Cardiac Output Monitoring: A Contemporary Assessment and Review

Robert H. Thiele, MD[1]; Karsten Bartels, MD[2]; Tong J. Gan, MD, MHS, FRCA[3]

Objective: An increasing number of minimally or noninvasive devices are available to measure cardiac output in the critical care setting. This article reviews the underlying physical principles of these devices in addition to examining both animal and human comparative studies in an effort to allow clinicians to make informed decisions when selecting a device to measure cardiac output.

Data Sources: Peer-reviewed manuscripts indexed in PubMed.

Study Selection: A systematic search of the PubMed database for articles describing the use of cardiac output monitors yielded 1,526 sources that were included in the analysis.

Data Extraction: From all published cardiac output monitoring studies reviewed, the animal model, number of independent measurements, and correlation between techniques was extracted.

Data Synthesis: Comparative studies in animals and humans between devices designed for measurement of cardiac output and experimental reference standards indicate thermodilution and Doppler-based techniques to have acceptable accuracy across a wide range of hemodynamic conditions, with bioimpedance techniques being less accurate. Thermodilution devices are marginally more accurate than Doppler-based devices but suffer from slower response time, increased invasiveness, and require stable core temperatures, good operator technique, and a competent tricuspid valve. Doppler-based techniques are less invasive and offer beat-to-beat measurements and excellent trending ability, but are dependent on accurate beam alignment and knowledge of aortic cross-sectional area. Studies of newer devices, such as pulse contour analysis, partial rebreathing, and pulse wave velocity, are far less in number and are primarily based on comparisons with thermodilution-based cardiac output measurements. Studies show widely ranging results.

Conclusion: Thermodilution is relatively accurate for cardiac output measurements in both animals and humans when compared to experimental reference standards. Doppler-based techniques appear to have similar accuracy as thermodilution pulmonary artery catheters. Bioimpedance, pulse contour, partial rebreathing, and pulse wave velocity-based devices have not been studied as rigorously; however, the majority of studies included in this analysis point towards decreased accuracy. (*Crit Care Med* 2015; 43:177–185)

Key Words: cardiac output; echocardiography; goal-directed therapy; hemodynamic monitoring; minimally invasive monitoring; pulmonary artery catheter

The combination of thermodilution (1) with the balloon-tipped pulmonary artery catheter (PAC) (2) by Swan and Ganz led to the intermittent thermodilution PAC (3), making the measurement of cardiac output (CO) a clinical reality by the early 1970s. However, a succession of large, prospective, randomized controlled trials assessing the efficacy of PACs failed to show improvements in mortality when applied to critically ill patients (4–6), leading to a decline in PAC use (7, 8). Still, the idea that optimization of CO might improve outcomes was not abandoned. The failure of CO optimization to improve outcomes might be related to the complications of PACs, counterbalancing its potential benefits. Therefore, investigators began to develop less-invasive strategies for measuring CO (9). The PAC, which was the clinical reference standard during this time period of development, was also interpreted by many to be the experimental reference standard.

Experimental reference standards include electromagnetic and transit time flow meters as well as measurements of CO using a method described by the German physician Adolf Eugen Fick (1829–1901). Fick described the relationship of CO, oxygen uptake (Vo_2), and the difference between arterial and venous blood oxygen content ($Cao_2 - Cvo_2$) (10):

$$CO = Vo_2 / \left(Cao_2 - Cvo_2\right) \quad (1)$$

Although the principles Fick described are used in many applications when an indicator is injected upstream and

[1]Department of Anesthesiology, University of Virginia, Charlottesville, VA.

[2]Department of Anesthesiology, University of Colorado Denver, Aurora, CO.

[3]Department of Anesthesiology, Stony Brook University, Stony Brook, NY.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (http://journals.lww.com/ccmjournal).

Supported, in part, by departmental sources.

Dr. Thiele's institution consulted for Teleflex (Airway Advisory). Dr. Gan consulted for Merck, Edwards, Covidien, and Deltex. His institution received grant support from Fresenius. Dr. Bartels has disclosed that he does not have any potential conflicts of interest.

For information regarding this article, E-mail: thiele@virginia.edu

DOI: 10.1097/CCM.0000000000000608

measured downstream, here the term "Fick method" will be used only for algebraic Fick-based CO measurements: Oxygen uptake is measured using exhaled gases from a Douglas bag. Following invasive measurement of mixed venous oxygen or carbon dioxide content, the Fick equation is then solved for CO and alternative measurements of CO can be assessed comparatively. Certainly, the accuracy of a reference is crucial when measurement comparisons are made (11). The purpose of this review is to assess the ability of CO monitors to accurately measure CO as well as to succinctly describe the physical principles on which they are based.

METHODS

We systematically performed a search to identify all published articles describing the use of CO monitors, which used, for purposes of historical consistency, regression analysis. Bias and limits of agreement analysis are a recent addition to the method comparator's statistical toolkit, and studies incorporating these techniques were not neglected (12). However, in order to appreciate the performance characteristics of presently available technology over wide ranges of hemodynamic conditions, it cannot be overemphasized that although earlier techniques were often validated against experimental reference standards in both animal and human subjects, present technology is almost exclusively validated against PACs in humans. All reviewed data (device, animal model, number of independent measurements, and correlation coefficients), including references, are summarized in **Appendix 1** (Supplemental Digital Content 1, http://links.lww.com/CCM/B53).

When available, we included animal studies in our search. Although, in one sense, these data may not be as persuasive as human data, they add value in that investigators are able to achieve a wider range of hemodynamic conditions. This is particularly useful in view of the statistical technique (regression analysis) used by early investigators. Indeed, criticisms of the linear regression approach include its dependence on a wide range of measurements and the inordinate effect of outliers. In situations in which measured values (e.g., CO) are relatively stable (as they tend to be in humans), methods which agree closely can exhibit very little correlation (13).

THERMODILUTION

Physical Basis

Stewart's "indicator-dilution" method of measuring CO (14) relies on injection of an indicator (e.g., dye) and subsequent measurement of a time-concentration curve. Flow is calculated in accordance with derivatives of the Conservation of Indicator Principle known as the "Stewart-Hamilton equations":

$$m = Q\int_0^\infty c(t)\mathrm{d}t \qquad (2)$$

where m is the mass of indicator injected, Q = flow, and $c(t)$ is a function describing the change in concentration over time (15). Fegler (1) adapted Stewart's technique, using temperature as the indicator (unlike the modern PAC, Fegler injected into a femoral venous catheter and measured temperature in the aorta). To apply this principle in Swan thermodilution measurements, additional factors have to be considered. CO is calculated using the following equation:

$$\mathrm{CO} = V_\mathrm{I}\left(T_\mathrm{B} - T_\mathrm{I}\right) K_1 \times K_2 / \int_0^\infty \Delta T_\mathrm{B}(t)\mathrm{d}t \qquad (3)$$

With V_I being injectate volume, T_B blood temperature, T_I injectate temperature, K_1 density factor defined as the specific heat multiplied by the specific gravity of the injectate divided by the product of the specific heat and gravity of blood, and K_2 is a computation constant taking into account the catheter dead space, the heat exchange in transit, and the injection rate. This product is divided by the change in blood temperature over time ($\int_0^\infty \Delta T_\mathrm{B}(t)\mathrm{d}t$) (16).

Three important assumptions are made by this technique—first, that measuring the temperature curve over a finite period of time (as opposed to indefinitely) will not meaningfully impact the estimate of its integral. Second, that the injectate and bloodstream are perfectly mixed. Third, that the measured temperature difference is accurate. These assumptions may not be valid in common clinical scenarios, such as in the setting of tricuspid regurgitation (17), frequent repeated measurements (18), low flow states (19), or rapid temperature changes following cardiopulmonary bypass (20, 21). The effects of these conditions are not always intuitive. In the case of tricuspid regurgitation, for example, regurgitation of cold indicator fluid into the right atrium causes a distortion of the thermodilution curve similar to as seen in low CO states. In practice, however, this effect seems to be dependent on flow, thus making simple adjustments of the cutoff point for the thermodilution curve challenging (22). Furthermore, Swan thermodilution measurements occur between the right atrium and the pulmonary artery, hence representing only right-sided CO and thereby dismissing shunt.

Clinical Considerations

The thermodilution technique has been validated in a greater number and variety of experimental models than any other clinically available techniques, including both ex vivo mechanical models and experimental reference standards in animals and humans. The consistent accuracy of thermodilution in addition to its "first to market" position (3) explain why thermodilution PACs were adopted as the clinical reference standard and subsequently used in later comparison studies (the precision error of PACs is only 13% for triplicate readings) (23). Continuous thermodilution catheters use a heating element (as opposed to room temperature saline) to generate temperature changes and appear to offer comparable clinical accuracy, albeit with a time lag of up to 5 minutes (24–26).

The thermodilution PAC is unique among CO monitoring devices in that it is capable of measuring pulmonary artery pressure and "occlusion" pressure. However, the ability of

practicing physicians to accurately interpret pulmonary artery tracings is in doubt (27).

ULTRASOUND-BASED TECHNIQUES

Physical Basis

The Doppler equation relates the frequency change of a returning ultrasound beam (Δf), the speed of sound in tissue (c), the frequency of the incident ultrasound beam (f_0), and the angle of incidence (θ) to the velocity of a moving reflector (v) by the following equation:

$$v = c\Delta f / (2f_0 \cos(\theta)) \quad (4)$$

When used to measure stroke volume, the velocity of blood flow must be integrated over one entire heart beat ("velocity time integral") and multiplied by cross-sectional area. In reality, cross-sectional area may change significantly over the course of a heartbeat, but this source of error is neglected. Lastly, it is assumed that the measured velocity is the same at all points in the measured vessel (i.e., a "flat" velocity profile) (28).

Clinical Considerations

As with the PAC, Doppler-based devices have been validated in ex vivo models of flow as well as experimental reference standards in animals and humans. These data suggest a slight decrease in accuracy of Doppler-derived CO compared with thermodilution-derived CO. However, the magnitude of this difference is of questionable clinical significance (**Table 1**). A major advantage of Doppler devices is their noninvasive nature.

Esophageal Doppler monitoring uses a small, dedicated Doppler probe (placed through the mouth or nose) in order to image the descending thoracic aorta. Unlike the suprasternal approach, which was used in the majority of validation studies, the esophageal Doppler approach cannot directly measure CO (since 30% of CO is diverted proximal to the descending thoracic aorta). That said, comparisons of esophageal Doppler and Fick methods have revealed correlations just slightly worse than what would be expected from a PAC (29–31).

Modern esophageal Doppler devices provide, in addition to CO, "corrected flow time" and stroke volume variation (SVV). Both are indicators of fluid responsiveness and have been used as therapeutic endpoints. Note that esophageal Doppler cannot be more accurate than thermodilution, as the algorithm used to convert stroke distance to stroke volume is based on a Doppler/thermodilution-derived database (32).

BIOIMPEDANCE AND BIOREACTANCE

Physical Basis

Thoracic electrical bioimpedance (TEB) is based on the assumption that the electrical resistance of the thorax is related to intrathoracic blood volume. TEB also assumes that changes in thoracic impedance are exclusively a function of changes in intrathoracic blood volume. Furthermore, the maximum impedance change

TABLE 1. Simultaneous Comparisons of Thermodilution and Doppler to Reference Standards

Study/Author	Subjects	*n*	Doppler	*n*	Thermodilution-Derived Cardiac Output
Fick					
Welch (31)	Pigs	28	0.88	28	**0.91**
Christie (65)	Humans	42	0.81	42	**0.94**
Gola (55)	Humans	73	**0.9**	73	0.81
Electromagnetic flow meter					
Gregoretti (34)	Pigs	128	0.87	128	**0.95**
Segal (39)	Sheep	341	**0.89**	81	0.85
Heerdt (41)	Humans	46	0.64	46	**0.8**
Segal (269)	Humans	44	0.82	44	**0.85**
Transit time flow meter					
Wong (81)[a]	Dogs	95	0.74	95	**0.9**
Aadahl (44)	Pigs	70	0.73	70	**0.9**
Dicorte (46)	Humans	170	0.49	170	**0.55**
Bajorat (45)	Pigs	366	0.84	366	**0.93**
Mean-weighted averages			**0.80**		**0.85**

[a]Comparisons between changes in cardiac output, not absolute values.

Boldface values are the larger values between Doppler and thermodilution-derived cardiac output in the respective rows.

over time is related to peak aortic flow rate (and peak aortic flow rate, when averaged over the ejection period, is proportional to mean aortic flow rate). Ventricular ejection time is discerned from the electrocardiogram (ECG) tracing. Based on the above assumptions, bioimpedance is highly sensitive to electrode positioning, pulmonary edema, and electrical noise.

Clinical Considerations

Bioimpedance devices have been compared to experimental reference standards in both animal models and humans as well as between clinically used CO monitors in animals and humans. The results of which suggest that bioimpedance devices are less accurate than thermodilution- or Doppler-based devices. The magnitude of this difference and the technology's propensity for interference in the operating room environment suggest that alternative techniques should be considered, when available.

Electrical Velocimetry. Electrical velocimetry reflects an effort to increase the accuracy of the original bioimpedance devices and assumes that thoracic conductivity is related to the velocity of blood flow in the aorta (as opposed to the volume of blood in the thorax). Available data comparing electrical velocimetry to thermodilution and Doppler-based methods of estimating CO are insufficient to determine adequate accuracy of this approach in order to recommend widespread clinical use.

Bioreactance. The bioreactance technique was developed in an effort to decrease erroneous readings secondary to electrode positioning, body size, temperature, and humidity that are typically encountered with the bioimpedance technique. The intrathoracic blood behaves as both an electrical capacitor and an inductor. These properties affect the phase shift between applied and received voltage, which are related to stroke volume (33). The only currently available device designed to measure CO using the bioreactance technique is the NICOM (Cheetah Medical, Vancouver, WA; http://www.cheetah-medical.com). Bioreactance has been compared to Doppler (34) as well as thermodilution-based techniques (mean weighted correlation coefficient of 0.80 based on three studies containing 171 comparisons) (33, 35, 36). Of note, the NICOM device also estimates SVV.

PARTIAL REBREATHING

Physical Basis

Carbon dioxide can be used to measure CO, using a modified version of the Fick equation:

$$CO = Vco_2 / \left(Cpaco_2 - Csaco_2\right) \quad (5)$$

where CO represents cardiac output, Vco_2 represents the production of carbon dioxide, $Cpaco_2$ represents the concentration of carbon dioxide in the pulmonary arterial compartment, and $Csaco_2$ represents the concentration of carbon dioxide in the systemic arterial compartment.

The partial rebreathing technique assumes that CO does not change between periods of non-rebreathing (minimal dead space) and a partial rebreathing (dead space added to the ventilator circuit). CO in both states can be written as:

$$\begin{aligned} CO &= Vco_{2,non} / \left(Cpaco_{2,non} - Csaco_{2,non}\right) \\ &= Vco_{2,rebr} / \left(Cpaco_{2,rebr} - Csaco_{2,rebr}\right) \end{aligned} \quad (6)$$

CO can be written as:

$$CO = \frac{Vco_{2,non} - Vco_{2,rebr}}{\left[\begin{array}{l}\left(Cpaco_{2,non} - Csaco_{2,non}\right) \\ -\left(Cpaco_{2,rebr} - Csaco_{2,rebr}\right)\end{array}\right]} \quad (7)$$

If one assumes that $Cpaco_2$ does not change between the non-rebreathing and partial rebreathing time periods, this equation can be simplified as (37–39):

$$CO = Vco_{2,non} - Vco_{2,rebr} / \left(Csaco_{2,rebr} - Csaco_{2,non}\right) \quad (8)$$

$Csaco_2$ can be estimated based on knowledge of the concentration of hemoglobin and the partial pressure of co_2 in arterial blood. Nunn iso-shunt plots (which relate Q_s/Q_T to both Pao_2 and Fio_2) are used to estimate Q_s/Q_T, which accounts for intrapulmonary shunts.

Clinical Considerations

Partial rebreathing techniques have primarily been validated against thermodilution in animals although one study used a transit time flow probe (40). Human comparisons between the partial rebreathing technique and thermodilution CO have included more than 800 paired measurements from over 250 patients in at least nine studies (41–49). The accuracy of the partial rebreathing technique appears to be related to both tidal volume (44, 45) and shunt fraction (43). Furthermore, partial rebreathing techniques have a relatively long response time.

The NICO system (Philips Respironics, Andover, MA) is the only commercially available system designed to measure CO using the partial rebreathing technique (**Table 2**). In order to be completely noninvasive, the NICO device assumes that the difference between end-tidal co_2 and $Csaco_2$ is approximately 6 mm Hg.

PULSE CONTOUR ANALYSIS

Two classes of arterial waveform analyzers are currently in existence—calibrated devices, which periodically recalibrate based on a second measurement technique (e.g., transpulmonary thermodilution and lithium dilution), and uncalibrated devices. The derivation and physical assumptions that underlie most of these devices has been reviewed in detail elsewhere (50) but for the sake of completeness will be presented in abbreviated form here.

Physical Basis

Frank's Windkessel model of blood flow formed the basis of most early attempts at measuring CO from the arterial pulse

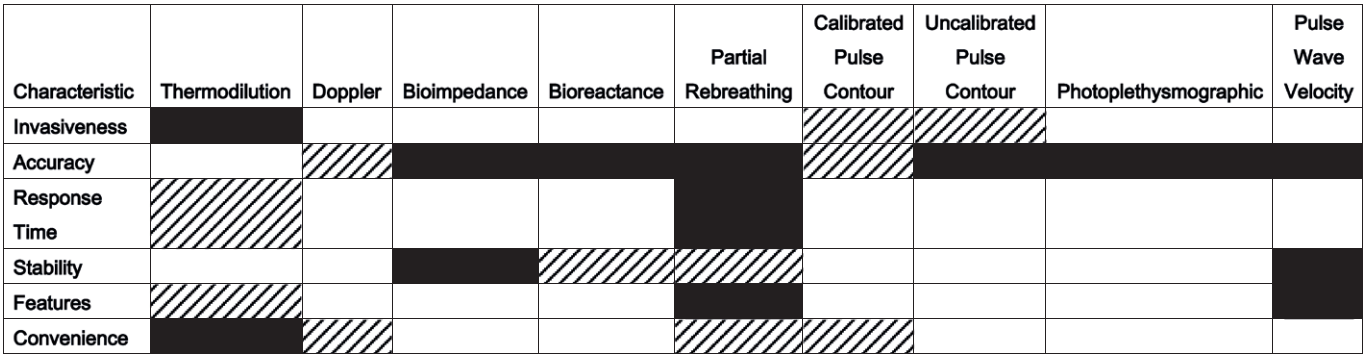

Figure 1. Qualitative comparison of commercially available cardiac output monitoring technology. *White* represents above average, *lined* represents average, and *black* represents below average (or not enough data to assess).

contour (51). Modern pulse contour devices are an extension of this technique. Frank's model assumes that the volume of blood entering a vessel of infinite length must equal the volume of blood leaving a vessel over the period of cardiac contraction and that during systole, the vessel will expand, whereas during diastole, it will contract. The aorta acts as a capacitor and the systemic arterioles act as a resistor. This is known as the "two-element Windkessel model," although models of increasing complexity have been developed (52). The characteristic impedance (cZ) technique uses blood pressure and heart rate to estimate impedance (resistance to pulsatile flow) (53).

Clinical Considerations

Pulse contour devices, as a class, must be used with caution in the setting of aortic insufficiency, which alters the shape of the arterial waveform and may decrease the accuracy of a device. As with the esophageal Doppler and bioreactance devices, many of the pulse contour devices provide the user with estimates of pulse pressure variation, SVV, and in some cases, dP/dt_{max}, and extravascular lung water.

Calibrated Arterial Waveform Devices. Transpulmonary Thermodilution (PiCCO). The PiCCO system (Pulsion Medical Systems, Munich, Germany; http://www.pulsion.com) treats compliance as a dynamic variable dependent on pressure ($C(p)$, based on waveform analysis distal to the dicrotic notch) and includes both compliance and instantaneous pressure changes (dP/dt) into its estimate of stroke volume (54).

$$\mathrm{SV} = k \int_{\text{end-diastole}}^{\text{end-systole}} \left[P(t)/\mathrm{SVR} + C(p) \times dP/dt \right] dt \qquad (9)$$

The PiCCO modifications are intended to better take into account the fraction of ventricular output, which is stored in capacitance vessels, but requires calibration (transpulmonary thermodilution) to determine k.

Transpulmonary thermodilution has been compared to experimental reference standards and thermodilution in multiple animal models (40, 55) as well as to experimental reference standards (56) and thermodilution (57–62) in humans. These studies suggest that transpulmonary thermodilution is noninferior to conventional thermodilution. Interestingly, Fegler's original thermodilution curves relied on arterial temperature measurements (1), and Goodyer's comparison of pulmonary thermodilution and aortic thermodilution curves to experimental reference standards suggested that the latter is more accurate (63).

Lithium Dilution (LiDCO Plus). The PulseCO system (LiDCO Group PLC, London, UK; http://www.lidco.com) incorporates characteristic impedance into its model using a transfer function (64) to estimate aortic blood pressures. The PulseCO system can be used as an uncalibrated device or combined with lithium dilution curve (referred to as the "LiDCO").

Lithium, especially when injected centrally, is a reliable indicator for CO measurements (65). Invasive animal data suggest that lithium injected into the right atrium and measured in a femoral catheter is more accurate than conventional thermodilution (66) and that injection through a peripheral as opposed to central site reduces its accuracy (67). The LiDCO Plus device has been compared to thermodilution in humans and, while fewer subjects have been studied as compared to the PiCCO, appears to correlate well with conventional thermodilution (68–70).

Uncalibrated Arterial Waveform Devices. Empiric Approach (FloTrac). The FloTrac device, which focuses on the development of an empirically derived mathematical model, rather than a physical model, represents a significant paradigm shift in arterial waveform analysis (71). The uncalibrated nature of the device likely comes at the expense of decreased accuracy (36, 72–79).

Pressure Recording Analytical Method. The pressure recording analytical method (PRAM) is based on the principle that volumetric changes in a blood vessel primarily occur in the radial direction and are based on the interaction of left ventricular ejection force, arterial compliance, impedance, and peripheral resistance to flow (due to wave reflections originating from bifurcations and changing vessel diameter) (80). Preliminary studies in animals using Doppler (81) as well as human data based on comparisons with both experimental reference standards (80) and conventional thermodilution (82–84) preliminarily suggest it may offer comparable accuracy to its calibrated counterparts. Given that the PRAM method has been studied primarily by a single group, further validation is needed.

Calibrated Versus Uncalibrated?

A simultaneous comparison of the LiDCO, PiCCO, and FloTrac monitors to intermittent thermodilution revealed narrower limits of agreement for the LiDCO and PiCCO devices compared with the FloTrac (85). The difference in the limits of agreement between uncalibrated and calibrated devices has also been reported in comparisons of the FloTrac and both LiDCO (86) and PiCCO (79, 87) to thermodilution. In liver transplantation, the LiDCO Plus outperforms the FloTrac in its ability to detect large changes in CO (88).

The accuracy of the PulseCO, PiCCO, and Flotrac devices appear to suffer during hemodynamic instability. Although the benefits of calibration have not been universally demonstrated (88), the majority of data suggest that calibrated devices outperform uncalibrated devices (89–91).

PHOTOPLETHYSMOGRAPHIC

Although the photoplethysmographic (PPG) waveform is related to the arterial pressure waveform and may be related to stroke volume in idealized conditions (92), this relationship is not clinically useful in the acute care setting (93).

Physical Basis

Peñáz developed the "volume clamp" technique in which changes in finger arterial blood volume could be monitored by an infrared transmitter and receiver combination (similar to a pulse oximeter), which is connected to an inflatable finger bladder and driven by a feedback control mechanism. The finger cuff is inflated and deflated to maintain a constant level of infrared absorption (or blood volume). When the artery is "unstretched," the volume clamp technique assumes that the pressure in the finger cuff is equal to the arterial pressure. Thus, by maintaining the artery in an "unstretched" state based on PPG estimates of volume, finger pressure can be measured continuously (94). Once a peripheral arterial pressure waveform is acquired, it can then be used to estimate stroke volume using the methods described in the *Pulse Contour Analysis* section.

Clinical Considerations

For the measurement of blood pressure, the volume clamp technique has been compared to invasive arterial pressure measurements in a variety of clinical settings, including pediatric critical care (95) and both pediatric (96) and adult (97) cardiac surgeries. The results of these studies suggest that the agreement between the volume clamp technique and invasive blood pressure monitors is reasonable.

The Finapres and ^{cc}Nexfin devices, which use the volume clamp-derived pressure waveform to estimate stroke volume, have been compared to the PAC, echocardiographic indices, Co_2 rebreathing, and inert gas rebreathing techniques in humans. Based on these limited data, this class of devices cannot yet be recommended for the reliable measurement of CO.

PULSE WAVE VELOCITY

Physical Basis

The Moens-Korteweg Equation describes the velocity of a pulse wave through an elastic tube using the tube's elasticity (E), wall thickness (h), and diameter (D) as well as the density (ρ) of the fluid within the tube (98, 99).

$$V = k\left(Eh/\rho D\right)^{1/2} \quad (10)$$

The pulse wave velocity technique assumes that changes in vascular impedance (which are mediated by changes in vascular tone that differentially affect both cross-sectional diameter and vessel compliance) (100) will result in changes in the speed at which the systemic arterial pressure wave travels (99). The pulse wave velocity makes two major assumptions: first, that stroke volume is proportionate to pulse pressure, and second, that pulse pressure is related to pulse wave velocity (or pulse wave transit time [PWTT]) (101).

Clinical Considerations

Nihon Kohden (Tokyo, Japan; http://www.nihonkohden.com) recently developed the esCCO, a device designed to estimate CO based on the principles mentioned above. The esCCO incorporates both PWTT (based on the ECG and pulse oximeter waveforms) and mean arterial pressure into its estimate of stroke volume, the details of which are proprietary. The esCCO device is not yet Food and Drug Administration approved but is marketed in Japan. It has not demonstrated sufficient accuracy to recommend widespread clinical use.

CONCLUSIONS

Thermodilution is relatively accurate when compared to reference standards such as the oximetric Fick method or electromagnetic and transit time flow meters. When indirectly compared to experimental reference standards, Doppler-based techniques have similar accuracy as thermodilution PACs. They have the added advantages of offering beat-to-beat monitoring as well as being less invasive (**Fig. 1**). Direct comparisons between Doppler and thermodilution with experimental reference standards suggest that thermodilution is more accurate than Doppler-based techniques. The assumptions made, when deriving CO from Doppler-based or thermodilution-based techniques, should be known and considered in a given clinical context. Bioimpedance devices do not correlate with direct Fick methods as closely as either thermodilution or Doppler. Electrical velocimetry and bioreactance will require additional data prior to making meaningful comparisons with more established techniques.

The body of literature available to assess the accuracy of newer devices is significantly smaller than for thermodilution, Doppler, and bioimpedance and is primarily based on comparisons with thermodilution-based CO. Uncalibrated pulse contour devices appear to track changes in CO when afterload is stable. Calibrated pulse contour devices are more accurate than their uncalibrated counterparts in hemodynamically unstable patients but require

periodic operator intervention. Partial rebreathing techniques and pulse wave velocity-based devices have not demonstrated sufficient accuracy to justify widespread clinical use.

ACKNOWLEDGMENTS

We acknowledge Dr. Marcel E. Durieux, MD, PhD, for his particularly detailed and insightful critique of this article prior to its submission for publication.

REFERENCES

1. Fegler G: Measurement of cardiac output in anaesthetized animals by a thermodilution method. *Q J Exp Physiol Cogn Med Sci* 1954; 39:153–164
2. Swan HJ, Ganz W, Forrester J, et al: Catheterization of the heart in man with use of a flow-directed balloon-tipped catheter. *N Engl J Med* 1970; 283:447–451
3. Ganz W, Donoso R, Marcus HS, et al: A new technique for measurement of cardiac output by thermodilution in man. *Am J Cardiol* 1971; 27:392–396
4. Sandham JD, Hull RD, Brant RF, et al; Canadian Critical Care Clinical Trials Group: A randomized, controlled trial of the use of pulmonary-artery catheters in high-risk surgical patients. *N Engl J Med* 2003; 348:5–14
5. Richard C, Warszawski J, Anguel N, et al; French Pulmonary Artery Catheter Study Group: Early use of the pulmonary artery catheter and outcomes in patients with shock and acute respiratory distress syndrome: A randomized controlled trial. *JAMA* 2003; 290:2713–2720
6. Harvey S, Harrison DA, Singer M, et al; PAC-Man study collaboration: Assessment of the clinical effectiveness of pulmonary artery catheters in management of patients in intensive care (PAC-Man): A randomised controlled trial. *Lancet* 2005; 366:472–477
7. Wiener RS, Welch HG: Trends in the use of the pulmonary artery catheter in the United States, 1993-2004. *JAMA* 2007; 298:423–429
8. Berthiaume LR, Peets AD, Schmidt U, et al: Time series analysis of use patterns for common invasive technologies in critically ill patients. *J Crit Care* 2009; 24:471.e9–471.e14
9. Porhomayon J, El-Solh A, Papadakos P, et al: Cardiac output monitoring devices: An analytic review. *Intern Emerg Med* 2012; 7:163–171
10. Geerts BF, Aarts LP, Jansen JR: Methods in pharmacology: Measurement of cardiac output. *Br J Clin Pharmacol* 2011; 71:316–330
11. LaMantia KR, O'Connor T, Barash PG: Comparing methods of measurement: An alternative approach. *Anesthesiology* 1990; 72:781–783
12. Bland JM, Altman DG: Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; 1:307–310
13. Bland JM, Altman DG: Agreed statistics: Measurement method comparison. *Anesthesiology* 2012; 116:182–185
14. Stewart GN: The output of the heart in dogs. *Am J Physiol* 1921; 57:27–50
15. Profant M, Vyska K, Eckhardt U: The Stewart-Hamilton equations and the indicator dilution method. *SIAM J Appl Math* 1978; 34:666–675
16. Nishikawa T, Dohi S: Errors in the measurement of cardiac output by thermodilution. *Can J Anaesth* 1993; 40:142–153
17. Cigarroa RG, Lange RA, Williams RH, et al: Underestimation of cardiac output by thermodilution in patients with tricuspid regurgitation. *Am J Med* 1989; 86:417–420
18. Maruschak GF, Potter AM, Schauble JF, et al: Overestimation of pediatric cardiac output by thermal indicator loss. *Circulation* 1982; 65:380–383
19. van Grondelle A, Ditchey RV, Groves BM, et al: Thermodilution method overestimates low cardiac output in humans. *Am J Physiol* 1983; 245:H690–H692
20. Bazaral MG, Petre J, Novoa R: Errors in thermodilution cardiac output measurements caused by rapid pulmonary artery temperature decreases after cardiopulmonary bypass. *Anesthesiology* 1992; 77:31–37
21. Latson TW, Whitten CW, O'Flaherty D: Ventilation, thermal noise, and errors in cardiac output measurements after cardiopulmonary bypass. *Anesthesiology* 1993; 79:1233–1243
22. Heerdt PM, Blessios GA, Beach ML, et al: Flow dependency of error in thermodilution measurement of cardiac output during acute tricuspid regurgitation. *J Cardiothorac Vasc Anesth* 2001; 15:183–187
23. Yang XX, Critchley LA, Joynt GM: Determination of the precision error of the pulmonary artery thermodilution catheter using an in vitro continuous flow test rig. *Anesth Analg* 2011; 112:70–77
24. Philip JH, Long MC, Quinn MD, et al: Continuous thermal measurement of cardiac output. *IEEE Trans Biomed Eng* 1984; 31:393–400
25. Aranda M, Mihm FG, Garrett S, et al: Continuous cardiac output catheters: Delay in in vitro response time after controlled flow changes. *Anesthesiology* 1998; 89:1592–1595
26. Goldstein LJ: Response time of the Opti-Q continuous cardiac output pulmonary artery catheter in the urgent mode to a step change in cardiac output. *J Clin Monit Comput* 1999; 15:435–439
27. Iberti TJ, Fischer EP, Leibowitz AB, et al: A multicenter study of physicians' knowledge of the pulmonary artery catheter. Pulmonary Artery Catheter Study Group. *JAMA* 1990; 264:2928–2932
28. Schuster AH, Nanda NC: Doppler echocardiographic measurement of cardiac output: Comparison with a non-golden standard. *Am J Cardiol* 1984; 53:257–259
29. Smith HJ, Grøttum P, Simonsen S: Doppler flowmetry in the lower thoracic aorta. An indirect estimation of cardiac output. *Acta Radiol Diagn (Stockh)* 1985; 26:257–263
30. Davies JN, Allen DR, Chant AD: Non-invasive Doppler-derived cardiac output: A validation study comparing this technique with thermodilution and Fick methods. *Eur J Vasc Surg* 1991; 5:497–500
31. Valtier B, Cholley BP, Belot JP, et al: Noninvasive monitoring of cardiac output in critically ill patients using transesophageal Doppler. *Am J Respir Crit Care Med* 1998; 158:77–83
32. Lowe GD, Chamberlain BM, Philpot EJ, et al: Oesophageal Doppler Monitor (ODM) guided individualised goal directed fluid management (iGDFM) in surgery–A technical review. Deltex Medical Technical Review 2010. Available at: http://www.deltexmedical.com/downloads/TechnicalReview.pdf. Accessed February 16, 2013
33. Keren H, Burkhoff D, Squara P: Evaluation of a noninvasive continuous cardiac output monitoring system based on thoracic bioreactance. *Am J Physiol Heart Circ Physiol* 2007; 293:H583–H589
34. Weisz DE, Jain A, McNamara PJ, et al: Non-invasive cardiac output monitoring in neonates using bioreactance: A comparison with echocardiography. *Neonatology* 2012; 102:61–67
35. Raval NY, Squara P, Cleman M, et al: Multicenter evaluation of noninvasive cardiac output measurement by bioreactance technique. *J Clin Monit Comput* 2008; 22:113–119
36. Marqué S, Cariou A, Chiche JD, et al: Comparison between Flotrac-Vigileo and Bioreactance, a totally noninvasive method for cardiac output monitoring. *Crit Care* 2009; 13:R73
37. Nugent AM, McParland J, McEneaney DJ, et al: Non-invasive measurement of cardiac output by a carbon dioxide rebreathing method at rest and during exercise. *Eur Heart J* 1994; 15:361–368
38. Jaffe MB: Partial CO_2 rebreathing cardiac output–Operating principles of the NICO system. *J Clin Monit Comput* 1999; 15:387–401
39. Haryadi DG, Orr JA, Kuck K, et al: Partial CO_2 rebreathing indirect Fick technique for non-invasive measurement of cardiac output. *J Clin Monit Comput* 2000; 16:361–374
40. Bajorat J, Hofmockel R, Vagts DA, et al: Comparison of invasive and less-invasive techniques of cardiac output measurement under different haemodynamic conditions in a pig model. *Eur J Anaesthesiol* 2006; 23:23–30
41. Suzuki M, Koda S, Nakamura Y, et al: 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; 100:1381–1383, table of contents

42. Kotake Y, Moriyama K, Innami Y, et al: Performance of noninvasive partial CO_2 rebreathing cardiac output and continuous thermodilution cardiac output in patients undergoing aortic reconstruction surgery. *Anesthesiology* 2003; 99:283–288
43. Rocco M, Spadetta G, Morelli A, et al: 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; 30:82–87
44. Tachibana K, Imanaka H, Miyano H, et al: Effect of ventilatory settings on accuracy of cardiac output measurement using partial CO(2) rebreathing. *Anesthesiology* 2002; 96:96–102
45. Tachibana K, Imanaka H, Takeuchi M, et al: 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; 98:830–837
46. Allardet-Servent J, Forel JM, Roch A, et al: Pulmonary capillary blood flow and cardiac output measurement by partial carbon dioxide rebreathing in patients with acute respiratory distress syndrome receiving lung protective ventilation. *Anesthesiology* 2009; 111:1085–1092
47. Valiatti JL, Amaral JL: Comparison between cardiac output values measured by thermodilution and partial carbon dioxide rebreathing in patients with acute lung injury. *Sao Paulo Med J* 2004; 122:233–238
48. Levy RJ, Chiavacci RM, Nicolson SC, et al: An evaluation of a noninvasive cardiac output measurement using partial carbon dioxide rebreathing in children. *Anesth Analg* 2004; 99:1642–1647, table of contents
49. van Heerden PV, Baker S, Lim SI, et al: Clinical evaluation of the noninvasive cardiac output (NICO) monitor in the intensive care unit. *Anaesth Intensive Care* 2000; 28:427–430
50. Thiele RH, Durieux ME: Arterial waveform analysis for the anesthesiologist: Past, present, and future concepts. *Anesth Analg* 2011; 113:766–776
51. Kouchoukos NT, Sheppard LC, McDonald DA: Estimation of stroke volume in the dog by a pulse contour method. *Circ Res* 1970; 26:611–623
52. Essler S, Schroeder MJ, Phaniraj V, et al: Fast estimation of arterial vascular parameters for transient and steady beats with application to hemodynamic state under variant gravitational conditions. *Ann Biomed Eng* 1999; 27:486–497
53. Wesseling KH, de Witt B, Weber AP, et al: A simple device for the continuous measurement of cardiac output. *Adv Cardiovasc Phys* 1983; 5:16–52
54. Gödje O, Höke K, Goetz AE, et al: Reliability of a new algorithm for continuous cardiac output determination by pulse-contour analysis during hemodynamic instability. *Crit Care Med* 2002; 30:52–58
55. Marx G, Schuerholz T, Sümpelmann R, et al: Comparison of cardiac output measurements by arterial trans-cardiopulmonary and pulmonary arterial thermodilution with direct Fick in septic shock. *Eur J Anaesthesiol* 2005; 22:129–134
56. Pauli C, Fakler U, Genz T, et al: Cardiac output determination in children: Equivalence of the transpulmonary thermodilution method to the direct Fick principle. *Intensive Care Med* 2002; 28:947–952
57. Goedje O, Hoeke K, Lichtwarck-Aschoff M, et al: Continuous cardiac output by femoral arterial thermodilution calibrated pulse contour analysis: Comparison with pulmonary arterial thermodilution. *Crit Care Med* 1999; 27:2407–2412
58. Sakka SG, Kozieras J, Thuemer O, et al: Measurement of cardiac output: A comparison between transpulmonary thermodilution and uncalibrated pulse contour analysis. *Br J Anaesth* 2007; 99:337–342
59. Della Rocca G, Costa MG, Pompei L, et al: Continuous and intermittent cardiac output measurement: Pulmonary artery catheter versus aortic transpulmonary technique. *Br J Anaesth* 2002; 88:350–356
60. Hamzaoui O, Monnet X, Richard C, et al: Effects of changes in vascular tone on the agreement between pulse contour and transpulmonary thermodilution cardiac output measurements within an up to 6-hour calibration-free period. *Crit Care Med* 2008; 36:434–440
61. Buhre W, Weyland A, Kazmaier S, et al: 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; 13:437–440
62. Gust R, Gottschalk A, Bauer H, et al: Cardiac output measurement by transpulmonary versus conventional thermodilution technique in intensive care patients after coronary artery bypass grafting. *J Cardiothorac Vasc Anesth* 1998; 12:519–522
63. Goodyer AV, Huvos A, Eckhardt WF, et al: Thermal dilution curves in the intact animal. *Circ Res* 1959; 7:432–441
64. Linton NW, Linton RA: Estimation of changes in cardiac output from the arterial blood pressure waveform in the upper limb. *Br J Anaesth* 2001; 86:486–496
65. Linton RA, Young LE, Marlin DJ, et al: Cardiac output measured by lithium dilution, thermodilution, and transesophageal Doppler echocardiography in anesthetized horses. *Am J Vet Res* 2000; 61:731–737
66. Kurita T, Morita K, Kato S, et al: Comparison of the accuracy of the lithium dilution technique with the thermodilution technique for measurement of cardiac output. *Br J Anaesth* 1997; 79:770–775
67. Kurita T, Morita K, Kato S, et al: Lithium dilution cardiac output measurements using a peripheral injection site comparison with central injection technique and thermodilution. *J Clin Monit Comput* 1999; 15:279–285
68. Linton RA, Band DM, Haire KM: A new method of measuring cardiac output in man using lithium dilution. *Br J Anaesth* 1993; 71:262–266
69. Costa MG, Della Rocca G, Chiarandini P, et al: Continuous and intermittent cardiac output measurement in hyperdynamic conditions: Pulmonary artery catheter vs. lithium dilution technique. *Intensive Care Med* 2008; 34:257–263
70. Mora B, Ince I, Birkenberg B, et al: Validation of cardiac output measurement with the LiDCO™ pulse contour system in patients with impaired left ventricular function after cardiac surgery. *Anaesthesia* 2011; 66:675–681
71. Pratt B, Roteliuk L, Hatib F, et al: Calculating arterial pressure-based cardiac output using a novel measurement and analysis method. *Biomed Instrum Technol* 2007; 41:403–411
72. Opdam HI, Wan L, Bellomo R: A pilot assessment of the FloTrac cardiac output monitoring system. *Intensive Care Med* 2007; 33:344–349
73. Cannesson M, Attof Y, Rosamel P, et al: Comparison of FloTrac cardiac output monitoring system in patients undergoing coronary artery bypass grafting with pulmonary artery cardiac output measurements. *Eur J Anaesthesiol* 2007; 24:832–839
74. Breukers RM, Sepehrkhouy S, Spiegelenberg SR, et al: Cardiac output measured by a new arterial pressure waveform analysis method without calibration compared with thermodilution after cardiac surgery. *J Cardiothorac Vasc Anesth* 2007; 21:632–635
75. Biais M, Nouette-Gaulain K, Cottenceau V, et al: Cardiac output measurement in patients undergoing liver transplantation: Pulmonary artery catheter versus uncalibrated arterial pressure waveform analysis. *Anesth Analg* 2008; 106:1480–1486, table of contents
76. Biancofiore G, Critchley LA, Lee A, et al: Evaluation of a new software version of the FloTrac/Vigileo (version 3.02) and a comparison with previous data in cirrhotic patients undergoing liver transplant surgery. *Anesth Analg* 2011; 113:515–522
77. Saraceni E, Rossi S, Persona P, et al: Comparison of two methods for cardiac output measurement in critically ill patients. *Br J Anaesth* 2011; 106:690–694
78. Eleftheriadis S, Galatoudis Z, Didilis V, et al: Variations in arterial blood pressure are associated with parallel changes in FlowTrac/Vigileo-derived cardiac output measurements: A prospective comparison study. *Crit Care* 2009; 13:R179
79. Sander M, Spies CD, Grubitzsch H, et al: Comparison of uncalibrated arterial waveform analysis in cardiac surgery patients with thermodilution cardiac output measurements. *Crit Care* 2006; 10:R164
80. Romano SM, Pistolesi M: Assessment of cardiac output from systemic arterial pressure in humans. *Crit Care Med* 2002; 30:1834–1841
81. Romagnoli S, Romano SM, Bevilacqua S, et al: Cardiac output by arterial pulse contour: Reliability under hemodynamic derangements. *Interact Cardiovasc Thorac Surg* 2009; 8:642–646
82. Franchi F, Silvestri R, Cubattoli L, et al: Comparison between an uncalibrated pulse contour method and thermodilution technique for cardiac output estimation in septic patients. *Br J Anaesth* 2011; 107:202–208
83. Romano SM, Conti AA, Giglioli C, et al: Blood flow assessment by arterial pressure wave without external calibration. *Comput Cardiol* 2006; 33:293–296

84. Scolletta S, Franchi F, Taccone FS, et al: An uncalibrated pulse contour method to measure cardiac output during aortic counterpulsation. *Anesth Analg* 2011; 113:1389–1395
85. Hadian M, Kim HK, Severyn DA, et al: Cross-comparison of cardiac output trending accuracy of LiDCO, PiCCO, FloTrac and pulmonary artery catheters. *Crit Care* 2010; 14:R212
86. Cecconi M, Dawson D, Casaretti R, et al: A prospective study of the accuracy and precision of continuous cardiac output monitoring devices as compared to intermittent thermodilution. *Minerva Anestesiol* 2010; 76:1010–1017
87. de Waal EE, Kalkman CJ, Rex S, et al: Validation of a new arterial pulse contour-based cardiac output device. *Crit Care Med* 2007; 35:1904–1909
88. Krejci V, Vannucci A, Abbas A, et al: Comparison of calibrated and uncalibrated arterial pressure-based cardiac output monitors during orthotopic liver transplantation. *Liver Transpl* 2010; 16:773–782
89. Johansson A, Chew M: Reliability of continuous pulse contour cardiac output measurement during hemodynamic instability. *J Clin Monit Comput* 2007; 21:237–242
90. Bein B, Meybohm P, Cavus E, et al: The reliability of pulse contour-derived cardiac output during hemorrhage and after vasopressor administration. *Anesth Analg* 2007; 105:107–113
91. Zöllner C, Haller M, Weis M, et al: 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; 14:125–129
92. McGrath SP, Ryan KL, Wendelken SM, et al: Pulse oximeter plethysmographic waveform changes in awake, spontaneously breathing, hypovolemic volunteers. *Anesth Analg* 2011; 112:368–374
93. Thiele RH, Colquhoun DA, Patrie J, et al: Relationship between plethysmographic waveform changes and hemodynamic variables in anesthetized, mechanically ventilated patients undergoing continuous cardiac output monitoring. *J Cardiothorac Vasc Anesth* 2011; 25:1044–1050
94. Boehmer RD: Continuous, real-time, noninvasive monitor of blood pressure: Penaz methodology applied to the finger. *J Clin Monit* 1987; 3:282–287
95. Lemson J, Hofhuizen CM, Schraa O, et al: The reliability of continuous noninvasive finger blood pressure measurement in critically ill children. *Anesth Analg* 2009; 108:814–821
96. Hofhuizen CM, Lemson J, Hemelaar AE, et al: Continuous non-invasive finger arterial pressure monitoring reflects intra-arterial pressure changes in children undergoing cardiac surgery. *Br J Anaesth* 2010; 105:493–500
97. Martina JR, Westerhof BE, van Goudoever J, et al: Noninvasive continuous arterial blood pressure monitoring with Nexfin®. *Anesthesiology* 2012; 116:1092–1103
98. Hamilton W, Remington J, Dow P: The determination of the propagation velocity of the arterial pulse wave. *Am J Physiol* 1945; 144:521–535
99. Greene ES, Gerson JI: Arterial pulse wave velocity: A limited index of systemic vascular resistance during normotensive anesthesia in dogs. *J Clin Monit* 1985; 1:219–226
100. Aars H: Diameter and elasticity of the ascending aorta during infusion of noradrenaline. *Acta Physiol Scand* 1971; 83:133–138
101. Ishihara H, Okawa H, Tanabe K, et al: A new non-invasive continuous cardiac output trend solely utilizing routine cardiovascular monitors. *J Clin Monit Comput* 2004; 18:313–320