Original Article
Cardiac output measurement using a modified carbon dioxide Fick method: comparison analysis with pulmonary artery catheter method and pulse induced contour cardiac output method

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Abstract: Objectives: In the present study, cardiac output in mechanically ventilated patients were determined using three methods including modified CO$_2$-Fick (mCO$_2$F), pulmonary artery catheter (PAC), and pulse induced contour cardiac output (PiCCO) methods and the results were compared to assess the effectiveness of mCO$_2$F method in measuring the cardiac output. Method: Mechanically ventilated and hemodynamically unstable patients (n=39) were sedated and intubated with Swan-Ganz or PiCCO arterial catheters. At the beginning of the experiment and at 4 h after the experiment, the CO$_2$ concentration in expiratory air was measured through a CO$_2$ monitor and it was used further in the cardiac output calculation using mCO$_2$F method. The cardiac output was also determined using PAC and PiCCO methods. Results: The cardiac output determined by PAC and mCO$_2$F method was not significantly (P>0.05) different [5.53±2.85 L.min$^{-1}$ (PAC) and 5.96±2.92 L.min$^{-1}$ (mCO$_2$F)] at the beginning of the experiment and [6.22±2.7 L.min$^{-1}$ (PAC) and 6.36±2.35 L.min$^{-1}$ (mCO$_2$F)] at 4 h after the experiment; however, they were highly correlated (r=0.939 and 0.908, P<0.001). The cardiac output determined by PiCCO and mCO$_2$F method was also not significantly (P>0.05) different [6.05±2.49 L.min$^{-1}$ (PiCCO) and 5.44±1.64 L.min$^{-1}$ (mCO$_2$F)] at the beginning of the experiment and [6.17±2.04 L.min$^{-1}$ (PiCCO) and 5.70±1.72 L.min$^{-1}$ (mCO$_2$F)] at 4 h after the experiment; however, they were highly correlated (r=0.776 and 0.832, P<0.001). Conclusion: The mCO$_2$F method could accurately measure the cardiac output in mechanically ventilated patients without using any expensive equipment’s and invasive procedures.

Keywords: Cardiac output, modified Fick method, mechanical ventilation, thermo dilution, pulse induced contour cardiac output, pulmonary artery catheter

Introduction
Cardiac output is the volume of blood pumped by the heart per minute. It is an important parameter of cardiac function and also an indicator for evaluating the dynamic changes of cardiac functions. Cardiac output monitoring is necessary in the management of critically ill patients. As an important hemodynamic parameter, the accurate cardiac output estimation is helpful in developing a rational therapeutic regimen and in evaluating the response of patients to the intervention.

The cardiac output of an unstable hemodynamic patient is usually estimated from blood pressure, urine output, blood gas analysis, and capillary refill. However, the results estimated from these parameters are not satisfactory [1, 2]. Thus, researchers have been trying to find a reliable, continuous, accurate, and minimally invasive method of cardiac output monitoring.

Introduced by Swan and Ganz, the pulmonary artery catheter (PAC) became to be the gold standard for cardiac output monitoring for more than two decades [3, 4]. However, arrhythmia, infection, and possible pulmonary artery disruption have always been concerns related to the use of a PAC and led to a growing interest in the development of noninvasive hemodynamic monitoring devices [5-7]. One less invasive
Cardiac output measurement using mCO$_2$F method

The Fick method is a “gold standard” measurement of cardiac output. It involves measurement of $O_2$, $CO_2$, and para-aminobenzoic acid, especially $O_2$. The Fick method is based on $O_2$ consumption monitoring in a closed space to calculate the $CO_2$ exchange; however, it is unlikely to place the patients in such a confined space. Theoretically, the cardiac output in mechanically ventilated patients can be measured using a modified CO$_2$ Fick method (mCO$_2$F). The mCO$_2$F method is based on $CO_2$ generation, in which $CO_2$ generation and $O_2$ consumption are always in a linear relationship [9]. Studies on measurement of cardiac output in mechanically ventilated animals using the mCO$_2$F method have shown that the method is of high accuracy, good reproducibility, and easy to apply [10]. However, little information on monitoring cardiac output using the mCO$_2$F method is reported in China.

Hence, in the present study, the effectiveness of mCO$_2$F method in measuring the cardiac output was assessed by comparing the cardiac output measurement using three different methods including mCO$_2$F, pulmonary artery catheter (PAC), (also known as the Swan-Ganz catheter), and pulse induced contour cardiac output (PiCCO) methods in mechanically ventilated patients.

Materials and methods

Study design and patient enrollment

In this prospective study, a total of 39 patients under hemodynamic monitoring between July 2012 and December 2012 in Surgical Intensive Care Unit of the First Affiliated Hospital of College of Medicine, Zhejiang University, Zhejiang, China, were enrolled. The study inclusion criteria were as follows: mechanically ventilated patients with either unstable hemodynamics after cardiothoracic surgery or with septic shock. The study exclusion criteria were as follows: 1) Patients who had craniofacial trauma or who recently underwent intracranial surgeries (which would lead to changes in blood $CO_2$ gradient and intracranial pressure); 2) Patients who recently underwent intragastric surgery; 3) Patients with local infection (which resulted in higher $CO_2$ concentration gradient in local tissues); 4) Patients who underwent cardiac shunt to treat patent ductus arteriosus, atrial septal defect, or ventricular septal defect; and 5) Patients who had taken medicines which would affect the body’s pH level and $CO_2$ production and demand for ventilator parameters adjustment. The study protocol was approved by the Ethic Committee of Human Research of First Affiliated Hospital of College of Medicine, Zhejiang University, Zhejiang, China. All participants provided written informed consent.

Cardiac output monitoring

Cardiac output of the patients was determined using three different methods such as mCO$_2$F, PAC, and PiCCO. The PAC and PiCCO methods were regarded as controls. The time interval between the cardiac output measurements using different methods was less than 10 min.

During the experiment, patients were generally anesthetized or sedated by continuous intravenous injection of midazolam (2-3 mg/h) or propofol (20-40 mg/h). The level of sedation of the patients was assessed by Ramsay sedation scale, and the patients’ sedation level was maintained at 5-6 points per Ramsay sedation scale [11]. Later, the patients were intubated with catheters as described below and mechanically ventilated using Servo ventilator (Siemens Electrical Apparatus Ltd., Berlin, Germany). The patient seemed to be in steady state when the $CO_2$ concentration in the outlet air was stable for 6 min [12]. At the time of cardiac output measurement, the infusion speed, vasoactive drug dosage, and the ventilator parameters were kept constant. The patient’s hemodynamic parameters were collected. The blood temperature displayed on the PAC or PiCCO monitor was recorded and regarded as the body temperature of the patients. For nonbleeding patients, the blood was collected in the first 4 h of the experiment and the hemoglobin (Hb) content was measured. For bleeding patients, venous blood was collected during the experiment and the Hb content was measured. During the experiment, in order to minimize the human errors in data collection, the ice cold (0°C) nor-
Cardiac output measurement using mCO₂F method

The principle of the mCO₂F method

The mCO₂F method is based on the principle that CO₂ production in tissue (CO₂P) is equal to pulmonary CO₂ exchange (VCO₂) in a steady state. In mechanically ventilated patients, VCO₂ can be obtained from a computer-aided analysis of expiratory airflow (Qexp) and CO₂ fraction in expiratory air (FeCO₂) [13].

\[
VCO₂ = \int_0^T Q_{exp}(t) \cdot FeCO₂(t) \cdot dt \cdot T^{-1}
\]

Where, VCO₂ is pulmonary CO₂ exchange (L/min); Qexp is expiratory airflow (L/min); FeCO₂ is CO₂ fraction in expiratory air (%); and t is time (min).

CO₂P is the product of cardiac output (Q) and venous-arterial difference in CO₂ concentration (Cv-a CO₂).

\[
CO₂P = Q \cdot (Cv CO₂ - C_a CO₂)
\]

Where, CO₂P is CO₂ production in tissue (mL/min); Q is cardiac output (L/min); Cv CO₂ is venous CO₂ concentration (mL/L); and C_a CO₂ is arterial CO₂ concentration (mL/L).

Blood CO₂ concentration could be measured using many methods, depending on the calculation method of CO₂ concentration in the erythrocyte [11, 12, 14-16]. Here, Douglas equation was used [14, 15, 17-19]:

\[
C_v CO₂ = C_a CO₂ \cdot \left[ 1 - \left( \frac{0.0289}{3.352 \cdot 0.456 \cdot sO₂ \cdot (8.142 \cdot PH)} \right) \right]
\]

Where, C_v CO₂ is total CO₂ concentration in blood (mL/100 mL); C_a CO₂ is total CO₂ concentration in plasma (mL/100 mL); Hb is hemoglobin concentration (g/dL); and sO₂ is oxygen saturation (%).

Total CO₂ content in plasma is calculated using Henderson-Hasselbalch equation:

\[
c_{CO₂} = 2.226 \cdot s \cdot PCO₂ \cdot \left( 1 + 10^{-\alpha} \right)
\]

\[
s = 0.0307 + 0.00057(37 - T) + 0.00002(37 - T) \cdot PK' = 6.086 + \left[ 0.042 \cdot (7.4 - PH) \right] + \left[ (3.8 \cdot T) \cdot (0.0047 + 0.00139 \cdot (7.4 - PH)) \right]
\]

Where, c_{CO₂} is total CO₂ concentration (mL/100mL); 2.226 is a conversion factor for mEq into mL/100 mL; s is solubility coefficient of CO₂ concentration in plasma (mEq/mmHg); PK' is apparent pK; pCO₂ is partial CO₂ pressure; and T is temperature (°C).

For the calculations, CO₂P and VCO₂ are required to be converted to standard temperature, pressure, and dry (STPD) conditions using the equation of

\[
CO₂P_{STPD} = CO₂P_{STPD} \cdot \left( \frac{T}{T₀} \right)^{\left(\frac{P_{STPD} - pH₂O}{P₀} \right)}
\]

Where, CO₂P_{STPD} is CO₂ production under STPD conditions; BTPS is body temperature, pressure, and saturated condition; CO₂P_{ATPS} is CO₂ production under BTPS conditions; T₀ is standard temperature (273 K); T_BTPS is temperature under BTPS conditions (K); P_{STPD} is pressure under STPD conditions (kPa); pH₂O is partial pressure of water vapor at T_BTPS (kPa); and P₀ is standard pressure (101.4 kPa).

\[
VCO₂_{STPD} = VCO₂_{STPD} \cdot \left( \frac{T}{T₀} \right)^{\left(\frac{P_{STPD} - pH₂O}{P₀} \right)}
\]

Where, VCO₂_{STPD} is pulmonary CO₂ exchange under STPD conditions; ATPS is ambient temperature, pressure, and saturated condition; VCO₂_{ATPS} is pulmonary CO₂ exchange under ATPS conditions; T_{ATPS} is ambient temperature (K); P_{ATPS} is pressure under the ATPS conditions (kPa).

Then, cardiac output can be calculated using the equation of

\[
Q = \frac{VCO₂_{ATPS}}{(C_v CO₂).STPD}
\]

where, Q is cardiac output (L/min); VCO₂_{ATPS} is pulmonary CO₂ exchange under STPD conditions (mL/min); (C_v CO₂).STPD is venous-arterial difference in CO₂ concentration under STPD conditions (mL/L).

Cardiac output measurement using mCO₂F method

Patients were intubated with a double lumen central venous catheter via internal jugular or subclavian vein. The tip of the catheter was positioned in right atrium to draw the central venous blood samples. An X-ray examination (Mobile DaRt, Shimadzu Corporation, Beijing, China) was performed to ensure that the tip of the catheter was positioned exactly in the right atrium. The intubation catheter was then con-
Cardiac output measurement using mCO₂F method

Figure 1. The flow chart of cardiac output measurement using the modified CO₂ Fick method.

PiCCO method, patients were also intubated with 4F PiCCO arterial catheters through the femoral artery, which were then connected to a monitor (PULSION Medical Systems SE, Fedkirchen, Germany) for hemodynamic and cardiac output monitoring.

Statistical analysis

All data were expressed as mean±standard deviation. All statistical analyses were performed using SPSS software, Version 13.0 (SPSS Inc., Chicago, IL, USA). Paired t test and correlation analysis were used to perform intergroup comparisons. Scatter plots and trend lines were used to assess the agreement between cardiac output measurements using every two different methods. For all analyses, a probability less than an alpha value of 0.05 (P<0.05) was considered to be statistically significant.

Results

Patient characteristics

Demographic factors and disease status of patients in both groups were comparable at baseline. The mean age of all patients was 50.33 years, the mean weight was 59.37 kg, and the mean height was 164.89 cm. There were 5 patients using PAC and 19 patients using PiCCO after cardiac surgery. There were 4 patients using PAC and 11 patients using PiCCO with septic shock (Table 1).

Partial CO₂ pressure in mixed venous blood and in right atrium blood

The partial CO₂ pressure in mixed venous blood and in right atrium blood was measured at the beginning of and 4 h after the initial cardiac output measurement using the PAC method. There was no significant (P>0.05) difference in partial CO₂ pressure in the mixed venous blood and in the right atrium blood (Table 2).

Cardiac output determined by the mCO₂F and the PAC method

At the beginning of the experiment, cardiac outputs determined by the PAC and mCO₂F methods were 5.53±2.85 and 5.96±2.92 L min⁻¹, respectively, which were not significantly (P>0.05) different (Table 3); however, they were highly correlated (r=0.939, P<0.001) (Table 4;
Cardiac output measurement using mCO$_2$F method

Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Patients using Swan-ganz catheter (n=9)</th>
<th>Patients with PICCO monitoring (n=30)</th>
<th>Total Patients using mCO$_2$F (n=39)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>52.46±23.41</td>
<td>47.81±18.23</td>
<td>50.33±17.14</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>53.42±43.27</td>
<td>60.51±39.75</td>
<td>59.37±27.82</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>163.77±12.84</td>
<td>166.90±17.94</td>
<td>164.89±15.76</td>
</tr>
<tr>
<td>Diseases</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After cardiac surgery</td>
<td>5</td>
<td>19</td>
<td>24</td>
</tr>
<tr>
<td>Septic shock</td>
<td>4</td>
<td>11</td>
<td>15</td>
</tr>
</tbody>
</table>

Table 2. Comparison of partial CO$_2$ pressure in mixed venous blood (P$_{\text{VCO}_2}$) and in right atrium blood (P$_{\text{vCO}_2}$) (mmHg)

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>P$_{\text{VCO}_2}$</th>
<th>P$_{\text{vCO}_2}$</th>
<th>T</th>
<th>P</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>48.65±9.24</td>
<td>48.34±8.14</td>
<td>0.164</td>
<td>0.873</td>
<td>9</td>
</tr>
<tr>
<td>4</td>
<td>46.80±7.35</td>
<td>46.32±5.40</td>
<td>0.275</td>
<td>0.791</td>
<td>9</td>
</tr>
</tbody>
</table>

Table 3. Cardiac output (L/min) comparison between the pulmonary artery catheter ($Q_{\text{PAC}}$) and the modified CO$_2$ Fick method ($Q_{\text{mCO}_2\text{F}}$) using paired t test

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>$Q_{\text{PAC}}$</th>
<th>$Q_{\text{mCO}_2\text{F}}$</th>
<th>t</th>
<th>P</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5.53±2.85</td>
<td>5.96±2.92</td>
<td>-1.257</td>
<td>0.244</td>
<td>9</td>
</tr>
<tr>
<td>4</td>
<td>6.22±2.71</td>
<td>6.36±2.35</td>
<td>-0.351</td>
<td>0.735</td>
<td>9</td>
</tr>
</tbody>
</table>

Table 4. Correlation of cardiac output (L/min) between pulmonary artery catheter ($Q_{\text{PAC}}$) and the modified CO$_2$ Fick method ($Q_{\text{mCO}_2\text{F}}$)

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>$Q_{\text{PAC}}$</th>
<th>$Q_{\text{mCO}_2\text{F}}$</th>
<th>Pearson-r</th>
<th>P</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5.53±2.85</td>
<td>5.96±2.92</td>
<td>0.939</td>
<td>0.000***</td>
<td>9</td>
</tr>
<tr>
<td>4</td>
<td>6.22±2.71</td>
<td>6.36±2.35</td>
<td>0.908</td>
<td>0.000***</td>
<td>9</td>
</tr>
</tbody>
</table>

Cardiac outputs determined by the two methods are highly correlated ($P<0.001$).

Table 5. Cardiac output (L/min) comparison between the pulmonary artery catheter ($Q_{\text{PAC}}$) and the modified CO$_2$ Fick method ($Q_{\text{mCO}_2\text{F}}$) using paired t test

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>$Q_{\text{PAC}}$</th>
<th>$Q_{\text{mCO}_2\text{F}}$</th>
<th>t</th>
<th>P</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5.53±2.85</td>
<td>5.96±2.92</td>
<td>-1.257</td>
<td>0.244</td>
<td>9</td>
</tr>
<tr>
<td>4</td>
<td>6.22±2.71</td>
<td>6.36±2.35</td>
<td>-0.351</td>
<td>0.735</td>
<td>9</td>
</tr>
</tbody>
</table>

Cardiac outputs determined by the two methods are highly correlated ($P>0.05$) different (Table 5); however, they were highly correlated ($r=0.776, P<0.001$) (Table 6 and Figure 4). At 4 h after the experiment, cardiac outputs determined by the PiCCO and mCO$_2$F methods were 6.17±2.04 and 5.70±1.72 L min$^{-1}$, respectively, which were not significantly ($P>0.05$) different (Table 5); however, they were highly correlated ($r=0.832, P<0.001$) (Table 6 and Figure 5).

Discussion

Cardiac output monitoring is essential in the treatment of critically ill patients, and the accurate hemodynamic parameters reflecting the cardiac performance are very helpful in guiding the clinical treatment. The present study demonstrated that the mCO$_2$F method is a reliable method for measuring cardiac output in mechanically ventilated and hemodynamically unstable patients.

In 1870, Adolph Fick proposed a method for cardiac output measurement based on the principle of preservation of oxygen [20]. Cardiac output can be calculated using the amount of oxygen consumed and arteriovenous oxygen concentration difference. It can also be modified by using CO$_2$ exchange and arteriovenous CO$_2$ concentration difference. The Fick principle has been widely used in many clinical methods of cardiac output monitoring. In Fick-derived noninvasive methods, oxygen consumption is calculated based on respiratory quotient and the measurement of CO$_2$ exchange. In CO$_2$ rebreathing method, derived from indirect Fick principle, the fluctuation of partial CO$_2$ pressure in blood may affect the cerebral blood flow of some patients and hence the method cannot be used for patients with cerebral trauma, newborn babies, or children [16]. In general, the direct oxygen Fick method is considered as the...
Cardiac output measurement using mCO₂F method

Figure 2. Correlation of cardiac output (L/min) determined by pulmonary artery catheter (PAC) and the modified CO₂ Fick method (mCO₂F) at the beginning of the experiment.

Figure 3. Correlation of cardiac output (L/min) determined by pulmonary artery catheter (PAC) and the modified CO₂ Fick method (mCO₂F) at 4 h after the experiment.

golden standard for measuring the cardiac output [21]. Many previous studies have confirmed that for cardiac output measurement, the mCO₂F method is more accurate than the O₂ Fick method or heat dilution [10, 22, 23], which is further supported by the present study results. The present study results demonstrated that the cardiac output in mechanically ventilated and hemodynamically unstable patients determined by the mCO₂F method was highly correlated with the results obtained using PAC or PiCCO methods.

In the present study, blood samples drawn from pulmonary artery and right atrium during cardiac output measurement were analyzed using the PAC method, and it was found that the partial CO₂ levels in blood taken from pulmonary artery and right atrium were not significantly different but highly correlated. It is indicated that the cardiac output measurement would not be affected by sampling position (right atrium or pulmonary artery). Hence, it is possible to replace P\text{VCO₂} in pulmonary artery with that in right atrium. Moreover, mCO₂F method would be easier to use in clinical settings. For cardiac output monitoring, tips of central venous catheter could be exactly positioned in right atrium, which could be confirmed by an x-ray examination.

Theoretically, one prerequisite for using CO₂ Fick equation in calculating systemic blood flow is to exclude all the influence of intracardial shunt and pulmonary shunt on blood flow. Therefore, patients with patent ductus arteriosus, atrial septal defect, and ventricular septal defect were ruled out in this study. The other prerequisite for using CO₂ Fick equation is that the cardiac output measurement should performed in steady state because the CO₂ exchange is equal to CO₂ production only in steady state. Hence, in the present study, the steady state was assumed to be attained when the CO₂ exchange was kept constant for at least 6 min, with unchangeable CO₂ concentration in outlet air, for cardiac output measurement in mechanically ventilated and hemodynamically unstable patients. As such, the present study results were reliable. However, in the present study, all patients were mechanically ventilated through an endotracheal cannula during the cardiac output measurement using this method. The pulmonary CO₂ exchange could be underestimated if there was air leak around the cannula, leading to lowered cardiac output estimation.

Despite of high risk and cost, the PAC method is regarded as a gold standard measurement of cardiac output [24]. The PiCCO method is often applied in intensive care unit because the catheter and instrument are easily connected and it also can yield many important data including cardiac output, cardiac index, and pulmonary pressure. In addition, it is sensitive to cardiac performance of patients and is more easily operated than the PAC method. However, the expensive specialized catheter and equipments are required to perform this method. Using mCO₂F method, blood-gas analysis of arterial blood and right atrium blood for determination of pH, pCO₂, and sO₂ can be performed. Measurement of CO₂ concentration in expiratory air in mechanically ventilated patients, the body temperature, and hemoglobin concentration can also be determined using the mCO₂F method, which should be the routine test for critically ill
Cardiac output measurement using mCO\textsubscript{2}F method

Table 5. Cardiac output (L/min) comparison between the PiCCO method (Q\textsubscript{PiCCO}) and the modified CO\textsubscript{2} Fick method (Q\textsubscript{mCO2F}) using paired t test

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Q\textsubscript{PiCCO}</th>
<th>Q\textsubscript{mCO2F}</th>
<th>t</th>
<th>P</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>6.04±2.64</td>
<td>5.59±1.94</td>
<td>1.475</td>
<td>0.151</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>6.35±2.47</td>
<td>5.85±1.95</td>
<td>2.018</td>
<td>0.053</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 6. Correlation of cardiac output (L/min) between the PiCCO method (Q\textsubscript{PiCCO}) and the modified CO\textsubscript{2} Fick method (Q\textsubscript{mCO2F})

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Q\textsubscript{PiCCO}</th>
<th>Q\textsubscript{mCO2F}</th>
<th>Pearson-r</th>
<th>P</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>6.04±2.64</td>
<td>5.59±1.94</td>
<td>0.776</td>
<td>0.000***</td>
<td>30</td>
</tr>
<tr>
<td>4</td>
<td>6.35±2.47</td>
<td>5.85±1.95</td>
<td>0.832</td>
<td>0.000***</td>
<td>30</td>
</tr>
</tbody>
</table>

***Cardiac outputs determined by the two methods are highly correlated (P<0.001).

Figure 4. Correlation of cardiac output (L/min) determined by pulse induced contour cardiac output (PiCCO) and the modified CO\textsubscript{2} Fick method (mCO\textsubscript{2}F) at the beginning of the experiment.

Figure 5. Correlation of cardiac output (L/min) determined by pulse induced contour cardiac output (PiCCO) and the modified CO\textsubscript{2} Fick method (mCO\textsubscript{2}F) at 4 h after the experiment.

patients in the intensive care unit. Hence, the cardiac output can be calculated using the mCO\textsubscript{2}F method without additional requirement of expensive instruments. This method is cost-effective, and it has no risk of disability and death. However, it takes time to reach the steady state before the experiment. Hence, continuous measurement of cardiac output cannot be performed. In addition, too small arteriovenous CO\textsubscript{2} concentration difference may result in calculation errors, which is a limitation of this method. It was confirmed in the present study with completely sedated and generally anesthetized adult patients. Further research is warranted to measure the accuracy of the mCO\textsubscript{2}F method and its applications in various disease conditions, especially patients with cardiac disorder.

The present study has several limitations. Firstly, because of different blood samples required to be tested to obtain the final result by calculation, the data for each sample were likely to cause total error. Secondly, instant results couldn’t be obtained because the parameters needed to be monitored over a period of time to obtain the data for final calculation. Thirdly, requirement of steady state in mechanically ventilated patients further pose a significant challenge in monitoring cardiac output. Fourthly, the sample size was not large enough and it further warranted increased sample size to get more reliable results.

In summary, cardiac output could be accurately determined using the mCO\textsubscript{2}F method if the patients were without any intracardiac or intrapulmonary shunt and if the CO\textsubscript{2} exchange reached the steady state during measurement. Blood samples withdrawn from the right atrium could be used for the measurement. The mCO\textsubscript{2}F method is a more reliable, cost-effective method for cardiac output monitoring in critically ill patients in intensive care unit.

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Disclosure of conflict of interest

None.

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