Central Peripheral Temperature Gradient Correlated with the Simultaneous ScvO₂ and Lactate Level in Severe Sepsis and Septic Shock Patients

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Objective: To evaluate whether the central peripheral temperature gradient (CPTG) correlated with the simultaneous central venous oxyhemoglobin saturation (ScvO₂) and serum lactate levels in severe sepsis and septic shock patients.

Design: A retrospective observational study design was used with temporal artery thermometry (TAT) to measure CPTG.

Results: A total of 61 patients with severe sepsis or septic shock in the intensive care unit (ICU) were analyzed and monitored for CPTG, mean arterial pressure (MAP), ScvO₂, and lactate level. Four patients were excluded due to peripheral arterial occlusive disease. The correlation between the binary CPTG (high CPTG ≥5℃ and low CPTG < 5℃) and simultaneous ScvO₂ and lactate level was evaluated. The effect of coexistent MAP (< 65 mmHg and ≥ 65 mmHg) on the lactate level and ScvO₂ (< 70% or ≥ 70%) was also investigated. Compared with the low CPTG group, the high CPTG group had lower ScvO₂ (60.1 ± 13.6% vs 66.5 ± 12.7%; p = 0.001) and higher lactate levels (6.0 ± 4.5 mmol/L vs 3.2 ± 2.1 mmol /L; p < 0.001). The binary CPTG correlated to the ScvO₂ (p < 0.001) after adjustment for the effect of MAP. The adjusted mean difference of ScvO₂ between those patients with high CPTG and low CPTG was -4.4% (95% confidence interval [CI]: -7.0 to -1.8). The binary CPTG also correlated with the lactate level (p < 0.001) after adjustment for the effect of MAP. The adjusted mean difference of the lactate level between those patients with high CPTG and low CPTG was 2.5 mmol/L (95% CI, 1.6-3.4 mmol/L). In a multivariate analysis predicting the lactate level by the coexistent MAP, binary CPTG, and ScvO₂, only the binary CPTG and MAP (< 65 mmHg or ≥ 65 mmHg) were independent predictors (both p < 0.001).

Conclusions: CPTG correlated with the ScvO₂ and serum lactate level in severe sepsis and septic shock patients.

Key words: central peripheral temperature gradient, ScvO₂, lactate level, severe sepsis, septic shock

Introduction

To avoid or improve global tissue hypoxia and oxygen debt resulting from an imbalance between systemic oxygen delivery (DO₂) and oxygen demands, hemodynamic monitoring plays an important role in guiding oxygen support to vital organs in severe sepsis and septic shock patients in the intensive care unit (ICU). The magnitude and duration of oxygen debt play a major role in the
development of multiple organ failure and increased mortality\(^{(1-3)}\).

Central venous oxyhemoglobin saturation (ScvO\(_2\)) reflects the degree of oxygen extraction from the brain and the upper part of the body\(^{(4,5)}\). By targeting resuscitation to ScvO\(_2\) ≥ 70% in the early hemodynamic support of severe sepsis and sepsis shock patients, a reduction in lactic acidosis, number of organ dysfunctions, and in-hospital mortality\(^{(6)}\) can be accomplished.

Unlike the ScvO\(_2\), an elevated serum lactate level may be a relatively delayed finding in patients with impaired tissue oxygenation. Lactic acidosis is frequently encountered in the ICU when an imbalance exists between the production and clearance of lactate. Several investigators have shown the value of lactate levels in predicting survival in patients with severe sepsis and septic shock\(^{(7,8)}\).

Clinically, one of the common manifestations of low cardiac output is cold, pale skin. Experimental evidence shows a close correlation between the temperature of the skin and its blood flow\(^{(9)}\). In a healthy patient under stable room temperature, the central (rectal) to peripheral (toe) temperature gradient was stable (3.5 to 4.38°C)\(^{(10)}\). Temporal artery thermometry (TAT) is a method of temperature assessment using infrared technology to detect the heat naturally emitting from the skin surface and has been compared with core temperature measurement; however, it is not always the same as\(^{(11-14)}\) or has significant disagreement\(^{(15,16)}\) from the core temperature. The utilization of the difference between the central temperature (across the forehead to the neck area behind the ear lobe) and peripheral temperature (across the lateral side to the medial side of the sole of the foot) to reflect the state of dynamic peripheral circulation during severe sepsis or septic shock may be an easy and attractive procedure compared to the previous measurement of central peripheral temperature gradient (CPTG) by the rectal and great toe temperature difference.

The aim of our study was to evaluate whether the level of CPTG correlated with the simultaneous ScvO\(_2\) and lactate levels in severe sepsis and septic shock patients. Furthermore, the value of ScvO\(_2\) and lactate level was evaluated when considering the binary CPTG and the coexistent mean arterial pressure (MAP).

**Patients and Methods**

**Design**

This was a retrospective observational study in the medical ICU of a tertiary care hospital.

**Patients**

Consecutive patients with severe sepsis and septic shock admitted to the ICU from September 2006 to August 2009 were eligible for study participation. The measurements of serial ScvO\(_2\), serum lactate level, MAP, and CPTG by TAT were determined by the ICU intensivists every 4 hours after ICU admission. This study was approved by the Institutional Review Board of the hospital. Sepsis was defined as suspected infection in the presence of two or more systemic inflammatory response syndrome criteria\(^{(17)}\). Severe sepsis was defined as sepsis associated with organ dysfunction, hypoperfusion, or hypotension\(^{(6,17-20)}\). Septic shock was defined as hypotension (systolic blood pressure < 90 mmHg) despite adequate fluid resuscitation (> 1500 mL) or the use of vasoactive agents\(^{(6,17-20)}\).

**Exclusion criteria**

Patients with peripheral arterial occlusive disease were ineligible for this study.

**Data collection**

The demographic information, simultaneous MAP, CPTG, ScvO\(_2\), and lactate level
measurements were obtained from all patients.

CPTG

CPTG was measured by temporal artery thermometer (TAT-5000, Exergen, US) to compare the central temperature (across the forehead to the neck area behind the ear lobe) and the peripheral temperature (across the lateral side to the medial side of the sole of the foot) difference. The binary CPTG was defined as either high CPTG (either right or left CPTG ≥5°C) or low CPTG (both right and left CPTG < 5°C).

Lactate

Lactate levels were measured in the central venous blood using blood gas and electrolytes analyzers (GEM Premier 3000, Instrumentation Laboratory Company, US, upper normal limit 2.0 mmol/L).

Statistical analysis

Data were described by mean ± standard deviation (SD) for continuous data, count, and percentage for categorical data. MAP and CPTG were dichotomized to binary variables for clinical reasons. Repeated measurements of MAP, CPTG, lactate, and ScvO₂ on the same patient were treated as clustered data. Considering the correlations among clustered measurements, univariate and multivariate linear generalized estimating equation (GEE) was adapted to construct the relationships between MAP, CPTG, serum lactate level, and ScvO₂, and between MAP, CPTG, and serum lactate level. An exchangeable working correlation matrix was chosen to construct GEE analysis on the basis of clinical implications and assessment of the model fitness using quasi-likelihood under the independence model criterion (QIC). All p-values were calculated from GEE and were considered statistically significant at <0.05. Data analysis was performed by SPSS for windows, version 17.0 (SPSS Inc., Illinois, USA).

Results

A total of 61 patients were analyzed; four patients were excluded due to peripheral arterial occlusive disease. The clinical characteristics of the remaining 57 patients are displayed in Table 1. In total, 727 measurements were available, which corresponded to an average of 13 measurements per patient (range, 1-55). Among the 710 measurements of the MAP, 6.3% of MAP were < 65 mmHg. High CPTG occurred in 42.1% of the 721 measurements. More than half of the 651 ScvO₂ measurements were < 70%, and 26.1% of the 655 lactate levels were > 5 mmol/L.

Compared to patients with low CPTG, patients with high CPTG demonstrated lower ScvO₂ (60.07% ± 13.61% vs 66.49% ± 12.37%; p = 0.001) and higher lactate levels (5.99 ± 4.53

<table>
<thead>
<tr>
<th>Table 1 Clinical characteristics</th>
<th>Values, % or mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>57</td>
</tr>
<tr>
<td>Age</td>
<td>67 ± 16</td>
</tr>
<tr>
<td>Sex, % male: % female</td>
<td>63:37</td>
</tr>
<tr>
<td>APACHE II</td>
<td>27.3 ± 9.1</td>
</tr>
<tr>
<td>Ventilator duration, d</td>
<td>12.7 ± 10.3</td>
</tr>
<tr>
<td>ICU length of stay, d</td>
<td>13.6 ± 10.3</td>
</tr>
<tr>
<td>ICU mortality rate, %</td>
<td>56.1</td>
</tr>
<tr>
<td>In-hospital mortality rate, %</td>
<td>61.4</td>
</tr>
</tbody>
</table>
Fig. 1 Central venous oxyhemoglobin saturation (ScvO₂) in low central peripheral temperature gradient (CPTG) and high CPTG

Fig. 2 Lactate levels in low central peripheral temperature gradient (CPTG) and high CPTG

Fig. 3 Central venous oxyhemoglobin saturation (ScvO₂) in high central peripheral temperature gradient (CPTG), low CPTG, and coexistent MAP (≥ 65 mmHg, < 65 mmHg)
mmol/L vs 3.15 ± 2.09 mmol/L; p < 0.001) (Fig. 1
and 2). Considering the coexistent CPTG and MAP,
a MAP-stratified analysis showed that a higher
level of ScvO₂ with low CPTG was found in those
patients with MAP ≥ 65 mmHg (66.84 ± 12.08 vs.
60.34 ± 13.31), but not in those patients with MAP
< 65 mmHg (59.50 ± 16.72 vs. 59.54 ± 14.58)
(Fig. 3). With respect to the serum lactate level,
patients in the low CPTG group had a decreased
level of lactate regardless of the MAP (3.00 ±
1.94 vs. 5.52 ± 4.12 mmol/L in those with MAP
≥ 65 mmHg; 6.06 ± 2.98 vs. 9.67 ± 5.95 mmol/L
in those with MAP < 65 mmHg) (Fig. 4).

A multivariate analysis showed that the
binary CPTG correlated to ScvO₂ (p < 0.001) after
adjustment for the effect of MAP. The adjusted
mean difference of ScvO₂ between the high and low
CPTG groups was -4.4% (95% confidence interval
[CI], -7.0% to -1.8%). Unlike the CPTG, MAP was
not correlated with the ScvO₂ (p=0.543)
CPTG correlated with the lactate level (p < 0.001)
after adjustment for the effect of MAP. The adjusted
mean difference of the lactate level between those
patients with high and low CPTG was 2.5 mmol/L
(95% CI, 1.6 to 3.4 mmol/L) (Table 2).

In a multivariate analysis predicting the lactate
level according to the coexistent MAP, binary CPTG,
and ScvO₂, only the binary CPTG and MAP were
independent predictors (both p < 0.001) (Table 3).

| Table 2 Multivariate analyses predicting the levels of ScvO₂ and lactate using CPTG and MAP |
|---------------------------------|---------------------------------|---------------------------------|
| ScvO₂ (%) | Lactate (mmol/L) |
| Intercept | Beta (95% CI) | P-value | Beta (95% CI) | P-value |
|          |              |         |              |         |
| CPTG, °C (≥ 5 vs. <5) | -4.40 (-7.00, -1.80) | <0.001 | 2.50 (1.58, 3.41) | <0.001 |
| MAP, mmHg (≥ 65 vs. <65) | -1.76 (-7.43, 3.91) | 0.543 | 1.89 (0.85, 2.92) | <0.001 |
Table 3  Multivariate analysis of predicting the levels of lactate using CPTG, MAP, and ScvO₂

<table>
<thead>
<tr>
<th>Variable</th>
<th>Beta (95% CI)</th>
<th>P-value</th>
</tr>
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<tbody>
<tr>
<td>Intercept</td>
<td>3.02</td>
<td></td>
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<tr>
<td>CPTG, °C (≥5 vs. &lt;5)</td>
<td>2.43 (1.50, 3.36)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MAP, mmHg (≥65 vs. &lt;65)</td>
<td>1.83 (0.80, 2.86)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ScvO₂, % (≥70 vs. &lt;70)</td>
<td>0.58 (-0.26, 1.41)</td>
<td>0.177</td>
</tr>
</tbody>
</table>

**Discussion**

A clear correlation between the level of CPTG (≥ 5°C and < 5°C) monitored by TAT and the simultaneous ScvO₂ and lactate levels in severe sepsis or septic shock patients in the ICU was demonstrated, and the correlation remained significant after considering the coexistent MAP. Only the binary CPTG and MAP were independent predictors of the lactate levels in a multivariate analysis.

Hemodynamic monitoring is a cornerstone in the intensive care of severe sepsis and septic shock patients, and the goals of hemodynamic support focus on adequate perfusion pressure and perfusion, however, perfusion correlates better with cardiac output and DO₂. Clinically, the heart rate, blood pressure, peripheral perfusion, urine output, SvO₂, ScvO₂, and lactate level were monitored in order to guide resuscitation in severe sepsis and septic shock patients; however, no single parameter guaranteed the adequacy of hemodynamic support. With impaired oxygen delivery, ScvO₂ or SvO₂ may be high due to maldistribution of blood flow, and with the inability of cellular oxygen utilization, lactate level may be normal (a relatively delayed finding in patients with impaired tissue oxygenation).

Blood flow brings warmth to the peripheral circulation, and cardiac output guarantees blood flow; the absence of cold and mottled skin has been considered a marker of adequate perfusion in patients with acute lung injury. Traditionally, it was assessed by inspection and palpation; however, to avoid subjective bias, directly recording and evaluating temperature changes by the difference between the rectal and great toe temperatures has been used. Measuring the CPTG by TAT represents a more simple and noninvasive method to reflect the state of the dynamic peripheral circulation after considering the effect of air flow and peripheral vascular resistance.

TAT was developed to address concerns about the inaccuracy of ear thermometry and parents’ growing dislike to rectal thermometry. TAT has been compared with the measurement of core temperature in adults, although inconsistent findings have been reported. Inaccuracies have not been reported in the measurement of the central and peripheral temperature difference. The correlation between the CPTG monitored by TAT and the simultaneous ScvO₂ and lactate levels during severe sepsis and septic shock has not been evaluated.

This study clearly demonstrated lower ScvO₂ and higher lactate levels in patients with high CPTG. Furthermore, when comparing the binary CPTG and coexistent MAP (< 65 mmHg or ≥ 65 mmHg), only the binary CPTG correlated to both ScvO₂ and lactate level, and the MAP only correlated with the lactate level. Considering the importance of the ScvO₂ and lactate level in determining the adequacy of hemodynamic support in severe sepsis and septic shock, the correlation between the CPTG and perfusion seemed more
significant than the MAP and perfusion.

Finally, in the multivariate analysis predicting the lactate level by the MAP (<65 mmHg or ≥65 mmHg), binary CPTG, and ScvO₂ (<70% or ≥70%), only the binary CPTG and MAP were independent predictors.

In this study, the lactate level was 9.7 ± 5.9 mmol/L when the CPTG was high and the coexistent MAP was <65 mmHg. The lactate level was 3.0 ± 1.9 mmol/L when the CPTG was low and the coexistent MAP was ≥65 mmHg. Currently, lactic acidosis is generally defined as a lactate level >5 mmol/L and may be classified by the association with imbalance of oxygen delivery and oxygen consumption (type A lactic acidosis) or other clinical conditions unrelated to oxygen debt (type B lactic acidosis). There is growing concern about the development of type B lactic acidosis in severe sepsis and septic shock over the past two decades, and the clinical distinction between Type A and Type B lactic acidosis is often obscure. Our study confirmed the presence of type A lactic acidosis in severe sepsis and septic shock patients and the potential role of CPTG measured by TAT in hemodynamic monitoring during severe sepsis and septic shock.

There were several limitations in this study. First of all, this was a single center, retrospective, observational study. Additionally, 5°C was chosen as the cut-off value to define high and low CPTG because the stable CPTG was 3.5 to 4.38°C. The normal or optimal CPTG measured by TAT needs further investigation. Furthermore, whether integrating the CPTG monitored by TAT into the resuscitation protocol improves the outcome of severe sepsis and septic shock patients needs clinical validation.

In conclusion, this study showed the level of CPTG (≥5°C or <5°C) measured by TAT during severe sepsis or septic shock was significantly correlated with the simultaneous ScvO₂ and lactate level.

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嚴重敗血症及敗血性休克病患的中心及周邊溫差與同一時間測量的中央靜脈氧氣飽合度和乳酸鹽濃度具有相關性

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呂瑾立3 鄭高珍4

目的：研究嚴重敗血症及敗血性休克病患的中心及周邊溫差與同一時間测量的中央靜脈血氧氣飽合度和乳酸鹽濃度是否具有相關性。

研究設計：回溯性的觀察性研究。

結果：61位接受同一時間監測中心及周邊溫差、平均動脈壓、中央靜脈血氧氣飽合度、及乳酸鹽濃度的加護病房中嚴重敗血症或敗血性休克病患，進入本研究，其中4位有周邊動脈血管阻塞的病患予以排除。我們調查「高的中心及周邊溫差」(右或左邊的中心及周邊溫差大於或等於5℃)及「低的中心及周邊溫差」(右或左邊的中心及周邊溫差都小於5℃)和同一時間测量的中央靜脈血氧氣飽合度和乳酸鹽濃度的相關性，並計算同一考量高與低的中心及周邊溫差和高與低的平均動脈壓(≥65 mmHg，<65 mmHg)時的中央靜脈血氧氣飽合度和乳酸鹽濃度，及評估同一時間測量時，高與低的中心及周邊溫差、高與低的平均動脈壓、高與低的中心及周邊溫差和乳酸鹽濃度的相關性。結果顯示，相較於「低的中心及周邊溫差」病患於「高的中心及周邊溫差」時的中央靜脈血氧氣飽合度較低(60.1 ± 13.6% vs. 66.5 ± 12.7%, p = 0.001)，但乳酸鹽濃度則較高(6.0 ± 4.5 mmol/L vs. 3.2 ± 2.1 mmol/L, p < 0.001)。同時考量中心及周邊溫差與平均動脈壓共同對中央靜脈血氧氣飽合度及乳酸鹽濃度的影響，只有在平均動脈壓≥65 mmHg時，中心靜脈血氧氣飽合度於「低的中心及周邊溫差」時較「高的中心及周邊溫差」為低(66.84 ± 12.08 vs. 60.34 ± 13.31)，但在平均動脈壓<65 mmHg時，則否(59.50 ± 16.72 vs. 59.54 ± 14.58)。但不論平均動脈壓≥65 mmHg或<65 mmHg，乳酸鹽濃度於「低的中心及周邊溫差」時都較「高的中心及周邊溫差」為低(3.00 ± 1.94 vs. 5.51 ± 4.12 mmol/L，平均動脈壓≥65 mmHg時，及6.06 ± 2.98 vs. 9.67 ± 5.95 mmol/L，平均動脈壓<65 mmHg時)。多變項分析也顯示「高與低的中心及周邊溫差」和「中央靜脈血氧氣飽合度」有顯著相關(p = 0.001)，調整後的中央靜脈血氧氣飽合度於「高的中心及周邊溫差」和「低的中心及周邊溫差」的平均差異是4.4% (95%信賴區間：-7.0 to -1.8)，高與低的中心及周邊溫差也和乳酸鹽濃度有顯著相關(p < 0.001)，調整後的乳酸鹽濃度於「高的中心及周邊溫差」和「低的中心及周邊溫差」的平均差異是2.5 mmol/L (95%信賴區間：1.6 to 3.4 mmol/L)。在預測乳酸鹽濃度的多變項分析中，只有同一時間測量的「高與低的中心及周邊溫差」及「高與低的平均動脈壓」是獨立的預測因子(both p < 0.001)，「高與低的中央靜脈血氧氣飽合度」則否。

結論：嚴重敗血症及敗血性休克病患的中心及周邊溫差與同一時間測量的中央靜脈血氧氣飽合度及乳酸鹽濃度有顯著的相關性。

關鍵詞：中心及周邊溫差，中央靜脈血氧氣飽合度，乳酸鹽濃度，嚴重敗血症，敗血性休克

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