

Performance of Noninvasive Partial CO_2 Rebreathing Cardiac Output and Continuous Thermodilution Cardiac Output in Patients Undergoing Aortic Reconstruction Surgery

Yoshifumi Kotake, M.D.,* Kiyoshi Moriyama, M.D.,* Yasushi Innami, M.D.,* Hideyuki Shimizu, M.D.,† Toshihiko Ueda, M.D.,‡ Hiroshi Morisaki, M.D.,§ Junzo Takeda, M.D.‖

Background: **In the partial CO_2 rebreathing method, monitored changes in CO_2 elimination and end-tidal CO_2 in response to a brief rebreathing period are used to estimate cardiac output. However, dynamic changes in CO_2 production during ischemia and reperfusion may affect the accuracy of these estimates. This study was designed to compare measurements of cardiac output as produced by the partial CO_2 rebreathing (NICO), bolus (BCO), and continuous thermodilution (CCO) methods of monitoring cardiac output.**

Methods: **Cardiac output was continuously monitored using both NICO and CCO in 28 patients undergoing aortic reconstruction. BCO measurements were taken at the following intervals when hemodynamic stability was achieved: (1) after anesthetic induction; (2) during aortic cross-clamp; (3) at reperfusion of the iliac artery; and, (4) during peritoneal closure.**

Results: **The bias and precision (1 SD) derived from all the measurements between NICO and BCO was −0.58 ± 0.9 l/min, whereas for CCO and BCO it was 0.38 ± 1.17 l/min. The bias between NICO and BCO was small after anesthetic induction and during cross-clamp, but increased following reperfusion. The bias between CCO and BCO was relatively small until reperfusion but increased significantly at peritoneal closure.**

Conclusions: **Results indicate that in aortic reconstruction surgery the performance of NICO monitoring is comparable with that of CCO; however, the direction of bias in these continuous measurement devices is the opposite.**

MAINTAINING optimal cardiac output results in improved outcomes and therefore is an important goal of intraoperative hemodynamic management.[1–3] However, the pulmonary artery catheter, which is used as a reference method to measure cardiac output, is invasive, and several investigations report less favorable outcomes associated with its use.[4–7] To address this problem, several less invasive and continuous cardiac output monitoring methods were developed, such as transesophageal Doppler, arterial pulse contour analysis, thoracic bioimpedance, and partial CO_2 rebreathing.[8] Of these methods, the partial CO_2 rebreathing method offers several advantages as an intraoperative monitor, including noninvasiveness, nonreliance on operator skill, and resistance to electromagnetic interference. However, the accuracy and clinical applicability of the Noninvasive Cardiac Output Monitor (NICO, Novametrix Medical Systems, Wallingford, CT) has not been fully evaluated. This system uses changes in CO_2 elimination and end-tidal CO_2 measured in response to a brief rebreathing period to calculate pulmonary blood flow. Because the NICO system relies on stable CO_2 production and a constant Et_{CO_2}-Pa_{CO_2} gradient during the measurements,[9,10] the dynamic changes in CO_2 production during ischemia and reperfusion that characterize patients undergoing aortic reconstruction may affect the accuracy of this method. We designed this prospective study to compare the accuracy of the NICO monitor and continuous thermodilution cardiac output *versus* standard bolus thermodilution in patients undergoing aortic reconstruction surgery.

Materials and Methods

After institutional review board approval, 28 patients undergoing elective aortic reconstruction for infrarenal abdominal aortic aneurysm were enrolled in this study when their informed consent was obtained. Anesthetic management was standardized in these patients as follows. After epidural catheterization at the Th10/11 or 11/12 interspace, anesthesia was induced with intravenous fentanyl and propofol and maintained with sevoflurane inhalation with or without nitrous oxide. Patients were paralyzed with vecuronium and mechanically ventilated with either the AS/3 ADU (Datex-Ohmeda, Helsinki, Finland) or KION (Siemens, Solna, Sweden) anesthesia machine. Tidal volume and respiratory rate were initially set at 10 ml/kg and 10 breaths per minute, respectively, and were adjusted to maintain Pa_{CO_2} at 35–45 mmHg. After tracheal intubation, cardiac output was continuously monitored using the NICO monitor (software version 3.1). Cardiac output data obtained with the NICO in average mode were downloaded to a computer for analysis. The NICO sensor was placed distal to the heat and moisture exchanger (Hygrobac S, DAR-Mallinckrodt, Mirandola, Italy). Meticulous attention was paid to maintenance of adequate rebreathing circuit volume during monitoring. An 8-French pulmonary artery catheter (746HF8, Baxter Healthcare, Irvine,

* Instructor, § Assistant Professor, ‖ Professor and Chairman, Department of Anesthesiology, † Instructor, ‡ Assistant Professor, Department of Cardiovascular Surgery, Keio University.

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Address reprint requests to Dr. Kotake: Department of Anesthesiology, Keio University School of Medicine, 35 Shinanomachi, Shinjuku, Tokyo, 160-8582, Japan. Address electronic mail to: ykotake@sc.itc.keio.ac.jp. Individual reprints may be purchased through the Journal Web site, www.anesthesiology.org.

Table 1. Demographic and Operative Data

Age, y	71.7 ± 7.9
Gender, M/F	21/7
Height, cm	161 ± 9
Weight, kg	59 ± 9
Body surface area, m^2	1.61 ± 0.17
Duration of surgery, min	252 ± 66
Duration of aortic cross-clamp, min	61 ± 14

Data are expressed as mean ± SD.

CA) was inserted *via* the right internal jugular vein. Continuous thermodilution cardiac output (CCO) and mixed venous oxygen saturation were continuously monitored with a Vigilance monitor (Baxter Healthcare, Irvine, CA). The calibration of mixed venous oxygen saturation and subsequent blood gas analysis were performed using a standard blood gas analyzer with Cooximeter (Stat Profile M, Nova Biochemicals, Waltham, MA). These data were downloaded to another computer every 30 s, and data averaged for 3 min before bolus thermodilution cardiac output (BCO) measurement were used for analysis. Fluid administration, blood transfusion, epidural injection of local anesthetics, administration of inotropic and vasodilatory drugs, and other anesthetic management procedures were performed at the discretion of the attending anesthesiologist.

BCO measurements were made at the following predetermined time points: (1) after anesthetic induction (Postinduction); (2) during aortic cross-clamping (XC); (3) at reperfusion of unilateral iliac artery (Declamp); and (4) during peritoneal closure (Endop). The injection of ice-cold saline was repeated four times within 3 min and averaged data were used for analysis. These BCO measurements were performed following the stabilization of intravascular fluid status and cardiac performance. This period was arbitrarily defined as being at least 5 min, during which there was no fluid challenge or change in pharmacologic intervention. Blood gas analysis data were input to the NICO monitor before each BCO measurement to allow precise estimations of shunt fraction and NICO values. At each BCO measurement, the shunt fraction was calculated using the standard formula (see Appendix).

NICO monitoring was terminated postoperatively, but CCO monitoring was continued during the postoperative period in some patients when clinically indicated. After patients were fully awake and showed stable hemodynamics and acceptable ventilation and oxygenation, they were extubated in the operating room before being transferred to the intensive care unit.

Data are expressed as mean ± SD and were statistically analyzed using the Statview 5.0 software (SAS Institute, Chicago, IL). Correlations between NICO and BCO data and between CCO and BCO data sets were determined by linear regression. A Bland-Altman plot was used to compare the bias (the mean of the differences) and precision (SD of bias) of NICO and CCO against BCO.[11] In addition, the relative error (expressed in %) was defined as 100*([either NICO or CCO–BCO]/BCO).[12] Intraoperative changes in other parameters were analyzed using a one-way ANOVA with repeated measurements. A value of $P < 0.05$ was considered significant. Multiple comparisons with Scheffé correction were performed when significant changes were detected.

Results

Demographic and operative data are summarized in table 1. Intraoperative cardiac output as measured by NICO, CCO, and BCO; other variables are summarized in table 2. The interval between the aortic cross-clamp and

Table 2. Intraoperative Data at Four Operative Stages

	Postinduction	XC	Declamp	Endop
HR, bpm	62 ± 13	64 ± 14	72 ± 12	75 ± 13
Systolic BP, mmHg	99 ± 14	118 ± 22	128 ± 23	121 ± 19
Diastolic BP, mmHg	56 ± 11	56 ± 11	57 ± 12	58 ± 10
NICO, l/min	3.7 ± 1.5	3.6 ± 1.7	4.2 ± 1.0	4.7 ± 1.4
CCO, l/min	3.9 ± 1.3	4.4 ± 1.6	5.5 ± 1.6	6.4 ± 2.5
BCO, l/min	3.7 ± 1.1	4.1 ± 1.5	5.3 ± 1.1*	5.6 ± 1.2*
P/F ratio, mmHg	460 ± 86	358 ± 113	371 ± 96*	375 ± 96*
Qs/Qt, %	11 ± 5	11 ± 5	12 ± 5	16 ± 10*
$Paco_2$, mmHg	41.3 ± 5.7	41.1 ± 5.1	44.9 ± 5.2*	41.7 ± 4.0
$PETCO_2$, mmHg	33.6 ± 4.6	30.6 ± 5.4	36.4 ± 4.7	34.6 ± 5.0
Da-et CO_2, mmHg	7.4 ± 4.9	10.5 ± 4.8	9.0 ± 5.6	7.1 ± 4.4
Vco_2, ml/min	108 ± 29	102 ± 27	129 ± 32*	131 ± 30*
Svo_2, %	81 ± 7	79 ± 7	79 ± 6	82 ± 7
Bladder temp. °C	35.8 ± 0.5	35.1 ± 0.6	35.1 ± 0.6	35.6 ± 0.7

Data are collected from 28 patients and expressed as mean ± SD. P/F ratio: Pao_2/Fio_2.

* $P < 0.05$ *vs.* after anesthetic induction. $P < 0.05$ vs. unilateral iliac reperfusion and peritoneal closure. Qs/Qt was calculated using the following equation: Qs/Qt = $(Cco_2 \cdot Cao_2)/(Cco_2 \cdot Cvo_2)$*100.

BCO, CCO, and NCO = bolus thermodilution, continuous thermodilution, and noninvasive cardiac output; Cco_2, Cao_2, and Cvo_2 = oxygen content of capillary, arterial, and mixed venous blood, respectively; Da-$etco_2$ = difference between $Paco_2$ and $PETCO_2$; declamp = at reperfusion of unilateral iliac artery; endop = during peritoneal closure; postinduction = after anesthetic induction; XC = during aortic cross-clamping.

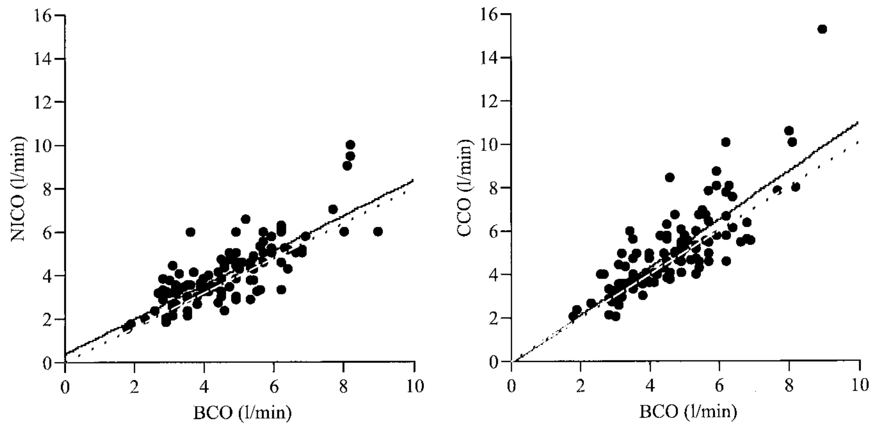

Fig. 1. Scatter plot of individual NICO and bolus thermodilution (BCO) values (*left*) and continuous thermodilution (CCO) and BCO values (*right*). Values from both CCO monitors significantly correlated with BCO (NICO = 0.80 * BCO + 0.35, r = 0.80) and with CCO (CCO = 1.11 * BCO − 0.14, r = 0.81). *Filled line* = correlation line; *dotted line* = line of identity.

the second measurement (XC), and the aortic declamp and the third measurement (Declamp) were 17 ± 5 and 20 ± 6 min, respectively. Overall correlations between NICO and BCO and CCO and BCO are expressed in figure 1. These data show that both NICO and CCO measurements correlated significantly with BCO, and that the correlation coefficients were remarkably similar (r = 0.80 and 0.81, respectively). Figure 2 shows the Bland-Altman plots of NICO and CCO against BCO. Overall, the bias and precision between NICO and BCO was −0.58 ± 0.90 l/min. The bias and precision between CCO and BCO for all measurements was 0.38 ± 1.17 l/min. These data show that NICO underestimated cardiac output, whereas CCO overestimated cardiac output, when compared with BCO measurements.

A comparison of bias and precision of both NICO and CCO against BCO at four intraoperative stages during aortic reconstruction is shown in table 3. The bias between NICO and BCO was small before cross-clamping, but increased following aortic cross-clamp and peaked after reperfusion of the unilateral iliac artery. However, the precision of the data remained within the same range. The bias and precision of CCO against BCO was comparable with that of NICO after anesthetic induction, and remained low during the aortic cross-clamp and early reperfusion periods. At the end of surgery, however, CCO overestimated cardiac output by 0.72 l/min and the deviation was larger than that observed in the NICO system. The relative error for all measurements as compared with BCO was −11.5 ± 19.4% for NICO and 8.2 ± 23.0% for CCO. Among the total number of measurements (n = 112), 20 NICO measurements and 18 CCO readings exceeded the relative error by 30%. The time-dependent change of the relative error is summarized in table 3. Figure 3 shows the relationship between the bias of NICO against BCO and four other parameters with the potential to affect the precision of NICO measurements: Pa_{CO_2}–Pet CO_2 difference, P/F ratio, V_{CO_2}, and shunt fraction (Qs/Qt). The data indicate that deviations in these parameters did not directly account for the differences between NICO and BCO because no specific trend was noted in the relationship between the bias and the value of these parameters.

Discussion

This study had four main findings. The first was that the NICO monitor provides a reasonably accurate overall estimate of cardiac output. The second finding, however, was that the NICO system experienced decreases in accuracy following aortic cross-clamping and declamping and that it consistently underestimated cardiac output as compared with BCO. The third finding was that, overall, in terms of bias and precision, NICO and CCO methods are comparable relative to BCO. The fourth finding was that analyses of the Pa_{CO_2}–P_{ETCO_2} difference, P/F ratio, V_{CO_2} and shunt fraction showed that none of these parameters could account for the increased bias in NICO estimates of cardiac output following reperfusion.

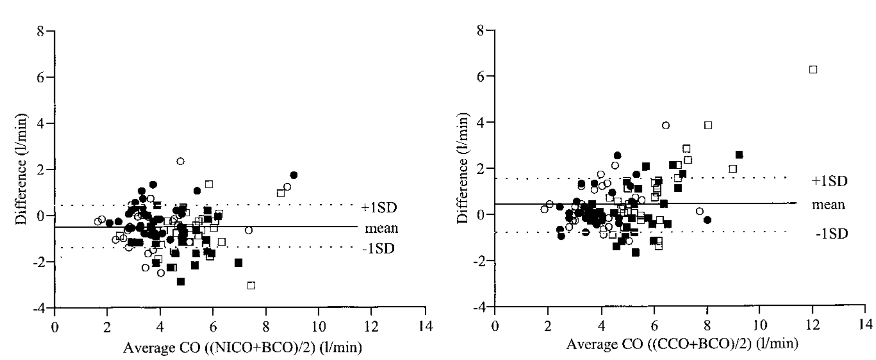

Fig. 2. Bland-Altman plot of cardiac output measurements from bolus thermodilution (BCO) and NICO (*left*) and from BCO and continuous thermodilution (CCO) (*right*). *Filled circle* = after anesthetic induction (Postinduction); *open circle* = during aortic cross-clamping (XC); *filled box* = at reperfusion of unilateral iliac artery (Declamp); *open box* = during peritoneal closure (Endop). n = 28 measurements in each stage; total = 112 measurements. Results show that NICO has a tendency to underestimate BCO, whereas CCO has a tendency to overestimate BCO.

Table 3. Bias, Precision and Relative Error of NICO and CCO against BCO at Four Operative Stages

	Postinduction	XC	Declamp	Endop
Bias ± precision, l/min				
NICO	−0.1 ± 0.61	−0.52 ± 0.95	−0.99 ± 0.86*	−0.72 ± 0.97*
CCO	0.23 ± 0.81	0.37 ± 1.05	0.2 ± 1.12	0.72 ± 1.57*
Relative error, %				
NICO	−1.2 ± 18.3	−11.1 ± 23.9	−19.1 ± 15.1	−14.9 ± 15.2
CCO	6.7 ± 23.4	10.9 ± 26.2	3.5 ± 19.6	12.1 ± 22.7

Data were collected from 28 patients and expressed as bias ± precision (1 SD of bias). Differences against BCO were statistically analyzed with repeated measure ANOVA. Relative error (%) is defined as [either (NICO or CCO) − BCO]/BCO and expressed in mean ± SD and is not subject to statistical analysis.

* $P < 0.05$ *vs.* after anesthetic induction.

BCO, CCO, and NCO = bolus thermodilution, continuous thermodilution, and noninvasive cardiac output; declamp = at reperfusion of unilateral iliac artery; Endop = during peritoneal closure; Postinduction = after anesthetic induction; XC = during aortic cross-clamping.

The NICO monitor uses the differential CO_2 Fick partial rebreathing method[9,10] to measure pulmonary capillary blood flow noninvasively and continuously in mechanically ventilated patients. The NICO algorithm is predicated on the following assumptions: (1) a stable CO_2 dissociation curve to convert P_{ETCO_2} to Ca_{CO_2}; (2) constant mixed venous CO_2 content; (3) constant dead space; and (4) stable pulmonary capillary blood flow during the measurement cycle. In addition to calculating cardiac output, it is necessary to estimate the shunt fraction correctly using Nunn's isoshunt plots by entering hemoglobin, Pa_{O_2}, and Pa_{CO_2} values. This device requires minimal operator experience and is not subject to electromagnetic interference during surgery. These characteristics suggest clinical advantages to the use of this device, but only a limited number of studies regarding the accuracy of the NICO monitor have been conducted.[13–17]

In our study, the agreement between NICO and CCO after anesthetic induction (−0.1 ± 0.61 l/min) was comparable with these previous findings, and we suggest that NICO provides an accurate estimate of cardiac output in stable conditions. However, the reports cited above did not specifically address the accuracy of the NICO monitor in the context of intraoperative events. This prompted us to investigate how aortic cross-clamping and declamping affect the accuracy of NICO monitoring and we found that bias increased significantly after aortic cross-clamp release.

Several factors are implicated in the difference between NICO and thermodilution cardiac output monitoring. Tachibana *et al.* reported a bias and precision of 0.28 ± 2.04 l/min during large tidal ventilation, but more discrepant results (−1.6 ± 2.24 l/min) during low tidal ventilation.[16] They speculated that slower changes in CO_2 stored in the body and decreased mixed venous

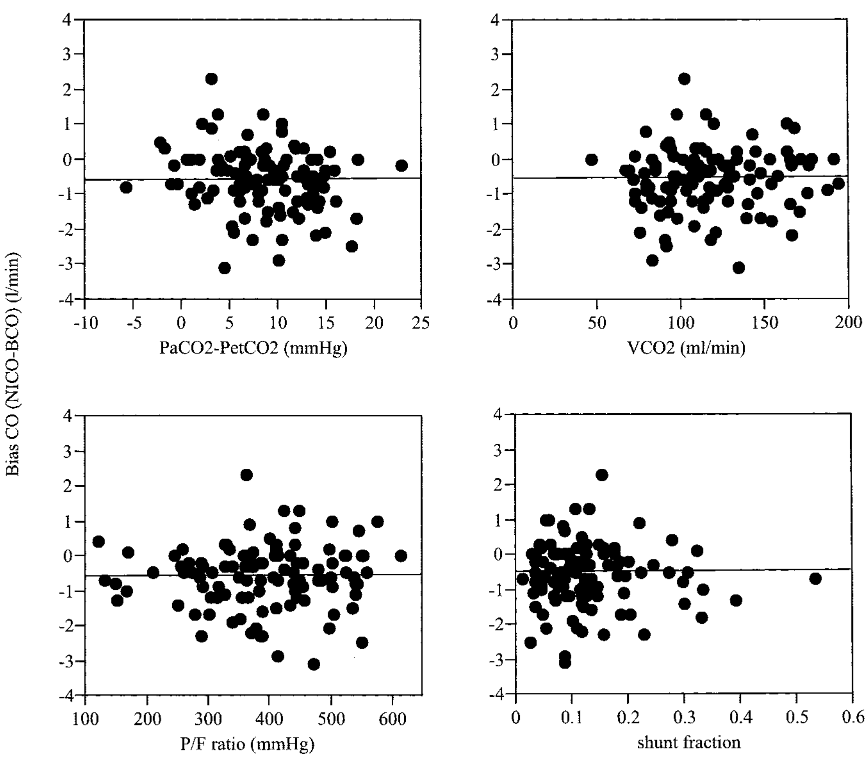

Fig. 3. Scatter plot between changes of four potentially significant parameters (Pa_{CO_2}–Pet CO_2 difference, P/F ratio, V_{CO_2}, and shunt) and bias of NICO monitoring compared with bolus thermodilution (BCO). No significant relationship was found between these changes in these parameters and the bias between NICO and BCO.

CO_2 content following the decrease in tidal volume result in increased bias.[16] It is conceivable that the increased bias immediately following reperfusion may be caused by an abrupt increase in $\dot{V}CO_2$ that cause similar effects to decreasing tidal volume. However, this mechanism may not fully account for our finding because the measurement was performed after $\dot{V}CO_2$ had stabilized. Alternatively, subclinical pulmonary dysfunction might negatively affect estimates of the shunt fraction and, consequently, of cardiac output. Maxwell *et al.* used a porcine model of severe chest trauma and hemorrhagic shock in an experimental setting to compare the performance of the NICO monitor with CCO.[15] In that study, bias and precision was reported as 0.01 ± 0.69 l/min. In addition, Odenstedt *et al.* reported good agreement between NICO and both CCO and BCO (bias ± 1 SD, −0.04 ± 1.72 l/min) in critically ill patients, although they noted significant underestimation of shunt fraction and $\dot{V}CO_2$.[17] Although pulmonary oxygenation remains relatively stable during surgery, subclinical pulmonary dysfunction, especially increased dead space caused by ischemia–reperfusion, may contribute to the increase in bias. However, in our study no factor could be singled out to account for the increase in bias in NICO measurements after reperfusion. We speculate that relatively acute changes in $\dot{V}CO_2$ and mixed venous CO_2 content persisting more than 15 min after reperfusion may be responsible for the underestimation of cardiac output as measured by the NICO monitor after aortic declamping. Alterations in pulmonary dead space and intrapulmonary shunt not reflected in the blood gas analysis may also contribute to this change. In addition, intraoperative fluctuations in such parameters as pH, temperature, hemoglobin concentration $\dot{V}CO_2$, dead space, and shunt can also be potential sources of error. Further study is obviously needed to clarify which factors influence the accuracy of NICO after reperfusion.

Comparisons between NICO and other continuous cardiac output monitoring systems provide clinically relevant information about the usefulness of NICO, which, all other considerations aside, is important because continuous and automatic monitoring is preferable in a clinical setting. Previous investigations report the bias and precision between CCO and BCO as 0.49 ± 1.01, 0.12 ± 0.84, and 0.40 ± 1.26 l/min, respectively, in either the Baxter Vigilance or Abbott Opti-Q system (Abbott, Chicago, IL).[18–20] Our data show a comparable degree of agreement between CCO and BCO. Although we are not able to specifically address the reason of increased bias of CCO at the end of surgery, increased cardiac output during this period may account for the increased bias of CCO.[21]

In regard to patient outcome, the routine use of pulmonary artery catheters in aortic surgery is associated with conflicting results. Berlauk *et al.* report that preoperative hemodynamic optimization through the use of pulmonary artery catheters improved outcome in atherosclerotic aortic occlusive disease patients.[22] On the contrary, Valentine *et al.* concluded that the routine use of pulmonary artery catheters is not beneficial and may be associated with a higher rate of intraoperative complications.[6]

These conclusions prompted us to investigate whether monitoring cardiac output using less invasive methods is adequate for intraoperative monitoring during elective aortic surgery. Several studies demonstrate that the monitoring of cardiac output and related parameters during aortic cross-clamping provides clinically useful information. For example, it has been shown that changes in cardiac output and CO_2 production during aortic cross-clamping are a predictor of hypotension at declamping.[23] Whalley *et al.* reported that the increase in systemic vascular resistance during aortic cross-clamping positively correlated with a base deficit after reperfusion.[24] These findings indicate that cardiac output and systemic vascular resistance, which can be monitored by NICO and the central venous catheter, may make it possible to predict declamping shock and take preventive measures. However, NICO cannot provide information regarding intravascular fluid status and may not be useful in the guidance of intraoperative fluid administration for patients with significant cardiac or pulmonary dysfunction. In this regard, it cannot be recommended as a replacement for pulmonary artery catheter monitoring.

In conclusion, it was determined that NICO provides an accurate estimate of cardiac output after anesthetic induction but underestimates cardiac output after aortic cross-clamping and declamping. Changes in $\dot{V}CO_2$ and subsequent total body CO_2 content change may be responsible for this bias. CCO shows a relatively smaller degree of bias than NICO but overestimates cardiac output at the end of the surgery. The performance of NICO is comparable with CCO in this clinical setting, and we believe that with cautious evaluation of data NICO may prove to be useful during elective aortic reconstruction surgery.

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Appendix: Calculation of Parameters

Shunt fraction = $(Cc_{O_2} - Ca_{O_2}) / (Cc_{O_2} - Cv_{O_2})$.

$Cc_{O_2} = ([Hb] * 1.39) + PA_{O_2} * 0.031$.

$Ca_{O_2} = 1.39 * Sa_{O_2}\ [Hb] + 0.0031 * Pa_{O_2}$.

$Cv_{O_2} = 1.39 * Sv_{O_2} * [Hb] + 0.0031 * Pv_{O_2}$.

$PA_{O_2} = Fi_{O_2}(P_B - P_{H_2O}) - Pa_{CO_2} / R$.

Where $P_B = 760$, $P_{H_2O} = 47$, $R = 0.8$.

Ca_{O_2} = oxygen content of arterial blood; Cc_{O_2} = oxygen content of pulmonary capillary blood; Cv_{O_2} = oxygen content of mixed venous blood; Fi_{O_2} = fraction of inhaled oxygen concentration; Hb = blood hemoglobin concentration; Pa_{CO_2} = carbon dioxide partial pressure of arterial blood; PA_{O_2} = oxygen partial pressure of alveolar gas; Pa_{O_2} = oxygen partial pressure of arterial blood; P_B = barometric pressure; P_{H_2O} = partial pressure of water vapor; Pv_{O_2} = oxygen partial pressure of mixed venous blood; R = respiratory quotient.