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ORIGINAL ARTICLE

Continuous cardiac output estimation using a new modified Fick method during off-pump coronary artery bypass graft surgery: a retrospective observational study

Chahyun Oh[1,2] · Hyung-Chul Lee[3,4] · Soomin Lee[1,2] · Man-Shik Shim[5] · Soo Bin Yoon[4] · Jinsik Jung[1] · Seok-Hwa Yoon[1,2] · Yoon-Hee Kim[1,2] · Youngkwon Ko[1,2] · Boohwi Hong[1,2,6] · Yunseo Ku[7]

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Abstract

Purpose Several technical aspects of the Fick method limit its use intraoperatively. A data-driven modification of the Fick method may enable its use in intraoperative settings.

Methods This two-center retrospective observational study included 57 (28 and 29 in each center) patients who underwent off-pump coronary artery bypass graft (OPCAB) surgery. Intraoperative recordings of physiological data were obtained and divided into training and test datasets. The Fick equation was used to calculate cardiac output (CO-Fick) using ventilator-determined variables, intraoperative hemoglobin level, and SvO_2, with continuous thermodilution cardiac output (CCO) used as a reference. A modification CO-Fick was derived and validated: CO-Fick-AD, which adjusts the denominator of the original equation.

Results Increased deviation between CO-Fick and CCO was observed when oxygen extraction was low. The root mean square error of CO-Fick was decreased from 6.07 L/min to 0.70 L/min after the modification. CO-Fick-AD showed a mean bias of 0.17 (95% CI 0.00–0.34) L/min, with a 36.4% (95% CI 30.6–44.4%) error. The concordance rates of CO-Fick-AD ranged from 73.3 to 87.1% depending on the time interval and exclusion zone.

Conclusions The original Fick method is not reliable when oxygen extraction is low, but a modification using data-driven approach could enable continuous estimation of cardiac output during the dynamic intraoperative period with minimal bias. However, further improvements in precision and trending ability are needed.

Keywords Cardiac output · Coronary artery bypass · Hemodynamic monitoring · Intraoperative monitoring · Oxygen saturation · Oxygen consumption

Introduction

Cardiac output (CO) is a cardinal factor that determines organ perfusion and is directly related to blood pressure and oxygen delivery [1, 2]. Despite being a paramount hemodynamic

Chahyun Oh and Hyung-Chul Lee have contributed equally.

✉ Yunseo Ku
yunseo.ku@cnu.ac.kr

1 Department of Anesthesiology and Pain Medicine, Chungnam National University Hospital, Daejeon, Korea

2 Department of Anesthesiology and Pain Medicine, College of Medicine, Chungnam National University, Daejeon, Korea

3 Department of Anesthesiology and Pain Medicine Seoul National University College of Medicine, Seoul National University Hospital, Seoul, Korea

4 Department of Anesthesiology and Pain Medicine, Seoul National University Hospital, Seoul, Korea

5 Department of Thoracic & Cardiovascular Surgery, Chungnam National University Hospital, Daejeon, Korea

6 Big Data Center, Biomedical Research Institute, Chungnam National University Hospital, Daejeon, Korea

7 Department of Biomedical Engineering, Chungnam National University College of Medicine, 266 Munhwa-Ro(St), Jung-Gu, Daejeon 35015, Korea

factor, reliable measurement of CO is not easy intraoperatively. For example, direct measurements via transthoracic or transesophageal echocardiography are often impeded by surgical exposure, patient position, and suboptimal Doppler signal alignment.

One of the standard methods for measuring CO is a thermodilution technique via a pulmonary artery catheter [3, 4]. By intermittently injecting a bolus of cold crystalloid into the central venous circulation, this method calculates the CO by plotting a thermodilution curve over time. However, this method is susceptible to multiple sources of error, such as the volume, rate, timing, and temperature of the injectate [5].

These limitations can be partially relieved by a continuous thermodilution technique (CCO), which uses a thermal filament with a random on–off heating system [6]. This system has been compared with other measurements and well validated in previous studies [7, 8]. However, estimates using this method have time delays of about 4 to 12 min in hemodynamic fluctuations [6, 9–11]. In addition, this method remains susceptible to errors induced by regurgitant flow, such as tricuspid valve regurgitation, as in the intermittent bolus technique [6].

CO can also be estimated using the Fick method [12], which is based on the principle that the total uptake of oxygen is equal to the product of CO and the difference between arterial and venous oxygen content (AVO_2-diff). Because this method is based on a parameter that can be measured in near real-time (i.e., mixed venous oxygen saturation [SvO_2]), it may provide prompt estimates. Although this method is a standard for measuring CO, it has several technical issues that limit its use in intraoperative settings [13–15]. For example, a small AVO_2-diff may amplify errors; pulmonary oxygen consumption is ignored, resulting in a possible overestimation of CO; and a steady state is assumed, which is not always the case during dynamic intraoperative periods. Thus, at present, the use of Fick's method is usually confined to cardiac catheterization laboratories.

Pulmonary artery catheter-derived parameters can be readily determined during off-pump coronary artery bypass graft (OPCAB) surgery, with minimal confounding from mechanical circulatory support or hypothermia. The present study describes the derivation of a modification to the Fick method using a set of recordings of continuous intraoperative physiological data acquired during OPCAB surgery. The accuracy, precision, and trending ability of the new method was evaluated using CCO as a reference.

Patients and methods

The study protocol was approved by the Institutional Review Boards of Chungnam National University Hospital (Daejeon, Korea, IRB number: 2022-02-004-002, chairperson: Jeong Lan Kim, approval date: July 18, 2022) and Seoul National University Hospital (Seoul, Korea, IRB number: 2206-055-1331, chairperson: Yun-Chul Hong, approval date: June 5, 2022). All vital data were obtained from prospective registries of vital signs for surgical patients at Chungnam National University Hospital (Daejeon, Korea, IRB number: 2019-08-039, chairperson: Jeong Lan Kim, approval date: May 12, 2020) and Seoul National University Hospital (Seoul, Korea, IRB number: 1408-101-605, chairperson: Wooho Kim, approval date: August 28, 2014), both of which use a free data collection program (Vital recorder version 1.8 [16], accessed at https://vitaldb.net, Seoul, Republic of Korea). The requirement for written informed consent was waived by the IRB. This manuscript adheres to Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Study design

This retrospective study included patients who underwent OPCAB surgery with CCO and SvO_2 monitoring under general anesthesia from June 2021 to June 2022 at Chungnam National University Hospital (designated as institution A afterward in the study) and from January to December 2021 at Seoul National University Hospital (institution B). Patients were excluded if their vital records did not include information acquired from a ventilator, pulmonary artery catheter, and pulse oximeter; if one-lung ventilation was used intraoperatively; if intraoperative central venous pressure wave form or postoperative chest radiography showed a mal-positioned pulmonary artery catheter; if SvO_2 showed a persistent poor signal quality index; or if a mechanical circulatory assist device was used. Other data collected from the patient records included age, sex, weight, and height.

Data acquisition (institution A)

CCO and SvO_2 data were acquired using a Swan-Ganz catheter (7.5 F Swan-Ganz continuous cardiac output thermodilution catheter: CCOmbo V, model 774F75, Edwards Lifesciences, Irvine, CA, USA) and a HemoSphere advanced monitoring platform (Edwards Lifesciences), with CCO estimated and updated every 60 s (STAT mode, which displays an estimation without a moving average process). SvO_2 was

monitored continuously following in vivo calibration during the initial stage of surgery after the induction of anesthesia and stabilization of ventilatory settings and hemodynamics. Both variables were recorded at 0.5 Hz frequency.

Variables acquired from the ventilator (Flow-i Anesthesia Machine, Maquet, Solona, Sweden) included inspired and expired oxygen fractions (%) and minute ventilation (MV, L/min), which were recorded at 0.2 Hz frequency.

SpO_2 was monitored continuously using a disposable oximeter sensor (Nellcor™ Neonatal-Adult SpO_2 sensor, Covidien, Mansfield, MA, USA) and a patient monitor (Intellivue MX800, Philips, Boeblingen, Germany), with recordings at a frequency of 1 Hz.

The intraoperative hemoglobin level (Hb; g/dL) was determined from the results of arterial blood gas analysis, which was routinely performed every one to two hours and at any other time clinically indicated. If Hb concentrations at 11:00 and 12:00 were 11 and 13 g/dL, respectively, then the Hb concentration was considered 11 g/dL before 11:00 and 13 g/dL from 11:00 to 12:00. As this assumption results in an unrealistic step-like Hb chart, a smoothing process using a 30-min window moving average (60 s × 30 min = 1,800 data points) was applied to construct a more realistic chart (Supplementary material 1).

Detailed information regarding the dataset from the institution B is summarized in Supplementary material 2.

Data pre-processing

The collected data were extracted at a frequency of 1 Hz and filtered for extreme and unreliable values based on the data distribution and clinical judgements, so that SpO_2 was ≥ 80%, SvO_2 was ≤ 90%, signal quality index was < 4 for SvO_2, SvO_2 was lower than SpO_2, inspired oxygen fraction was greater than expired oxygen fraction, the difference between inspired and expired oxygen fraction was ≥ 2% and ≤ 10%, MV was ≥ 2 and ≤ 10 L/min, the absolute difference between inspired and expired MV was ≤ 0.5 L/min, and CCO was ≥ 2 and ≤ 7 L/min. After these filtrations, all measured variables were averaged every 60 s, so that all parameters could be matched at each minute.

Data partitioning

After data preprocessing, we generated two distinct datasets: one for model derivation (training dataset) and another for validation (test dataset). To ensure balance in CO values and maintain proportionality between the institutions in the datasets, the data acquired from each institution were sorted based on mean CCO values. Subsequently, odd-numbered subjects were assigned to the training dataset, while even-numbered subjects were allocated to the test dataset.

Fick method

Initially, the original Fick equation was used without considering dissolved oxygen (CO-Fick; Eqs. 1–3):

$$VO_2(\mathrm{mL/min}) = 1000 \times \text{I-E } O_2(\%)/100 \times \mathrm{MV(L/min)} \quad (1)$$

$$\begin{aligned} AVO_2\text{-diff (mL/L)} = & 1.36 \times 10 \\ & \times \text{ Hb (g/dL)} \\ & \times \left(SpO_2 - -SvO_2\right)/100 \end{aligned} \quad (2)$$

$$\text{CO-Fick (L/min)} = VO_2/AVO_2\text{-diff} \quad (3)$$

where VO_2 is oxygen consumption, I-E O_2 is inspired–expired oxygen fraction, and AVO_2-diff is the difference in arteriovenous oxygen content.

Time adjustment

To compensate for the time delay of CCO [9, 11], we conducted a cross-correlation analysis between CCO and CO-Fick in the training dataset. This analysis involved matching varying degrees of time-shifted CCO values with real-time CO-Fick, and subsequently calculating the corresponding R squared (R^2) values. The time shift that resulted in the highest R^2 value was determined, and the mean value of these time shifts was applied to the test dataset. In other words, delayed values of CCO were matched with the real-time values of CO-Fick.

Resampling

To minimize potential bias arising from unequal lengths obtained from each subject, we conducted resampling with replacement (n = 250). The number of resampling iterations was determined based on the mean number of data points per subject. By applying this process, we aimed to create equal-length data points for each subject, thereby ensuring a more balanced and unbiased dataset for the subsequent analysis.

Modification of CO-Fick: CO-Fick-AD (adjusting denominator)

The modification of CO-Fick was based on the following finding: the deviation between CCO and CO-Fick increased as SvO_2 values increased (and as AVO_2-diff values decreased; Fig. 1). To address this issue, following modification to the Fick method was derived from the training dataset. The expected AVO_2-diff value (AVO_2-diff-e) was

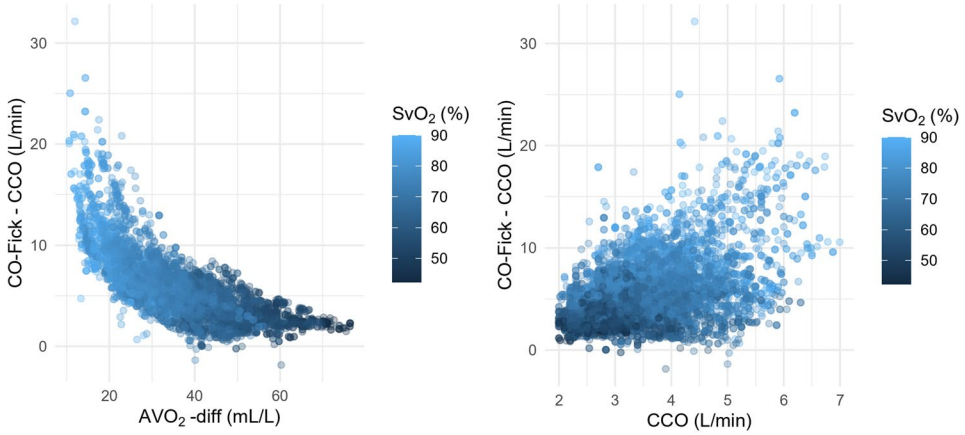

Fig. 1 Scatter plots showing the errors between cardiac output estimated by the Fick method (CO-Fick) and continuous thermodilution (CCO). The difference between CO-Fick and CCO increased as AVO_2-diff decreased (left), and CCO increased (right). Lighter colors of the points indicate higher mixed venous oxygen saturation (SvO_2, %) and lower oxygen extraction ratio. Note the scale difference between the axes. The figures were plotted using the training dataset

calculated based on CCO and VO_2 (AVO_2-diff-e = VO_2/CCO). The difference between AVO_2-diff-e and AVO_2-diff, called error-AVO_2-diff, was subsequently included in multivariable analyses with variables other than CCO (i.e., I-E O_2, MV, VO_2, and AVO_2-diff). Using a multivariable linear regression model derived from the former process, a modification called 'CO-Fick-AD (adjusting denominator)' was calculated, as shown in Eq. 4.

$$\text{CO-Fick-AD} = VO_2/(AVO_2\text{-diff} + \text{error - } AVO_2\text{-diff}) \quad (4)$$

Sensitivity analysis

Because the time delay between CCO and CO-Fick can vary widely among patients, and the degree of time adjustment may affect the results, sensitivity analysis was performed to examine the extent to which the results were affected by the adjustment. The entire analysis process (including model derivation) was repeated after individual time adjustments and without adjustments. For individual time adjustments, the time shifts with the highest R^2 value between CCO and CO-Fick in each case was applied individually.

Statistical analysis

Based on a literature review[17, 18], a sample size of 25 subjects per each dataset (training and test) was considered adequate for the current study. The data acquisition period was set to achieve this target sample size, and all feasible data were included in the analysis. All statistical analyses were performed using R software version 4.0.3 (R Project for Statistical Computing, Vienna, Austria). Continuous variables are reported as mean ± SD or as median (interquartile range [IQR]), depending on their distribution. Correlations between continuous variables were assessed using the Spearman's correlation coefficient. The errors between CO-Fick and CCO, as well as CO-Fick-AD and CCO, were quantified by calculating root mean square error (RMSE).

The mean biases, limits of agreement, and concordance correlation coefficients [19] between the new method and CCO were calculated using the R package 'SimplyAgree', which considered adjustment for repeated measurements per patient [20]. The concordance correlation coefficient was regarded as a comprehensive performance metric for a model that evaluates accuracy and precision at the same time. Percentage error was calculated as the limit of agreement divided by the mean CCO of the corresponding dataset [21].

Trending ability was assessed using four-quadrant plot analysis, with interval changes of 10 and 30 min. Two sizes of exclusion zones for changes in CO, < 0.5 L/min and < 1.0 L/min, were used to calculate concordance rates.

Results

Of the 107 enrolled patients (47 and 60 patients in each institution), 50 were excluded and 57 (28 and 29 in the institution A and B, respectively) were included in the final analysis. One patient with persistently high SvO_2 (> 95%) and 19 patients with insufficient hemoglobin data (intraoperative laboratory data frequency < 3) were excluded, despite not being prespecified exclusion criteria (Fig. 2). None of the patients had an equal or greater than moderate degree of tricuspid valve regurgitation in the entire dataset. The clinical characteristics and measurements of the training and test datasets are summarized in Table 1. A detailed comparison of the measurements of the datasets from the two institution is presented in Supplementary material 2.

A 6 min of time shift was applied to the CCO values in the test dataset according the cross-correlation analysis in the training dataset. As a result of multivariable analysis of

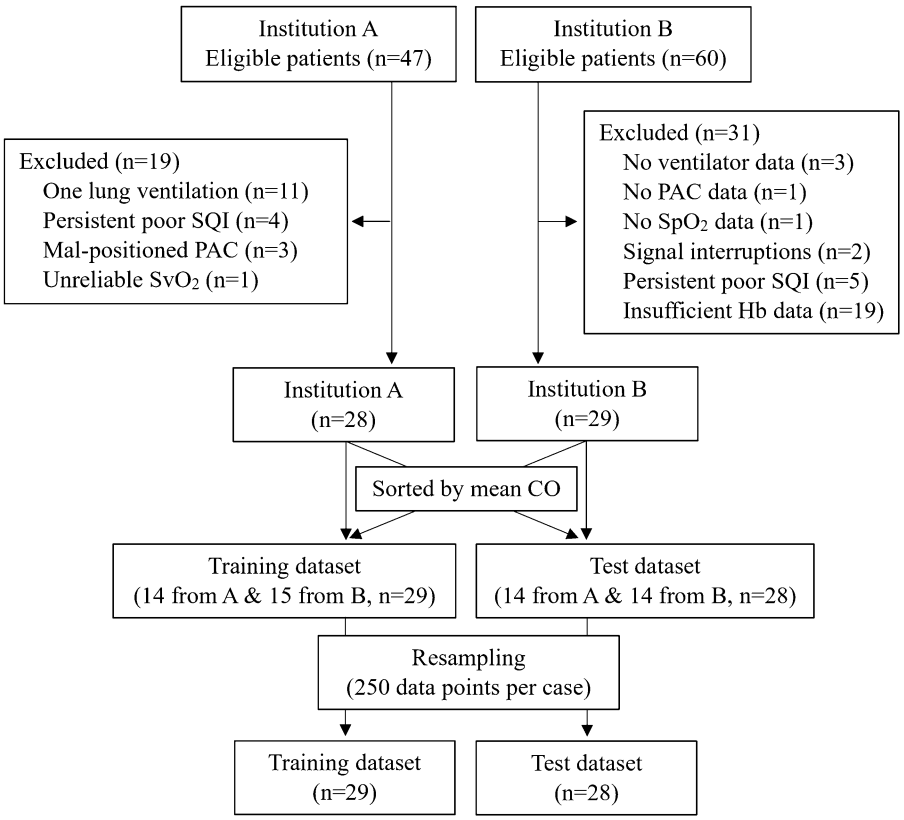

Fig. 2 Flow diagram of the patients. *PAC* pulmonary artery catheter, SpO_2 peripheral oxygen saturation, *SQI* signal quality index, SvO_2 mixed venous oxygen saturation, *Hb* hemoglobin concentration, *CO* cardiac output

the training dataset, a model for estimating error-AVO_2-diff was derived as Eq. 5, where Log_2CO-Fick denotes the binary logarithmic conversion of CO-Fick. The scale of the SvO_2 value was adjusted (divided by 100).

$$\begin{aligned}\text{Error-AVO}_2\text{-diff} &= 85.18 \times \text{Log}_2\text{CO-Fick} + 90.47 \\ &\times \text{SvO}_2/100 - 79.43 \times \text{Log}_2\text{CO-Fick} \\ &\times \text{SvO}_2/100 - 98.29\end{aligned} \tag{5}$$

The interaction term (Log_2CO-Fick × SvO_2/100) included in the equation signifies that the magnitude of the increase in error-AVO_2-diff associated with the increase in CO-Fick depends on SvO_2. Finally, the predicted error-AVO_2-diff from Eq. 5 was incorporated into Eq. 4 to calculate CO-Fick-AD. Detailed information regarding the derivation of the modification and a web-based calculation are presented in Supplementary Material 3.

A scatter plot illustrating the relationships between CCO and both CO-Fick and CO-Fick-AD are presented in Fig. 3. The RMSE of CO-Fick was decreased from 6.07 L/min to 0.70 L/min after the modification (CO-Fick-AD). The result of the Bland–Altman analysis of CO-Fick-AD in the test dataset are shown in Table 2 and Fig. 3. CO-Fick-AD showed a mean bias of 0.17 (95% CI, 0.00 to 0.34) L/min, with a 36.4% (95% CI, 30.6 to 44.4%) error. The concordance rates of CO-Fick-AD ranged from 73.3% to 87.1% depending on the time interval and exclusion zone (Fig. 4).

The results of the Bland–Altman analysis during sensitivity analysis are presented in Table 2. The analysis after individual time adjustment demonstrated minimal changes in bias and precision compared with the results after 6 min of time shift. The concordance rates also exhibited minimal changes after individual time adjustment, ranging from 74.5% to 87.6% depending on the time interval and exclusion zone. On the other hand, the analysis without time adjustment showed compromised performance, particularly in the short-term (10 min) interval trending ability (concordance rate of 59.7% and 60.8% with 0.5 L/min and 1.0 L/min exclusion zone).

Discussion

In this study, we aimed to address the considerable error observed in CO-Fick by introducing an adjustment in the denominator of the original equation. The results demonstrated that this adjustment effectively reduces the error with minimal bias. However, it is essential to acknowledge that despite this improvement, CO-Fick-AD

Table 1 Patient characteristics and measurements in the training and test datasets

Variables	Training ($n=29$, data points = 7250)	Test ($n=28$, data points = 7000)
Age (yr)	66.6 ± 9.1	67.5 ± 8.6
Sex (F)	8 (27.6)	3 (10.7)
Height (cm)	165.4 (156.0, 170.0)	167.3 (158.4, 170.9)
Weight (kg)	66.3 ± 8.4	67.8 ± 7.1
BMI (kg/m^2)	24.7 ± 2.5	25.1 ± 2.3
Record duration (min)[a]	267.3 ± 65.5	243.4 ± 52.4
CCO (L/min)	3.5 (3.0, 4.2)	3.6 (3.1, 4.2)
Hb (g/dL)	9.7 (8.7, 10.7)	10.3 (9.0, 11.3)
SvO_2 (%)	73.9 (65.9, 79.8)	74.2 (66.7, 80.5)
SpO_2 (%)	100.0 (100.0, 100.0)	100.0 (99.6, 100.0)
CaO_2 (mL/L)	131.7 (119.1, 145.5)	138.5 (122.4, 153.7)
CvO_2 (mL/L)	94.0 (79.4, 109.2)	101.1 (86.5, 121.5)
AVO_2-diff (mL/L)	35.4 (26.0, 45.5)	35.8 (26.8, 46.0)
Inspired O_2 fraction (%)	47.8 (37.4, 56.7)	47.6 (39.0, 57.9)
Expired O_2 fraction (%)	42.6 (32.0, 51.1)	42.6 (33.5, 53.2)
I-E O_2 (%)	5.4 (5.0, 6.0)	5.1 (4.8, 5.7)
MV (L/min)	5.6 (4.8, 6.4)	5.7 (4.8, 6.4)
VO_2 (mL/min)	307.3 (256.6, 353.6)	290.0 (239.0, 340.8)

Values are presented as count (%), mean ± SD, or median (IQR)

BMI body mass index, *CCO* continuous thermodilution cardiac output, *Hb* hemoglobin concentration, *SvO_2* mixed venous oxygen saturation, *SpO_2* peripheral oxygen saturation, *CaO_2* arterial oxygen content, *CvO_2* venous oxygen content, *AVO_2-diff* difference in arteriovenous oxygen content, *I-E O_2* inspired—expired oxygen fraction, *MV* minute ventilation, *VO_2* oxygen consumption

[a]The original length of the record before resampling. After resampling, each record was equalized to 250 data points (1 min per data point)

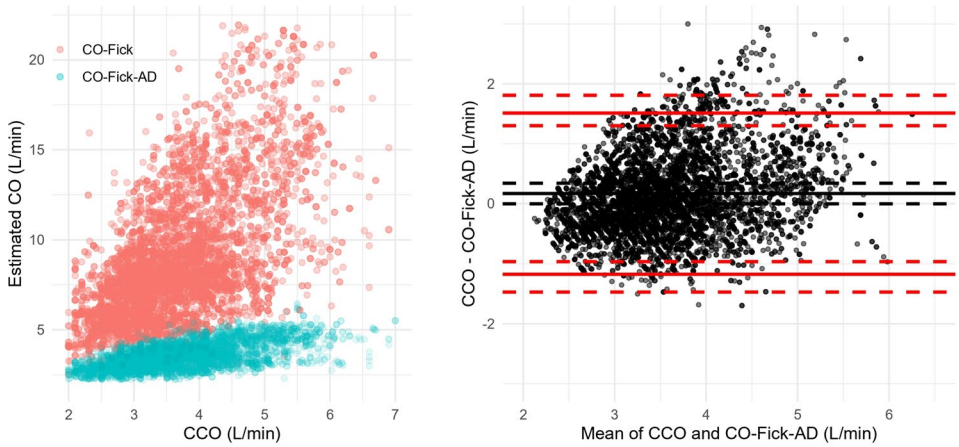

Fig. 3 Scatter plot (left) and Bland–Altman plot (right) showing decreased error between cardiac output estimated by the modified Fick method (CO-Fick-AD) and continuous thermodilution (CCO). The root mean squared error of CO-Fick was decreased from 6.07 L/min to 0.70 L/min after the modification (CO-Fick-AD). Note the scale difference between the axes of the scatter plot. Black and red solid lines in the Bland–Altman plot indicate mean bias and limits of agreement, respectively. Dashed lines indicate 95% confidence intervals of the corresponding parameters

did not reach the acceptable criteria of precision (percentage error < 30%)[21] and trending ability (concordance rate > 92%)[22]. This finding indicates that further refinements are necessary to enhance the performance of the method to be reliably used in clinical practice.

Table 2 Results of the modified Fick method (CO-Fick-AD), and sensitivity analysis in the test dataset

	Main analysis	Sensitivity analysis	
	CO-Fick-AD	No time adjustment	Individual time adjustment
CCC (95% CI)	0.593 (0.580, 0.605)	0.513 (0.499, 0.526)	0.601 (0.588, 0.613)
Mean bias, L/min (95% CI)	0.17 (0.00, 0.34)	0.18 (0.01, 0.34)	0.15 (–0.02, 0.33)
LOA-lower, L/min (95% CI)	− 1.17 (− 1.47, − 0.96)	− 1.24 (− 1.51, − 1.04)	− 1.18 (− 1.48, − 0.97)
LOA-upper, L/min (95% CI)	1.51 (1.30, 1.81)	1.59 (1.39, 1.87)	1.49 (1.28, 1.79)
% Error (95% CI)	36.4 (30.6, 44.4)	38.3 (32.9, 45.8)	36.2 (30.5, 44.2)

CO-Fick-AD modified version of CO-Fick using a term for adjusting denominator, *CCC* concordance correlation coefficient, *CI* confidence interval, *LOA* limit of agreement

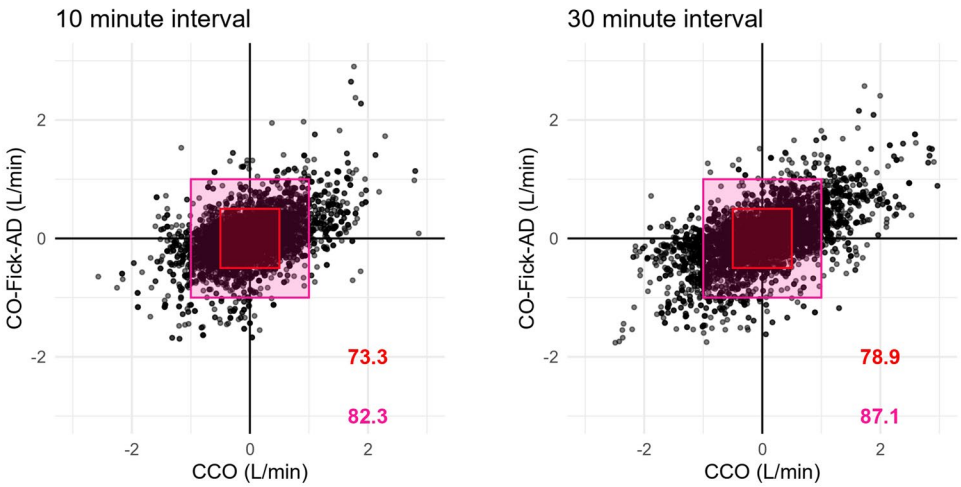

Fig. 4 Four-quadrant plots of cardiac output estimated by the modified Fick method (CO-Fick-AD) vs. continuous thermodilution (CCO) in the test dataset. Each axis indicates an interval change in the corresponding parameter. The red (inner) and pink (outer) rectangles indicate exclusion zones of 0.5 L/min and 1.0 L/min, respectively. The concordance rates (red and pink numbers) were calculated as the proportion of points in the first and third quadrants after excluding the central exclusion zone

For a new CO estimation method to be accepted, it should have a precision equivalent to that of the reference method. The combined precision of a reference and a test method can be calculated as $\sqrt{[(precision\ of\ reference)^2 + (precision\ of\ test\ method)^2]}$ [21]. A meta-analysis found that the pooled percentage error (i.e. combined precision) between continuous and intermittent thermodilution techniques was 29.7% [23], whereas the precision of the intermittent bolus thermodilution technique is regarded as 20% [21]; hence we assumed the precision of the CCO to be 20% ($\sqrt{20^2 + 20^2} = 28.3$). In this context, a 30% error was defined as the cut-off for interchangeability in this study. Although the precision of CO-Fick-AD could not meet this criterion, it is closer to the criterion than other conventional methods, which often showed percentage errors over 40%[24]. Additionally, there is an argument regarding the criterion of 30% being too strict to be met in a clinical context, with a suggestion of using 45% as an alternative [24]. Considering these context, CO-Fick-AD's performance becomes even more noteworthy, as it offers a promising alternative with improved precision and reduced bias.

Determining cardiac output is essential for determining the cause of hypotension as well as being a target for hemodynamic optimization [2]. Unfortunately, however, the determination of cardiac output is more complicated than measuring blood pressure. Various techniques have been developed, but none has replaced the intermittent bolus thermodilution technique [24, 25], which is still considered the gold standard for measuring CO [3, 4].

Although studies assessing methods for measuring CO have utilized the intermittent bolus thermodilution technique as the reference standard [26, 27], use of this method during the dynamic intraoperative period is cumbersome and susceptible to various sources of error [5], Moreover, this method is not compatible with continuous recording. The continuous thermodilution technique has been regarded as a good alternative to the intermittent bolus thermodilution technique [28], despite the time delay of the former [9–11]. The present study attempted

to overcome this time delay by applying a 6 min time adjustment.

The present study has highlighted the impact of oxygen, the indicator used in the Fick method, on inducing errors. Notably, when the indicator amount was limited, as indicated by a small AVO_2-diff, the Fick method exhibited a significant overestimation of CO, aligning with a prior finding by Lin et al. that reported increased errors in the presence of high inspired O_2 levels (> 0.85) and the resulting elevated SvO_2 [15]. However, it's important to note that the magnitude of error observed in our study surpassed the previous report, which can be attributed to several factors. First, our study calculated VO_2 using ventilator-derived variables, resulting in an average VO_2 of 168.6 ± 39.5 mL/min/m^2 (adjusted with body surface area), whereas the previous study employed the LaFarge equation, yielding VO_2 values of 158.8 ± 10.2 mL/min/m^2 in patients treated with conventional levels of inspired O_2 (< 0.7). Second, the previous study incorporated dissolved oxygen content into their CO-Fick calculation, a consideration omitted in our study. Based on their reported arterial and venous O_2 partial pressures, the dissolved oxygen content averaged 5.7 mL/L in patients receiving conventional levels of inspired O_2. When we incorporated this value into our calculations, the RMSE decreased from 6.07 L/min to 4.28 L/min. Third, while our intraoperative setting aligns with theirs, they conducted measurements before surgical incision, once a stable condition was achieved. This difference in the condition during measurement may also account for some of the discrepancies between our study and previous laboratory findings [29, 30]. Furthermore, it's worth noting that previous laboratory studies demonstrating high accuracy of the Fick method typically operated within lower ranges of SvO_2, whereas in our study, elevated SvO_2 levels emerged as a major source of error.

One of the strengths of this study was the inclusion of the datasets from two different institutions. Because the variables included in the newly derived modification can be sensitive to institutional factors such as ventilator type and settings and anesthetic protocols, this inclusion was crucial for deriving a more generalizable modification. Specifically, VO_2 and SvO_2 differed between the two institutions, perhaps due to differences in the type of anesthetic agent used [31, 32]. Patients in the institution A were anaesthetized with the inhalation agent sevoflurane, whereas those in the institution B were anesthetized with the intravenous agent propofol. Additionally, other factors such as the depth of anesthesia, opioid dose, and administration of vasopressors and/or inotropes could have contributed to the observed differences.

The current study had several limitations. First, the hemoglobin levels used in these analyses were not measured in real-time but were concentrations based on intermittently measured laboratory results. As laboratory tests in normal clinical practice can be performed only at intervals, errors due to this process were unavoidable. Refinement with more accurate data would yield a more reliable method. Alternatively, continuous noninvasive hemoglobin monitoring (SpHb, Masimo, Irvine, CA, USA) [33] may overcome this limitation. Second, the use of newly derived method can be limited when hemoglobin levels fluctuate, or laboratory tests are not readily available. Third, the present study did not explicitly evaluate the effects of dead space ventilation [34] and pulmonary oxygen consumption [14]. Fourth, the model was based only on data acquired from patients undergoing OPCAB surgery, indicating the need to test this model in patients undergoing other types of surgery. Fifth, the new method still needs an invasive measurement, SvO_2, thereby hampers its clinical utility over CCO. However, it can serve as a supplement or a suitable alternative to CCO in cases where the usage or fidelity of CCO is limited, such as in tricuspid regurgitation. Moreover, the new method could pave the way for future noninvasive modalities that utilize the Fick principle.

In conclusion, the modification of the Fick method can aid in the continuous estimation of cardiac output during the dynamic intraoperative period with minimal bias. However, this method requires further improvements in precision and trending ability.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00540-023-03260-x.

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Data availability The data that support the findings of this study are available from the corresponding author upon a reasonable request.

Declarations

Conflict of interest No potential conflict of interest relevant to this article was reported.

References

1. Meng L, Wang Y, Zhang L, McDonagh DL. Heterogeneity and variability in pressure autoregulation of organ blood flow: lessons learned over 100+ years. Crit Care Med. 2019;47:436–48.
2. Meng L. Heterogeneous impact of hypotension on organ perfusion and outcomes: a narrative review. Br J Anaesth. 2021;127:845–61.
3. Argueta EE, Paniagua D. Thermodilution cardiac output: a concept over 250 years in the making. Cardiol Rev. 2019;27:138–44.
4. Drummond KE, Murphy E. Minimally invasive cardiac output monitors. Contin Educ Anaesth Crit Care Pain. 2012;12:5–10.

5. Nadeau S, Noble WH. Limitations of cardiac output measurements by thermodilution. Can Anaesth Soc J. 1986;33:780–4.
6. Bootsma IT, Boerma EC, Scheeren TWL, de Lange F. The contemporary pulmonary artery catheter. Part 2: measurements, limitations, and clinical applications. J Clin Monit Comput. 2022;36:17–31.
7. Medin DL, Brown DT, Wesley R, Cunnion RE, Ognibene FP. Validation of continuous thermodilution cardiac output in critically ill patients with analysis of systematic errors. J Crit Care. 1998;13:184–9.
8. Sun Q, Rogiers P, Pauwels D, Vincent JL. Comparison of continuous thermodilution and bolus cardiac output measurements in septic shock. Intensive Care Med. 2002;28:1276–80.
9. Aranada M, Mihm Frederick G, Garrett S, Mihm Megan N, Pearl RG. Continuous cardiac output catheters: delay in in vitro response time after controlled flow changes. Anesthesiology. 1998;89:1592–5.
10. Lazor MA, Pierce ET, Stanley GD, Cass JL, Halpern EF, Bode RH Jr. Evaluation of the accuracy and response time of STAT-mode continuous cardiac output. J Cardiothorac Vasc Anesth. 1997;11:432–6.
11. Siegel LC, Hennessy MM, Pearl RG. Delayed time response of the continuous cardiac output pulmonary artery catheter. Anesth Analg. 1996;83:1173–7.
12. Seely RD, Nerlich WE, Gregg DE. A comparison of cardiac output determined by the fick procedure and a direct method using the rotameter. Circulation. 1950;1:1261–6.
13. Visscher MB, Johnson JA. The fick principle: analysis of potential errors in its conventional application. J Appl Physiol. 1985;1953(5):635–8.
14. Light RB. Intrapulmonary oxygen consumption in experimental pneumococcal pneumonia. J Appl Physiol. 1985;1988(64):2490–5.
15. Lin SY, Chang FC, Lin JR, Chou AH, Tsai YF, Liao CC, Tsai HI, Chen CY. Increased FIO2 influences SvO2 interpretation and accuracy of Fick-based cardiac output assessment in cardiac surgery patients: a prospective randomized study. Medicine (Baltimore). 2021;100: e27020.
16. Lee HC, Jung CW. Vital Recorder-a free research tool for automatic recording of high-resolution time-synchronised physiological data from multiple anaesthesia devices. Sci Rep. 2018;8:1527.
17. Truijen J, Westerhof BE, Kim YS, Stok WJ, de Mol BA, Preckel B, Hollmann MW, van Lieshout JJ. The effect of haemodynamic and peripheral vascular variability on cardiac output monitoring: thermodilution and non-invasive pulse contour cardiac output during cardiothoracic surgery. Anaesthesia. 2018;73:1489–99.
18. Montenij LJ, Buhre WF, Jansen JR, Kruitwagen CL, de Waal EE. Methodology of method comparison studies evaluating the validity of cardiac output monitors: a stepwise approach and checklist. Br J Anaesth. 2016;116:750–8.
19. Carrasco JL, King TS, Chinchilli VM. The concordance correlation coefficient for repeated measures estimated by variance components. J Biopharm Stat. 2009;19:90–105.
20. Zou GY. Confidence interval estimation for the Bland-Altman limits of agreement with multiple observations per individual. Stat Methods Med Res. 2013;22:630–42.
21. Critchley LA, Critchley JA. A meta-analysis of studies using bias and precision statistics to compare cardiac output measurement techniques. J Clin Monit Comput. 1999;15:85–91.
22. Critchley LA, Lee A, Ho AMH. A critical review of the ability of continuous cardiac output monitors to measure trends in cardiac output. Anesth Analg. 2010;111:1180–92.
23. Kouz K, Michard F, Bergholz A, Vokuhl C, Briesenick L, Hoppe P, Flick M, Schön G, Saugel B. Agreement between continuous and intermittent pulmonary artery thermodilution for cardiac output measurement in perioperative and intensive care medicine: a systematic review and meta-analysis. Crit Care. 2021;25:125.
24. Peyton PJ, Chong SW. Minimally invasive measurement of cardiac output during surgery and critical care: a meta-analysis of accuracy and precision. Anesthesiology. 2010;113:1220–35.
25. Saugel B, Hoppe P, Nicklas JY, Kouz K, Körner A, Hempel JC, Vos JJ, Schön G, Scheeren TWL. Continuous noninvasive pulse wave analysis using finger cuff technologies for arterial blood pressure and cardiac output monitoring in perioperative and intensive care medicine: a systematic review and meta-analysis. Br J Anaesth. 2020;125:25–37.
26. Kusaka Y, Ohchi F, Minami T. Evaluation of the fourth-generation FloTrac/Vigileo system in comparison with the intermittent bolus thermodilution method in patients undergoing cardiac surgery. J Cardiothorac Vasc Anesth. 2019;33:953–60.
27. Maeda T, Hamaguchi E, Kubo N, Shimokawa A, Kanazawa H, Ohnishi Y. The accuracy and trending ability of cardiac index measured by the fourth-generation FloTrac/Vigileo system™ and the Fick method in cardiac surgery patients. J Clin Monit Comput. 2019;33:767–76.
28. de Lange F, Bootsma IT, Boerma EC. Letter to the editor in response to "Agreement between continuous and intermittent pulmonary artery thermodilution for cardiac output measurement in perioperative and intensive care medicine: a systematic review and meta-analysis." Crit Care. 2021;25:215.
29. Nakanishi N, Yoshioka T, Okano Y, Nishimura T. Continuous Fick cardiac output measurement during exercise by monitoring of mixed venous oxygen saturation and oxygen uptake. Chest. 1993;104:419–26.
30. Hoeper MM, Maier R, Tongers J, Niedermeyer J, Hohlfeld JM, Hamm M, Fabel H. Determination of cardiac output by the Fick method, thermodilution, and acetylene rebreathing in pulmonary hypertension. Am J Respir Crit Care Med. 1999;160:535–41.
31. Liao R, Li J, Liu J. Volatile induction/maintenance of anaesthesia with sevoflurane increases jugular venous oxygen saturation and lumbar cerebrospinal fluid pressure in patients undergoing craniotomy. Eur J Anaesthesiol. 2010;27:369–76.
32. Jeong H, Jeong S, Lim Hoi J, Lee J, Yoo KY. Cerebral oxygen saturation measured by near-infrared spectroscopy and jugular venous bulb oxygen saturation during arthroscopic shoulder surgery in beach chair position under sevoflurane-nitrous oxide or propofol-remifentanil anesthesia. Anesthesiology. 2012;116:1047–56.
33. Barker SJ, Shander A, Ramsay MA. Continuous noninvasive hemoglobin monitoring: a measured response to a critical review. Anesth Analg. 2016;122:565–72.
34. Ritchie-McLean S, Shankar R. Calculating oxygen consumption during low-flow anaesthesia. Anaesthesia. 2017;72:789.