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REVIEW

Newer methods of cardiac output monitoring

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Abstract

Cardiac output (CO) is the volume of blood ejected by each ventricle per minute and is the product of stroke volume and heart rate. CO can thus be manipulated by alteration in heart rate or rhythm, preload, contractility and afterload. Moreover it gives important information about tissue perfusion and oxygen delivery. CO can be measured by various methods and thermodilution method using pulmonary artery catheter (PAC) is till date considered as gold standard method. Complications associated with PAC led to development of newer methods which are minimally or non-invasive. Newer methods fulfil other properties like continuous and reproducible reading, cost effective, reliable during various physiological states and have fast response time. These methods are validated against the gold standard with good level agreement. In this review we have discussed various newer methods of CO monitoring and their effectiveness in clinical use.

Key words: Cardiac output; Pulse contour analysis; Pulse power analysis; Bioimpedance; Doppler; Echocardiography

Core tip: This is review of newer methods of cardiac output monitoring which are minimally invasive and have lesser complications as compared to gold standard methods.

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INTRODUCTION

Cardiac output (CO) monitoring is an important tool in high risk critically ill surgical patients in whom large fluid shifts are expected along with bleeding and hemodynamic instability. It is an important component of goal directed therapy (GDT), *i.e.*, when a monitor is used in conjunction with administration of fluids and vasopressors to achieve set therapeutic endpoints thereby improving patient care and outcome. CO cannot be measured reliably by clinical examination and routine assessment. There are various methods of CO monitoring based on Ficks principle, thermodilution, Doppler, pulse contour analysis and bioimpedance. Each method has its own merits and demerits (Table 1). An ideal CO monitor should be minimally or non-invasive, continuous, cost effective, reproducible, reliable during various physiological states and have fast response time[1]. Advances in the computer software and hardware have led to development of newer methods of CO monitoring with minimal or no vascular access.

Methods of CO monitoring are broadly classified as follows: (1) Invasive-Intermittent bolus pulmonary artery thermodilution, Continuous pulmonary artery thermodilution; (2) Minimally invasive-Lithium dilution CO (LiDCO), Pulse contour analysis CO (PiCCO and FloTrac), Esophgeal Doppler (ED), transesophgeal echocardiography (TEE); and (3) Non-invasive-Partial gas rebreathing, Thoracic bioimpedance and bioreactance, endotracheal cardiac output monitor (ECOM), Doppler method and Photoelectric plethysmography.

Table 1 Advantages and disadvantages of methods of cardiac output monitoring

No	Device	Type	Advantages	Disadvantages
1	PAC	Invasive	Gold standard	Catheter related complications
2	Continous CO by PAC	Invasive	Continous CO measurement	Catheter related complications Cost
3	LiDCO	Minimally invasive	Only one arterial line Continuous CO measurements Measure SV and SVV	Requires good arterial waveform Requires Calibration Contraindicated in Lithium therapy
4	PiCCO	Minimally invasive	Continuous CO measurement Effective during hemodynamic instability	Requires good arterial waveform Requires calibration
5	FloTrac	Minimally invasive	Continuous CO measurement No calibration	Requires good arterial waveform
6	PRAM	Minimally invasive	No calibration	Still not validated
7	ED	Minimally invasive	Simple to use Reliable Useful in GDT	Measure flow only in descending thoracic aorta Assumptions about aortic size may not be accurate
8	TEE	Minimally invasive	Evaluate cardiac anatomy preload and ventricular function	Cost Skilled personnel
9	Partial non-rebreathing systems	Non invasive	Ease of use Continuous CO measurement	Affected by changes in dead space or V/Q matching
10	Thoracic bioimpedance	Non invasive	Continuous CO measurement	Affected by electrical noise, movement, temperature and humidity Requires hemodynamic stability Not useful in dysrhythmias
11	ECOM	Non invasive	Continuous CO measurement	Coronary blood flow not recorded Electrocautery produces interference

CO: Cardiac output; LiDCO: Lithium dilution CO; PiCCO and FloTrac: Pulse contour analysis; PRAM: Pressure recording analytic method; ED: Esophgeal Doppler; TEE: Transesophgeal echocardiography; ECOM: Endotracheal cardiac output monitor; PAC: Pulmonary artery catheter; SV: Stroke volume; SVV: SV variation; GDT: Goal directed therapy.

INVASIVE METHODS

Cardiac output measurement by pulmonary artery catheter

Pulmonary artery catheter (PAC) as a monitor to measure flow and pressure was developed by Dexter[2] and modified later on by Swan *et al*[3] to measure CO and central filling pressures. It is still considered as gold standard monitor to measure CO since 1970's[4]. It has been used as a monitoring tool in high risk surgeries and critical care units.

However, its use has been associated with various complications like pneumothorax, arrhythmia, infection, pulmonary artery rupture, valve injury, knotting and thrombosis leading to embolism[5,6]. Also, various technical errors may lead to false readings like loss of injectate, variability of temperature, thermistor malfunction, clot over catheter tip, coiling of catheter or timing of injectate > 4 s. Moreover, intracardiac shunts, mechanical ventilation or valvular dysfunction may lead to incorrect readings. These errors and adverse effects led to the development of less invasive methods of CO monitoring[7,8]. Thus the main objective of present review article is to focus on the newer methods of CO monitoring that are validated with the gold standard method and have ease of use and lesser complications.

CONTINUOUS CO MEASUREMENT BY PAC

Continuous CO (CCO, Edwards Lifesciences, Irvine, California, United States) is a modification of PAC with copper filament in the catheter that remains in the right ventricle. There is intermittent heating of blood in the right heart by the filament and the resultant signal is captured by thermistor near the tip of the catheter. Average value of CO measured over time is displayed on the monitor. Main advantages of CCO over conventional PAC are avoidance of repeated boluses thus reducing the infection risk and operator errors[5]. Moreover, continuous monitoring of stroke volume (SV), systemic vascular resistance (SVR) and mixed venous saturation can also be performed with this catheter. We found CCO to be comparable to conventional intermittent thermodilution CO in patients undergoing off pump coronary artery bypass grafting surgery (OPCAB) at various time points[9].

Literature review regarding use of PAC in operating room and intensive care units (ICU) revealed both benefits and risks. Gore *et al*[10] showed that PAC use increased mortality after myocardial infarctionand SUPPORT trial also showed increased mortalityat 30 d[11]. Complications have led some authors to call for complete moratorium on PAC use[12]. Various randomized controlled trials (RCT) also demonstrated increased incidence of adverse events in comparison to central venous pressure 1.5% *vs* 0.7% with no significant difference in mortality and length of stay in hospital[13]. Later on PAC-MAN trial failed to show any benefit or harm with the use of PAC[14]. Its use in patients undergoing OPCAB also showed no difference in mortality and final outcome[15]. ESCAPE trial demonstrated functional improvement with PAC guided

therapy used in patients with congestive heart failure[16].

Inspite of various arguments PAC is still considered as the "Gold Standard" for monitoring of CO. However, due to inherent risk associated with its use investigators are trying to develop a minimally or non-invasive monitor for CO which has all the characteristics of an ideal monitor. Various methods based on arterial pulse contour analysis, plethysmography, Fick's principle or bioimpedance have been developed. Its values should be within limits of agreement (Bland Altman analysis)[17] of the "gold standard". We will discuss these methods in the present review.

MINIMALLY INVASIVE METHODS

Pulse power analysis

This method is based on the principle that change of the blood pressure about the mean is directly related to the SV. Various factors affect its accuracy like compliance of the arterial tree, wave reflection, damping of the transducer and aortic systolic outflow[18].

LiDCO (Cambridge, United Kingdom) system combines pulse contour analysis with lithium indicator dilution for continuous monitoring of SV and SV variation (SVV). Root mean square method is applied to the arterial pressure signal and called "nominal SV" and using a patient specific calibration factor is further scaled to an "actual SV"[19]. It is a minimally invasive technique first described in 1993[18] and requires a venous (central or peripheral) line and an arterial catheter. A bolus of lithium chloride is injected into venous line and arterial concentration is measured by withdrawing blood across disposable lithium sensitive sensor containing an ionophor selectively permeable to Li. CO is calculated based on Li dose and area according to the concentration time circulation[20].

It requires calibration every 8 h and during major hemodynamic changes. It is contraindicated in patients on Li therapy and calibration is also affected by neuromuscular blockers as quaternary ammonium residue causes electrode to drift[20]. Its accuracy is affected by aortic regurgitation, intraaortic balloon pump (IABP), damped arterial line, postaortic surgery, arrhythmia and intra or extracardiac shunts[5,20].

This device has been studied in relation with PAC. Linton *et al*[18] found good correlation with PAC. Good correlation with PAC has also been found in patients undergoing liver transplantation[21]. Pearse *et al*[22] studied it for early goal directed therapy and revealed fewer complications and shorter length of hospital stay.

Pulse contour analysis

It is based on the principle that area under the systolic part of the arterial pressure waveform is proportional to the SV[23]. It was first described by Erlanger and Hooker in 1904 and suggested that CO was proportional to arterial pulse pressure[24]. In this method the area is measured post diastole to end of ejection phase divided by aortic impedance that measures SV. It also measures SVV and pulse pressure variation (PVV) which is useful in predicting fluid responsiveness. SVV is the difference between maximum and minimum SV over the respiratory cycle and is caused by changes in preload with alteration in intrathoracic pressure. In addition to that shape of the arterial waveform (dP/dt), arterial compliance, SVR and patient specific calibration factors are also required for calibration[24]. In 1970's first algorithm was developed to continuously analyse the pressure waveform from arterial line[25].

PICCO system: The PiCCO system (PULSION medical system, Munich, Germany) was the first pulse contour device introduced and was replaced with PiCCO2 in 2007[26]. It requires both central venous (femoral or internal jugular) and arterial cannulation (femoral/radial). Indicator solution injected *via* central venous cannula and blood temperature changes are detected by a thermistor tip catheter placed in the artery. Thus, it combines pulse contour analysis with the transpulmonary thermodilution CO to determine hemodynamic variables. It requires manual calibration every 8 h and hourly during hemodynamic instability[27].

In addition, thermodilution curve can be used to measure intrathoracic blood volume (ITBV), global end diastolic volume (GEDV) and extravascular lung water (EVLW). GEDV and ITBV are a measure of cardiac preload and EVLW (interstitial, intracellular or intra alveolar) is a mean to quantify pulmonary edema. It also measures SVV/PVV which is marker of fluid responsiveness[28].

PiCCO is a relatively invasive method as it requires both arterial and venous cannulation. Its accuracy may be affected be vascular compliance, aortic impedence and peripheral arterial resistance. Moreover, air bubble, clots and inadequate indicator may also affect the accuracy. Valvular regurgitation, aortic aneurysm, significant arrhythmia and rapidly changing temperature may also affect its accuracy[29].

Various validation studies have found good correlation with PAC during coronary artery bypass grafting[30]. However, that is not the case in patients undergoing OPCAB[31]. Innon-cardiac and critically ill patients good correlation has been observed[32]. Significant errors have been reported during hemodynamic instability requiring recalibration[33].

FloTrac system: FloTrac (Edwards LifeSciences. Irvine, United States) is a pulse contour device introduced in 2005 and is a minimally invasive method as it requires only an arterial line (femoral or radial).The system does not need any external calibration, is operator independent and easy to use. It is based on the principle that there is a linear relationship between the pulse pressure and SV[19,34].

The algorithm used in this system uses SD of 2000 arterial waveform points which is calculated by arterial pressure waveform sampled each 20 s at 100 Hz. It in-

corporates characteristics of the arterial waveform with patient specific demographics. The SV is estimated by following equation:

$$SV = SD_{AP} X \mu$$

SD_{AP} = Standard deviation of data points that reflects pulse pressure.

μ = Conversion factor depends on arterial compliance, mean arterial pressure, waveform characteristics.

Vascular compliance is patient's biometric values (sex, age, height and sex)[35] and waveform characteristics assessed by skewness (degree of asymmetry) and kurtosis (degree of peakedness) of the individual arterial pressure waveform. A change in vascular tone is represented by skewness and kurtosis. The conversion factor μ enables calculation of SV without external calibration. Second generation devices also developed that calibrate every minute leading to improved CO measurement[36]. A third generation device with Dynamo tone technology that has automatic adjustment for change in the vascular tone has also been made[37]. Good arterial waveform quality is a prerequisite for accurate reading of CO. Accuracy is affected in patients with significant arrhythmias, IABP or morbid obesity[38].

Various studies have validated the efficacy of FloTrac with PAC and find good correlation. We have studied FloTrac with PAC in patients undergoing OPCAB and found good agreement. The mean bias and limits of agreement (2 standard deviations) expressed in liters per minute at respective points of measurement were -0.54 ± 1.12, -0.37 ± 1.0, -0.42 ± 1.50, -0.25 ± 1.18, -0.31 ± 1.28, 0.41 ± 1.0, 0.06 ± 1.50, and 0.09 ± 1.40[39]. However, in patients with low SVR undergoing liver transplantation or septicemia it is not found as accurate as PAC[40-42]. It is found to be useful in patients undergoing major abdominal surgery who received GDT[43]. Moreover, the site of the arterial cannulation is also an important determinant of accuracy. In severe vasoconstriction radial artery reading will underestimate the CO while in volume responsive patient volume redistribution to cerebral circulation will also impair the pulse contour analysis through radial artery[3].

Pressure recording analytic method: Pressure recording analytic method (PRAM)-MostCare (Vytech, Padova, Italy) measures the area under the curve of arterial waveform. Major advantage is that it does not require external calibration and internal calibration is done by morphology of the arterial waveform. PRAM technology analyses whole cardiac cycle and area under the pressure wave (P/t) is determined[44]. The P/t is divided into diastolic and systolic phase with 2 impedances based on different characteristics. However the accuracy of this method is still not proven.

EV1000/Volume view: A new calibrated pulse wave analysis method (VolumeView™/EV1000™, Edwards Lifesciences, Irvine, CA, United States) has been developed. It is based on pulse pressure analysis, which is calibrated by transpulmonarythermodilution and is currently under trial. Its comparison with PICCO2 system in critically ill patients found comparable results[45]. However; very few studies are available for its validation. We have just finished a study on its use for GDT in OPCAB and found it to be very useful.

Esophageal doppler

Esophageal Doppler uses a flexible probe with transducer at the tip. It is of the size of anorogastric tube and can be placed for longer period in intubated patients. At the midthoracic level it measures flow as it is presumed to be parallel to the descending aorta. Since aorta is considered as a cylinder, the flow can be measured by multiplying cross-sectional area (CSA) and velocity. Doppler ultrasound is used to measure the SV. Once an optimal flow profile has been obtained, the blood flow velocity is determined from the shift in frequency of red blood cells. This is done by the ultrasound processor using the Doppler equation:

$$V = f_d \times c/2 \times f_0 \times \cos\theta$$

V = velocity of blood, f_d = Doppler shift in frequency, c = speed of ultrasound in tissue (1540 m s21), f_0 = initial ultrasound frequency, and θ = the angle of ultrasound beam in relation to the blood flow.

The velocity-time integral (VTI) is calculated from the area under the velocity-time curve and used as the stroke distance. The area can be calculated by nomogram or direct measurement. Thus SV is calculated as CSA × VTI and CO is calculated as SV × HR[24]. FTc *i.e.*, corrected time flow can also be determined which is used as measure of cardiac preload[46].

Major limiting factor is that it measures flow only in descending thoracic aorta which is 70% of total flow. A correction factor needs to be added to compensate aortic arch flow. Moreover discrepancies in flow may be seen in aortic coarctation, aneurysm or crossclamp, IABP and various metabolic states. Various factors like changes in pulse pressure, vascular compliance, volume status or inotropes may affect the CSA. In circulatory failure, it has been shown that CSA should be measured directly to prevent any inaccuracy in readings. Unchanged CSA may lead to underestimation of CO[24]. Accurate velocity can only be determined by proper positioning of the probe which must be within 20° of the axial flow.

Various studies have compared ED with PAC and found good agreement with low bias. A meta analysis revealed it as a reliable method with low bias with limited efficacy[47]. ED has also been used in GDT and shown greater improvement in SV and CO with faster recovery and shorter length of stay[48]. In cardiac surgery, decreased hospital and ICU stay with decreased incidence of gut mucosal perfusion, without major complications has been shown with ED[49]. We also studied this device in patients undergoing OPCAB and found that in comparison with PAC it cannot be used as a sole method for CO monitoring[50].

TEE

TEE has now been a widely used monitor in periopera-

tive setting. It is an important tool for the assessment of cardiac structures, filling status and cardiac contractility[51]. Moreover, aortic pathology can also be detected by TEE. Doppler technique is used to measure CO by Simpson's rule measuring SV multiplied by HR. Flow is measured by area under the Doppler velocity waveform that gives VTI and CSA is calculated by planimetry. Measurement can be done at the level of pulmonary artery, mitral or aortic valve. TEE views used for measurement are mid-esophageal aortic long axis view and deep transgastric long axis view with pulsed and continuous wave Doppler respectively. The ultrasound beam is parallel to the blood flow in transgastric view.

TEE has been validated with PAC with good limits of agreement[52]. It is a useful tool in hemodynamically unstable patient under mechanical ventilation[53]. However, a skilled operator is required, limited availability and cost factor are major limitations for its use.Standard TEE probe cannot be kept in the patient for too long. Hemodynamic TEE is a disposable thinner TEE probe which can be left *in situ* for several days.

NON INVASIVE METHODS

Partial gas rebreathing

It is also known as the NICO system (Novametrix Medical Systems, Wallingford, Conn, United States) or partial gas re-breathing monitor and uses indirect Fick's principle to calculate CO. It is used in intubated patients under mechanical ventilation. At steady state, the amount of CO2 entering the lungs *via* the pulmonary artery is proportional to the CO and equals the amount exiting the lungs *via* expiration and pulmonary veins.

During 30 s of re-breathing, the amount entering does not change, but the amount eliminated by expiration decreases and endtidal CO2 increases in proportion to the CO[24]. CO is calculated according to following formula:

$$CO = VCO2/CvCO2 - CaCO2$$

Here VCO2 is CO2 consumption, CaCO2 and CvCO2 is arterial and venous CO2 content respectively. The diffusion rate of carbon dioxide is 22 times more rapid than that of oxygen, it is assumed that no difference in venous CO2 (CvCO2) will occur, whether under normal or rebreathing conditions. A disposable circuit is connected to the ventilator circuit along with infrared CO2 sensor, pneumotachometer and a rebreathing valve. Partial rebreathing is initiated every three minutes by opening the valve and pulmonary blood flow is calculated by difference between normal and rebreathing ratio[54].

Major limitation is that tracheal intubation with fixed ventilator setting is required. It is also not very accurate in patients with severe chest trauma, significant intrapulmonary shunt, high CO states and low minute ventilation[24]. Validation studies have not found accuracy of this device with PAC. Studies have shown underestimation preoperatively and overestimation postoperatively after cardiac surgery[55]. Thus it has limited clinical applicability in comparison to PAC.

Thoracic bioimpedance

Thoracic bioimpedance (TEB) is a non-invasive method of CO monitoring. Initially it was used by astronauts in 1960s[56]. It is based on the hypothesis by considering thorax as a cylinder perfused with fluid with specific resistivity. It measures the electrical resistance of the thorax to a high frequency, low amplitude current[24].

Electrodes six in number are placed (two on either side of neck and four in lower thorax) on the patient and the resistance to current flowing from the outermost to innermost electrodes is measured. The bioimpedance is indirectly proportional to the content of thoracic fluid. Tissue fluid volume, pulmonary and venous blood, and the aortic blood volume all contribute to the TEB measurement. Changes in CO will change the amount of aortic blood and will be reflected in a change TEB[5]. SV is calculated using the formula[24]:

$$SV = VEPT \times VET \times EPCI$$

VEPT = volume of electrically participating tissue (gender, height, and weight).

VET = ventricular ejection time taken from the R-R interval.

EPCI = ejection phase contractility index which is indirectly proportional to TEB.

Major limitations like interference with electrocautery, proper electrode placement, patient's movements and arrhythmia may affect its accuracy. Studies in cardiac surgical patients revealed good correlation intraoperatively with a mean bias of -0.28 L/min. Presence of sternal wires, orarrythmia may lead to inaccurate readings in the postoperative period[57]. Results were also not encouraging in critically ill patients. Moreover, it has been considered as trend analysis monitor rather than a diagnostic one[58].

Thoracic bioreactance

Thoracic bioreactance (NICOM device, Cheetah medical, Portland, Oregon) is a modification of TEB which avoids interferences by noise and external sources. It analyses changes in the phase of electrical voltage signal to the current applied across the thorax. Changes in electrical capacitive and inductive properties occurs secondary to change in intrathoracic volume.

The method involves placement of two dual electrodes on either side of the thorax. Sine-wave high-frequency (75 kHz) current is transmitted into the body through one electrode and other electrode is used by the voltage input amplifier. The mean of two will give final value[59].

Electrocautery also affects its accuracy however if the device receives signal for atleast 20 s over a minute the CO value can be determined. Major advantage is the ease of use in intubated patients, arrhythmias, emergency room (ER), ICU and operating room (OR). Validating studies with PAC showed good correlation between the two methodswith minimal bias[57]. Moreover comparison with pulse contour devices like PiCCO and ED also showed comparable results[58,60].

ECOM

ECOM (Con-Med, Irvine, Calif, United States) measures CO using impedance plethysmography. It is based on the principle of bioimpedance and current is passed through electrodes attached to endotracheal tube shaft and cuff. Current is passed from electrode on the shaft of endotracheal tube (ETT) and change in impedance secondary to aortic blood flow is detected by electrode on the cuff of ETT. An algorithm calculates SV based on impedance changes and CO can be calculated. Impedance is affected by aortic blood flow[61].

Electrocautery affects its accuracy and coronary blood flow is not calculated. Moreover the technology is still adequately not validated in humans, is costly and has not become very popular.

Portable doppler device

Ultrasonic Cardiac Output Monitors (USCOM, Sydney, Australia) is a portable device which is non-invasive and uses a probe placed suprasternally to measure flow through the aorta or on the left chest to measure transpulmonary flow[62]. It uses the Doppler principle as used with ED and TEE. Main advantage is the portability of the device and it can be used with ease in ER, OR, ICU and even in wards. Since it is a non-invasive device it can be used by trained nursing staff and is an important screening tool for postoperative cardiac surgical patients as well.

Major limitations are probe positioning as misalignment of ultrasound beam with blood flow may lead to errors and estimation of proper CSA in various physiological states is also important[24].

We have used USCOM device in post cardiac surgical patients for both left and right sided CO, CI and SV measurements and found good agreement with PAC. On comparing the right-sided CO, SV, and CI with those of PAC, the mean bias was 0.03 L/min, 1.6 mL, and 0.02 L/min per square meters, respectively. The comparison of left-sided CO, SV, and CI with those of thermodilution revealed a means bias of 0.14 L/min, 1.0 mL, and 0.08 L/min per square meters, respectively[63]. We further studied this device in OPCAB and found good correlation with PAC. The CO had a mean bias of -0.13 L/min and limits of agreement (mean bias ± 2SD) at -0.86 and 0.59 L/min[64].

Photoelectric plethysmography

The Nexfin HD (BMEYE B.V, Amsterdam, Netherlands) is a completely non-invasive pulse pressure analysis device that assesses pulse pressure using photoelectric plethysmography in combination with a volume-clamp technique (inflatable finger cuff). CO is derived byModelflow method. There are very few validation studies to state its efficacy[65].

CONCLUSION

There are various newer devices for CO monitoring available in clinical practice that are validated against the gold standard method. Newer devices have the advantage of being minimally or non-invasive and portable. Hence, a few of them can be used outside the OR and ICU. Validation with PAC and other limitations may still be an obstacle for their usein different clinical scenarios. The criteria for selection of newer devices should be based on the institutional protocol and clinical condition of the patients. More RCT's are needed to prove their efficacy and cost benefit. PAC will remain a gold standard for CO monitoring, however, use of newer devices based on pulse contour analysis, pulse pressure analysis and Doppler methods should be encouraged.

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