Central venous-to-arterial carbon dioxide difference as a useful complementary goal of fluid resuscitation for septic shock patients.

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Abstract

Introduction: Central venous oxygen saturation has inevitable limitation when it serves as a goal of fluid resuscitation. The objective of this study was to assess the capacity of central venous-to-arterial carbon dioxide difference (P(cv-a)CO_2) as a complementary marker to guide fluid resuscitation when ScvO_2 has reached its threshold in septic shock patients.

Methods: This is a single-center, observational study of septic shock patient. Patients were randomly divided into two groups with ScvO_2 normalized and both ScvO_2 and P(cv-a)CO_2 normalized as a target of fluid resuscitated respectively. Compared the variables at the beginning of study (T0) and 6 h after fluid resuscitated (T6) for both groups. Lactate clearanc were calculated, and dose of vasoactive drugs, duration of mechanical ventilation and ICU stay and 28-day mortality were recorded.

Results: 68 septic shock patients were included in study. At T0, no difference were found between the two groups. Heart rate and lactic acid decreased significantly at T6 in both groups, but lactate clearance rate of ScvO_2+P(cv-a)CO_2 group (30.1 ± 17.2) were significantly higher than ScvO_2 group (21.6 ± 14.3) (p<0.05). Mechanical ventilation time and duration of ICU stay of ScvO_2+P(cv-a)CO_2 group were shorter than ScvO_2 group (11.7 ± 4.9 days vs 14.7 ± 6.2 days and 9.3 ± 4.4 days vs 13.2 ± 6.2 days respectively). No significant difference was observed in 28-days mortality for the two groups.

Conclusion: P(cv-a)CO_2 is a valuable complementary goal to guide the fluid resuscitation for septic shock patients. The inclusion of P(cv-a)CO_2 into resuscitation protocol would be a safely and effectively practice. But P(cv-a)CO_2 may not availably enough to serve as a predictor of prognosis and mortality.

Keywords: Septic shock, Fluid resuscitation, Hemodynamics, P(cv-a)CO_2.

Introduction

Severe sepsis and septic shock is a life-threatening condition with an incidence of 300 per 100000, and still a common cause of death for patients of intensive care unit (ICU) [1,2]. Promoted practice for septic shock therapy is largely based on a study by Rivers et al. which developed a protocol known as early goal-directed therapy (EGDT) [3]. EGDT is the key to early treatment of septic shock, which could maintain effective circulating blood volume and improve tissue perfusion. According to Rivers et al. several predefined resuscitation end point should be achieved in EGDT: CVP 8-12 mmHg, MAP 65-90 mmHg, urine output >0.5 mL/kg/hr, mixed venous oxygen saturation (ScvO_2)>65% or central venous oxygen saturation (SvO_2)>70%, haematocrit>30% [3].

Among those parameters, SvO_2 or ScvO_2 has been considered as a reliable and sensitive indicator to reflect systemic oxygen supply and demand relationship in septic shock patients, low SvO_2 or ScvO_2 always indicated unbalance state of tissue oxygen delivery and consumption, and always associated with increased postoperative complications [4,5]. But SvO_2 or ScvO_2 serves as an estimate of oxygen delivery/uptake relationship are not sufficiently precise to detect tissue hypoxia thus may not efficacious to improve tissue perfusion and metabolism [6,7]. Several studies have reported that EGDT goals achieved and ScvO_2 over 70% cannot rule out hypoxic tissue metabolism and hemodynamic abnormalities [8,9]. Recently, some multicenter studies also failed to demonstrate ScvO_2>70% was effective in septic shock therapy [10,11]. These finding triggers the discussion if ScvO_2 alone is accurate enough to guide fluid resuscitation and vasoactive drugs application effectively. To address the limitation of ScvO_2, some candidate parameters such as tissue oxygen saturation [12], lactate clearance [13] and carbon dioxide partial pressure [14] have been investigated as substitutable or complementary target to guide fluid resuscitation.

In recent years, some studies have reported the inverse correlation between mix venous to arterial carbon dioxide difference (P(v-a)CO_2) and cardiac index (CI) in septic patient or non-septic circulatory failure patients [15-17]. Carbon dioxide produced by peripheral tissues is removed by venous blood, therefore the reduced of blood flow and development of anaerobic metabolism could be indicated by elevated P(v-a)CO_2, experimental studies has suggested P(v-a)CO_2 could be...
used as a marker of tissue hypoxia [18,19]. Unfortunately, the measurement of P(v-a)CO₂ requires pulmonary artery catheter insertion, which is seldom utilized in clinic today [20]. Central venous-to-arterial carbon dioxide difference (P(cv-a)CO₂) as an estimate of P(v-a)CO₂, is derived from the insertion of central venous catheter that has been applied to most patients with septic shock [20]. As P(v-a)CO₂ potentially represents a more accessible parameter than P(v-a)CO₂, P(v-a)CO₂ have also been investigated of its possibility to assess tissue hypoperfusion, Cusheriet al. showed a strong agreement between P(v-a)CO₂ and (P(cv-a)CO₂), and found (P(cv-a)CO₂) and CI also present a negative correlation [21].

Therefore, we aim to investigate the possibility of P(cv-a)CO₂ as a useful complementary marker to guide fluid resuscitation when ScvO₂ has reach its threshold in septic shock patients, and assess its potential to evaluate the severity of the disease and prognostic of patients in present study.

**Materials and Methods**

**Patients**

Patients with septic shock admitted to ICU of Xiangya Hospital Center of Zhongnan University from September 2010 to September 2011 were studied. All patients were diagnosed following the criteria defined by 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference [22]. All recruited patients required tracheotomy and assisted breathing with ventilator to improve hypoxia condition. Exclusion criteria were: age under 18, dying or predict death within 24 h; the presence of irreversible underlying disease; underlying heart disease or acute myocardial infarction, cardiogenic shock; patient or family members refused to have the operation; history of renal insufficiency and hemodialysis. All patients were randomly divided into two groups according to different fluid resuscitated goals, ScvO₂ group and ScvO₂+P(cv-a)CO₂ group; and all resuscitated prectice were following the international guidelines for management of severe sepsis and septic shock in 2008 [4].

**Resuscitation protocol and hemodynamic management**

The fluid resuscitated targets of ScvO₂+P(cv-a)CO₂ group as follow: CVP8~12 mmHg (12~15 mmHg with mechanical ventilation), MAP ≥ 65 mmHg, urine volume ≥ 0.5 mL/kg/h, ScvO₂>70% and P(cv-a)CO₂<6 mmHg; and goals of ScvO₂ group were the same as ScvO₂+P(cv-a)CO₂ group except P(cv-a)CO₂ was not monitored and controlled.

When a patient was included in the study, a central venous catheter was inserted with right internal jugular or right subclavian vein approach and a pulse indicator continuous cardiac output (PiCCO) catheter was placed in the same time for continuous central venous pressure (CVP) and ScvO₂ monitoring. Blood pressure after invasive and noninvasive opiration and arterial blood gas analysis were also monitored. In ScvO₂+P(cv-a)CO₂ group, P(cv-a)CO₂ was calculated every hour. Cultivate blood and/or hematuria and/or phlegm before antibiotics administered. Isotonic crystalloid was administered first to target CVP achieved 8~12 mmHg, if systolic blood pressure less than 80 mmHg, vasoactive drug would be administered at the same time. In any case of CVP decreased, retitation treatment would be adopted, and do not need to deal with the case of CVP higher than upper limit. Second, if CVP achieved 8~12 mmHg but MAP<65 mmHg, 2~20 μg/kg/min dopamine would be administered, and 0.1~2 μg/kg/min norepinephrine would be administered if blood pressure still cannot maintain. Fanally, if CVP achieved 8~12 mmHg and MAP achieved 65~90 mmHg, urine volume ≥ 0.5 mL/kg/h, but ScvO₂ still lower than 70%, following treatment would be conduct: (1) blood transfusion until haematoerit (HCT)>30%; (2) if HCT>30% but ScvO₂<70%, combined with dobutamine (start dose is 3 μg/kg/min, increase by 1~2 μg/kg/min every 10 min, stop admitted when heart rate>150/min); (3) if ScvO₂ still cannot reach 70% by increase oxygen supply, treatment that such as cooling, sedative and analgesic could be adopted to lowering oxygen consumption. All goals must be achieved for a maximum of 6 h. For ScvO₂+P(cv-a)CO₂ group, when P(cv-a)CO₂<6 mmHg, CVP achieved 8~12 mmHg and MAP achieved 65~90 mmHg, urine volume ≥ 0.5 mL/kg/h, ScvO₂>70% should maintained in 6 h, if P(cv-a)CO₂ ≥ 6 mmHg, adopt retitation therapy.

Blood glucose control within 6~8.3 mmol/L, volume replacement was performed with ringer’s solution and hydroxethyl starch as appropriate, some patient required to infuse concentrated red blood cells and albumin with crystalloid ratio at 3:4-1.

**Data collection**

General information of patient includes sex, age, basic desease, type of disease, Acute Physidogy and Chronic Health Evaluation (APACHE) II score, Sequential Organ Failure Assessment (SOFA) score were collected. Patient's heart rate, respiration, invasive and noninvasive blood pressure, pulse oximetry, OI, CVP, hourly urine output, arterial blood gas analysis, central venous blood gas analysis and other indicators were monitored hourly. Blood lactate concentration, CI, EVLW1, liquid equilibrium state were determined in T0 (at the start of the study) and T6 (6 h after inclusion) and calculated lactate clearance by following formula: lactate clearance=(blood lactate at T0-blood lactate at T6)/(blood lactate at T0). Dose of vasoactive drugs (integral dose of norepinephrine and dobutamine) comparison within 6 h, duration of mechanical ventilation, 28 day mortality and ICU stay were also recorded.

**Statistical analysis**

The data were analyzed using SPSS17.0, all results are presented as mean ± standard deviation. Pairwise comparison of geometric mean were used SNK-q test (student newmankeulea, SNK method), analysis of attribute data used chi-square test, P<0.05 was considered statistically significant.
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All data were checked by normality test and homogeneity of variance test.

**Result**

During the study period, a total of 128 patients with septic shock were admitted into the ICU of Xiangya hospital center of Zhongnan University. Among those patient, 60 were excluded according to the following criteria: septic shock over 24 h when enter ICU (n=28), refusal of PICCO catheter placement (n=12), death within 24 h (n=12), ScvO$_2$<70% after fluid resuscitation (n=8). Finally, 68 patients were eligible for this study. No patients were found complications such as bleeding, infection, pneumothorax, air embolism in puncture site. Basic information was shown in Table 1.

**Table 1. Baseline characteristics of patients.**

<table>
<thead>
<tr>
<th></th>
<th>ScvO$_2$ group (n=30)</th>
<th>ScvO$_2$+P(cv-a)CO$_2$ group (n=38)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male/fermale)</td>
<td>16/14</td>
<td>22/16</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Age (years)</td>
<td>54.1 ± 15.0</td>
<td>53.6 ± 14.0</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Infection site</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>12</td>
<td>14</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Enterocoelia</td>
<td>12</td>
<td>14</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Urinary tract</td>
<td>3</td>
<td>5</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Other</td>
<td>3</td>
<td>5</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Basic deseases</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>COPD</td>
<td>8</td>
<td>10</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Hematological</td>
<td>8</td>
<td>10</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>malignancy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autoimmune disease</td>
<td>8</td>
<td>8</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3</td>
<td>5</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Hypertension</td>
<td>5</td>
<td>6</td>
<td>p&gt;0.05</td>
</tr>
</tbody>
</table>

**Table 2. Effect evaluation indices of fluid resuscitation at T0 and T6.**

<table>
<thead>
<tr>
<th></th>
<th>T0</th>
<th>T6</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP</td>
<td>ScvO$_2$ group</td>
<td>55.3 ± 4.9</td>
</tr>
<tr>
<td></td>
<td>ScvO$_2$+P(cv-a)CO$_2$ group</td>
<td>50.6 ± 5.6</td>
</tr>
<tr>
<td>Heart rate</td>
<td>ScvO$_2$ group</td>
<td>122.5 ± 18.6</td>
</tr>
<tr>
<td></td>
<td>ScvO$_2$+P(cv-a)CO$_2$ group</td>
<td>125.3 ± 15.3</td>
</tr>
<tr>
<td>APACHE II score</td>
<td>ScvO$_2$ group</td>
<td>20.0 ± 6.0</td>
</tr>
<tr>
<td></td>
<td>ScvO$_2$+P(cv-a)CO$_2$ group</td>
<td>19.5 ± 5.9</td>
</tr>
<tr>
<td>SOFA score</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Significant difference between T0 and T6 in the same group, P<0.05

Demographic and clinical characteristics such as sex, age, basic disease and infection site at baseline were similar in the two groups (p>0.05). Before fluid resuscitation practice, there are no significantly different in heart rate, MAP, CVP, ScvO$_2$, APACHE II score, SOFA score between the two groups either. As shown in Table 2, lactic acid level of patients in ScvO$_2$+P(cv-a)CO$_2$ group was slightly higher than ScvO$_2$ group patients, but no statistical difference was found between the two groups. Mean arterial pressure of all patients were lower than 60 mmHg, IOI lower than 200, CI in both groups were high normal, and MAP, IOI, CI, EVLWI and SOFA score have no difference between the two groups (p>0.05).

**Comparison between patients in ScvO$_2$ group and ScvO$_2$+P(cv-a)CO$_2$ group at T0**

**Comparison between patients in ScvO$_2$ group and ScvO$_2$+P(cv-a)CO$_2$ group at T6**

After fluid resuscitation 6 h, heart rate and lactic acid decreased significantly in both ScvO$_2$+P(cv-a)CO$_2$ and ScvO$_2$
group, and CVP, MAP and ScvO₂ increase significantly (p<0.05), but no statistically significant were observed between the two groups (p>0.05). Lactate clearance rate of ScvO₂+P(cv-a)CO₂ group (30.1 ± 17.2) was higher than ScvO₂ group (21.6 ± 14.3) (p<0.05). After 6 h, liquid equilibrium state of ScvO₂+P(cv-a)CO₂ group (3011 ± 1198) mL were higher than ScvO₂ group (2415 ± 680) mL (p<0.05), but vasoactive drug dose were significantly less than ScvO₂ group (dose of dobutamine and norepinephrine were (87.8 ± 24.1) mg vs. (111.7 ± 45.1) mg and (13.1 ± 5.7) mg vs. (16.8 ± 6.0) mg respectively) (p<0.05). After 6 h, CVP and CI of ScvO₂+P(cv-a)CO₂ group were also higher than ScvO₂ group (p<0.01), but incidence of pulmonary edema and EVLWI (12/30) vs. (14/38) between the two group have no significant difference (p>0.05). After recovery, oxygenation index in both groups were significantly improve, but no difference were found between two groups (p>0.05).

Table 3. Practice in fluid resuscitation and outcomes comparison between ScvO₂+P(cv-a)CO₂ group and ScvO₂ group.

<table>
<thead>
<tr>
<th></th>
<th>ScvO₂ group</th>
<th>P(cv-a)CO₂ + ScvO₂ t-value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norepinephrine (ng)</td>
<td>16.8 ± 6.0</td>
<td>13.1 ± 5.7</td>
<td>0.011</td>
</tr>
<tr>
<td>Fluid balance (mL)</td>
<td>2415 ± 680</td>
<td>3011 ± 1198</td>
<td>0.017</td>
</tr>
<tr>
<td>Pulmonary edema (%</td>
<td>6/30 (20%)</td>
<td>8/38 (21%)</td>
<td>-</td>
</tr>
<tr>
<td>Mechanical ventilation time (day)</td>
<td>14.7 ± 6.2</td>
<td>11.7 ± 4.9</td>
<td>0.028</td>
</tr>
<tr>
<td>duration of ICU stay (day)</td>
<td>13.2 ± 6.2</td>
<td>9.3 ± 4.4</td>
<td>0.003</td>
</tr>
<tr>
<td>28 days mortality (%)</td>
<td>8/30 (27%)</td>
<td>11/38 (29%)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Discussion

The main findings of present study are as follows: for fluid resuscitation in patients with septic shock, when ScvO₂>70% is achieved, the presence of P(cv-a)CO₂ within normal range is relevant to elevated CVP, CI; reduce dose of vasoactive drugs; correlate with higher lactate clearance; and less mechanical ventilation and ICU stay. Therefore P(cv-a)CO₂ may be a useful complementary target for EGDT.

P(cv-a)CO₂ with better CI and tissue perfusion

Sufficient tissue perfusion is an essential component of oxygenation for patients with septic shock. When oxygen delivery could not reach oxygen demand, it would trigger tissue hypoxia, eventually lead to organ failure [23]. Therefore, the use of early and efficient tool to identify and correct hypoperfusion state is the key for fluid resuscitation practice of patients with septic shock patients, and then improves outcomes. Since the landmark study by Rivers et al. [3], ScvO₂ was used as measurement of the balance of oxygen delivery and consumption, and serve as a goal for EGDT. But ScvO₂ alone has its limitation as it is measured downstream from tissue [5]. Oxygenation index (OI) basically independent of anaerobic metabolism, in septic condition, capillary shunting and mitochondrial damage will affect tissue oxygen extraction, but the heterogeneity of microcirculation may cover up low local oxygen venous saturation [24,25]. In that case, tissue hypoxia would present while ScvO₂ over its threshold, therefore ScvO₂ maybe an inaccuracies indicator to reflect the global tissue perfusion. Because the solubility of carbon dioxide is around 20 times than oxygen, carbon dioxide is more likely to spread out of ischemic tissue into veins, making it an extremely sensitive indicator of hypoperfusion [26]. Some studies have confirmed that the increase of CO₂ partial pressure is capable to reflect tissue perfusion than other normal indicator (eg, blood lactate) although its pathophysiology is still unclear [27].

In our study, we have investigated the potential of P(cv-a)CO₂ as a complementary target in fluid resuscitation while ScvO₂>70%. By maintaining P(cv-a)CO₂ within normal range in a group of septic shock patients that ScvO₂ already over 70%, and with another group of patients only normalize ScvO₂>70% s a control group, we found that both groups mean arterial pressure and CVP were significantly higher in T6, and...
heart rate decrease significantly than T0, indicated fluid resuscitation is effective. But CI of patients in ScvO2+P(cv-a)CO2 group increased significantly than control group, which revealed that P(cv-a)CO2 as a complementary target is beneficial to elevate cardiac output, then improve tissue perfusion.

The normal range of P(cv-a)CO2 is 2–5 mmHg, over 6 mmHg would indicated inadequate cardiac output and tissue hypoperfusion [26]. Although ScvO2 were higher than 70% in all 30 cases of ScvO2 group, but 12 (40%) patients have P(cv-a)CO2>6 mmHg, which indicated tissue hypoperfusion of those patients. This is consistent with the reports of Varpuls, and in agreement with reports found that P(cv-a)CO2 have a negative relationship with cardiac output [25,28]. And this may contributed to the higher CI of ScvO2+P(cv-a)CO2 group. In other research, patients whose P(cv-a)CO2 over 6 mmHg always present great lactate level than whose P(cv-a)CO2 less than 6 mmHg, and CI, ScvO2 lower than patients that P(cv-a)CO2<6 mmHg [29]. Insufficient CI would lead to hypoxia because of low flow state, and the shortage of blood flow cannot take CO2 away from tissue, which would elevate P(cv-a)CO2.

The significantly higher blood lactate clearance observed in ScvO2+P(cv-a)CO2 group also support patients in this group reach a better perfusion state. Arterial blood lactate is a sensitive indicator of tissue ischemia and hypoxia, so dynamic monitor of arterial lactate is importance for early diagnosis of shock and tissue hypoxia. Oxygen delivery restoration in resuscitation would be indicated by the reduction of blood lactate concentration [30]. Studies have found that a lactate clearance of 10% or more is evidence of adequate tissue oxygen delivery, and serve as an independent predictor of prognosis and survival from septic shock [7,31,32]. In this study, blood lactate in both groups were decrease significantly than previous, and lactate clearance of both groups were above 10%, but ScvO2+P(cv-a)CO2 group (30.1% ± 17.2%) have higher lactate clearance than ScvO2 group (21.6% ± 14.3%), indicated ScvO2+P(cv-a)CO2 group could reach a better resuscitation state, and improve body tissue perfusion; while ScvO2 group maybe just reach the lower limit of capacity requirements. Therefore, normalize both P(cv-a)CO2 and ScvO2 may be beneficial to patients with septic shock in aspect of cardiac output and tissue hypoperfusion improvement.

**P(cv-a)CO2 and fluid resuscitation practice**

By fluid resuscitation, abundance crystal and colloid liquids may be use during early aggressive treatment, which may damage alveolar capillaries, resulting in pulmonary interstitial edema, increased lung damage and even lead to acute respiratory distress syndrome [33]. Extravascular lung water index (EVLWI) is a sensitive indicator of pulmonary edema, was monitored by PiCCO to assess the degree of pulmonary edema during the early period of fluid resuscitation, reduce the incidence of lung injury. The balance fluid volume of ScvO2 group and ScvO2+P(cv-a)CO2 group was 2415 ± 680 mL and 3011 ± 1198 mL respectively, data shows statistically significant difference. Although patients in ScvO2+P(cv-a)CO2 group received more crystal and colloid fluid than did patients in the ScvO2 group during early aggressive treatment, which may cause acute lung injury, but the slight increased of EVLWI in ScvO2+P(cv-a)CO2 group (7.6 ± 3.3) did not show any significant difference compare with control group (7.3 ± 3.4). The incidence of pulmonary edema in 28-days following (20% vs. 21%) also support more intravenous fluids received in patients of ScvO2+P(cv-a)CO2 group did not cause significant harm to the lungs than control group. In contrast, ScvO2+P(cv-a)CO2 group (11.7 ± 4.9 days) effectively reduce the duration of mechanical ventilation than control group (14.7 ± 6.2 days). This may be because patients in ScvO2+P(cv-a)CO2 group got adequately fluid resuscitation, cardiac output increased, body tissue perfusion improved effectively, lung perfusion and cell metabolism also improved, fanally shorten the duration of mechanical ventilation. Those datas indicated that normalize both ScvO2 and P(cv-a)CO2 in fluid resuscitation could be practiced safely by balance the demand of cardiac preload and the occur of pulmonary edema.

There are some patients in both group needed dobutamine because of ScvO2 lower than 70%. Dobutamine is an strong agonist for β1 and β2 adrenergic receptor. The active effect to β1 receptor could improve cardiac index by 25% to 50%, and heart rate increase by 10% to 20% [7]. β2 receptor activation could reduce pulmonary wedge pressure and improve cardiac output then improve tissue perfusion [34]. Therefore, dobutamine can increase oxygen delivery but also increase myocardial oxygen consumption. In our study, patients of ScvO2+P(cv-a)CO2 group required less vasoactive drugs than ScvO2 group after fluid resuscitation in 6 h. In consideration of more adequate resuscitation state were receives in patients of ScvO2+P(cv-a)CO2 group, they also enhanced cardiac preload to increase cardiac output, raised effective circulating volume, thereby reducing the amount of vasoactive drugs.

**P(cv-a)CO2 with prognosis and mortality**

SOFA score and APACHE II score are scoring system commonly used in critically ill patients, for evaluating severity of patients with septic shock and predict prognosis or mortality [35]. Fabrice V point out SOFA score obvious decrease in low P(cv-a)CO2 group patients in 24 h [29] and research from Emmanuel et al. have investigated the use of P (cv-a) CO2 as an individualized goal to guide orientation treatment for 70 high-risk surgical patients, recording the patient’s CI, CVP, and P (cv-a)CO2, analyzed their prognosis, found that patients with complications have higher P(cv-a)CO2 value than patients didn’t have complications; for patients whose ScvO2 ≥ 71% and with complications, P(cv-a)CO2 value is significantly higher than patients who without complications occur [36]. Bakker and other studies suggest that surviving septic shock patients have lower P(cv-a)CO2 than the patients who died, although they have a very similar CI, oxygen supply and oxygen consumption values [28]. In this study, SOFA score and APACHEII score have no significant difference between two groups when enter the program, and SOFA score and APACHEII score decreased significantly in T6. But there are
also no significant difference in SOFA score and APACHE II score in T6 between the two groups. Although the length of stay in ICU was much shorter in ScvO2+P(cv-a)CO2 group (9.3 ± 4.4 days vs. 13.2 ± 6.2 days), no significant difference were observed in 28 days mortality for the two groups. The 28 days mortality rate in both groups were similar with previous studies [3,11], indicated that the resuscitation practice in our study is effective.

But as a single-center preliminary research, the studied patients group is small, we may not get sufficient data to indentify some significant finding. Further multi-center clinical trials with larger sample are required to confirm the effective of P(cv-a)CO2 as a complementary goal to guide the fluid resuscitation.

**Conclusion**

P(cv-a)CO2 is a valuable complementary goal to guide the fluid resuscitation for septic shock patients. The inclusion of P(cv-a)CO2 into resuscitation protocol would be a safely and effectively practice. But P(cv-a)CO2 may not available enough to serve as a predictor of prognosis and mortality.

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