Original Article

Is Noninvasive Continuous Cardiac Output Technique Based on Pulse Wave Transit Time Applicable in Cardiac Output Monitoring during Thoracic Aortic Aneurysm Surgery?

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ABSTRACT

Introduction: The present study compared the precision of estimated continuous cardiac output (esCCO) and the use of a pulmonary artery catheter (PAC) in continuous measurement of cardiac output (paCCO) in total arch replacement (TAR).

Methods: Cardiac output was measured continuously, using esCCO and paCCO, for 24 h from the time of arrival in the operating room until admission to the intensive care unit (ICU). Continuous cardiac output measurements obtained using the above devices were compared using Bland-Altman analysis to evaluate bias, precision, and percent error (%error) and four-quadrant plots to evaluate the concordance rate.

Results: The examination of 17 patients was held at 3 setting points: starting anesthesia to before cardiopulmonary bypass (pre-CPB), after CPB to the end of surgery (post-CPB), and after ICU admission (ICU). Data were obtained at 2,513, 2,426, and 23,533 points, respectively. Bias ± precision of esCCO to paCCO was −0.24 ± 0.88 L/min, 0.22 ± 1.42 L/min, 0.61 ± 0.84 L/min and % error was 48%, 56%, and 44% respectively. The concordance rate of four-quadrant plot was 64.9%, 68.0%, 73.8% respectively.

Conclusions: When we have compared compatibility, concordance, and trending ability of esCCO to paCCO in pre-CPB, post-CPB, and ICU, it is difficult to estimate cardiac output with esCCO during TAR. The results might have been influenced by direct effects on the cardiac contraction associated with surgical procedures, and changes in the physical properties of vascular elasticity with vascular prosthesis implantation.

esCCO failed to track changes on Cardiac output (CO) adequately during TAR.

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KEYWORDS: esCCO, cardiac output, pulmonary artery catheter, total arch replacement surgery

1. Introduction

Cardiac output (CO) is an important indicator in cardiovascular management during cardiovascular surgery. Measurement of CO based on thermodilution, using a pulmonary artery catheter (PAC), is now a standard method.[1)]

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However, in many clinical studies, CO measurement using a PAC has not improved outcomes in patients with severe conditions.[2–5] Furthermore, the risk of complications associated with PAC insertion, such as arrhythmia, pulmonary artery injury, infection, and thrombus formation, and the cost of a PAC itself, have led to a reduction in its use.[6, 7] These issues have led to the clinical introduction of various alternative methods of CO measurement that are less invasive or noninvasive.[8]

Estimated continuous cardiac output (esCCO) is a method of measuring CO using pulse wave transit time (PWTT). This method enables noninvasive, continuous measurement of CO using basic parameters under general anesthesia. PWTT, which is the length of time between the electrocardiogram R wave and the upstroke of the plethysmogram wave in percutaneous oxygen saturation (SpO_2) monitoring, is a completely noninvasive method for measuring CO.[9, 10]

Several studies have compared the precision of thermodilution-based intermittent CO (ICO) and esCCO measurements and have proven that these devices were interchangeable[11–13] in various surgical settings and postoperative ICU settings. However, very few studies have compared esCCO and continuous CO measurements using a pulmonary artery catheter (paCCO) using continuous and simultaneous measurements in cardiac surgery[14] especially during thoracic aortic surgeries.

Therefore, selecting adult patients scheduled to undergo total arch replacement (TAR) as subjects, the present study examined changes in the concordance and trending ability of esCCO and paCCO before and after cardiopulmonary bypass (CPB) and on admission to the intensive care unit (ICU).

2. Methods

2.1 Patients

The research protocol and consent form for the present study were approved by the Kawasaki Saiwai Hospital Institutional Review Board (application number, 29-04) and registered with the UMIN Clinical Trials Registry prior to the start of the study (UMIN000030441). Informed consent was obtained from all patients prior to their participation in the study.

The subjects comprised patients who met the following inclusion criteria: scheduled to undergo TAR, an American Society of Anesthesiologists Physical Status class 2-3, age ≥ 18 years, and scheduled to undergo PAC insertion. The exclusion criteria were as follows: persistent arrhythmia, low cardiac function (ejection fraction [EF] ≤ 35%), severe aortic regurgitation, and severe tricuspid valve regurgitation.

2.2 Monitoring and anesthesia

As standard monitoring during general anesthesia, after starting monitoring with an electrocardiogram (ECG) and SpO_2 monitor (BSM-9101, Nihon Kohden, Tokyo, Japan), we secured a 22-G peripheral arterial pressure line (A-line) through the right radial artery and a 16-G peripheral venous line (V-line) through the left forearm. In the ECG monitoring, we used lead II. A pulse oximeter probe was attached to the patient's fingertip of right hand. Body temperature was measured in terms of bladder and tympanic temperature.

After confirming that hemodynamics were stable and initiating oxygen administration, we induced general anesthesia using fentanyl (1-3 μg/kg), propofol (1-2.5 mg/kg), and rocuronium (0.6-0.9 mg/kg). We performed intubation and inserted a transesophageal echocardiography (TEE) probe (Hitachi, Tokyo, Japan). Subsequently, we inserted an 8.5-Fr central venous catheter (Edwards oximetry central venous catheter™) and 7.5-Fr PAC (Swan-Ganz™ CCO/CEDV thermodilution catheter, Edwards Lifesciences, CA, USA) through the right internal jugular vein, and we confirmed that the tip of the PAC was positioned at the entrance of the right pulmonary artery in the pressure waveform[6] and TEE.[15] Body temperature was measured in terms of bladder and tympanic temperature in the operating room, and only bladder temperature was measured in the ICU.

Anesthesia was maintained with sevoflurane 1.0-3.0 vol% and fentanyl 1-3 μg/kg/h. Mechanical ventilation conditions were as follows: F_IO_2 0.4-0.5, tidal volume 7-8 mL/kg, ventilation frequency 10-15 times/min, and positive end-expiratory pressure 4-8 cmH_2O. Fluid transfusion volume and administration of vasopressors/antihypertensive drugs were according to the discretion of the attending anesthesiologist and the cardiothoracic surgeon. Vascutek Triplex® grafts (Terumo, Scotland, UK) were used as vascular prostheses.

2.3 Measurements, data collection, and patient management

Signals for ECG, SpO_2, and arterial blood pressure were recorded from the monitor (BSM-9101, Nihon Kohden, Tokyo, Japan) to a recording terminal, while esCCO was calculated post-processing. esCCO was corrected after induc-

tion of anesthesia and ICU admission based on arterial pressure values obtained from the A-line. We connected the PAC to a Vigilance II™ monitor (Edwards Lifesciences, CA, USA) and recorded paCCO measurements. Data was collected from the start of surgery to before the start of CPB (pre-CPB), from weaning from CPB to completion of surgery (post-CPB), and from ICU admission to 6:00 AM the following day (ICU). Systemic vascular resistance (SVR) during each data collection period was calculated as follows: SVR = (MAP−CVP) × 79.992/paCCO.

2.3.1 Start of surgery until initiation of CPB (Pre-CPB)

Medical monitors were attached to patients, and recording of biological information for determining esCCO started after arterial cannula insertion. Measurement continued until just before the start of CPB.

2.3.2 During CPB (suspension of CO measurement)

Once CPB was started, body temperature was set to moderate hypothermia. The target temperatures for deep hypothermic cardiac arrest were set at ≤ 25.0℃ for the bladder and ≤ 20.0℃ for the tympanic membrane.

2.3.3 Weaning from CPB to end of TAR (post-CPB)

Once the target temperature (36.0℃) was confirmed, patients were weaned from CPB. At this point, measurement of esCCO and paCCO was resumed. After surgery, esCCO and paCCO measurements were suspended, and patients were transferred to the ICU as mechanical ventilation was continued.

2.3.4 After ICU admission (ICU)

Monitoring (ECG, SpO_2, arterial blood pressure, central venous pressure, and pulmonary artery pressure) was resumed immediately after ICU admission (BSM-9101). The PAC was connected to the Vigilance II™ monitor, and paCCO measurement was resumed. The use of vasopressors/antihypertensive drugs, fluid transfusion, and blood transfusion were based on the discretion of the attending cardiothoracic surgeon. Propofol was administered until before the patients were weaned from mechanical ventilation (6:00 AM the following day).

2.4 Statistical analysis

The concordance and compatibility of esCCO and paCCO measurements were analyzed using a Bland-Altman plot. The trending ability of esCCO in regard to paCCO was assessed using a four-quadrant plot of ΔesCCO in relation to ΔpaCCO. With the Bland-Altman analysis, in accordance with a report by Critchley and Critchley,[16] we determined and assessed the bias (mean of the difference) and precision (standard deviation (SD) of the difference) of the reference paCCO and esCCO. The paired t-test was conducted in relation to mean paCCO and mean esCCO value at pre-CPB, post-CPB and ICU. The precision was corrected for repeated measures.[17] A P-value less than 5% was considered to be significant. Moreover, % error was calculated as (2 × precision) / (mean paCCO), with a result ≤ 30% considered to constitute reliability. The 95% limits of agreement (LOA) show the range demonstrated by bias ± 2 × precision. The trending ability of esCCO in relation to paCCO was assessed using four-quadrant plots with the exclusion zones defined as a reference CO of 0.5-1.0 L/min or 10-15% change in CO.[18, 19] A concordance rate of ≥ 90% to 95% indicated reliability. Regarding trending ability, to assess precision (r) and accuracy (C_b), we calculated the concordance correlation coefficient (CCC) (CCC = r × C_b). CCCs that are closer to 1 represent higher concordance.[20] In the assessment of the trending ability of esCCO in relation to paCCO, delays in paCCO must be considered. In the present study, delay in paCCO was corrected using moving averages of waveforms (supplement).

The sample size was calculated with a test with the alpha error set at 5% and power set at 80%. In the Bland-Altman analysis, bias (mean of the difference) was set at 0.18 L/min in a pilot study of five patients, the maximum value was adopted, and the difference of the population mean was set at ± 0.3 L/min. The maximum precision (SD) for each patient was 1.07 L/min. Based on an SD of 1.07 L/min and a significant difference of 0.3, we calculated that we would need at least 102 points as a sample size. Measurements of paCCO involved delays of 5-15 min.[21] Therefore, when assessing trending ability, we determined data using moving averages with 25-min intervals. The mean operative time in the five patients of the pilot study was 8 h. During this time, paCCO could be measured for 2 h 55 min. Therefore, we determined that 149 points could be obtained intraoperatively for a single patient. Data were shown as mean ± SD or, when necessary, as median (interquartile range). Statistical analysis was performed using Microsoft Excel 2010® (Microsoft Corporation, VA, USA).

3. Results

The present study was conducted from October 2017 to April 2018. Of 21 potential subjects who were scheduled to undergo TAR, four were excluded from the study. Three of these patients presented with persistent paroxysmal atrial fibrillation once they entered the operating room,

Table 1 Patient characteristics

Number of patients	17
Gender (Male/Female)	15/2
Age (years)	74.2 ± 9.3
Height (cm)	163.9 ± 8.8
Weight (kg)	64.5 ± 14.1
BSA (m^2)	1.69 ± 0.2
BMI	23.6 ± 4.3
Type of surgery	
TAR	15
TAR + CABG	2
Measurement duration (min)	
Operation time	364.2 ± 71.6
Anesthesia time	459.2 ± 99.9
CPB time	232.3 ± 55.5
Rewarming time	117.6 ± 30.2
DHCA	65.4 ± 19.4
Temeprature (℃)	
During DHCA	
Tympanic	19.6 ± 1.3
Bladder	22.7 ± 1.4
at the end of surgery	35.9 ± 0.3
Infusion amount (ml)	
Crystalloid + Colloid	1461 ± 409.2
Transfusion	1807 ± 556.9

Data are expressed as number of patients or mean ± SD, as appropriate.
BSA: body surface area; BMI: body mass index
TAR: total arch replacement; CABG: coronary artery bypass grafting
CPB: cardiopulmonary bypass; DHCA: deep hypothermic cardiac arrest; OR: operating room

while one patient presented with pulmonary artery injury following CPB. Pulmonary artery injury was conceivably caused by either surgical maneuvers or advancement of the PAC. However, we could not identify the cause.

Characteristics of the patients in the present study are shown in Table 1.

From the 17 subjects, we obtained 2,513 data points pre-CPB, 2,426 points post-CPB, and 23,533 data points in the ICU. Mean paCCO and mean esCCO were 3.64 L/min, 3.40 L/min on pre-CPB, 5.04 L/min, 5.26 L/min on post-CPB and 3.85 L/min and 4.46 L/min on ICU respectively and P-value was ≤ 0.01 at 3 setting points.

We used obtained data points to conduct Bland-Altman analysis, in which we calculated bias, precision, 95% LOA, and % error in the pre-CPB, post-CPB, and ICU periods (Fig. 1). The bias was −0.24 L/min, 0.22 L/min, 0.61 L/min, and precision was 0.88 L/min, 1.42 L/min, and 0.84 L/min in pre-CPB, post-CPB and ICU respectively. The lower and upper 95%LOA for paCCO and esCCO was −2.00 and 1.52 L/min, 2.62 and 3.06 L/min, −1.08 and 2.30 L/min in pre-CPB, post-CPB, and ICU, respectively. Furthermore, % error was 48%, 56%, and 44% accordingly at the 3 setting points. In four-quadrant plots, in pre-CPB, post-CPB, and ICU, there were 368, 412, and 1,410 data points, respectively, that served as subjects for analysis. The concordance rates were 64.9%, 68.0%, and 73.8%, respectively, while the CCCs were 0.282, 0.275, and 0.245, respectively (Fig. 2).

The only correlation observed between esCCO and SVR was a weak correlation in the pre-CPB period (pre-CPB, r = 0.22; post-CPB, r = 0.03; ICU, r = 0.06).

4. Discussion

In the data collection periods before, during, and after TAR in the present study, there was little compatibility between paCCO and esCCO and concordance, and the trending ability was low in these devices. The trending ability was especially low in the post-CPB period. In surgeries such as TAR, in which the surgical procedure extends directly to the heart and vascular prosthesis implantation can change the physical properties of the aorta and peripheral arteries, the accuracy of CO measurement was shown to be low with devices such as esCCO that uses PWTT. This result was likely due to continued measurement after performing correction only once after starting measurement.

In the Bland-Altman plot, Critchley et al.[17] reported that clinical use is permissible when 95% LOA was 1 L/min and % error was less than 30%. In the present study, both 95% LOA were higher and percentage error was > 30% at pre-CPB, post-CPB, and ICU periods, meaning that compatibility between the two devices was not high.

In the four-quadrant plots, the concordance rates in the pre-CPB, post-CPB, and ICU periods were 64.9%, 68.0%, and 73.8%, respectively. When the exclusion zone is 0.5-1.0 L/min or 15%, a concordance rate of > 90-95% is considered to constitute reliability.[19] Under both of the above conditions, the trending ability in the present study was considered low. Magliocca et al. assessed the trending ability using CCCs.[21] In the present study, CCCs in the pre-CPB, post-CPB, and ICU periods were 0.282, 0.275, and 0.245, respectively. All of these were low, indicating the trending ability was also low.

esCCO is a noninvasive method of measuring CO that

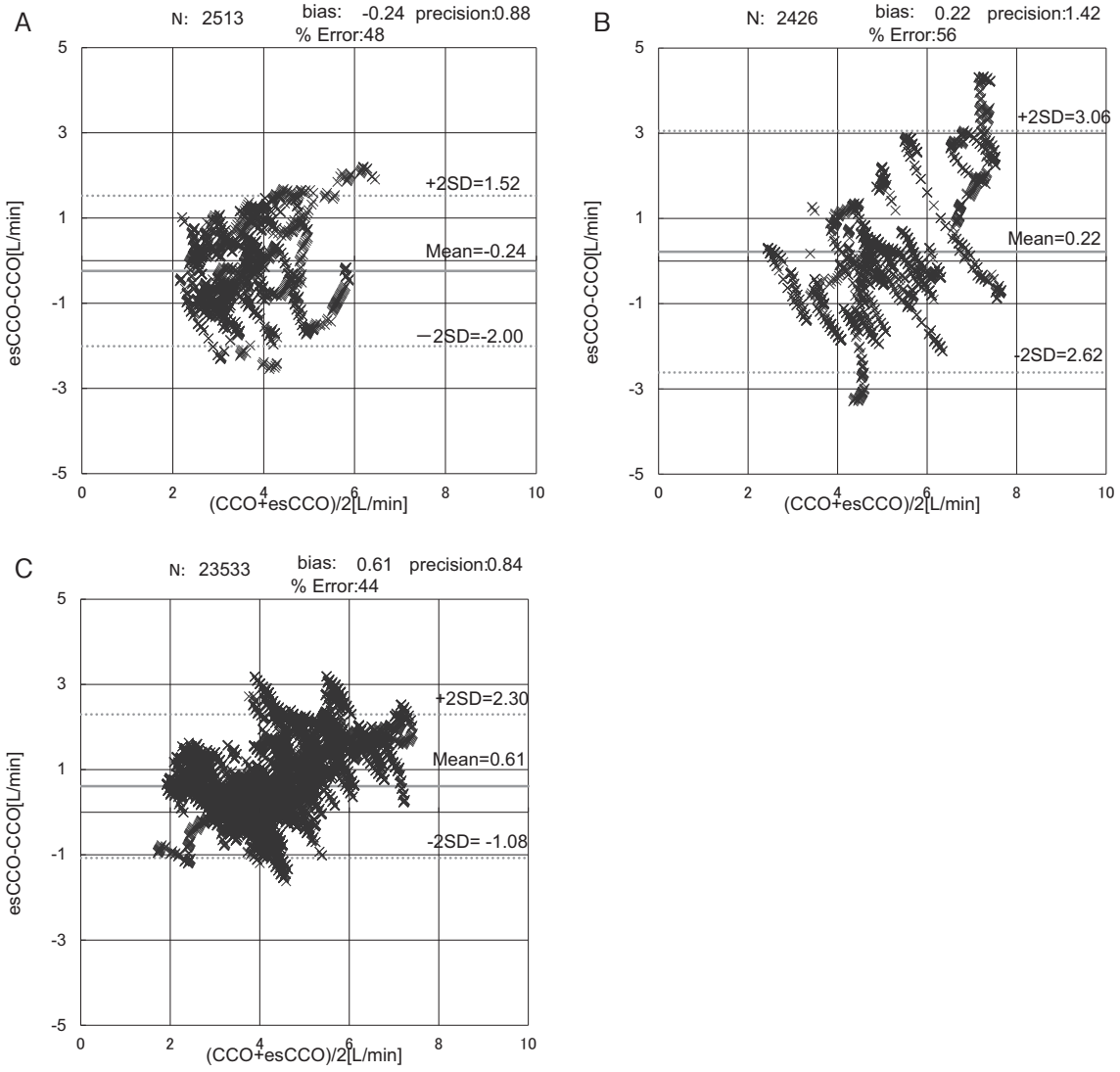

Fig. 1 Bland-Altman plots of paCCO and esCCO data
A. Pre-CPB: n = 2513, bias = −0.24 L/min, precision = 0.88, % error = 48%
B. Post-CPB: n = 2426, bias = 0.22 L/min, precision = 1.42 L/min, % error = 56%
C. ICU: n = 23533, bias = 0.61 L/min, precision = 0.84 L/min, % error = 44%

uses conventional monitoring techniques. PWTT is composed of the pre-ejection period (PEP), PWTT1, and PWTT2. PEP refers to the period prior to myocardial contraction; PWTT1 refers to aortic transit time, which reflects the physical characteristics of the great vessels; and PWTT2 refers to peripheral artery transit time, which reflects vascular properties of peripheral arteries (Fig. 3).[22]

Blood vessels are classified primarily as elastic and myogenic blood vessels. Elastic blood vessels are large in diameter and located near the heart, whereas myogenic blood vessels are peripherally located.[23] The aorta, which was replaced in TAR in the present study, is an elastic blood vessel that has multiple elastic laminae in its tunica media and possesses a Windkessel function, in which the vessel itself has a buffering capacity. This function is generally considered to reduce cardiac afterload and enables efficient contraction. Replacement of a proximal blood vessel with a prosthesis, such as in TAR, can change blood vessel elasticity and affect afterload,[24] resulting in changes in the characteristics of pulse wave transit.

The PEP, which represents the time from the onset of the ECG Q wave to the opening of the aortic valve, includes the time from the onset of the Q wave to the closure of the mitral valve and the isovolumetric contraction phase. As reported in a previous study, PEP has been shown to change in the same manner as isovolumetric con-

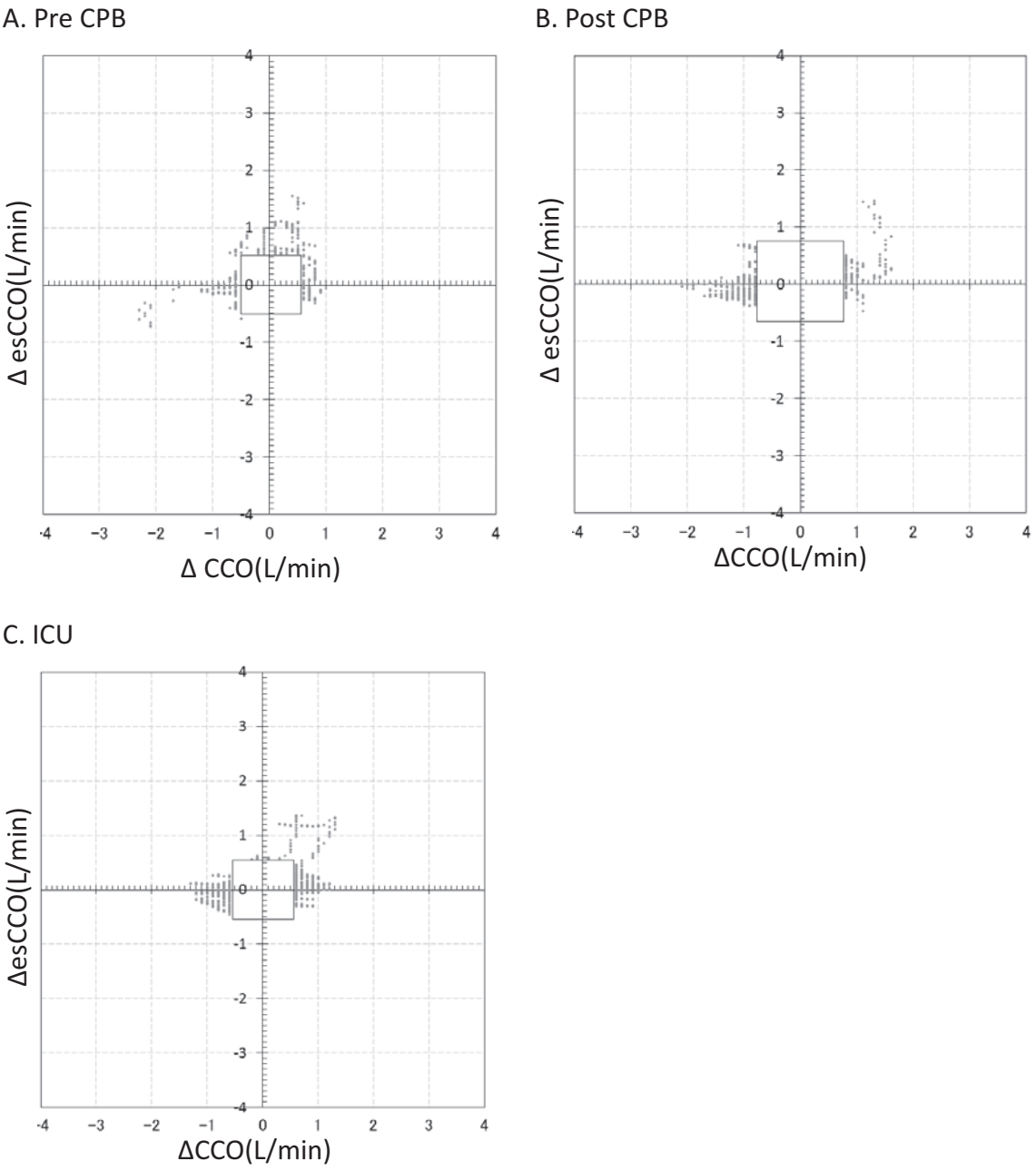

Fig. 2 Trending ability of esCCO compared with that of paCCO (four-quadrant plot)
A. Pre-CPB: exclusion zone = 0.55 L/min
B. Post-CPB: exclusion zone = 0.77 L/min
C. ICU: exclusion zone = 0.57 L/min

traction pressure, and increases or decreases in afterload are equivalent to increases and decreases in isovolumetric contraction pressure.[25] Therefore, as blood vessel prostheses increase the compliance of the great vessels, increased afterload increases isovolumetric contraction pressure, which may consequently prolong the isovolumetric contraction phase and PEP. It is conceivable that PEP was prolonged in this manner, thereby affecting esCCO measurements.

Then, as for the post-vascular prosthesis implantation effect on PWTT1, because the esCCO parameter K is calibrated using pulse pressure, changes in aortic elastance may have resulted in changes in K, thereby affecting esCCO measurements in the post-CPB period.

However, PWTT2 is considered to change due to SVR. In a previous study,[20] the bias of both esCCO and ICO

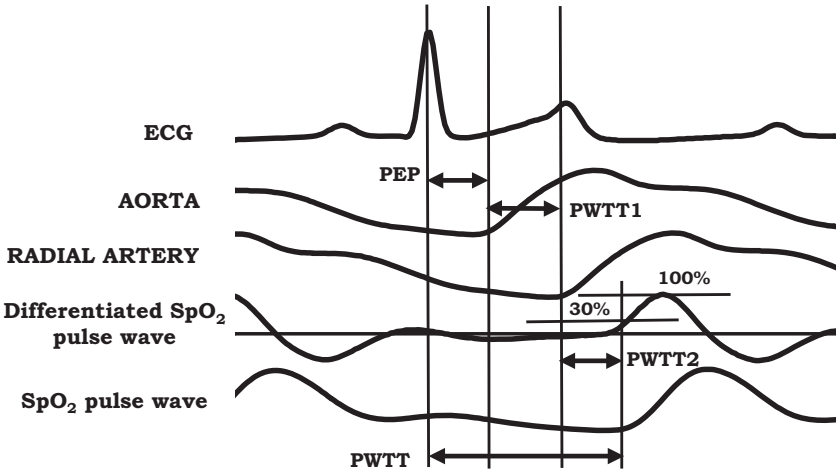

Fig. 3 Relationship of the time-related components of PWTT
PWTT = PEP + PWTT1 + PWTT2
PWTT: pulse wave transit time
PEP: pre-ejection period
SpO2: plethysmographic waveform of pulse oximetry

demonstrated correlations with SVR (r = 0.61), indicating that reduced SVR reduces the accuracy of esCCO measurements. Although we performed a similar comparison in the present study, only a weak correlation (r = 0.22) was observed in the pre-CPB period. In the post-CPB and ICU periods, the correlation coefficients were 0.03 and 0.06, respectively, thus demonstrating that SVR did not have a pronounced effect. The large effect on K may have obscured the effect of changes in SVR on esCCO in TAR.

Lastly, in the present study, esCCO and paCCO were calibrated only before surgery and after ICU admission. A study that compared the PiCCO® system (Getinge Group, Tokyo, Japan) and PAC revealed that CO can be assessed more accurately by correcting 1 h after the initial correction.[26] Further studies regarding the timing of correction may be necessary.

5. Conclusions

The present study assessed the concordance and compatibility between esCCO and paCCO and trending ability of esCCO in relation to paCCO. Despite of our estimation, concordance, compatibility, and trending ability were low, conceivably due to the measurement accuracy of esCCO during TAR. Results may have been influenced by direct effects on the cardiac contraction associated with operation, and changes in the physical properties of vascular elasticity with vascular prosthesis implantation. It suggests that esCCO failed to adequately track CO changes. Therefore, esCCO is not useful to measure continuous CO in TAR.

Supplement: Adjusting for delays in paCCO using moving averages

We calculated the moving average of a simulated waveform. In previous studies, values displayed by paCCO were delayed 5-15 min after actual changes in CO. In an experiment using sheep, the length of time required for paCCO to reflect 80% of rapid CO change was 14.5 ± 4.1 min, whereas the required length of time for this change to be displayed by a simultaneously used ultrasonic flow probe, which is considered to be capable of immediately reflecting changes in CO, was 1.8 ± 0.9 min[22]. If esCCO is assumed to be similarly capable of instant response, the response time of paCCO would be 14.4-1.8 = 12.6 min. If the optimal interval of moving average time yields 1 data point per minute, the interval can be calculated as 25 min. When assessing the trending ability of esCCO and paCCO, calculating simple moving averages of esCCO in 25-min intervals could minimize the effect of delays in paCCO.

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Authors' contributions: R.O.: Study design and writing the first draft of the paper

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