Minimally Invasive Cardiac Output Monitoring in the Perioperative Setting

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With advancing age and increased co-morbidities in patients, the need for monitoring devices during the perioperative period that allow clinicians to track physiologic variables, such as cardiac output (CO), fluid responsiveness and tissue perfusion, is increasing. Until recently, the only tool available to anesthesiologists to monitor CO was either a pulmonary artery catheter or transesophageal echocardiograph. These devices have their limitations and potential for morbidity. Several new devices (including esophageal Doppler monitors, pulse contour analysis, indicator dilution, thoracic bioimpedance and partial non-rebreathing systems) have recently been marketed which have the ability to monitor CO noninvasively and, in some cases, assess the patient's ability to respond to fluid challenges. In this review, we will describe these new devices including the technology, studies on their efficacy and the limitations of their use.

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An integral role of the anesthesiologist in patient care is to monitor and interpret physiologic variables. Treatment strategies are guided by both clinical skills and information provided by monitoring tools. The value of patient monitors to real-time decision making during patient care is especially important when caring for critically ill patients. Routine monitoring of circulatory function includes heart rate (HR), arterial blood pressure, electrocardiography (ECG) and oxygenation. Clinical signs, such as jugular venous distension and urine output, are often used to judge intravascular volume status and adequacy of end organ blood flow but are not as reliable in critically ill patients. Anesthesiologists and intensivists have devoted most of their monitoring devices to the measurement of pressures. However, most organs are dependent on flow as well as pressure to achieve adequate function.

To this end, there have been several monitors developed that allow the clinician to monitor cardiac output (CO) and the response to fluid therapy. When these monitors are used in conjunction with the administration of fluids and vasopressors to specific therapeutic end points, patient care and outcome may be improved. These interventions, termed "goal-directed therapy" have been used widely both in the operating room (OR) and the intensive care unit (ICU).[1,2]

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The most well-known monitor for measuring flow and pressure is the pulmonary artery catheter (PAC) described initially by Dexter,[3] and later modified by Swan et al.,[4] to measure CO and central filling pressures. Since that time, investigators have tried to develop the ideal monitor of CO measurement. Such a monitor would be totally noninvasive or minimally invasive as this would allow its use in a variety of clinical settings that may not be amenable to invasive hemodynamic monitoring, such as the labor suite, emergency room, during medical transport, ambulatory surgery suites or the recovery room. The ideal monitor would also need to be accurate and reproducible and have limits of agreement (as assessed by Bland–Altman[5] analysis) that compared favorably with values derived from the PAC, often considered the "gold standard" when other devices are compared. Furthermore, such a monitor would also need to be reliable under many different physiologic conditions, such as different shock states or other conditions when dynamic changes in intravascular volume status and peripheral resistance are occurring. Finally, the ideal CO monitor would need to be continuous, and have the ability to assess the efficacy of therapeutic interventions (e.g., the hemodynamic response to administration of fluid challenges or vasoactive drugs). At present, no device meets all of these criteria. This article aims to discuss the minimally invasive technologies available to measure CO that require very little additional specialized training. The technologies that will be discussed include partial carbon dioxide rebreathing systems, pulse contour analysis, thoracic electrical bioimpedance (TEB), esophageal Doppler (ED) and indicator dilution methods, (e.g., lithium dilution).

The information presented is based upon a PubMed search for English language articles published up to

and including February 2008 using the following medical subject headings with the term CO: noninvasive, dye dilution, Fick principle, thermodilution, PAC, lithium dilution, pulse contour analysis, transpulmonary thermodilution, ED, Doppler echocardiography, carbon dioxide rebreathing, electrical velocimetry, bioimpedance and electrical impedance.

References were screened by title and by abstract before the full text was acquired. The bibliographies of original papers and review articles were also searched for any papers that may have been missed with the initial search criteria. When necessary, companies were contacted for further information. Representative articles from the search criteria were then used to create the review, including a description of the technology and representative studies.

When available, Bland–Altman analysis of bias, precision, and levels of agreement is reported.[5] The Bland–Altman approach, which has become the preferred method of statistical analysis for assessing agreement between two methods of clinical measurement, is unfortunately not universally reported in studies investigating different methods of measuring CO, making comparison of different monitoring modalities difficult.

History of CO Measurements

Of the 27 million patients who undergo surgery in the United States each year, approximately 8 million have coronary artery disease or risk factors for cardiovascular disease. One million of these patients have perioperative cardiac ischemic events.[6] Moreover, the prevalence of cardiovascular disease increases with age. The proportion of the United States population that is older than 65 years is predicted to increase from 25% to 35% within the next 30 years.[6,7] This is also the patient group that has the largest number of surgical procedures performed. Thus, in an attempt to reduce cardiac morbidity, anesthesiologists have used the hemodynamic data obtained from the PAC to diagnose and treat these high-risk patients.

A major concern with the use of PACs is the risk associated with central venous catheterization. These risks include arrhythmias, pulmonary infarction, infection, pulmonary embolus, and rupture of the pulmonary artery to name just a few.[8] Furthermore, PACs add significant cost to the care of the patient. These disadvantages of PAC use have motivated the search for a less invasive method to determine CO.

Minimally Invasive CO Monitors

Minimally invasive CO monitors include ED monitors, carbon dioxide rebreathing systems, indicator dilution methods, TEB and pulse contour analysis devices. We will discuss the theory behind the operation of these devices as well as studies addressing the use of these technologies for goal-directed therapy and, where available, the reliability of these devices when compared with gold standards, such as the PAC. Table 1 summarizes the advantages and disadvantages of the currently available CO monitors.

Esophageal Doppler Monitor

ED monitoring was first introduced in the 1970s as a noninvasive means to measure aortic blood flow. Suprasternal or transthoracic probes were used initially, but the difficulty of probe positioning and instability on the chest wall made their use for repeated measurements limited. This led to the development of the ED probe. It had several advantages, including the ability to remain in position for days to weeks and its proximity to the aorta. The ED probe is approximately the size of a nasogastric tube and can be positioned easily.

Since the Doppler methodology measures velocity not flow, certain assumptions are required to use this technology to estimate CO. The aorta is assumed to be a cylinder and the flow through it is calculated by multiplying the cross-sectional area (CSA_a) by the velocity (V_f). Blood flow in the aorta is pulsatile and the velocity changes over time. V_f can thus be described as the area under a curve of a velocity-time graph. This area is computed mathematically as the integral of the derivative of velocity over time (dV/dt) from T_0 to T_1 (where T_0 is the start of aortic blood flow and T_1 is the end of flow). This value is then multiplied by the CSA_a (which is the area of a circle πr^2) to give a value for stroke volume (SV). The radius of the descending aorta (which is used to calculate the area of the aorta) is derived from published nomograms based on age, sex, weight, and height (Deltex, West Sussex, England, www.deltexmedical.com) or through direct measurement (Arrow's HemoSonic® Reading, PA,). CO is then calculated by multiplying SV by HR ($CO = HR \times SV$).

Esophageal Doppler also has the ability to measure the corrected flow time (FT_c) as a measure of cardiac preload. The FT_c is the time from the beginning of the aortic pulse waveform upstroke to its return to baseline. The FT_c is the systolic flow time corrected for HR of 60 bpm. Several studies have compared this measurement with other measures of cardiac preload (such as pulmonary artery occlusion pressure) and have found good agreement between the two (discussed below).[9–11] One of the advantages of using the ED probe is that changes in SV after the administration of fluid challenges can be used to guide fluid administration. It thus functions as a monitor for titrating fluid to optimize preload.

There are several limitations to the use of ED. First, the ED only measures descending aortic blood flow, and excludes flow to the aortic arch vessels. CO is therefore calculated only from this descending aortic blood flow value. Aortic blood flow is approximately 70% of CO with 30% going to the cephalic blood vessels, and thus a correction, or *K*-factor of 30% must be introduced to account for blood flow to the arch

Table 1. Advantages and Disadvantages of the Currently Available Minimally Invasive CO Monitors

Device	Advantages	Disadvantages
Esophageal Doppler	Simple to use	Mathematical assumptions about aortic size might be erroneous
	Does not require access to the circulation	
	Many clinical studies proving utility	Only measures descending aortic blood flow
	Reliable	Occasional difficulty in obtaining optimal probe position
	Can use as a monitor of volume responsiveness in goal directed therapy	Learning curve
Thoracic electrical bioimpedance	Completely noninvasive	Difficult to set up
		Numerous mathematical assumptions
		Not useful for patients with dysrhythmias
		"Noise" from OR limits use
		Requires hemodynamic stability
		Have not been reported for use in goal directed therapy
Partial non-rebreathing systems	Easy to set up	Have not been reported for use in goal directed therapy
	Does not require access to the circulation	Changes in dead space or V/Q matching may erroneously change CO measurement
	Provides for continuous CO measurement	
Arterial pulse contour	Simple to use	Requires access to the circulation
	Only require arterial line	Requires high fidelity arterial tracing
	Can be used in goal directed therapy	Requirement for calibration (some systems)
	Validated in clinical studies under many different conditions	Need to re-calibrate during periods of hemodynamic instability (some systems)
	Continuous CO measurements	
	Can be used to measure stroke volume and stroke volume variation	
Lithium dilution	Ease of set up	Requires access to the circulation
	Only require arterial line	Repetitive blood draws
	Continuous CO measurements	Calibration interfered in the presence of neuromuscular blocking drugs
	Can be used to measure stroke volume and stroke volume variation	
	Can be used with goal directed therapy	
Trans-pulmonary thermodilution techniques	Can use pre-existing arterial line or central line	Requires access to the central circulation
		Radial artery not suitable
	Continuous CO measurements	Not truly a noninvasive technology
	Provides estimation of extravascular lung water	Limited use in the OR
	Can be used with goal directed therapy	

CO = cardiac output; OR = operating room.

vessels. Although valid in young healthy patients, this ratio may not be constant due to changes in metabolic activity between different organs, or hemodynamic status.

Second, CSA_a is not a constant, but rather dynamic due to changes in pulse pressure, vascular tone, aortic compliance, volume status or catecholamine use. The CSA_a determination is crucial to CO calculation since any change in radius of the aorta is squared before use in the final equation. Thus, even small changes in aortic area can significantly affect CO determinations. This has led to the development of an ED probe that can directly measure CSA_a (Arrow's HemoSonic®) rather than calculating it from a nomogram of typical aortic radii.[12]

Finally, probe position is critical to obtain accurate V_f. The Doppler beam must be within 20° of axial flow to obtain a good measure of aortic blood flow. This has led to the suggestion that ED monitoring is somewhat operator dependent,[13–15] and that additional training is required to become proficient in its use.[16] However, the learning curve is steep with some studies demonstrating a dramatic improvement in skill with only 10 to 12 insertions.[14,16] Inter and intraobserver reliability of the technique is clinically acceptable, between 8% and 12%.[17,18]

There have been several studies that have compared ED measurements of CO with PAC-derived thermodilution CO (PAC_{TD}). A meta-analysis of 11 ED studies demonstrated a pooled median bias of 0.19 L/min (range: −0.69–2.0 L/min) for CO.[19] Based on three individual studies, the pooled limits of agreement were −2.21 to 2.33 L/min.[20] These studies were conducted in hemodynamically stable patients or those who were undergoing coronary artery bypass grafting (CABG).

A completely noninvasive Doppler technology, the USCOM (Ultrasound CO monitor, USCOM, Sydney, Australia, www.uscom.com.au), is also available which uses Doppler technology to measure CO from a suprasternal Doppler probe. This nascent technology has been studied in a few patient population groups (mostly stable ICU patients) and has shown reasonable correlation with PAC_{TD}.[21,22] There is a concern that during the learning phase of the device, CO measurements may not be accurate.

Numerous clinical studies have demonstrated improvement in patient outcome with goal-directed fluid therapy using ED. Sinclair et al., conducted a randomized controlled trial of patients undergoing femur

fracture repair.[23] Patients were randomized to either routine care or ED-guided fluid loading. Study patients received significantly more fluid and had a statistically significant decrease in the primary outcome of median time to be declared fit for discharge (10 vs 15 days) and length of stay (12 vs 20 days) when compared with controls.[23] A similar trial conducted by Venn et al., showed that, when compared to a control group of patients (central venous pressure monitoring), ED-monitored patients had less intraoperative hypotension and were considered medically fit for discharge sooner than the control group.[24]

Gan et al., randomized elective noncardiac surgical patients to either routine care or goal-directed fluid therapy with an ED monitor. Patients in the intervention group received more colloid and had significantly shorter median length of stay (5 vs 7 days) and an earlier ability to tolerate solid food (3 vs 5 days, $P < 0.05$).[2] In another study, Mythen and Webb prospectively randomized elective cardiac surgery patients to usual care or extra boluses of a hydroxyethyl starch solution to maintain maximum SV based on ED monitoring. Patients in the intervention group had a statistically significant decrease in gut mucosal hypoperfusion, major complications, hospital and ICU stay.[11] In a study by Wakeling et al., intraoperative ED-guided fluid management was associated with a 1.5-day median reduction in postoperative hospital stay. Patients recovered gut function significantly faster and suffered significantly less gastrointestinal and overall morbidity and had higher quality of recovery scores.[25] A relevant finding of all these studies was a greater sensitivity of SV and CO when compared with arterial blood pressure and HR as measures of adequate intravascular volume status. It appeared that compensatory tachycardia tended to maintain CO in the face of moderate hypovolemia.[26]

In a similar trial, Noblett et al., randomized patients undergoing elective colorectal surgery to either standard care with respect to fluid loading to those with an ED-titrated fluid regimen.[27] They found that patients in the intervention group had higher COs and SVs. This translated into the clinically relevant findings that patients in the intervention group tolerated an oral diet earlier, had fewer postoperative complications, and had a shorter length of stay. Interestingly, patients in the intervention group also had lower levels of interleukin-6, which suggested an attenuated inflammatory response to surgery, perhaps due to the improved organ perfusion.

A study by Conway et al., (using the same algorithm as Sinclair et al.[23]) in patients undergoing major bowel surgery compared ED-derived CO and goal-directed fluid therapy in a group of patients who underwent major bowel surgery.[28] They demonstrated less use of critical care beds postoperatively in the intervention group. Furthermore, this trial of 57 patients also showed less congestive heart failure than the control group.

When comparing goal-directed studies of CO with ED, it is unclear as to whether the FTc or SV should be used to guide fluid therapy. It appears that the ability to respond to a fluid challenge is best determined by FTc. However, to use this value as a marker of fluid optimization may be potentially misleading. FTc is inversely proportional to systemic vascular resistance (SVR).[29] In conditions in which SVR may be elevated, (heart failure, excessive vasopressor use or hypothermia) FTc is reduced and might lead clinicians to give more fluid without a clinical improvement in CO or organ flow. Furthermore, in pathological conditions such as pericardial tamponade, pulmonary embolus, or mitral stenosis, in which there is a pathological limitation of left ventricular filling, FTc will be reduced and not respond to a volume challenge and might lead the clinician to give fluid in a state where the patient might be on the optimal portion of their starling curve resulting in no improvement in CO with the risk of precipitating pulmonary edema.[29]

For this reason, the SV might be a better variable to measure fluid optimization. In a study by Bundgaard-Nielsen et al., SV was compared with FTc to determine fluid optimization in radical prostatectomy patients.[30] This study found that the change in FTc was inconsistent when used for fluid optimization and that SV was the preferable method in these patients.

ED monitoring has proven itself to be a reliable tool to monitor goal-directed therapy. It has the ability to measure CO, but its utility in situations with low CO is limited when compared with PAC_{TD}. Initial investigations also show its utility in reducing morbidity when coupled with a goal-directed fluid approach to surgical patients. Further clinical trials, however, are needed to determine its utility in different patient populations, specifically those who are hemodynamically unstable requiring vasopressor support and those with dynamic changes in SVR. Concerns about its precision in measurement need to be addressed and the optimal variable to measure for fluid optimization (either SV or FTc) in different patient populations needs to be clarified. Also, some have called into question the accuracy of this technology because of wide limits of agreement in some of the studies.[31] ED may lead to fewer operative patients undergoing PAC placement in the future.

THORACIC ELECTRICAL BIOIMPEDANCE

TEB is the least invasive method of measuring CO. First proposed by Kubicek in 1966, TEB is based on the theory that the thorax is a cylinder that is perfused with a fluid (blood) of a specific resistivity. Thoracic bioimpedance is the electrical resistance to high frequency low amplitude current that is transmitted from electrodes placed on the upper and lower thorax. Six electrodes are placed on the patient, two on either side of the neck and four in the lower thorax. After injection of current by way of the outermost electrodes

on the body surface, the impedance of flow through the thorax is sensed by the innermost set of electrodes on the body surface. This value is indirectly proportional to the volume of thoracic fluids such that increasing fluid in the thorax results in less TEB. Therefore, the inverse of TEB, and thus changes in CO, are reflected as a change in total bioimpedance or fluid conductivity.

The measurement in changes in TEB to estimate SV is based on the equation:

$$SV = p\left(\frac{L^2}{Z\phi^2}\right) \cdot \left[VET_x\left(\frac{d_7}{dt_{max}}\right)\right]$$

where p is the resistivity of blood (ohm-cm), L is the distance between the electrodes (cm), Z_ϕ is the mean thoracic impedance between electrodes (ohm), VET is the ventricular ejection time (sec) and $(d_Z/d_t)_{max}$ is the maximum negative slope of the bioimpedance signal (ohm/sec).[32] SV is then derived based on several assumptions. First, the rate of change over time in TEB corresponds to aortic blood flow (and assumes that other factors that change impedance do not change). Second, $(d_Z/d_t)_{max}$ corresponds to peak aortic blood flow. Third, the ejection phase contractility index (EPCI) which is used in the calculation of SV is equal to EPCI = $(d_Z/d_t)_{max}$ × total fluid conductivity. Fourth, VET can be measured from the distance between the QRS intervals of the surface ECG. Finally, the volume of electrically participating tissues (VEPT) is estimated from the patient's height, weight, age, and sex.[33,34] SV is thus estimated by the formula SV = (VEPT)(VET)(EPCI), and CO is determined by CO = SV × HR. This equation has been modified by Bernstein to account for the non-cylindrical shape of the chest, which might result in an erroneous determination of the CO.[35]

It is readily apparent that an accurate determination of CO requires significant assumptions and hemodynamic stability. Thoracic bioimpedance is affected by tissue fluid volume and changes in the volume of pulmonary and venous blood induced by respiration. This "noise" must be filtered out from the desired changes in volumetric blood flow of the aorta. Any alteration in the position or contact of the electrodes will thus affect these measurements. Also, determining the VET by using the interval between QRS complexes precludes its use in patients with arrhythmias, since errors in CO determination will undoubtedly result. Any acute change in tissue water, such as the development of pulmonary edema or pleural effusions or chest wall edema, will alter bioimpedance readings and affect CO measurements.

The intraoperative environment is not conducive to TEB measurements of CO due to interference by noise from electrocautery, mechanical ventilation and surgical manipulation. In addition, alterations in myocardial contractility that are induced by anesthetics, loading conditions and ischemia can cause errors in TEB measurements of CO, further reducing its usefulness in patients with coronary artery disease and poor ventricular function (ironically, the patient population the clinician would be most interested in).[36] Clinical trials of TEB have been shown to be reliable in young healthy volunteers, but in critically ill or surgical patients, the results have been inconsistent.[36–38] A meta-analysis of TEB studies found an r^2 value of 0.53 when compared with a reference method which led the authors to conclude that the interpretation of CO values from TEB in cardiac patients should be undertaken with caution.[39] Unfortunately, this meta-analysis did not use the Bland–Altman approach to analyze their data.

A new generation of TEB devices, including the BioZ (Cardiodynamics Intl., San Diego, CA, www.bioz.com) overcomes some of the initial limitations of the first generation TEB devices by having 1) faster signal processing, 2) better signal filtering, 3) improved ECG triggering, 4) improved arrhythmia detection, and 5) respiratory filtering.

In an intraoperative study of patients undergoing CABG surgery, the BioZ device did well initially in determining CO when compared with PAC_{TD}, however, during the immediate postoperative period, the correlation as measured by Bland–Altman analysis was not as robust.[40] This could have been secondary to changes in the amount of fluid in the pleural spaces or changes in the intrinsic contractility of the heart or the use of steel wires to reapproximate the sternum. The lack of correlation at the end of surgery did not seem to be due to the effects of opening the chest as the correlation between PAC_{TD} and TEB remained good with the initial opening of the chest.

Further studies in postoperative CABG patients showed good bias and precision when compared with PAC_{TD}. These studies suggest that, while the new generation devices might be better than the first generation TEB machines, questions still remain about their ability to measure CO during dynamic conditions.

Without improvements in signal processing techniques, it is unlikely that TEB will become a standard monitor in the anesthesia or critical care setting.[41] A newer monitor, the Aesculon (Osypka Medical, LA Jolla, CA) uses electrical velocimetry, which interprets the maximum rate of change of TEB to calculate CO. This monitor has shown some promise in postoperative cardiac surgical patients (both hemodynamically stable and unstable).[42] Further studies are required to validate this technology. There have been no clinical studies demonstrating outcome benefits or studies discussing the use of TEB with goal-directed therapy.

Methods Using the Fick Principle

Use of the Fick method is another noninvasive way of determining CO. First proposed by Adolf Fick in 1870, it is based on the conservation of mass, such that the total uptake or release of a substance by an organ

is the product of the blood flow to that organ multiplied by the arteriovenous concentration difference. Rearranging the original equation allows us to solve for CO

$$CO = \frac{VO_2}{Ca_{O_2} - Cv_{O_2}}$$

where VO_2 is oxygen consumption, Ca_{O_2} is arterial oxygen content, and Cv_{O_2} is mixed venous oxygen content. This technique is commonly used in cardiac catheterization laboratories and is considered the gold standard for measuring CO. The procedure, however, is invasive and methodological error is common. It is not used in the OR secondary to the difficulty in measuring oxygen uptake and the need for hemodynamic and respiratory stability to accurately measure CO.

The Fick principle can use many different indicators and, more recently, technologies have become available that have used CO_2 as an indicator.[43] The Fick equation can then be rewritten as

$$CO = \frac{\dot{V}CO_2}{Cv_{co_2} - Ca_{co_2}} \quad (1)$$

where VCO_2 is the CO_2 elimination, and Ca_{co_2} and Cv_{co_2} are the arterial and venous CO_2 contents, respectively. It is possible to calculate Ca_{co_2} from $Paco_2$ or estimate it from the end tidal CO_2. This estimation only holds true in patients with no diffusion abnormalities. VCO_2 can be calculated from the difference between inspired and expired gas CO_2 content. Measuring Cv_{co_2} is much more difficult.

Instead of using direct measurements of Cv_{co_2}, it can be estimated with the help of a partial rebreathing technique. This technique is called the differential CO_2 Fick partial rebreathing method. To estimate Cv_{co_2}, 150 mls of dead-space are added to the ventilator circuit by opening a rebreathing valve and measurements of the change in CO_2 elimination and end tidal CO_2 are made first during a period of non-rebreathing and a subsequent rebreathing period. The Fick equation for the non-rebreathing (nonrebr) and the rebreathing (rebr) periods can then be combined

$$CO = \frac{\dot{V}CO_{2nonrebr}}{Cv_{CO_{2nonrebr}} - Ca_{CO_{2nonrebr}}} \quad (2)$$

$$CO = \frac{\dot{V}CO_{2rebr}}{Cv_{CO_{2rebr}} - Ca_{CO_{2rebr}}} \quad (3)$$

$$CO = \frac{\dot{V}CO_{2nonrebr} - \dot{V}CO_{2rebr}}{(Cv_{CO_{2nonrebr}} - Ca_{CO_{2nonrebr}}) - (Cv_{CO_{2rebr}} - Ca_{CO_{2rebr}})} \quad (4)$$

The body has large stores of CO_2 and CO_2 has a slow time constant for diffusion, therefore, it can be assumed that the mixed venous CO_2 concentration will remain relatively constant throughout the breathing and non-rebreathing periods and as a result these terms cancel out. The equation then becomes

$$CO = \frac{\dot{V}CO_{2nonrebr} - \dot{V}CO_{2rebr}}{Ca_{CO_{2rebr}} - Ca_{CO_{2nonrebr}}} \quad (5)$$

Thus

$$CO = \frac{\Delta\dot{V}CO_2}{\Delta Ca_{CO_2}} \quad (6)$$

where $\Delta\dot{V}CO_2$ is the change in CO_2 elimination and ΔCa_{CO_2} is the change in alveolar blood CO_2 content between the baseline and rebreathing periods. To calculate the alveolar CO_2 content, the following equation is used

$$Ca_{CO_2} = (6.957[Hgb] + 94.864) * \log(1.0 + 0.1933\, PaCO_2) \quad (7)$$

where Hgb is hemoglobin concentration in g/L. The arterial CO_2 content is estimated using the $Paco_2$ and the CO_2 dissociation curve.

This technique only measures non-shunted blood and, therefore, to get an accurate measure of CO, the shunt fraction must be estimated by using the shunt equation:

$$\frac{Q_s}{Q_T} = \frac{CcO_2 - CaO_2}{CcO_2 - CvO_2} \quad (8)$$

where Ca_{O_2}, C_vO_2, and CaO_2 are the end-capillary, venous and arterial oxygen contents. In order to measure these noninvasively, Nunn's iso-shunt plots are used.[44] These plots are a series of curves that describe the relationship between Pao_2 and FIO_2 for different levels of intrapulmonary shunt. Thus, shunt can be determined simply by using the Pao_2 and FIO_2.

Several technical problems are encountered with this method. The difference between mixed venous and arterial CO_2 is usually only about 6 mm Hg. If this were to increase due to increases in dead-space, the calculated CO would change as well. The relationships between the $Paco_2$ and Pv_{CO_2} levels are only valid when the $Paco_2$ is more than 30 mm Hg, and when the CO_2-Hgb dissociation curve is linear. Thus, an increase in minute ventilation which reduces $Paco_2$ to <30 mm Hg would render the CO inaccurate. There are very few intraoperative situations where the $Paco_2$ would need to be decreased below this level (severe metabolic acidosis or decreases in intracranial elastance). Also, changes in mechanical ventilation that alter either the dead-space or ventilation perfusion matching may result in the calculated CO changing when, in fact, none has occurred. The only system currently on the market is the NICO® system (NICO® Sensor, Respironics, Wallingford, CT, www.nico.respironics.com).

Several studies have investigated the accuracy of the partial-rebreathing system for determining CO, mostly in patients undergoing cardiac surgery or in hemodynamically stable ICU patients with differing degrees of intrapulmonary shunt.[41,45–53] Overall, this system seems to correlate well with traditional PAC_{TD}-derived measurements of CO. The system seems to perform best at normal CO, but suffers lack of agreement when CO is high,[46] minute ventilation is decreased,[49,50] during periods of increased intrapulmonary shunt,[47] or during severe chest trauma.[51] In the study by Rocco et al., bias was −2.3 L/min when $\dot{Q}s/\dot{Q}p$ exceeded 35%.[47]

Overall, the studies on the CO_2 rebreathing system have shown significant bias (range: −0.58 to −1.73 L/min) in several patient populations, e.g., intraoperative general or cardiac surgery, or stable postoperative patients. There have been no reports on the device when used in hemodynamically unstable patients.[47–49,52,54]

Another drawback to the partial-rebreathing technique is that it is only a measure of CO and has no method of monitoring intravascular volume status or fluid responsiveness. There have been no clinical studies demonstrating outcome benefits using the CO_2 rebreathing device.

Lithium Dilution Devices

Indicator dilution methods of measuring CO were initially described in 1932 by Hamilton.[55] The initial indicator used was usually indocyanine green. The technique of using lithium dilution to measure CO was first described in 1993 by Linton et al.[56] A bolus of lithium chloride is injected into either a peripheral or central vein, and the subsequent lithium concentration decay is measured with a lithium-sensitive electrode in a preexisting arterial line. This electrode uses the Nernst equation to relate the voltage change across the electrode with the lithium concentration while applying a correction factor for plasma sodium, as the electrode has a low sensitivity for distinguishing these two cations. This information is then used to calculate a concentration versus time graph and the CO is then calculated from integrating the area under the curve. This technique requires an approximately 3 mL blood sample to obtain the lithium concentration. One of the advantages of this technique is that lithium does not naturally occur in plasma, therefore, it has a high signal-to-noise ratio. This allows very small doses to be used, and therefore toxic levels are virtually impossible to achieve.[57] Further, lithium is rapidly redistributed and has no first pass loss from the circulation.

Some of the concerns regarding the lithium dilution method are the need for the repetitive blood draws (and the concern of this precipitating blood transfusions) and the lack of ability to measure cardiac preload. Furthermore, the use of nondepolarizing neuromuscular antagonists has been shown to affect the lithium sensor. If this system is used intraoperatively, the recommendation is that the sensor be re-calibrated before injection of these drugs or after the peak concentration of the drug has had time to subside.[58]

Currently there is only one product on the market that uses a lithium dilution to measure CO (LiDCO®, LiDCO, London, UK, www.lidco-ir.co.uk). This device measures CO and then uses a pulse contour device to obtain subsequent continuous measurements of CO and assessment of preload.

Pulse Contour Devices

The theory behind using the arterial pulse waveform to measure CO dates back to 1899 when Otto Frank described the circulation in terms of a Windkessel model. It was Frank's goal to be able to calculate CO from arterial pulse pressure. Windkessel is the German word for an air chamber. This model described the loads faced by the heart when pumping against the pulmonary or systemic circulation and the relationship between the arterial blood pressure and flow in the systemic and pulmonary arteries.[58] The model compares a hydraulic pump in a closed circuit that is comprised of a water pump connected to a chamber with a pocket of air in it to the heart and systemic arterial system. When water is pumped into the chamber, the pocket of air is compressed and water is pushed back out of the chamber into the pump. The compressibility of air in this chamber represents the elasticity and distensability of the arterial system, commonly referred to as the arterial systems compliance. The resistance that is met by the water leaving the Windkessel and flowing back to the pump represents the SVR. This model is called a two element Windkessel model. Further refinements to this theory have led to the development of the three and four element Windkessel model.

In 1904, Erlanger and Hooker theorized that CO was proportional to arterial pulse pressure. Despite this early observation, it was only during the last several years that the technology to accurately measure CO with the arterial waveform has become available. It was soon discovered that, to accurately measure CO using the pulse waveform, some other method was needed to calibrate the system.

Further, the compliance of the arterial tree was a major impediment to the accurate measurement of CO. Simply stated, the compliance of the arterial tree is nonlinear. That is, when a volume of blood is introduced into the vasculature at higher pressures, the compliance decreases more rapidly than when the same volume of blood is introduced at a lower pressure. Such corrections for the nonlinearity of the system were not available until more information on the compliance of human aortas became known in 1948.[59] This led to measuring the systolic area from a waveform. The waveform was then calibrated with

another method for measuring CO, and then corrected for aortic compliance.

In 1983, Wesseling et al. developed an algorithm that can be used to define an area under the systemic arterial pulse waveform that establishes SV.[60] By integrating the area under the pressure time curve from end systole to end diastole the SV can be calculated.

Changes in the systolic pressure between the inspiratory and expiratory phase during mechanical ventilation can be used to ascertain intravascular volume status.[61,62] By calculating the systolic pressure variation and the SV variation (SVV) (derived from the continuous CO measurement), the pulse contour systems can also function as volume status monitors.

Since their inception, pulse contour devices have been extensively studied and validated with many studies showing a bias of 0.03 to 0.3 L/min.[63–67] These studies were conducted in a variety of patient populations (postcardiac surgery, medical ICU patients) and bias and precision were clinically acceptable. The accuracy of CO measurement remained despite changes induced with esmolol in one study.[64] However, in another study with cardiac surgical patients, the CO lost its correlation with PAC_{TD}-derived CO when SVR was artificially increased with phenylephrine.[68] The lack of correlation between pulse contour devices and PAC_{TD} has also been demonstrated in conditions in which the arterial waveform is altered, such as aortic regurgitation and the use of an intraaortic balloon pump. Pulse contour devices are affected by extrinsic factors such as positive end-expiratory pressure and tidal volume. Several studies have shown that alterations in tidal volume or the level of positive end-expiratory pressure can alter the derived CO.[32,69,70]

Pulse contour devices have some advantages over other devices used to measure CO. They require little training, are simple to calibrate and provide an estimation of intravascular volume status. Their use in high-risk surgical patients in whom more invasive hemodynamic monitoring is desired will likely increase in the future.

A newer device to measure CO noninvasively is the FloTrac (FloTrac® Edwards LifeSciences LLP, Irvine CA, www.edwards.com/products/mininvasive). This device also uses the arterial pressure waveform to measure CO. The difference over other monitors (such as the LiDCO®) is that it does not need to be calibrated with an indicator, such as lithium or with a transpulmonary-derived measure of CO. The essence of this technology is the application of advanced statistical principles to the arterial pressure tracing that result in the creation of a proprietary algorithm that recalibrates itself constantly. By measuring the arterial pressure over a 20 s period at 100 Hz, the system obtains 2000 data points for analysis. The standard deviation of these points is then compared with empirical data stored in the proprietary algorithm of the software correlating the standard deviation of the arterial pressure measurements with the appropriate SV. The FloTrac® is also able to account for changes in arterial compliance which allows for the device to remain accurate and reliable during periods when CO, vasomotor tone or both are changing.

A recent study in cardiac surgical patients comparing the FloTrac with PAC_{TD} CO showed good correlation with the PAC with a bias of 0.55 L/min.[71] The FloTrac also has the advantage of being able to determine SVV as a monitor of preload responsiveness. It is these features (the lack of need of a standard calibration and the ability to remain accurate in dynamic physiologic states) that could potentially make the FloTrac a useful addition to the group of noninvasive CO monitors. The disadvantages of the FloTrac and other pulse contour analysis systems (lack of correlation with PAC_{TD} when the hemodynamics or arterial waveform are altered) are being rectified by the manufacturers. Newer generation pulse contour analysis monitors calculate the pulsatility of the arterial waveform more frequently, thus leading to better correlation with PAC_{TD} when patients' hemodynamics are changing.

The pulse contour devices are perhaps the most promising with regard to their ease of use, precision when compared with PAC_{TD} ease of calibration, and their ability to measure intravascular volume responsiveness. However, more studies demonstrating clinical utility in different patient populations (such as those who are hemodynamically unstable) are needed.

TRANSPULMONARY THERMODILUTION TECHNIQUES

This technique uses a central venous catheter and an arterial line to intermittently measure the CO via transpulmonary thermodilution. The arterial catheter (that must be placed in a femoral, brachial or axillary artery) is then used as a pulse contour device to measure CO continuously. Radial artery catheterization is not sufficient, as the damped waveform that can occur with the use of vasopressors or changes in SVR has shown to invalidate the CO measurements. The PiCCO system (Pulsion Medical Systems, Munich, Germany, www.pulsion.com) uses this technology and provides the operator with several continuous variables to monitor patient's hemodynamic status. SV and SVV are continuously measured, whereas variables, such as extravascular lung water are measured intermittently. Extravascular lung water is a potentially important measurement as it may be able to predict a patient's risk of developing pulmonary edema with intravascular volume loading.

This technology is more widely used in Europe and has good agreement with other standard measures of CO. In patients undergoing liver transplant or CABG surgery bias ranged from 0.04 to 0.3 L/min.[72–74] When trialed in patients with hemodynamic instability, the PiCCO system was not as accurate, with one study

Table 2. Summary of Studies Utilizing Goal Directed Therapy

Author and reference	Patient population	Number of patients	Device used	Outcome variable	Results (primary outcome)	Other findings
Mythen and Webb[11]	Cardiac Surgery	60	Esophageal Doppler	Gut Mucosal Perfusion	Increased gut mucosal perfusion	Decreased hospital & ICU LOS, decreased complications
Sinclair et al.[23]	Femoral Fracture	40	Esophageal Doppler	Time to fitness for discharge, mortality, CO, SV	Decreased Hospital LOS increased SV & CO	No change in mortality
Conway et al.[28]	Major bowel surgery	55	Esophageal Doppler	CO, Hospital LOS, Complications	Increased CO, No change in LOS or complications	Decreased ICU admissions
Gan et al.[2]	General, gynecological and urological surgery	100	Esophageal Doppler	LOS, GI, and renal complications	Decreased Hospital LOS	Less PONV, earlier tolerance of enteral nutrition
Venn et al.[24]	Hip Fracture patients	90	Esophageal Doppler	Fitness to discharge, LOS, Post-op morbidity	Faster time to fitness for discharge	No change in LOS or morbidity
McKendry et al.[77]	Cardiac Surgery	174	Esophageal Doppler	Hospital and ICU LOS, complications	Decreased hospital LOS	No change in ICU LOS or complications
Wakeling et al.[25]	Major bowel surgery	128	Esophageal Doppler	Hospital LOS, gut function	Decreased Hospital LOS	Decreased GI morbidity
Pearse et al.[78]	Major General Surgery	122	LiDCO	Complications, LOS	Decreased Hospital LOS, complications	
Noblett et al.[27]	Colorectal resection	103	Esophageal Doppler	LOS	Decreased Hospital LOS	Tolerated enteral nutrition earlier
Kapoor et al.[79]	Cardiac Surgery	30	Pulse Contour	Cardiac Index	Increased Cardiac Index	Shorter duration of ventilation, ICU LOS

CO = cardiac output; SV = stroke volume; LOS = length of stay; GI = gastrointestinal; PONV = postoperative nausea and vomiting; LiDCO = lithium dilution cardiac output.

reporting bias of 0.68 L/min and limits of agreement of ±1.94 L/min.[75] Such degree of bias and wide limits of agreement led the authors to conclude that this method has to be used with caution when used in unstable patients.

Goal-directed therapy with this technology has been reported in patients undergoing CABG surgery.[76] The study found that when an algorithmic approach to fluid management that included the titration of colloids to a global end-diastolic volume index was used, patients received less total dose and shorter duration of vasopressor support, shorter periods of mechanical ventilation and a reduced time to achieve fitness for ICU discharge.

The drawback to this system is the need for a central line and the need for cannulation of a large artery. This technology has been more widely used in the intensive care settings but the suitability for use in the OR is somewhat limited as it does not negate the need for central venous access and therefore is not a "minimally" invasive device.

CONCLUSIONS

With the advancing age of the surgical population and the increasing prevalence of ischemic heart disease, the need for monitoring of organ flow is likely to increase. Because of the inherent limitations and complications of the use of a PAC, clinicians (both in the OR and the critical care setting) are looking more toward the use of minimally or noninvasive monitors of CO.

Of the available monitors, the ED and the arterial pulse contour devices seem to have the greatest potential at replacing the PAC for CO measurement. Some of the limitations of these devices, such as the inability to measure pressures in the central circulation (i.e., pulmonary artery occlusion pressure) will limit their use in patients in whom concern over the development of pulmonary edema is present. Furthermore, the inability of these devices to measure either central or true mixed venous oxygen saturation limits their use in the assessment of global tissue perfusion. However, some of the noninvasive CO monitors have the ability to predict fluid responsiveness. The ED and arterial pulse contour monitors have been shown (when combined with an intraoperative goal-directed fluid strategy) to reduce postoperative morbidity. A summary table of the studies that have demonstrated benefits of goal-directed therapy is shown in Table 2.

All of the currently available noninvasive monitors have advantages and limitations. With an increasing

number of clinical studies being published on the applicability, suitability, and clinical utility of these monitors and more importantly demonstrating outcome differences, their use should continue to gain popularity.

REFERENCES

1. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, Peterson E, Tomlanovich M. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001;345:1368–77
2. Gan TJ, Soppitt A, Maroof M, el-Moalem H, Robertson KM, Moretti E, Dwane P, Glass PS. Goal-directed intraoperative fluid administration reduces length of hospital stay after major surgery. Anesthesiology 2002;97:820–6
3. Dexter L. Cardiac catheterization in the diagnosis of congenital heart disease. Bull N Y Acad Med 1950;26:93–102
4. Swan HJ, Ganz W, Forrester J, Marcus H, Diamond G, Chonette D. Catheterization of the heart in man with use of a flow-directed balloon-tipped catheter. N Engl J Med 1970;283:447–51
5. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307–10
6. Fleisher LA, Eagle KA. Clinical practice. Lowering cardiac risk in noncardiac surgery. N Engl J Med 2001;345:1677–82
7. Mangano DT, Goldman L. Preoperative assessment of patients with known or suspected coronary disease. N Engl J Med 1995;333:1750–6
8. Domino KB, Bowdle TA, Posner KL, Spitellie PH, Lee LA, Cheney FW. Injuries and liability related to central vascular catheters: a closed claims analysis. Anesthesiology 2004; 100:1411–8
9. DiCorte CJ, Latham P, Greilich PE, Cooley MV, Grayburn PA, Jessen ME. Esophageal Doppler monitor determinations of cardiac output and preload during cardiac operations. Ann Thorac Surg 2000;69:1782–6
10. Madan AK, UyBarreta VV, Aliabadi-Wahle S, Jesperson R, Hartz RS, Flint LM, Steinberg SM. Esophageal Doppler ultrasound monitor versus pulmonary artery catheter in the hemodynamic management of critically ill surgical patients. J Trauma 1999;46:607–11; discussion 11–12
11. Mythen MG, Webb AR. Perioperative plasma volume expansion reduces the incidence of gut mucosal hypoperfusion during cardiac surgery. Arch Surg 1995;130:423–9
12. Cariou A, Monchi M, Joly LM, Bellenfant F, Claessens YE, Thebert D, Brunet F, Dhainaut JF. Noninvasive cardiac output monitoring by aortic blood flow determination: evaluation of the Sometec Dynemo-3000 system. Crit Care Med 1998;26:2066–72
13. Mark JB, Steinbrook RA, Gugino LD, Maddi R, Hartwell B, Shemin R, DiSesa V, Rida WN. Continuous noninvasive monitoring of cardiac output with esophageal Doppler ultrasound during cardiac surgery. Anesth Analg 1986;65:1013–20
14. Freund PR. Transesophageal Doppler scanning versus thermodilution during general anesthesia. An initial comparison of cardiac output techniques. Am J Surg 1987;153:490–4
15. Spahn DR, Schmid ER, Tornic M, Jenni R, von Segesser L, Turina M, Baetscher A. Noninvasive versus invasive assessment of cardiac output after cardiac surgery: clinical validation. J Cardiothorac Anesth 1990;4:46–59
16. Lefrant JY, Bruelle P, Aya AG, Saissi G, Dauzat M, de La Coussaye JE, Eledjam JJ. Training is required to improve the reliability of esophageal Doppler to measure cardiac output in critically ill patients. Intensive Care Med 1998;24:347–52
17. Singer M, Clarke J, Bennett ED. Continuous hemodynamic monitoring by esophageal Doppler. Crit Care Med 1989; 17:447–52
18. Valtier B, Cholley BP, Belot JP, de la Coussaye JE, Mateo J, Payen DM. Noninvasive monitoring of cardiac output in critically ill patients using transesophageal Doppler. Am J Respir Crit Care Med 1998;158:77–83
19. Dark PM, Singer M. The validity of trans-esophageal Doppler ultrasonography as a measure of cardiac output in critically ill adults. Intensive Care Med 2004;30:2060–6
20. Boulnois JL, Pechoux T. Non-invasive cardiac output monitoring by aortic blood flow measurement with the Dynemo 3000. J Clin Monit Comput 2000;16:127–40
21. Tan HL, Pinder M, Parsons R, Roberts B, van Heerden PV. Clinical evaluation of USCOM ultrasonic cardiac output monitor in cardiac surgical patients in intensive care unit. Br J Anaesth 2005;94:287–91
22. Chand R, Mehta Y, Trehan N. Cardiac output estimation with a new Doppler device after off-pump coronary artery bypass surgery. J Cardiothorac Vasc Anesth 2006;20:315–9
23. Sinclair S, James S, Singer M. Intraoperative intravascular volume optimisation and length of hospital stay after repair of proximal femoral fracture: randomised controlled trial. BMJ 1997;315:909–12
24. Venn R, Steele A, Richardson P, Poloniecki J, Grounds M, Newman P. Randomized controlled trial to investigate influence of the fluid challenge on duration of hospital stay and perioperative morbidity in patients with hip fractures. Br J Anaesth 2002;88:65–71
25. Wakeling HG, McFall MR, Jenkins CS, Woods WG, Miles WF, Barclay GR, Fleming SC. Intraoperative oesophageal Doppler guided fluid management shortens postoperative hospital stay after major bowel surgery. Br J Anaesth 2005;95:634–42
26. Singer M. Cardiac output in 1998. Heart 1998;79:425–8
27. Noblett SE, Snowden CP, Shenton BK, Horgan AF. Randomized clinical trial assessing the effect of Doppler-optimized fluid management on outcome after elective colorectal resection. Br J Surg 2006;93:1069–76
28. Conway DH, Mayall R, Abdul-Latif MS, Gilligan S, Tackaberry C. Randomised controlled trial investigating the influence of intravenous fluid titration using oesophageal Doppler monitoring during bowel surgery. Anaesthesia 2002;57:845–9
29. Singer M. The FTc is not an accurate marker of left ventricular preload. Intensive Care Med 2006;32:1089; author reply 91
30. Bundgaard-Nielsen M, Ruhnau B, Secher NH, Kehlet H. Flow-related techniques for preoperative goal-directed fluid optimization. Br J Anaesth 2007;98:38–44
31. Laupland KB, Bands CJ. Utility of esophageal Doppler as a minimally invasive hemodynamic monitor: a review. Can J Anaesth 2002;49:393–401
32. Kubicek WG, Karnegis JN, Patterson RP, Witsoe DA, Mattson RH. Development and evaluation of an impedance cardiac output system. Aerosp Med 1966;37:1208–12
33. Chaney JC, Derdak S. Minimally invasive hemodynamic monitoring for the intensivist: current and emerging technology. Crit Care Med 2002;30:2338–45
34. Summers RL, Shoemaker WC, Peacock WF, Ander DS, Coleman TG. Bench to bedside: electrophysiologic and clinical principles of noninvasive hemodynamic monitoring using impedance cardiography. Acad Emerg Med 2003;10:669–80
35. Bernstein DP. A new stroke volume equation for thoracic electrical bioimpedance: theory and rationale. Crit Care Med 1986;14:904–9
36. Perrino AC Jr, Lippman A, Ariyan C, O'Connor TZ, Luther M. Intraoperative cardiac output monitoring: comparison of impedance cardiography and thermodilution. J Cardiothorac Vasc Anesth 1994;8:24–9
37. Barin E, Haryadi DG, Schookin SI, Westenskow DR, Zubenko VG, Beliaev KR, Morozov AA. Evaluation of a thoracic bioimpedance cardiac output monitor during cardiac catheterization. Crit Care Med 2000;28:698–702
38. Imhoff M, Lehner JH, Lohlein D. Noninvasive whole-body electrical bioimpedance cardiac output and invasive thermodilution cardiac output in high-risk surgical patients. Crit Care Med 2000;28:2812–8
39. Raaijmakers E, Faes TJ, Scholten RJ, Goovaerts HG, Heethaar RM. A meta-analysis of three decades of validating thoracic impedance cardiography. Crit Care Med 1999;27:1203–13
40. Spiess BD, Patel MA, Soltow LO, Wright IH. Comparison of bioimpedance versus thermodilution cardiac output during cardiac surgery: evaluation of a second-generation bioimpedance device. J Cardiothorac Vasc Anesth 2001;15:567–73
41. Botero M, Kirby D, Lobato EB, Staples ED, Gravenstein N. Measurement of cardiac output before and after cardiopulmonary bypass: comparison among aortic transit-time ultrasound, thermodilution, and noninvasive partial CO_2 rebreathing. J Cardiothorac Vasc Anesth 2004;18:563–72

42. Suttner S, Schollhorn T, Boldt J, Mayer J, Rohm KD, Lang K, Piper SN. Noninvasive assessment of cardiac output using thoracic electrical bioimpedance in hemodynamically stable and unstable patients after cardiac surgery: a comparison with pulmonary artery thermodilution. Intensive Care Med 2006;32:2053–8
43. Jaffe MB. Partial CO_2 rebreathing cardiac output–operating principles of the NICO system. J Clin Monit Comput 1999;15:387–401
44. Nunn J. Applied respiratory physiology. 4th ed. Oxford: Butterworth Ltd, 1993
45. Suzuki M, Koda S, Nakamura Y, Kawamura N, Shimada Y. The relationship between cardiac output measured by the thermodilution method and that measured by the carbon dioxide rebreathing technique during laparoscopic surgery. Anesth Analg 2005;100:1381–3; table of contents
46. Jover JL, Soro M, Belda FJ, Aguilar G, Caro P, Ferrandis R. Measurement of cardiac output after cardiac surgery: validation of a partial carbon dioxide rebreathing (NICO) system in comparison with continuous thermodilution with a pulmonary artery catheter. Rev Esp Anestesiol Reanim 2005;52:256–62
47. Rocco M, Spadetta G, Morelli A, Dell'Utri D, Porzi P, Conti G, Pietropaoli P. A comparative evaluation of thermodilution and partial CO_2 rebreathing techniques for cardiac output assessment in critically ill patients during assisted ventilation. Intensive Care Med 2004;30:82–7
48. Kotake Y, Moriyama K, Innami Y, Shimizu H, Ueda T, Morisaki H, Takeda J. Performance of noninvasive partial CO_2 rebreathing cardiac output and continuous thermodilution cardiac output in patients undergoing aortic reconstruction surgery. Anesthesiology 2003;99:283–8
49. Tachibana K, Imanaka H, Takeuchi M, Takauchi Y, Miyano H, Nishimura M. Noninvasive cardiac output measurement using partial carbon dioxide rebreathing is less accurate at settings of reduced minute ventilation and when spontaneous breathing is present. Anesthesiology 2003;98:830–7
50. Tachibana K, Imanaka H, Miyano H, Takeuchi M, Kumon K, Nishimura M. Effect of ventilatory settings on accuracy of cardiac output measurement using partial CO(2) rebreathing. Anesthesiology 2002;96:96–102
51. Maxwell RA, Gibson JB, Slade JB, Fabian TC, Proctor KG. Noninvasive cardiac output by partial CO_2 rebreathing after severe chest trauma. J Trauma 2001;51:849–53
52. Nilsson LB, Eldrup N, Berthelsen PG. Lack of agreement between thermodilution and carbon dioxide-rebreathing cardiac output. Acta Anaesthesiol Scand 2001;45:680–5
53. Binder JC, Parkin WG. Non-invasive cardiac output determination: comparison of a new partial-rebreathing technique with thermodilution. Anaesth Intensive Care 2001;29:19–23
54. Mielck F, Buhre W, Hanekop G, Tirilomis T, Hilgers R, Sonntag H. Comparison of continuous cardiac output measurements in patients after cardiac surgery. J Cardiothorac Vasc Anesth 2003;17:211–6
55. Hamilton WF, Moore WJ, Kinsman JM. Studies on the circulation IV. Further analysis of the injection methods and of changes in hemodynamics under physiological conditions. Am J Physiol 1932;99:534–51
56. Linton RA, Band DM, Haire KM. A new method of measuring cardiac output in man using lithium dilution. Br J Anaesth 1993;71:262–6
57. Jonas MM, Tanser SJ. Lithium dilution measurement of cardiac output and arterial pulse waveform analysis: an indicator dilution calibrated beat-by-beat system for continuous estimation of cardiac output. Curr Opin Crit Care 2002;8:257–61
58. Rhodes A, Sunderland R. Arterial pulse power analysis: the LIDCO plus system. Update Intensive Care Emerg Med 2005;42:183–92
59. Remington JW, Noback CR, Hamilton WF, Gold JJ. Volume elasticity characteristics of the human aorta and the prediction of stroke volume from the pressure pulse. Am J Physiol 1948;153:198–308
60. Wesseling KH, de Wit B, Weber JAP, Smith NT. A simple device for the continuous measurement of cardiac output. Adv Cardiovasc Phys 1983;5:16–52
61. Michard F, Boussat S, Chemla D, Anguel N, Mercat A, Lecarpentier Y, Richard C, Pinsky MR, Teboul JL. Relation between respiratory changes in arterial pulse pressure and fluid responsiveness in septic patients with acute circulatory failure. Am J Respir Crit Care Med 2000;162:134–8
62. Michard F. Changes in arterial pressure during mechanical ventilation. Anesthesiology 2005;103:419–28; quiz 49–5
63. Jansen JR, Schreuder JJ, Mulier JP, Smith NT, Settels JJ, Wesseling KH. A comparison of cardiac output derived from the arterial pressure wave against thermodilution in cardiac surgery patients. Br J Anaesth 2001;87:212–22
64. Buhre W, Weyland A, Kazmaier S, Hanekop GG, Baryalei MM, Sydow M, Sonntag H. Comparison of cardiac output assessed by pulse-contour analysis and thermodilution in patients undergoing minimally invasive direct coronary artery bypass grafting. J Cardiothorac Vasc Anesth 1999;13:437–40
65. Goedje O, Hoeke K, Lichtwarck-Aschoff M, Faltchauser A, Lamm P, Reichart B. Continuous cardiac output by femoral arterial thermodilution calibrated pulse contour analysis: comparison with pulmonary arterial thermodilution. Crit Care Med 1999;27:2407–12
66. Zollner C, Briegel J, Kilger E, Haller M. Retrospective analysis of transpulmonary and pulmonary arterial measurement of cardiac output in ARDS patients. Anaesthesist 1998;47:912–7
67. Zollner C, Haller M, Weis M, Morstedt K, Lamm P, Kilger E, Goetz AE. Beat-to-beat measurement of cardiac output by intravascular pulse contour analysis: a prospective criterion standard study in patients after cardiac surgery. J Cardiothorac Vasc Anesth 2000;14:125–9
68. Rodig G, Prasser C, Keyl C, Liebold A, Hobbhahn J. Continuous cardiac output measurement: pulse contour analysis vs thermodilution technique in cardiac surgical patients. Br J Anaesth 1999;82:525–30
69. Kubitz JC, Annecke T, Forkl S, Kemming GI, Kronas N, Goetz AE, Reuter DA. Validation of pulse contour derived stroke volume variation during modifications of cardiac afterload. Br J Anaesth 2007;98:591–7
70. Reuter DA, Bayerlein J, Goepfert MS, Weis FC, Kilger E, Lamm P, Goetz AE. Influence of tidal volume on left ventricular stroke volume variation measured by pulse contour analysis in mechanically ventilated patients. Intensive Care Med 2003;29:476–80
71. Manecke GR Jr, Auger WR. Cardiac output determination from the arterial pressure wave: clinical testing of a novel algorithm that does not require calibration. J Cardiothorac Vasc Anesth 2007;21:3–7
72. Button D, Weibel L, Reuthebuch O, Genoni M, Zollinger A, Hofer CK. Clinical evaluation of the FloTrac/Vigileo system and two established continuous cardiac output monitoring devices in patients undergoing cardiac surgery. Br J Anaesth 2007;99:329–36
73. Della Rocca G, Costa MG, Pompei L, Coccia C, Pietropaoli P. Continuous and intermittent cardiac output measurement: pulmonary artery catheter versus aortic transpulmonary technique. Br J Anaesth 2002;88:350–6
74. Wiesenack C, Prasser C, Keyl C, Rodig G. Assessment of intrathoracic blood volume as an indicator of cardiac preload: single transpulmonary thermodilution technique versus assessment of pressure preload parameters derived from a pulmonary artery catheter. J Cardiothorac Vasc Anesth 2001;15:584–8
75. Compton FD, Zukunft B, Hoffmann C, Zidek W, Schaefer JH. Performance of a minimally invasive uncalibrated cardiac output monitoring system (Flotrac/Vigileo) in haemodynamically unstable patients. Br J Anaesth 2008;100:451–6
76. Goepfert MS, Reuter DA, Akyol D, Lamm P, Kilger E, Goetz AE. Goal-directed fluid management reduces vasopressor and catecholamine use in cardiac surgery patients. Intensive Care Med 2007;33:96–103
77. McKendry M, McGloin H, Saberi D, Caudwell L, Brady AR, Singer M. Randomised controlled trial assessing the impact of a nurse delivered, flow monitored protocol for optimisation of circulatory status after cardiac surgery. BMJ 2004;329:258
78. Pearse R, Dawson D, Fawcett J, Rhodes A, Grounds RM, Bennett ED. Early goal-directed therapy after major surgery reduces complications and duration of hospital stay. A randomised, controlled trial [ISRCTN38797445]. Crit Care 2005;9:R687–93
79. Kapoor PM, Kakani M, Chowdhury U, Choudhury M, Lakshmy, Kiran U. Early goal-directed therapy in moderate to high-risk cardiac surgery patients. Ann Card Anaesth 2008;11:27–34

