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Perioperative Cardiac Output Monitoring Utilizing Non-pulse Contour Methods

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Abstract
Purpose of Review The purpose of this review was to provide an overview of the recent concepts regarding cardiac output measurement devices that utilize non-pulse contour methods, especially in an intraoperative setting. The techniques include inert gas rebreathing method, partial CO_2 rebreathing method, impedance cardiography, and its derivative technologies such as electrical velocimetry and bioreactance, transesophageal echocardiography/Doppler, and transthoracic echocardiography/Doppler. We focused on the invasiveness of the devices and their underlying technology.
Recent Findings Although various types of cardiac output monitoring devices are available, none of them may be considered as an ideal device in terms of accuracy, trending ability of cardiac output changes, and reproducibility of measurements. There are increasing types of devices applicable for intraoperative use, yet only few data are available regarding the trending ability of cardiac output changes and reproducibility of the measurements. Therefore, the empirical application of these devices for various surgical patients may be done under the consideration of their invasiveness and their underlying technology, and it may provide us with more data over time.
Summary The non-pulse contour-derived cardiac output measurement devices are classified according to their underlying principles, which closely reflect their advantages and disadvantages in the perioperative setting.

Keywords Cardiac output · Hemodynamic monitoring · Intraoperative monitoring · Complications · Non-invasive · Non-pulse contour

Introduction

Cardiac output (CO) monitoring devices are used for detecting hemodynamic changes and guiding further therapy in both perioperative and postoperative periods. Perioperative CO monitoring has the potential benefits of reducing morbidity and mortality by optimizing perioperative fluid management. Less invasive CO monitoring devices are emerging as substitutes to the more invasive pulmonary artery catheterization (PAC). PAC is increasingly being avoided owing to its invasiveness [1]. The potential benefits of PAC are offset by its complications, which may also be responsible for the failure of PAC-based CO optimization in improving outcomes [2]. As the decision-making process in medical practice involves balancing the benefits and risks, the disadvantages of the various monitoring methods should be considered when adopting devices into clinical practice. The possible risks of CO monitoring devices are invasiveness, cost, and inaccuracy. Inaccuracy may result in incorrect decision-making owing to an incorrect interpretation of a situation (Fig. 1) Different monitoring devices have their own advantages and limitations related to their underlying technology. In this monograph, we classified and reviewed intraoperative non-pulse contour CO monitoring devices according to (1) their invasiveness and (2) their underlying technology.

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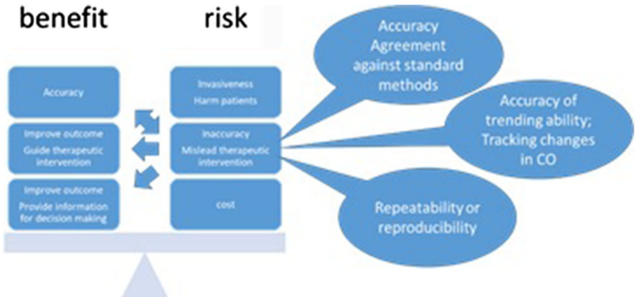

Fig. 1 Benefits and risks associated with CO monitoring devices

The pulse contour method is defined as a technique for measuring and monitoring stroke volume (SV) on a beat-to-beat basis based on the morphological information obtained on an arterial pulse pressure waveform [3•]. The arterial pressure waveform may be obtained invasively (by using an arterial catheter) or non-invasively (without the use of an arterial line: volume clamp method, applanation tonometry, and photoelectric plethysmography). Pulse contour analysis-derived CO measurements may be used in an uncalibrated form (not calibrated to biometric and physiological data) or calibrated to an external CO measurement (transpulmonary thermodilution [TPTD] and lithium dilution.) The commercially available devices that are based on pulse contour methods include the FloTrac System, PiCCO-Technology, LiDCO System, VolumeView System, CNAP Monitor, PRAM System, and T-Line System. There are several comprehensive reviews available concerning pulse contour methods [4].

Classification of CO Monitoring Devices by Their Invasiveness

The devices can be stratified into several levels based on their invasiveness (Table 1). Except for the direct aortic flow probe insertion and other invasive perivascular flow probe placements that require surgical procedures, PAC (thermodilution) may be considered as the most invasive of all CO monitoring techniques. Numerous complications of PAC have been identified such as dysrhythmia, infection, pulmonary artery rupture, injury to adjacent arteries, embolization, pulmonary infarction, cardiac valvular damage, pericardial effusion, and intracardiac catheter knotting [5–8] (Table 1). The complication rate of PAC is about 5–10% [8] and is higher if access-related complications are included. The group with the second level of invasiveness includes TPTD, lithium dilution technique, and ultrasound dilution technique, which require the placements of both arterial pressure catheters and central venous catheters (CVC). The complications related to CVC insertion are pneumothorax, hemothorax, thrombus, bleeding, hematoma, arterial catheterization, vascular injury, extravenous wire malposition, stroke or cerebral ischemia, infection (local or systemic), arrhythmia, and right atrial perforation or other heart-related complications [9]. The complication rate with these techniques is in the range of 1–20% [9–11]. Although ultrasound-guided insertion may reduce the complication rate, the risk of complications is still substantial [9, 12, 13]. The transpulmonary lithium dilution technique involves an additional risk of lithium toxicity. The third level of invasiveness includes insertion of arterial pressure lines or transesophageal ultrasonic probes. This group of devices includes pulse contour analyses and transesophageal echocardiography (TEE)/Doppler (TED). Arterial cannulation has generally been found to be a safe procedure, and the incidence of serious complications is less than 1% [14, 15]. Similarly, the major complication rate associated with TEE is less than 1% [16], while no complications have been reported for TED [17]. Finally, the least invasive techniques, also known as non-invasive or minimally invasive methods [18–20], include the bioimpedance/bioreactance method, partial CO_2 rebreathing method, inert gas rebreathing (IGR) method, transthoracic echocardiography (TTE)/Doppler (TTD) method, and non-invasive pulse contour method.

Classification of Non-pulse Contour CO Monitoring Devices by Their Underlying Technology

The determination of CO has been the subject of extensive developments over the last decade. The monitoring devices may be classified according to their underlying principles (Appendix).

CO Monitoring Devices: Principles and Practices

Fick's Principle

This is an invasive and time-consuming method that is not suitable for continuous measurement as it requires drawing of arterial/mixed venous blood samples from the arterial line and the PAC, in addition to the measurement of exhaled oxygen volume. Although this method is considered the gold standard for CO measurement, it is rarely used for intraoperative monitoring.

Partial Gas Rebreathing Method

The NICO system (Novametrix Medical Systems, Wallingford, CT, USA) measures CO via a disposable rebreathing circuit that is added to the ventilator tubing and automatically provides a non-invasive CO measurement at 3-min intervals. Its easy application and the availability of automatic and continuous measurement make it suitable for perioperative use. This technique was found to have good agreement with PAC thermodilution in animal models [21], surgical/ICU (intensive care unit) patients [22, 23], pediatric

Table 1 Invasive feature of CO monitoring devices; risk stratification and the complications

Level of invasiveness	Types of technique	Factors associated with risk	Complications	Complication rate
1	Pulmonary artery catheter thermodilution	Pulmonary artery catheter insertion	Dysrhythmia, infection, rupture of pulmonary artery, injury to adjacent arteries, embolization, pulmonary infarction, cardiac valvular damage, pericardial effusion, intracardiac catheter knotting	5–10%
2	1) Transpulmonary thermodilution 2) Transpulmonary ultrasound dilution 3) Transpulmonary lithium dilution (TPLD)	a) Central venous catheter insertion (common) b) Arterial catheter insertion (common) c) Lithium infusion (TPLD specific)	a) Pneumothorax, hemothorax, thrombus, bleeding, hematoma, arterial placement of catheter, vascular injury, extravenous wire malposition, stroke or cerebral ischemia, infection (local or systemic), arrhythmia, and right atrial perforation or other heart-related complications b) Listed in the box below c) Lithium intoxication	1–20%
3	Invasive pulse contour, transesophageal echocardiography/Doppler (TEE/TED)	a) Arterial catheter insertion (invasive pulse contour specific) b) Probe insertion into the esophagus (TEE/TED specific)	a) Permanent ischemic damage, sepsis, pseudoaneurysm formation b) Dental trauma, submucosal hematoma of pharyngeal area, jaw subluxation, tonsillar bleeding, perforations, bleeding from esophageal tract, dysphagia, vagal reflexes, sympathetic reflexes, infections	a) Less than 1%. Ultrasound-guided insertion may reduce the risks, although they still remain substantial b) Less than 1%
4	Bioimpedance/bioreactance method, inert gas rebreathing method, partial CO_2 rebreathing method Transthoracic echocardiography/Doppler, non-invasive pulse contour methods	None CO_2 rebreathing (partial CO_2 rebreathing method specific)	Hypercapnia	NA NA

The techniques are listed in order of decreasing invasiveness

CO cardiac output, *CO_2* carbon dioxide, *NA* not applicable

patients [24], and cardiac surgery patients [25]; moderate agreement in thoracic surgery patients [26] and cardiac surgery patients [27]; and poor agreement in post-cardiac surgery patients [28, 29] and acute lung injury patients [30]. The device appears to have a high repeatability (4%) [28, 31]. There is no study adequately analyzing the trending ability of CO on this device.

The drawbacks of this technique are the need for stable CO_2 elimination, which prevents its use in awake, spontaneously breathing subjects, and its unreliability in patients with chest trauma or pulmonary pathology, [28, 30, 32, 33]. Because CO_2 detection is crucial in this technique, ventilator setting is an important factor in ensuring the accuracy of measurements. Tidal volumes (TV) of 10 mL/kg result in good agreement between this method and PAC thermodilution, whereas lower TV (6 mL/kg) may result in underestimation of CO [33]. Similarly, measurement in children with low TV may also be less accurate [24]. The accuracy of this technique also depends on shunt fraction [34]. As patients with severe lung injury have increased shunt fractions, it is difficult to estimate CO using this technique. Further, arterial blood gas analysis is required for shunt estimation [35]. The device seems to be more accurate in low-to-moderate CO than in high CO [22, 23, 36].

Although the device is considered harmless to patients, there is a potential risk of elevated arterial CO_2 levels, which excludes its use in patients with critically increased intracranial pressure or pulmonary hypertension (PH). Arterial CO_2 partial pressures can rise by about 10% of their initial values owing to the intermittent addition of extra dead space. It is also unclear whether this technique may be used during laparoscopy and CO_2 insufflation. Despite these limitations, this device has the potential for intraoperative use in selected patients, provided its trending ability is validated.

Inert Gas Rebreathing Method

Innocor (Innovision, Glamsbjerg, Denmark) is the commercially available product that applies the IGR method for CO monitoring. This system utilizes two types of physiologically inert gases: a blood-soluble gas (0.5% nitrous oxide, N_2O) and an inert insoluble gas (0.1% sulfur hexafluoride, SF_6). The rebreathing bag is prefilled with an O_2-enriched mixture of these two gases. A photoacoustic infrared gas analyzer is used for the continuous and simultaneous measurement of the levels of the inert gases and of CO_2. Photoacoustic analyzers measure gas concentrations over a 5- to 6-breath or 10- to 20-s interval of rebreathing into the closed system. The concentration of the blood-insoluble SF_6 following equilibration aids in the calculation of the total system volume (lungs, valve, and rebreathing bag). Subsequently, the rate of disappearance of N_2O reflects its uptake by pulmonary blood flow (PBF). These data (total system volume and rate of N_2O disappearance) are used for calculating the total PBF that participates in gas exchange. This system was developed for spontaneously breathing patients and has been extensively validated in various types of spontaneously breathing patient populations including patients with heart failure [37, 38], PH [39, 40], atrial fibrillation [41, 42], and pulmonary disease [43, 44], as well as in pediatric patients [45]. Overall, IGR demonstrated good agreement with gold standard methods including PAC thermodilution, the Fick method, and cardiac magnetic resonance-derived CO in these patient populations. However, only few studies [46, 47••] validated its accuracy in ventilated patients, who are the main subjects of this review. Reutershan indicated good interchangeability with PAC thermodilution in mechanically ventilated patients with acute respiratory distress syndrome by using an older generation IGR device [46]. Similarly, Perak showed good agreement between CO determined by IGR and the Fick equation in pediatric patients [47••]. The authors indicated the need for a valve adapter that allowed for rebreathing. Data regarding the repeatability and trending ability of this device in mechanically ventilated patients are not available as of now. Peyton et al. reported the repeatability of this device as being less than 20% in spontaneously breathing cardiac patients and healthy volunteers [48].

The drawbacks of the IGR device are its lower accuracy in high CO conditions [41, 49] and its inability to provide continuous measurements. However, one study suggested that an IGR device could provide measurements once in every 5 min [48]. This is a potential intraoperative CO monitoring device as it is completely non-invasive, safe, easy-to-use, and accurate in various patient groups, especially patients with cardiac rhythm failure and pulmonary disease, who are unsuitable for monitoring with other techniques. Further validation of this technique is required in ventilated patients and in the perioperative setting.

Indicator Dilution Technique

The DDG pulsed dye densitometry series (Nihon Kohden, Tokyo, Japan) is one of the commercially available product using the indicator dilution technique. In this technique, signal detection in the arterial blood is performed in a manner similar to that of pulse oximetry. Transcutaneous measurements of two wavelengths (805 and 940 nm) are used to calculate the ratio between hemoglobin and the injected indicator, indocyanine green (pulse dye densitometry; PDD). Indocyanine green distributes exclusively in the intravascular space following a bolus injection and is cleared via hepatic elimination at a half-life of 4.1 min. Hemoglobin concentration is required for the calculation of the absolute indocyanine green concentration. CO is calculated from the indocyanine green dye-dilution curve (dye densitogram) according to the Stewart-Hamilton equation. Similar to pulse oximetry, factors that compromise signal detection, such as vasoconstriction, interstitial edema, movement, or ambient light artifacts, may limit the reliability of CO assessment by using this method [50, 51]. There are conflicting reports regarding the accuracy of PDD. The indocyanine green dye dilution CO measurement was found to have acceptable agreement with PAC thermodilution in various surgery patients [52], cardiac surgery patients with limited performance [51, 53], post-cardiac surgery patients [54], and critically ill pediatric animal models (acceptable bias and precision) [55]. Bremer et al. found the technique to be reliable only at CO values > 5.0 L/min [56]. A similar trend of increased overestimation in the low CO range was also reported by other studies [52]. Kroon et al. reported concordance rate of 81% for the trending ability of PDD, when compared with PAC thermodilution CO [54]. They also demonstrated that the device had good reproducibility. However, the intraoperative use of this technique may be limited owing to the following reasons: limited performance on trending ability and lack of continuous measurement of CO as subsequent measurements cannot be performed until indocyanine green is excreted. Theoretically, the total elimination of indocyanine green takes about three half-lives, and the residual plasma indocyanine green may contribute to errors.

Transpulmonary ultrasound dilution (TPUD) is another method that utilizes the indicator dilution technique. This is used in the commercially available product called COstatus (Transonic Systems Inc., Ithaca, NY, USA). This device consists of an extracorporeal arteriovenous loop set that is connected to an arterial catheter on one side and a CVC on the other side. Two reusable sensors for blood ultrasound velocity and flow are clamped on to the loop, and a roller pump circulates blood through the arteriovenous loop for each measurement session. Isotonic saline, which is used as the indicator, is injected into the venous side of the arteriovenous loop, randomly during a respiratory cycle, at the rate of 0.5–1.0 mL/kg, to a maximum volume of 30 mL for each measurement. The venous sensor detects the indicator and determines the time and volume of injection. Following its passage through the cardiopulmonary system, the arterial sensor records the travel time of the indicator and the changes in blood ultrasound velocity. At the end of three consecutive measurements, blood is returned to the patient by flushing the arteriovenous loop with heparinized saline, thus avoiding any blood loss. The device was found to have good agreement with PAC thermodilution in critically ill post-cardiac surgery patients [57], although this study did not provide any evidence of its use in the intraoperative setting. The reproducibility of TPUD is indicated by its coefficient of variance of 6% [57]. The device was found to have good agreement and trending ability in children undergoing heart surgery [58] and in neonatal animal models [59–61, 62•].

The limitations of this device are the following: arterial pressures are not available during the time that the CO is measured (5–6 min when the pump is operated); the volume of isotonic saline injections may be an issue in patients who are extremely hypervolemic; and an arterial catheter and CVC are required for monitoring. The device may have the potential for intraoperative use, especially in small children with arterial catheters and CVC.

Thermodilution Technique

A detailed description of PAC thermodilution and TPTD is beyond the scope of this review and is attempted elsewhere [1, 6, 63].

Impedance Cardiography

The conventional impedance cardiography (ICG) devices involve placing electrodes on the patient's body surface, which may interfere with the performance of surgical procedures. Several products incorporate the classic thoracic ICG, such as the Niccomo monitor (Medis GmbH, Ilmenau, Germany) and the BioZ monitor (Cardio Dynamics, San Diego, CA, USA). Niccomo is reported as lacking adequate accuracy [64, 65], although there is no evidence comparing it with PAC thermodilution. There was inadequate agreement between BioZ and PAC continuous thermodilution in patients undergoing off-pump coronary artery bypass graft, with a tendency to overestimate and underestimate CO in low CO and high CO conditions, respectively [66].

Another device, ECOM (ConMed, Irvine, USA), is based on a modification of the thoracic electrical bioimpedance method and involves electrodes attached to a specially designed endotracheal tube. There was inadequate agreement between ECOM and PAC thermodilution in patients undergoing cardiac surgery [67–70], along with poor trending ability [68, 70]. The repeatability of this device appeared to be good (10% of precision) [70]. ECOM is a simple system to employ in the perioperative setting, although it lacks the required accuracy. However, the direct evidence of improved postoperative outcomes following the use of ECOM encourages its perioperative use [71••].

NICaS (NIMedical, Petah Tikva, Israel) utilizes whole-body impedance, which is detected peripherally as impedance signals, for determining CO. Although it is not validated in the intraoperative setting, studies have reported poor agreement in PH patients [72] and good agreement in cardiac disease patients [73]. Although there are recent case series on its perioperative use in patients with pheochromocytoma [74] and those undergoing Cesarean sections [75], there is inadequate evidence to support its intraoperative use.

NICOM (Cheetah medical, Portland, USA) is a device that uses the bioreactance method and has been validated in various intraoperative settings. Studies have reported poor agreement with Doppler echo-derived CO in patients undergoing abdominal surgery [76–78] and with PAC thermodilution for living donor liver transplantation [79, 80]. This device seems to be unreliable in abdominal surgery, possibly owing to the massive fluid shifts and tissue retraction in these procedures. It has been demonstrated as having poor accuracy in pediatric population, although the studies involved inconsistent physical conditions and settings [78, 81–84]. The repeatability of the device is reported to be good [31], while its trending ability is relatively reliable [83, 85–87, 88•]. Although the device has inadequate accuracy, it may be useful in some perioperative settings, as it provides continuous CO measurement and SV variation, which are proven parameters to guide fluid therapy [84, 89–92].

There is no commercially available transbrachial electrical velocimetry device. A prototype of the device has been validated in volunteers with favorable results [93, 94••]. Although no study has been reported under perioperative setting, the precision of the device as well as its accuracy against magnetic resonance image-derived CO have been confirmed [94••]. Considering its potential for the perioperative use, its empirical perioperative use may be allowed and further analysis is expected in this field.

Aesculon and its portable version, Icon (Osypka Medical, Berlin, Germany), employ electrical velocimetry (EV) methods to determine CO. The device has been validated in intraoperative settings and found to have good agreement with TEE for coronary artery surgery [95]. However, other studies have identified it as having poor agreement with various reference methods in cardiac disease patients [96] and critically ill patients [97]. In contrast, the device may be useful as it has acceptable accuracy in pediatric patients with various conditions [98••, 99–107]. The device was found to have high reproducibility [106, 108], although data on its trending ability in humans are lacking. The device has the potential for intraoperative use in pediatric patients.

Continuous Doppler and Morphological Echocardiography

TTE has limited applicability in the perioperative setting owing to the difficulty in obtaining continuous and consistent measurement of CO with it. TEE is a currently used monitoring technique in the perioperative setting as it provides information concerning cardiac and aortic structures, cardiac contractility, and volume/fluid assessment. Similar to TTE, TEE has inaccuracy or inconsistency issues that are related to operator skill. To overcome the drawback of it being an operator-dependent measure, a TTD-based monitoring method called USCOM (Uscom, Sydney, Australia) and a TED-based monitoring method called CardioQ (Deltex Medical, Chichester, UK) have been developed. USCOM utilizes continuous wave Doppler to obtain velocity-time integrals of either transaortic blood flow at the left ventricular outflow tract or pulmonary valve blood flow, by applying a non-imaging probe in the suprasternal notch (aortic valve) or left parasternal site (pulmonary valve). The cross-sectional area of the aortic root may be a source of error as it is derived from nomograms based on patient height [109], without the use of 2-dimensional (2D) echo. Chong and Peyton conducted a meta-analysis of six studies that analyzed USCOM and identified a mean weighted bias of − 0.39 L/min, precision of 1.27 L/min, and percentage error of 42.7% [110]. Recently available data have confirmed it as having acceptable agreement with 3D-TTE in pregnant women [111•]. Further, USCOM was successful in detecting blood loss in healthy volunteers [112]. Another study demonstrated that the tandem use of USCOM and CardioQ provided reliable accuracy as well as trending ability of CO [113•]. The limitation of this device is its reliance on operator skill. Adequate training to achieve the appropriate angle of insonation for optimizing flow signal may improve the measurement accuracy [114, 115].

CardioQ utilizes a disposable probe that is inserted in the esophagus to measure blood flow in the descending aorta for the continuous measurement of CO [116]. It only measures flow in the descending thoracic aorta, which is 70% of the total flow. Therefore, an additional conversion factor is needed to compensate aortic arch flow. Similar to USCOM, the diameter of the descending aorta is not directly measured but estimated from nomograms based on patient characteristics. As the thoracic aorta elongates and unfolds with advancing age, the reliability of the technique reduces owing to probe displacement [117]. CardioQ is endorsed by the British guidelines for use in patients undergoing major or high-risk surgery [118]. Moller-Sorensen et al. found that this technique had poor agreement with PAC thermodilution in patients undergoing coronary artery bypass graft. However, they reported the device as having good precision (12.8%) and an acceptable trending ability [119•]. The device-derived SV respiratory variation accurately predicted fluid responsiveness under general anesthesia [120, 121].

Modified Pulse Wave Transient Time

The esCCO (Nihon Kohden, Tokyo, Japan) technique estimates CO by utilizing modified pulse wave transient time (mPWTT). This system uses an existing electrocardiogram and a specific type of pulse oximeter. Recently available data demonstrate its poor agreement and insufficient trending ability with TPTD in off-pump coronary artery surgery patients [122]. Similar results have been reported in critically ill patients [123–126, 127•, 128, 129•], cardiac surgery patients [130], and liver transplantation patients [131]. In contrast, it was found to have good agreement with acceptable trending ability in renal transplant patients [132] and poor agreement with acceptable trending ability in liver surgery patients [133]. The inaccuracy with this technique may be related to low systemic vascular resistance [126, 129, 131]. This device appears to have lower accuracy in low CO conditions [122]. It was found to have acceptable reproducibility [127, 128, 134]. Intraoperative interventions such as administration of vasoactive drugs and anesthetics, intrathoracic pressure changes, systemic vascular resistance changes, cardiac displacement, and arrhythmias are likely to affect the quality of the ECG and pulse oximetry signals. Further, its relatively low trending ability may also limit its intraoperative use.

Conclusions

Although various types of less invasive methods for CO measurement have been developed, none of them are entirely ideal for perioperative use. Each device has its own advantages and drawbacks related to its underlying technology. The current evidence for their perioperative use is limited. The empirical application of these devices for various surgical patients may provide us with more data over time.

Compliance with Ethical Standards

Conflict of Interest Yohei Fujimoto, Koichi Suehiro, Akira Mukai, and Kiyonobu Nishikawa declare they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- •• Of major importance

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