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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_2F), pulmonary artery catheter (PAC), and pulse induced contour cardiac output (PiCCO) methods and the results were compared to assess the effectiveness of mCO_2F 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_2F method. The cardiac output was also determined using PAC and PiCCO methods. Results: The cardiac output determined by PAC and mCO_2F 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_2F)] at the beginning of the experiment and [6.22±2.7 $L.min^{-1}$ (PAC) and 6.36±2.35 $L.min^{-1}$ (mCO_2F)] 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_2F 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_2F)] at the beginning of the experiment, and [6.17±2.04 $L.min^{-1}$ (PiCCO) and 5.70±1.72 $L.min^{-1}$ (mCO_2F)] at 4 h after the experiment; however, they were highly correlated (r=0.776 and 0.832, P<0.001). Conclusion: The mCO_2F 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 thermodilution-based technique consists of the pulse-induced cardiac output device (PiCCO), however, the requirement for intra-arterial and central venous catheterisation limits the use of PiCCO to those with evolving critical illness or at high risk of complex and severe haemodynamic derangement [8].

The Fick method is a "gold standard" measurement of cardiac output. It involves measurement of O_2, CO_2, and para-aminohippuric 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_2F). The mCO_2F 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_2F method have showed that the method is of high accuracy, good reproducibility, and easy to apply [10]. However, little information on monitoring cardiac output using the mCO_2F method is reported in China.

Hence, in the present study, the effectiveness of mCO_2F method in measuring the cardiac output was assessed by comparing the cardiac output measurement using three different methods including mCO_2F, 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 craniocerebral trauma or who recently underwent intracranial surgeries (which would leads 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 arterisus, 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, demanding 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_2F, 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 Servoi 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) normal saline injection and blood sampling at different time points were always performed by the same person. The cardiac output of each patient was measured two times within four hours of the experiment.

The principle of the mCO_2F method

The mCO_2F method is based on the principle that CO_2 production in tissue (CO_2P) is equal to pulmonary CO_2 exchange (VCO_2) in a steady state. In mechanically ventilated patients, VCO_2 can be obtained from a computer-aided analysis of expiratory airflow (Q_{exp}) and CO_2 fraction in expiratory air ($FeCO_2$) [13].

$$VCO_2 = \left\{ \int_0^T Q_{exp}(t) \cdot FeCO_2(t) \cdot dt \right\} \cdot T^{-1}$$

Where, VCO_2 is pulmonary CO_2 exchange (L/min); Q_{exp} is expiratory airflow (L/min); $FeCO_2$ is CO_2 fraction in expiratory air (%); and t is time (min).

CO_2P is the product of cardiac output (Q) and venous-arterial difference in CO_2 concentration ($C_{(v-a)}CO_2$).

$$CO_2P = Q \cdot \left(C_v CO_2 - C_a CO_2\right)$$

Where, CO_2P is CO_2 production in tissue (mL/min); Q is cardiac output (L/min); C_VCO_2 is venous CO_2 concentration (mL/L); and C_aCO_2 is arterial CO_2 concentration (mL/L).

Blood CO_2 concentration could be measured using many methods, depending on the calculation method of CO_2 concentration in the erythrocyte [11, 12, 14-16]. Here, Douglas equation was used [14, 15, 17-19]:

$$c_bCO_2 = c_pCO_2 \cdot \left[1 - \frac{(0.0289 \cdot Hb)}{(3.352 - 0.456 \cdot sO_2) \cdot (8.142 - PH)}\right]$$

Where, c_bCO_2 is total CO_2 concentration in blood (mL/100 mL); C_pCO_2 is total CO_2 concentration in plasma (mL/100 mL); Hb is hemoglobin concentration (g/dL); and sO_2 is oxygen saturation (%).

Total CO_2 content in plasma is calculated using Henderson-Hasselbalch equation:

$$c_pCO_2 = 2.226 \cdot s \cdot PCO_2 \cdot \left(1 + 10^{PH-PK'}\right)$$

$$s = 0.0307 + 0.00057(37 - T) + 0.00002(37 - T)^2$$

$$PK' = 6.086 + \left[0.042 \cdot (7.4 - PH)\right] + \left\{(3.8 - T) \cdot \left[0.0047 + 0.00139 \cdot (7.4 - PH)\right]\right\}$$

Where, c_pCO_2 is total CO_2 concentration (mL/100mL); 2.226 is a conversion factor for mEq into mL/100 mL; s is solubility coefficient of CO_2 concentration in plasma (mEq/mmHg); pK' is apparent pK; pCO_2 is partial CO_2 pressure; and T is temperature (°C).

For the calculations, CO_2P and VCO_2 are required to be converted to standard temperature, pressure, and dry (STPD) conditions using the equation of

$$CO_2P^{STPD} = CO_2P^{BTPS} \cdot \left\{\frac{T_0}{T^{BTPS}}\right\} \cdot \left\{\frac{\left(P^{BTPS} - pH_2O\right)}{P_0}\right\}$$

where, CO_2P^{STPD} is CO_2 production under STPD conditions; BTPS is body temperature, pressure, and saturated condition; CO_2P^{BTPS} is CO_2 production under BTPS conditions; T_0 is standard temperature (273 K); T^{BTPS} is temperature under BTPS conditions (K); P^{BTPS} is pressure under BTPS conditions (kPa); pH_2O is partial pressure of water vapor at T^{BTPS} (kPa); and P_0 is standard pressure (101.4 kPa).

$$VCO_2^{STPD} = VCO_2^{ATPS} \cdot \left\{\frac{T_0}{T^{ATPS}}\right\} \cdot \left\{\frac{\left(P^{ATPS} - pH_2O\right)}{P_0}\right\}$$

Where, VCO_2^{STPD} is pulmonary CO_2 exchange under STPD conditions; ATPS is ambient temperature, pressure, and saturated condition; VCO_2^{ATPS} is pulmonary CO_2 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

$$Q = \frac{VCO_2^{STPD}}{\left(C_{(v-a)}CO_2\right)^{STPD}}$$

where, Q is cardiac output (L/min); VCO_2^{STPD} is pulmonary CO_2 exchange under STPD conditions (mL/min); $(C_{(v-a)}CO_2)^{STPD}$ is venous-arterial difference in CO_2 concentration under STPD conditions (mL/L).

Cardiac output measurement using mCO_2F 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-

Figure 1. The flow chart of cardiac output measurement using the modified CO_2 Fick method.

nected to a CO_2 monitor (ST303 CO_2 analyzer, Sentry Optronics Corp., Taiwan). Before the measurement, ventilator sensor was exposed for zero calibration. A ventilator was connected to a vessel through its outlet as a bumper. After the gas flow was stable, the bumper was connected to the CO_2 monitor through its outlet for $FeCO_2$ measurement. Meanwhile, Q_{exp} was recorded. Based on $FeCO_2$ and Q_{exp}, VCO_2 could be calculated using the equation 1 mentioned above. Likewise, using the blood-gas analysis results of arterial and venous blood, body temperature, cardiac output, and other parameters were calculated by following the equations mentioned above. The flow chart of the cardiac output measurement using the mCO_2F method is shown in **Figure 1**.

Cardiac output measurement using mCO_2F method and PAC method

Nine patients were randomly selected for the cardiac output measurement simultaneously using the mCO_2F and PAC methods. For the cardiac output measurement using PAC method, patients were also intubated with Swan-Ganz catheter (Teleflex Medical, Limerick, USA) through the internal jugular or subclavian vein. Blood sample was collected at the beginning of the experiment and 4 h after the experiment. Mixed venous blood samples were obtained from the pulmonary artery. Arterial blood was also withdrawn from the left radial artery through direct puncture. Both arterial and venous blood samples were used for blood-gas analysis (GEM Premier 3000, Instrumentation Laboratory, Belgium). The partial CO_2 pressure in mixed venous blood and in right atrium blood was compared.

Cardiac output measurement using mCO_2F method and PiCCO method

For the remaining 30 patients, the cardiac output was simultaneously measured using the mCO_2F and PiCCO methods at the beginning of the experiment and 4 h after the experiment. For the cardiac output measurement using 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 CO_2 pressure in mixed venous blood and in right atrium blood

The partial CO_2 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 CO_2 pressure in the mixed venous blood and in the right atrium blood (**Table 2**).

Cardiac output determined by the mCO_2F and the PAC method

At the beginning of the experiment, cardiac outputs determined by the PAC and mCO_2F 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**;

Table 1. Patient Characteristics

	Patients using Swan-ganz catheter (n=9)	Patients with PiCCO monitoring (n=30)	Total Patients using mCO_2F (n=39)
Age (y)	52.46±23.41	47.81±18.23	50.33±17.14
Body weight (kg)	53.42±43.27	60.51±39.75	59.37±27.82
Height (cm)	163.77±12.84	166.90±17.94	164.89±15.76
Diseases			
After cardiac surgery	5	19	24
Septic shock	4	11	15

Table 2. Comparison of partial CO_2 pressure in mixed venous blood ($P\bar{V}CO_2$) and in right atrium blood ($PvCO_2$) (mmHg)

Time (h)	$P\bar{V}CO_2$	$PvCO_2$	T	*P*	n
0	48.65±9.24	48.34±8.14	0.164	0.873	9
4	46.80±7.35	46.32±5.40	0.275	0.791	9

Table 3. Cardiac output (L/min) comparison between the pulmonary artery catheter (Q_{PAC}) and the modified CO_2 Fick method (Q_{mCO2F}) using paired t test

Time (h)	Q_{PAC}	Q_{mCO2F}	t	*P*	n
0	5.53±2.85	5.96±2.92	-1.257	0.244	9
4	6.22±2.71	6.36±2.35	-0.351	0.735	9

Table 4. Correlation of cardiac output (L/min) between pulmonary artery catheter (Q_{PAC}) and the modified CO_2 Fick method (Q_{mCO2F})

Time (h)	Q_{PAC}	Q_{mCO2F}	Pearson-r	*P*	n
0	5.53±2.85	5.96±2.92	0.939	0.000***	9
4	6.22±2.71	6.36±2.35	0.908	0.000***	9

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

Figure 2). At 4 h after the experiment, cardiac outputs determined by the PAC and mCO_2F methods were 6.22±2.71 and 6.36±2.35 L min^{-1}, respectively, which were not significantly ($P>0.05$) different (**Table 3**); however, they were highly correlated ($r=0.908$, $P<0.001$) (**Table 4**; **Figure 3**).

Cardiac output determined by the mCO_2F and the PiCCO method

At the beginning of the experiment, cardiac outputs determined by the PiCCO and mCO_2F methods were 6.05±2.49 and 5.44±1.64 L min^{-1}, respectively, which were not significantly ($P>0.05$) 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_2F 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_2F 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 princple 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

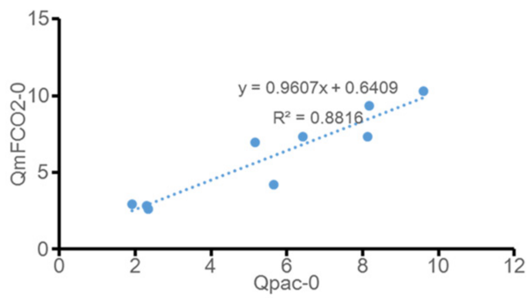

Figure 2. Correlation of cardiac output (L/min) determined by pulmonary artery catheter (PAC) and the modified CO_2 Fick method (mCO_2F) at the beginning of the experiment.

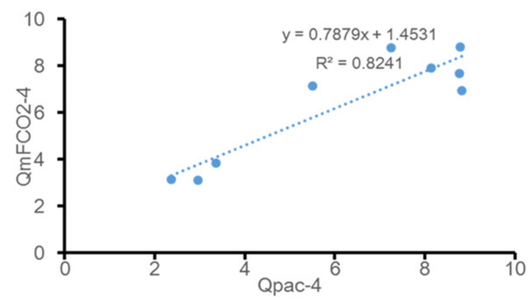

Figure 3. Correlation of cardiac output (L/min) determined by pulmonary artery catheter (PAC) and the modified CO_2 Fick method (mCO_2F) at 4 h after the experiment.

golden standard for measuring the cardiac output [21]. Many previous studies have confirmed that for cardiac output measurement, the mCO_2F method is more accurate than the O_2 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 mCO_2F 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 CO_2 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 $P\overline{V}CO_2$ in pulmonary artery with that in right atrium. Moreover, mCO_2F 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 CO_2 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 arterisus, atrial septal defect, and ventricular septal defect were ruled out in this study. The other prerequisite for using CO_2 Fick equation is that the cardiac output measurement should performed in steady state because the CO_2 exchange is equal to CO_2 production only in steady state. Hence, in the present study, the steady state was assumed to be attained when the CO_2 exchange was kept constant for at least 6 min, with unchangeable CO_2 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 CO_2 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 mCO_2F method, blood-gas analysis of arterial blood and right atrium blood for determination of pH, pCO_2, and sO_2 can be performed. Measurement of CO_2 concentration in expiratory air in mechanically ventilated patients, the body temperature, and hemoglobin concentration can also be determined using the mCO_2F method, which should be the routine test for critically ill

Table 5. Cardiac output (L/min) comparison between the PiCCO method (Q_{PiCCO}) and the modified CO_2 Fick method (Q_{mCO2F}) using paired t test

Time (h)	Q_{PiCCO}	Q_{mCO2F}	t	*P*	n
0	6.04±2.64	5.59±1.94	1.475	0.151	0
4	6.35±2.47	5.85±1.95	2.018	0.053	0

Table 6. Correlation of cardiac output (L/min) between the PiCCO method (Q_{PiCCO}) and the modified CO_2 Fick method (Q_{mCO2F})

Time (h)	Q_{PiCCO}	Q_{mCO2F}	pearson-r	*P*	n
0	6.04±2.64	5.59±1.94	0.776	0.000***	30
4	6.35±2.47	5.85±1.95	0.832	0.000***	30

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

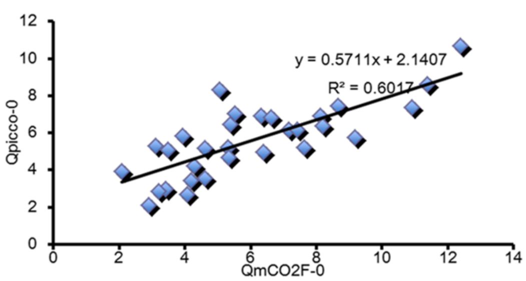

Figure 4. Correlation of cardiac output (L/min) determined by pulse induced contour cardiac output (PiCCO) and the modified CO_2 Fick method (mCO_2F) at the beginning of the experiment.

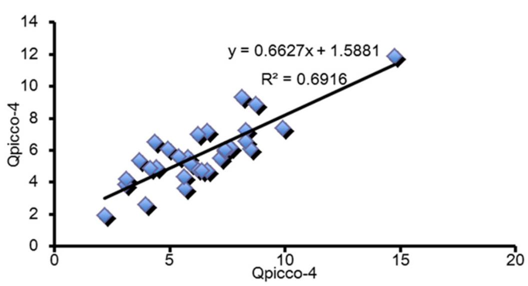

Figure 5. Correlation of cardiac output (L/min) determined by pulse induced contour cardiac output (PiCCO) and the modified CO_2 Fick method (mCO_2F) at 4 h after the experiment.

patients in the intensive care unit. Hence, the cardiac output can be calculated using the mCO_2F 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_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_2F 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_2F method if the patients were without any intracardiac or intrapulmonary shunt and if the CO_2 exchange reached the steady state during measurement. Blood samples withdrawn from the right atrium could be used for the measurement. The mCO_2F 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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References

[1] Magder S. Current tools for assessing heart function and perfusion adequacy. Curr Opin Crit Care 2014; 20: 294-300.

[2] Pearse RM, Harrison DA, MacDonald N, Gillies MA, Blunt M, Ackland G, Grocott MP, Ahern A, Griggs K, Scott R, Hinds C, Rowan K; OPTIMISE Study Group. Effect of a perioperative, cardiac output-guided hemodynamic therapy algorithm on outcomes following major gastrointestinal surgery: a randomized clinical trial and systematic review. JAMA 2014; 311: 2181-2190.

[3] Swan HJ and Ganz W. Measurement of right atrial and pulmonary arterial pressures and cardiac output: clinical application of hemodynamic monitoring. Adv Intern Med 1982; 27: 453-473.

[4] Ganz W, Donoso R, Marcus HS, Forrester JS and Swan HJ. A new technique for measurement of cardiac output by thermodilution in man. Am J Cardiol 1971; 27: 392-396.

[5] Boldt J. Clinical review: hemodynamic monitoring in the intensive care unit. Crit Care 2002; 6: 52-59.

[6] Cooper AB, Doig GS and Sibbald WJ. Pulmonary artery catheters in the critically ill. An overview using the methodology of evidence-based medicine. Crit Care Clin 1996; 12: 777-794.

[7] Sakka SG, Reinhart K, Wegscheider K and Meier-Hellmann A. Is the placement of a pulmonary artery catheter still justified solely for the measurement of cardiac output? J Cardiothorac Vasc Anesth 2000; 14: 119-124.

[8] Litton E and Morgan M. The PiCCO monitor: a review. Anaesth Intensive Care 2012; 40: 393-409.

[9] Siebenmann C, Rasmussen P, Sorensen H, Zaar M, Hvidtfeldt M, Pichon A, Secher NH and Lundby C. Cardiac output during exercise: A comparison of four methods. Scand J Med Sci Sports 2015; 25: e20-7.

[10] Mahutte CK and Jaffe MB. Effect of measurement errors on cardiac output calculated with O2 and modified CO_2 Fick methods. J Clin Monit 1995; 11: 99-108.

[11] Ramsay MA, Savege TM, Simpson BR and Goodwin R. Controlled sedation with alphaxalone-alphadolone. Br Med J 1974; 2: 656-659.

[12] de Boode WP, Hopman JC, Daniels O, van der Hoeven HG and Liem KD. Cardiac output measurement using a modified carbon dioxide Fick method: a validation study in ventilated lambs. Pediatr Res 2007; 61: 279-283.

[13] Sun XG, Hansen JE, Stringer WW, Ting H and Wasserman K. Carbon dioxide pressure-concentration relationship in arterial and mixed venous blood during exercise. J Appl Physiol (1985) 2001; 90: 1798-1810.

[14] McHardy GJ. The relationship between the differences in pressure and content of carbon dioxide in arterial and venous blood. Clin Sci 1967; 32: 299-309.

[15] Douglas AR, Jones NL and Reed JW. Calculation of whole blood CO_2 content. J Appl Physiol (1985) 1988; 65: 473-477.

[16] Greisen G. Autoregulation of cerebral blood flow in newborn babies. Early Hum Dev 2005; 81: 423-428.

[17] Henderson LJ, Bock AV, Field HJ and JL. S. Blood as a physicochemical system II. J Bio Chem 1924; 59: 379-431.

[18] Kelman GR. Digital computer procedure for the conversion of PCO_2 into blood CO_2 content. Respir Physiol 1967; 3: 111-115.

[19] Godfrey S. Manipulation of the indirect Fick principle by a digital computer program for the calculation of exercise physiology results. Respiration 1970; 27: 513-532.

[20] Acierno LJ. Adolph Fick: mathematician, physicist, physiologist. Clin Cardiol 2000; 23: 390-391.

[21] de Boode WP, Hopman JC, Wijnen MH, Tanke RB, van der Hoeven HG and Liem KD. Cardiac output measurement in ventilated lambs with a significant left-to-right shunt using the modified carbon dioxide fick method. Neonatology 2010; 97: 124-131.

[22] Mahutte CK, Jaffe MB, Sassoon CS and Wong DH. Cardiac output from carbon dioxide production and arterial and venous oximetry. Crit Care Med 1991; 19: 1270-1277.

[23] Mahutte CK, Jaffe MB, Chen PA, Sasse SA, Wong DH and Sassoon CS. Oxygen Fick and modified carbon dioxide Fick cardiac outputs. Crit Care Med 1994; 22: 86-95.

[24] Gonzalez J, Delafosse C, Fartoukh M, Capderou A, Straus C, Zelter M, Derenne JP and Similowski T. Comparison of bedside measurement of cardiac output with the thermodilution method and the Fick method in mechanically ventilated patients. Crit Care 2003; 7: 171-178.