients with a septic syndrome and cannot be used as a triage tool in this setting.

Measurements of blood lactate were performed using a POC portable analyzer. Our study support the use of POC lactate as a useful and accurate method to evaluate a blood lactate value in the ED, which is in agreement with previous data [14–16]. We found a small but significant bias between the reference arterial blood lactate measurement and that performed with the POC system: mean reference values were 0.2 mmol/l higher than mean POC-obtained values. The most likely explanation is that laboratory lactate was processed after 15- to 30-minute delay, during which blood tubes were transported to central laboratory and lactate production might have increased inside the tubes. This is especially true because blood samples were not delivered to central laboratory in iced packs.

Point-of-care device saves time [31], and a portable analyzer is particularly well suited to ED practice, allowing to early start intensive management of septic patients. A venous blood lactate measurement cannot be made within triage zone for practical reasons, but it may be easily done with a POC device as soon as the nurse has put the intravenous line and can use a residual drop of venous blood from the needle. In doing so, ED physicians may be able to detect early the patients at risk of severe sepsis and initiate early-goal-directed therapy as soon as possible. Therefore, a venous blood lactate measurement with a POC system can be a useful triage tool by early detecting severely septic patients, especially among those still sustaining a normal blood pressure.

High blood lactate values were associated with significant mortality at 28 days, as previously reported in many studies during sepsis [3,9,13,26,30,8,32]. Arterial, venous, and capillary values were not statistically different in their ability to discriminate the patients with poor prognosis. As expected, the severely septic patients had a higher mortality and the number of initial organ failures was also related to hospital mortality. We observed in our septic patients a high incidence of severe sepsis as compared with previously reported studies [5,13,33]. This is likely due to a high percentage of elderly patients who are at high risk for severe sepsis [34] and to our ED organization that addresses ambulatory patients directly from triage zone to general practitioners working nearby the ED.

We are aware of the existence of some limitations in this study. First, it was conducted in a single center with a high incidence of severe sepsis which makes it nonextendible to the general population of septic patients. Moreover, the number of patients included into the study may appear to be weak, even if the sample size was matched to the outcome measures. Second, the blood lactate was measured only once, except for the arterial sample which was measured in duplicate using 2 different methods. It is not possible to exclude that venous and capillary blood lactate concentrations would be different using a reference method of measurement. Moreover, we did not measure the tourniquet time necessary for taking the venous samples, which could artificially raise the venous blood lactate level. However, a previous work has shown that the tourniquet time seems to influence poorly the lactate level [18]. At last, because venous blood lactate was measured only once, this study does not support the use of venous blood lactate to control the effectiveness of the undertaken treatment.

In conclusion, this study shows that the peripheral venous blood lactate may usefully replace the arterial blood lactate measurement in order to early detect severely ill septic patients admitted to the ED. Venous blood lactate could even be more effective than the arterial one for early recognition of severe sepsis. We suggest that the use of POC devices for the measurement of venous blood lactate should be systematic for the triage of septic patients admitted to the ED. This would accelerate the recognition of severe septic patients and would allow to start early adequate and intensive care in these high-risk patients.

References


