Minimally invasive hemodynamic monitoring for the intensivist: Current and emerging technology

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Objective: **To review minimally invasive cardiac output monitoring devices currently available for use in the intensive care unit.**

Data Sources: Medline search from 1966 to present plus cited reference studies and abstracts from available product literature.

Study Selection: Selection criteria included published reports and abstracts comparing the accuracy of minimally invasive cardiac output monitors to a "gold standard."

Data Synthesis: Many reports have been published on the accuracy of individual minimally invasive cardiac output monitors, but cumulative data reviewing each type of monitor have not been synthesized and made available to the clinician.

Conclusions: Emerging noninvasive or minimally invasive means of cardiac output monitoring are based on varied physiologic principles and can be used for following hemodynamic trends. Each of these methods has advantages and disadvantages; it is important for the clinician to understand the strengths and limitations of each device to effectively use the information derived. (Crit Care Med 2002; 30:2338–2345)

Monitoring of physiologic variables comprises an integral part of the care of the critically ill patient and assists the intensivist in both diagnostic and treatment strategies. There has been much debate in the literature regarding the usefulness and safety of invasive hemodynamic monitoring in the intensive care unit (ICU). Several studies have shown improved outcomes from hemodynamic monitoring in high-risk surgical patients, but there is conflicting evidence as to benefits in the critically ill medical patient (1, 2). A recent retrospective study suggested that the use of a pulmonary artery catheter was associated with increased mortality rate of 39% compared with patients who did not receive the catheter (3). In 1997, a consensus statement was published which concluded that there was no basis for a proposed Food and Drug Administration moratorium on pulmonary artery catheter use (4). Complications associated with invasive techniques have led to growing interest in the development of newer noninvasive or minimally invasive means of hemodynamic monitoring including applications of the Fick principle, Doppler technology, thoracic-electrical bioimpedance, and pulse contour devices. The purpose of this review is to summarize the current less invasive technologies available, the physiologic principles underlying their applications, and the relative advantages and limitations associated with these devices. We have focused on technologies that can be readily used by the intensivist without requiring additional specialized training such as echocardiography. An improved understanding of these emerging technologies will assist the intensivist in applying the appropriate device to his or her particular practice setting.

Indirect Fick Method. Before we describe the indirect Fick method for determining cardiac output, it will be useful to review the Fick principle. Adolf Fick first introduced this concept in 1870 when he said, "the total uptake or release of a substance by an organ is the product of the blood flow to the organ and the arteriovenous concentration of the substance." This is simplistically translated into "rate of indicator out equals rate of indicator in plus rate of indicator added." This is represented mathematically by

$$CO = \frac{\dot{V}O_2}{CaO_2 - CvO_2} \qquad [1]$$

where CO is cardiac output, $\dot{V}O_2$ is oxygen consumption, CaO_2 is arterial oxygen content, and CvO_2 is mixed venous oxygen content.

Since the Fick principle can be used with a multitude of indicators and can be used if the indicator is added or removed, another plausible indicator is CO_2. Substituting CO_2 for oxygen in Equation *1* yields the indirect Fick equation

$$CO = \frac{\dot{V}CO_2}{CvCO_2 - CaCO_2} \qquad [2]$$

$\dot{V}CO_2$ is the clearance of CO_2, $CvCO_2$ is the mixed venous content of CO_2, and $CaCO_2$ is the arterial content of CO_2.

$\dot{V}CO_2$ can be calculated by the difference in CO_2 content between expired and inspired gasses. $CaCO_2$ can be obtained from arterial blood gas or estimated from end-tidal CO_2 (in healthy subjects with no diffusion abnormalities, alveolar CO_2 approximates arterial $PaCO_2$). $CvCO_2$ is much more difficult to get noninvasively.

A partial rebreathing technique has been used to eliminate the need to directly measure $CvCO_2$. By taking advantage of a mathematical technique known as the law of ratios, the clinician can manipulate the indirect Fick equation such that a measurement of $CvCO_2$ is not necessary to calculate cardiac output (Fig. 1).

The rebreathing values are obtained by introducing an additional 150 mL of dead space into the ventilator circuit and taking measurements once a new equilibrium has been established. Assuming that the mixed venous CO_2 concentration

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DOI: 10.1097/01.CCM.0000029186.57736.02

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does not change significantly throughout the rebreathing period, the terms associated with $CvCO_2$ cancel each other out of the equation and are not needed for the calculation.

There are several technical problems with the indirect Fick technique. First, the difference between $PvCO_2$ and $PaCO_2$ is usually only about 6 mm Hg; consequently, small errors in the measurement of either of these values results in a large change in calculated cardiac output. Second, the relationships assumed are only valid when the $PaCO_2$ is >30 torr when the CO_2-hemoglobin dissociation curve is linear (5). If the patient hyperventilates and the $PaCO_2$ is <30 torr, the relationship is no longer valid. Third, shunted blood is not measured. Fourth, changes in mechanical ventilator settings that alter dead space or ventilation/perfusion relationships may produce a calculated alteration in cardiac output when in fact none has occurred.

Table 1 summarizes the available experimental data for cardiac output determinations with this method (6–11). The partial rebreathing technique gives a better approximation of cardiac output in patients who are less critically ill and have normal alveolar gas exchange. In the study by Gama de Abreu et al. (6), sheep with severe lung injury were used, and the comparison to thermodilution cardiac output was relatively poor. Based on these results, this technique is probably best suited for monitoring trends in critically ill patients with stable lung function rather than diagnostic interpretation. Currently, one device is commercially available in the United States (NICO Sensor, Novametrix Medical Systems, Wallingford, CT).

Indirect Fick Equation

$$CO = \frac{VCO_2}{CvCO_2 - CaCO_2}$$

Applied with rebreathing circuit (r) and without (n)

$$CO = \frac{VCO_2{}^n}{CvCO_2{}^n - CaCO_2{}^n} = \frac{VCO_2{}^r}{CvCO_2{}^r - CaCO_2{}^r}$$

Combining to form the rebreathing Indirect Fick Equation

$$CO = \frac{VCO_2{}^n - VCO_2{}^r}{(CvCO_2{}^n - CaCO_2{}^n) - (CvCO_2{}^r - CaCO_2{}^r)} = \frac{\text{change in } VCO_2}{\text{change in } CaCO_2}$$

Figure 1. Partial CO_2 rebreathing differential Fick equation.

Table 1. Partial rebreathing vs. thermodilution (comparative studies)

Author	n	Patients	Comparison	Bias, L/min	Precision, L/min	r	r^2
Gama de Abreu et al. (6)	20	Sheep ARDS	PATD	−1.69	±1.90	.54	.51
Kuck et al. (7)	36	Cardiac surgery	PATD			.92	
Jopling et al. (8)	48	Unknown	PATD	−1.75	±2.28		
Kuck et al. (9)	134	CABG	PATD	0.69	±0.94	.78	
				0.34	±0.34	.82	
Loeb et al. (10)	12	Cardiac surgery	PATD	−0.19	±1.16		
Watt et al. (11)	5	Cardiac surgery	PATD	0.20	±0.79		

ARDS, acute respiratory distress syndrome; PATD, pulmonary artery thermodilution; CABG, coronary artery bypass graft.

Esophageal Doppler Monitoring

Doppler techniques have been employed in the suprasternal, transgastric, and transesophageal locations to estimate cardiac output noninvasively. The transesophageal approach is readily available to the intensivist and offers a number of advantages including close proximity to the descending aorta and stability of the probe within the esophagus. The use of esophageal Doppler monitoring (EDM) to measure cardiac output noninvasively was first described in 1971 and later refined in 1989 (12, 13). The technical basis for this technique is the concept that flow in a cylinder is equal to the area of the cross-section of the cylinder times the velocity of fluid in the cylinder. The cross-sectional area of a cylinder is equal to the area of a circle or Πr (2). In the case of aortic blood flow, the movement of blood is pulsatile and the velocity changes with time. Thus, the velocity can be characterized by the area under the velocity-time curve between two points in time (Fig. 2).

The area under the curve can be computed mathematically as the integral of the derivative of volume over time (dV/dt) from T1 to T2, where T1 represents the onset of flow and T2 represents the end of flow. This value is termed the time-integrated velocity. Stroke volume (SV) is calculated by multiplying the cross-sectional area by the time-integrated velocity. Once SV is known, cardiac output can be easily determined by the relationship, CO = heart rate (HR) × SV.

With Doppler technique, the velocity of blood flow across the aortic valve or in the descending aorta can be measured. In EDM, the Doppler probe measures flow in the descending aorta. The probe is approximately the size of a nasogastric tube and can be placed noninvasively with a similar technique to placing a nasogastric tube.

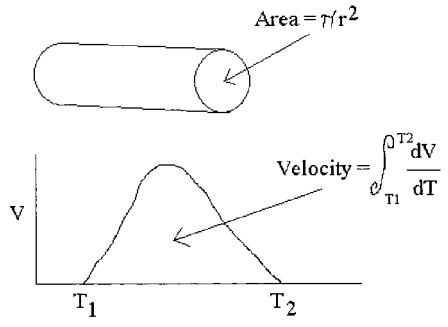

Figure 2. Determination of stroke volume in esophageal Doppler monitoring. *dV/dT*, derivative of volume over time; *T1*, onset of flow; *T2*, end of flow.

Several technical problems can limit the accuracy of cardiac output measurements by esophageal Doppler monitoring. The first thing to consider is that the descending aorta only receives a portion of the cardiac output, and the CO value derived from EDM is only an estimate of cardiac output based on descending aortic blood flow. Therefore, a correction factor must be added to account for this discrepancy. Another important consideration is the importance of positioning

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of the probe to get accurate measurements. To have a good approximation of velocity, the Doppler beam should be within 20° of axial flow. The accuracy of the cross-sectional area estimation is crucial to the calculation of cardiac output because any error in *r* is squared before it is used in the final equation. Also, the assumption that the aorta is cylindrical is not always valid. The cross-sectional area of the aorta is actually dynamic and is dependent on the pulse pressure and aortic compliance. Furthermore, flow in the aorta is not always laminar. Conditions such as tachycardia, anemia, and aortic valve disease can cause turbulent aortic blood flow and alter velocity measurements.

There have been limited studies concerning the accuracy and clinical benefits of EDM. In 1998, Cariou and colleagues (14) found that aortic blood flow is proportional to cardiac output over a wide range of cardiac output values (r = .80) and that aortic diameter can be reliably measured with m-mode ultrasound when compared with transesophageal echocardiography. Measurements of cardiac output by EDM have been correlated with both thermodilution and Fick methods (Table 2) (15–21). Of note, all of these studies used a nomogram based on the patient's age, gender, and weight to estimate cross-sectional area of the descending aorta. Although initial results are promising, more studies are needed to make a decision regarding the accuracy of this technique in critically ill patients. EDM-derived cardiac output using m-mode measurement of aortic diameter may yield more closely correlated values to thermodilution, but this has not yet been confirmed in clinical trials.

EDM allows the measurement of corrected flow time (FT_c) as a measure of cardiac preload and peak flow velocity as a measure of contractility. The FT_c is the systolic flow time corrected for heart rate expressed in milliseconds. In a small series of critically ill surgical patients, the FT_c correlated more strongly with cardiac output than pulmonary artery occlusion pressure (16). Additionally, the longest FT_c has been shown to correlate with the optimal level of left ventricular filling in mechanically ventilated patients (22). The FT_c was recently evaluated by using the end-diastolic short axis (derived from transesophageal echocardiography) as the "gold standard." In 34 patients undergoing coronary artery bypass grafting, the average correlation coefficient was .49 (23). Clinically, the EDM has proven beneficial for perioperative monitoring as a means to decrease morbidity in elective femur fracture fixation (24) and has been reported to yield beneficial information for treatment of sepsis in humans (25). EDM is well suited for the ICU and can be applied to a wide spectrum of patients with few contraindications (e.g., severe agitation, esophageal malignancy/perforation, severe bleeding diathesis, or aortic dissection). However, it is limited by the variability that can occur due to probe positioning, and additional training is required to ensure proficiency (26). Several commercially available devices estimate cardiac output by using Doppler esophageal monitoring technology: the CardioQ (Deltex Medical, Branford, CT), the Oesophageal Doppler Monitor II (Abbot Laboratories, North Chicago, IL), and the Dynemo 3000 (Sometec, Paris, France), which uses a nomogram to predict aortic diameter. The Hemosonic 100 (Arrow International, Reading, PA) uses m-mode ultrasound to measure aortic diameter.

Table 2. Esophageal Doppler monitor vs. "gold standard"

Author	n	Patients	Comparison	Bias, L/min	*r*
DiCorte et al. (15)	34	CABG	EM		.765
Madan et al. (16)	14	SICU	TD		.6
Valtier et al. (17)	46	MV	TD	.24	.95
Ballard et al. (18)	10	ICU	CCO	−.01	
Leather and Wouters et al. (19)	14	OR	TD	−.89	
Bernardin et al. (20)	22	MICU	TD		.92
Cuschien et al. (21)	10	SICU	TD		.846
			Fick		.811

CABG, coronary artery bypass graft; EM, electromagnetic flowmetry; SICU, surgical intensive care unit; TD, pulmonary artery thermodilution; MV, mechanically ventilated patients; ICU, intensive care unit; CCO, continuous pulmonary artery thermodilution; OR, operating room; MICU, medical intensive care unit; Fick, calculated by direct Fick.

Thoracic Electrical Bioimpedance

Thoracic electrical bioimpedance (TEB) is another noninvasive means by which cardiac output can be estimated. The thoracic bioimpedance is the electrical resistance of the thorax to a high-frequency, very low-magnitude current. This measure is indirectly proportional to the content of thoracic fluids such that as the amount of thoracic fluid increases, the TEB decreases. Therefore, total fluid conductivity (TFC) is equal to the inverse value of TEB (1/TEB). Changes in cardiac output may be reflected as a change in overall bioimpedance or TFC. In this technique, six electrodes are placed on the patient: two in the upper thorax/neck area and four in the lower thorax. The electrodes not only detect changes in bioimpedance; they also monitor electrical signals from the heart. The measurement of changes in TEB to estimate SV was originally described by Kubicek in the 1960s

$$SV = p\left(\frac{L}{Z_\phi}\right)Z[VET \times (dz/dt_{max})] \quad [3]$$

where p is the resistivity of blood (ohm-cm), L is the distance between the two inner voltage-sensing electrodes (cm), Z_0 is the mean thoracic impedance between the inner sensing electrodes (ohm), VET is the ventricular ejection time (sec), and $(dZ/dt)_{max}$ is the maximum negative slope of the bioimpedance signal (ohm/sec) (27).

This equation was later modified by Bernstein (28) to account for the noncylindrical shape of the thorax. Bernstein (28) also introduced a calibration factor that compensated for variation in gender and degree of obesity. Currently available bioimpedance hemodynamic monitors use some derivation of this calculation such that SV is derived according to the following logic:

1. The rate of TEB change over time (dZ/dt) corresponds to change in aortic blood flow (assuming other factors affecting impedance do not change between times the measurements were made).
2. $(dZ/dt)_{max}$ corresponds to peak aortic blood flow.
3. Ejection phase contractility index (EPCI) = $(dZ/dt)_{max} \times$ TFC.
4. Ventricular ejection time (VET) can be

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measured from the distance between the QRS intervals on the electrocardiogram sensing electrodes.

5. The volume of electrically participating tissues (VEPT) is estimated from the patient's gender, height, and weight.

These measurements have been used to estimate SV according to

$$SV = (VEPT)(VET)(EPCI) \qquad [4]$$

The determinants of overall thoracic bioimpedance are changes in tissue fluid volume, volumetric changes in pulmonary and venous blood induced by respiration, and volumetric changes in aortic blood flow produced by myocardial contractility. Accurate measurements of changes in aortic blood flow depend on the ability to accurately measure the third determinant while filtering out the "noise" produced by the first two determinants. This technique is very sensitive to any alteration in position or contact of the electrodes to the patient. Thus, the clinician must preferably use the same electrode and electrode position between measurements and attempt to minimize conditions that may interfere with electrode contact such as perspiration. Also, the accurate measurement of VET relies on a constant R-R interval. In patients with atrial arrhythmias such as frequent premature atrial contractions or atrial fibrillation/flutter, errors in measurement of VET can lead to significant errors in measurements of cardiac output. Importantly, any acute change in tissue water content, such as pulmonary edema, pleural effusions, or chest wall edema, can alter bioimpedance readings irrespective of any changes in cardiac output.

Many studies have examined the accuracy of thoracic electrical bioimpedance, including a recent meta-analysis in 1999 (29). This analysis reviewed 154 studies of thoracic bioimpedance versus a gold standard. The results related to accuracy are summarized in Table 3. The authors' conclusions were that TEB was probably useful for trend analysis but not accurate enough for diagnostic interpretation and that caution should be taken when the bioimpedance method is used with cardiac patients. Another study examined a large cohort of trauma patients, medical intensive care patients, and surgical intensive care patients (n = 2,192) and found an overall correlation of r = .85 (30). Interestingly, when patients with severe pulmonary edema, pleural effusions, or excessively high TFC were excluded, the correlation was $r = .93$. This subgroup comprised 8% of the total cohort.

TEB is the most noninvasive method of estimating cardiac output. This property can be particularly useful in the ICU setting when caring for patients with relative or absolute contraindications to more invasive methods or when arteriovenous access is problematic. However, TEB provides a less accurate estimate of cardiac output in patients with significant thoracic fluid overload such as pulmonary edema, pleural effusions, or massive peripheral edema (30). The prevalence of these conditions in the ICU will limit TEB use in that setting. When TEB is used in the ICU, the clinician should be mindful of the presence of these conditions and consider using an alternative method of hemodynamic monitoring. Many commercially available products incorporate bioimpedance technology. Products currently marketed for use in the ICU include BioZ (Cardiodynamics, San Diego, CA), IQ System (Renaissance Technologies, Newton, PA), and CircMon (JR Medical, Estonia).

Transpulmonary Cardiac Output

Cardiac output can also be measured noninvasively by using the transpulmonary thermodilution technique. Like pulmonary artery (PA) thermodilution, this method uses the Stewart-Hamilton equation to estimate cardiac output (see Equation *5*),

$$CO = \frac{(Ta - Tb) \times Vi \times K}{\int dT/dt} \qquad [5]$$

where CO is cardiac output, Ta is temperature before injection, Tb is temperature after injection, Vi is volume of injectate, K is a constant, and dT/dt is change in temperature per change in time.

Cold injectate is administered intravenously (usually in the central circulation), and the change in temperature is detected in the arterial system. There are several key differences between the transpulmonary technique and the pulmonary artery technique. First, the transpulmonary method does not require the insertion of a pulmonary artery catheter and is therefore less invasive. This may equate to a lower complication rate. Second, transpulmonary thermodilution measures left-sided cardiac output, and PA thermodilution measures right-sided cardiac output. In most circumstances, the left-sided CO approximates the right-sided CO; however, there are times when these values theoretically can diverge, for example, during positive pressure ventilation. Finally, transpulmonary thermodilution may be less dependent on respiratory variation given the difference in proximity to the thorax.

Several clinical validation studies have compared transpulmonary thermodilution to a gold standard (Table 4) (31–34). These data suggest a good correlation between transpulmonary thermodilution and PA thermodilution. As one can see in Table 3, transpulmonary CO values are often greater than corresponding PA thermodilution values. The reason for this is not entirely clear. Proposed mechanisms include loss of indicator (cold) with transpulmonary and/or cold-in-

Table 3. Meta-analysis by Raaijmakers et. al (29), r^2 values

	Healthy	Cardiac	Critically I11	Total
Repeated measurements	.71	.59	.67	.67
Single measurements	.74	.44	.74	.53

Table 4. Transpulmonary thermodilution vs. "gold standard"

Author	n	Patients	Comparison	r	Bias, L/min	Precision, L/min
Gust et al. (31)	75	s/p CABG	PATD	.72	0.46	±1.16
Tibby et al. (32)	24	Children	Fick	.97		
Sakka et al. (33)	51	Sepsis/vent	PATD	.98	0.73	±0.38
			Fick	.85	0.002	±1.19
			CCO	.93	0.30	±0.76
Godje et al. (34)	450	s/p CABG	PATD	.96	0.16	

s/p, status post; CABG, coronary artery bypass graft; PATD, pulmonary artery thermodilution; CCO, continuous cardiac output via pulmonary artery catheter heater probe.

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duced reduction in HR leading to decreased CO in the right heart compared with the left heart (33). Differences may also be partially explained by differences in sensitivity to respiratory variation, which would affect the PA thermodilution method to a greater extent. It appears that the correlation holds true for critically ill patients (33); however, confirmation studies are needed in an extended spectrum of clinical conditions.

Pulse Contour Analysis

In 1983, Wesseling and colleagues (35) developed an algorithm based on arterial pulse contour analysis to continually monitor CO. It is based on the concept that the contour of the arterial pressure waveform is proportional to SV, which can be estimated by the integral of the change in pressure from end diastole (t0) to end systole (t1) over time. The estimate of SV is also influenced by the impedance of the aorta (Z)

$$SV = \frac{\int_{t0}^{t1} dP/dt}{Z} \qquad [6]$$

Z is dependent on the CO and the individual elastic/mechanical properties of the aorta at that particular time (bolus effect). To determine what the individual impedance is at any one point, CO must be determined by another method and used to calibrate the pulse contour device. This can be accomplished by a transpulmonary thermodilution method.

Pulse contour analysis has been extensively studied, and there are many available validation studies (Table 5) (36–39). In the study by Buhre et al. (36), the close correlation between pulse contour CO and PA thermodilution remained despite significant changes in CO induced by esmolol. In another study, pulse contour was compared with PA thermodilution and continuous CO by heater probe (40). The results were documented before and after administration of phenylephrine. The close correlation between values obtained by continuous CO and PA thermodilution persisted after phenylephrine administration, but the values obtained by pulse contour and PA thermodilution diverged after the administration of vasoconstrictor. This discrepancy suggests loss of correlation with significant changes in hemodynamics.

Most studies of the pulse contour method show excellent correlation with PA thermodilution, including patients with acute respiratory distress syndrome (37). There are conflicting studies as to the influence of significant changes in SVR that may occur after calibration (36, 40). Frequent recalibration during times of hemodynamic instability will minimize such errors. Currently available commercial devices require manual input of a value for central venous pressure. The location of the arterial sensing catheter in pulse contour analysis is an important consideration. Although the manufacturer of PiCCO (Pulsion Medical, Munich, Germany) recommends placement in either the axillary or femoral position, the clinical validation studies for pulse contour were done with the arterial catheter in the femoral position. The accuracy of pulse contour seems to lessen when the arterial waveform analysis is obtained from a peripheral location such as the finger (41, 42). Use of the arterial sensing catheter in the radial position has not been clinically validated. The requirement of a proximal arterial catheter causes the pulse contour device to be more invasive than the other techniques described and may limit its usefulness.

Pulse contour devices also allow the measurement of global end diastolic volume (GEDV) to approximate intrathoracic blood volume (ITBV) and extravascular lung water (EVLW) as a surrogate for cardiac preload. ITBV and EVLW have traditionally been measured by the double indicator technique (thermodilution and indocyanine green) via a pulmonary artery catheter. ITBV is calculated by the product of CO and the mean transit time (MTT) of a plasma-bound indicator (ITBV = CO × MTT). With the less invasive transpulmonary technique, intrathoracic thermal volume (ITTV) is calculated by the product of CO and MTT of cold injectate. Also, the pulmonary thermal volume (PTV) is derived from the relationship PTV = CO × t, where t is the exponential decay time. This relationship assumes that the majority of temperature decay occurs in the largest mixing chamber (PTV; Fig. 3).

Once values for ITTV and PTV are obtained, they can be used to calculate GEDV from the equation GEDV = ITTV − PTV. A linear relationship has been found to exist between ITBV and GEDV (43–45) whereby ITBV = 1.25 × GEDV (this is an approximation based on the average of several trials). Also, EVLW can be calculated by subtracting ITBV from ITTV (EVLW = ITTV − ITBV).

Using EVLW to guide fluid management in medical intensive care patients has been suggested to reduce the duration of mechanical ventilation and length of stay in the ICU (44). The ITBV has been suggested to be a better indicator of cardiac preload than pulmonary artery occlusion pressure (PAOP) and central venous pressure (44–46). In mechanically ventilated patients, this may be due to an artificial elevation of PAOP and central venous pressure from increased airway pressure. Lichtwarck-Aschoff et al. (46) demonstrated a correlation between change in ITBV and change in cardiac

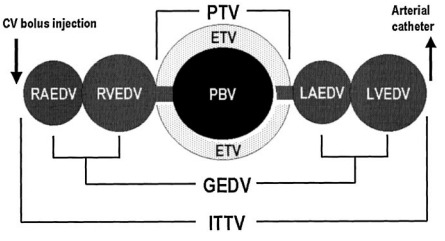

Figure 3. Blood volumes in measurement of global end diastolic volume (reproduced with permission from Pulsion Medical, Munich, Germany). *RAEDV*, right atrial end-diastolic volume; *RVEDV*, right ventricular end-diastolic volume; *PBV*, pulmonary blood volume; *ITTV*, intrathoracic thermal volume; *ETV*, extravascular thermal volume; *LAEDV*, left atrial end-diastolic volume; *LVEDV*, left ventricular end-diastolic volume; *GEDV*, global end-diastolic volume; *PTV*, pulmonary thermal volume.

Table 5. Pulse contour vs. pulmonary artery thermodilution

Author	n	Patients	Comparison	*r*	Bias, L/min	Precision, L/min
Buhre et al. (36)	36	MIDCAB	PATD	.94	0.003	1.26
Zollner et al. (37)	160	ARDS	PATD	.91	0.03	1.04
Goedje et al. (38)	216	Cardiac surgery	PATD	.92	0.07	1.4
Zollner et al. (39)	76	Cardiac surgery	PATD	.88	0.31	1.25

MIDCAB, minimally invasive coronary artery bypass; PATD, pulmonary artery thermodilution; ARDS, acute respiratory distress syndrome.

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index (r = .71) whereas change in PAOP and change in central venous pressure were not correlated with cardiac index (r = −.018 and r = −.069, respectively) (46). Similar results were found in 57 critically ill patients with sepsis or septic shock (47). ITBV and EVLW measured via single transpulmonary technique have been shown to have an excellent correlation with measurements of ITBV and EVLW with the double-indicator technique (r = .97 and r = .96, respectively) (48).

Based on accumulated clinical experience, ITBV may be an alternative measure to predict cardiac preload in critically ill patients. Errors in volume measurement may occur in the presence of large aortic aneurysms, intracardiac shunts, pulmonary embolism, or acute changes in chamber size (e.g., recent pulmonary lobectomy or pneumonectomy) (49). Also, measurement of ITBV via transpulmonary technique depends on a constant relationship between GEDV and ITBV. This method assumes that the majority of temperature decay occurs in the pulmonary blood volume (the largest mixing chamber). This technique offers an accurate measurement of cardiac output (compared with thermodilution) and can be readily applied to the critically ill patient. The most important clinical limitation is the requirement of a proximal arterial catheter. Currently, there is one commercially available pulse contour device that can estimate cardiac output and ITBV (PiCCO; Pulsion Medical, Munich, Germany).

Lithium Dilution Cardiac Output

As discussed earlier, pulse contour devices must be calibrated with a CO derived from another source (e.g., transpulmonary thermodilution). They also can be calibrated by using lithium dilution. In this technique, lithium chloride is injected into a central or peripheral venous catheter, and lithium is measured with a lithium-sensitive electrode in the peripheral arterial system. The electrode is outside the artery and thus requires withdrawal of a small (3-mL) sample of blood with each measurement. The change in voltage across a semipermeable membrane is related to the change in lithium concentration. A correction for serum sodium concentration is needed due to low selectivity of the membrane for lithium over sodium. A dilution curve for lithium is constructed, and cardiac output is calculated according to

$$\mathrm{CO(L/min)} = \frac{\mathrm{LiC1} \times 60}{\mathrm{Area} \times (1 - \mathrm{PCV})} \quad [7]$$

where LiCl is the dose of lithium chloride in mmol, Area is the area under the lithium-time dilution curve, and PCV is the packed cell volume, which is derived from the hemoglobin concentration.

Once the CO measurement is obtained, that value can be used to calibrate a pulse contour device.

Multiple trials have been done to study the accuracy of lithium dilution CO compared with various reference gold standards (Table 6) (50–52). Kurita et al. (53) found good correlation between lithium dilution and electromagnetic flowmeter-derived CO in the setting of hemodynamic changes induced by dobutamine and propanolol in an animal model. Data presented by Garcia-Rodriguez et al. (54) suggest that no accuracy is lost when the lithium is injected via a peripheral catheter.

Cardiac output values derived from lithium dilution correlate well with pulmonary artery thermodilution and transpulmonary thermodilution measurements (50–52). Compared with the thermodilution-derived pulse contour technique, lithium dilution cardiac output is less invasive because it does not require central circulation catheterization; however, it offers the clinician no direct assessment for cardiac preload. Also, the 3-mL blood draw required for each calibration may contribute to anemia and increase blood product transfusions. Although the lithium dilution method seems to perform well with only peripheral access, no accurate measurement of central venous pressure and thus SVR can be made without central venous catheterization. The lithium dilution method may be useful for the patient in whom cardiac output monitoring is required without a need for directly measured cardiac preload. For example, it could be useful in distinguishing high cardiac output versus low cardiac output in a patient with unexplained hypotension. Currently, there is one commercially available lithium dilution cardiac output monitor (LiDCO; LiDCO Ltd, London, UK).

CONCLUSIONS

Many methods are available to noninvasively measure cardiac output. The characteristics of each technique re-

Table 6. Lithium dilution cardiac output vs. pulmonary artery thermodilution

Author	n	Patients	Comparison	*r*	Bias, L/min	Precision, L/min
Linton et al. (50)	200	Cardiac surgery	PATD		−0.25	0.46
Young et al. (51)	69	Cardiac surgery	PATD		−0.53	1.25
Linton et al. (52)	48	Age 5days-9yrs	TPTD	.98	−0.1	0.3

PATD, pulmonary artery thermodilution; TPTD, transpulmonary thermodilution.

Table 7. General features of available minimally invasive cardiac output technologies

Method	Accuracy[a]	Estimate of Cardiac Preload	Special Considerations
Indirect Fick	++	No	Intubated, accuracy limited by cardiopulmonary disease
EDM	+++	Yes (FTc)	Patient movement, specialized training
TEB	+++	No	Decreased accuracy with abnormal cardiac rhythm, severe peripheral edema
Transpulmonary/pulse contour	++++	Yes (ITBV)	Requires proximal arterial access
Lithium dilution	++++	No	Does not require central circulation catheterization

[a]Compared with pulmonary artery thermodilution (highest accuracy corresponds to ++++ and lowest accuracy corresponds to +).

EDM, esophageal Doppler monitor; FTc, corrected flow time; TEB, thoracic electrical bioimpedance; ITBV, intrathoracic blood volume.

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It is important for the clinician to understand the strengths and limitations of each device to effectively use the information derived.

viewed are summarized in Table 7. In an era of questionable utility and safety of the invasive pulmonary artery catheter, a safe and reliable means by which to measure cardiac output more noninvasively in critically ill patients is welcomed. In general, most methods are based on sound physiologic principle and can be used for following hemodynamic trends. The indirect Fick methods are convenient and relatively easy to apply to mechanically ventilated patients but may not be accurate enough for initial diagnostic information in a patient with significant lung disease or multiorgan failure. The esophageal Doppler monitor, although slightly more invasive and operator dependent than others, is associated with low risk and may be a better alternative for the critically ill patient. More studies are needed to document accuracy of this method by using m-mode ultrasound for measurement of aortic diameter. The bioimpedance methods tend to lose accuracy in the setting of intrathoracic fluid shifts such as occur in acute respiratory distress syndrome, congestive heart failure, peripheral edema, or pleural effusions, which may limit its use in the intensive care setting. The pulse contour devices offer a beat-to-beat measurement of cardiac output and have shown good correlation with pulmonary artery thermodilution during times of stable hemodynamics. These devices should be recalibrated frequently in patients with unstable hemodynamics. Pulse contour devices also allow estimation of ITBV to assess cardiac preload. In some cases, ITBV may be more useful for volume resuscitation than the traditional pulmonary artery catheter derived PAOP (55). Each of these methods has advantages and disadvantages; it is important for the clinician to understand the strengths and limitations of each device to effectively use the information derived. Intensivists work in a rapidly changing environment and must be able to critically evaluate emerging technologies before widespread application in patients. In a time when the pulmonary artery catheter is coming under scrutiny due to safety and accuracy concerns, less invasive devices may be an appropriate alternative.

REFERENCES

1. Shoemaker WC, Appel PL, Kram HB, et al: Prospective trial of supranormal values of survivors as therapeutic goals in high-risk surgical patients. *Chest* 1998; 94:1176–1186
2. Boyd O, Grounds RM, Bennett ED: A randomized clinical trial of the effect of deliberate perioperative increase of oxygen delivery on mortality in high-risk surgical patients. *JAMA* 1993; 270:2699–2707
3. Connors AF Jr, Speroff T, Dawson NV, et al: The effectiveness of right heart catheterization in the initial care of critically ill patients. SUPPORT Investigators. *JAMA* 1996; 276:889–897
4. Pulmonary artery catheter consensus conference: Consensus statement. *Crit Care Med* 1997; 25:910–925
5. Magder S: Cardiac output. *In:* Principles and Practice of Intensive Care Monitoring. Tobin MJ (Ed). New York, McGraw-Hill 1998, pp 797–810
6. Gama de Abreu M, Quintel M, Ragaller M, et al: Partial carbon dioxide rebreathing: A reliable technique for noninvasive measurement of nonshunted pulmonary capillary blood flow. *Crit Care Med* 1997; 25:675–683
7. Kuck K, Ing D, Haryadi DG, et al: Evaluation of partial re-breathing cardiac output measurement during surgery. *Anesthesiology* 1998; 89:A542
8. Jopling MW: Noninvasive cardiac output determination utilizing the method of partial CO_2 rebreathing. A comparison with continuous and bolus thermodilution cardiac output. *Anesthesiology* 1998; 89:A544
9. Kuck K, Orr J, Haryadi DG, et al: Evaluation of the NICO partial rebreathing cardiac output monitor. *Anesthesiology* 1999; 91:A560
10. Loeb RG, Brown EA, DiNardo JA, et al: Clinical accuracy of a new non-invasive cardiac output monitor. *Anesthesiology* 1999; 91: A474
11. Watt RC, Loeb RG, Orr J: Comparison of a new non-invasive cardiac output technique with invasive bolus and continuous thermodilution. *Anesthesiology* 1998; 89:A536
12. Side CD, Gosling RJ: Non-surgical assessment of cardiac function. *Nature* 1971; 232: 335–336
13. Singer M, Clarke J, Bennett ED: Continuous hemodynamic monitoring by esophageal Doppler. *Crit Care Med* 1989; 17:447–450
14. Cariou A, Monchi M, Joly LM, et al: Noninvasive cardiac output monitoring by aortic blood flow determinations: Evaluation of the Sometec Dynemo-3000 system. *Crit Care Med* 1998; 26:2066–2072
15. DiCorte CJ, Latham P, Greilich PE, et al: Pulmonary artery catheter vs esophageal Doppler monitor: Measurement of cardiac output and left ventricular filling during cardiac surgery. *Anesth Analg* 1999; 88:SCA37
16. Madan AK, UyBarreta VV, Shaghayegh AW, et al: Esophageal Doppler ultrasound monitor versus pulmonary artery catheter in the hemodynamic management of critically ill surgical patients. *J Trauma* 1999; 46:607–611
17. 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
18. Ballard C, Cohen Y, Fosse JP, et al: Haemodynamic measurements (continuous cardiac output and systemic vascular resistance) in critically ill patients: Transoesophageal Doppler versus continuous thermodilution. *Anaesth Intensive Care* 1999; 27:33–37
19. Leather HA, Wouters PF: Oesophageal Doppler monitoring overestimates cardiac output during lumbar epidural anaesthesia. *Br J Anaesth* 2001; 86:794–797
20. Bernardin G, Tiger F, Fouche R, et al: Continuous noninvasive measurement of aortic blood flow in critically ill patients with a new esophageal echo-Doppler system. *J Crit Care* 1998; 13:177–183
21. Cuschien J, Rivers E, Caruso J, et al: A comparison of transesophageal Doppler, thermodilution and Fick cardiac output measurements in critically ill patients. *Crit Care Med* 1998; 26(Suppl):A82
22. Singer M, Bennett ED: Noninvasive optimization of left ventricular filling using esophageal Doppler. *Crit Care Med* 1991; 19: 1132–1137
23. DiCorte CJ, Latham P, Greilich PE, et al: Esophageal Doppler monitor determinations of cardiac out and preload during cardiac operations. *Ann Thorac Surg* 2000; 69: 1782–1786
24. Sinclair S, James S, Singer M: Intraoperative intravascular volume optimisation and length of stay after repair of proximal femoral fracture: Randomised controlled trial. *BMJ* 1997; 315:909–912
25. Eachempati SR, Young C, Alexander J, et al: The clinical use of an esophageal Doppler monitor for hemodynamic monitoring in sepsis. *J Clin Monit Comput* 1999; 15: 223–225
26. Lefrant JY, Bruelle P, Aya AGM, et al: Training is required to improve the reliability of esophageal Doppler to measure cardiac output in critically ill patients. *Intensive Care Med* 1998; 24:347–352
27. Kubicek WG: Development and evaluation of an impedance cardiac output system. *Aerospace Med* 1966; 12:1208–1212
28. Bernstein DP: A new stroke volume equation for thoracic electrical bioimpedance: Theory and rationale. *Crit Care Med* 1986; 14: 904–909
29. Raaijmakers E, Faes JC, Scholten RJ, et al: A meta-analysis of three decades of validating

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thoracic impedance cardiography. *Crit Care Med* 1999; 27:1203–1213
30. Shoemaker WC, Belzberg H, Wo CJ, et al: Multicenter study of noninvasive monitoring systems as alternatives to invasive monitoring of acutely ill emergency patients. *Chest* 1998; 114:1643–1652
31. 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
32. Tibby SM, Hatherill M, Marsh MJ, et al: Clinical validation of cardiac output measurements using femoral artery thermodilution with direct Fick in ventilated children and infants. *Intensive Care Med* 1997; 23: 987–991
33. Sakka SG, Reinhart K, Wegscheider K, et al: Is the placement of a pulmonary artery catheter still justified solely for the measurement of cardiac output? *J Cardiothorac Vasc Anesth* 2000; 14:119–124
34. Godje O, Peyerl M, Seebauer T, et al: Reproducibility of double indicator dilution measurements of intrathoracic blood volume compartments, extravascular lung water, and liver function. *Chest* 1998; 113:1070–1077
35. Wesseling KH, deWitt B, Weber AP, et al: A simple device for the continuous measurement of cardiac output. *Adv Cardiovasc Phys* 1983; 5:1–52
36. 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
37. Zollner C, Briegel J, Kilger E, et al: Retrospective analysis of transpulmonary and pulmonary arterial measurement of cardiac output in ARDS patients. *Anaesthesist* 1998; 47: 912–917
38. Goedje O, Hoeke K, Lichtwarck-Aschoff M, et al: Continuous cardiac output by femoral artery thermodilution calibrated pulse contour analysis: Comparison with pulmonary arterial thermodilution. *Crit Care Med* 1999; 27: 2407–2412
39. Zollner 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
40. Rodig G, Prasser C, Keyl C, et al: Continuous cardiac output measurement: Pulse contour analysis versus thermodilution technique in cardiac surgical patients. *Br J Anaesth* 1999; 82:525–530
41. Hirschl M, Binder M, Gwechenberger M, et al: Noninvasive assessment of cardiac output in critically ill patients by analysis of the finger blood pressure waveform. *Crit Care Med* 1997; 25:1909–1914
42. Hirschl M, Kittler H, Woisetschlager C, et al: Simultaneous comparison of thoracic bioimpedance and arterial pulse waveform-derived cardiac output with thermodilution measurement. *Crit Care Med* 2000; 28: 1798–1802
43. Sakka SG, Ruhl CC, Pfeiffer UJ, et al: Assessment of cardiac preload and extravascular lung water by single transpulmonary thermodilution. *Intensive Care Med* 2000; 26: 180–187
44. Mitchell JP, Schuller D, Calandrino FS, et al: Improved outcome based on fluid management in critically ill patients requiring pulmonary artery catheterization. *Am Rev Respir Dis* 1992; 145:990–998
45. Buhre W, Bendyk K, Weyland A, et al: Thermo-dye dilution technique versus single thermodilution technique. Assessment of intrathoracic blood volume (ITBV). *Anaesthesist* 1998; 47:51–53
46. Lichtwarck-Aschoff M, Zeravik J, Pfeiffer UJ: Intrathoracic blood volume accurately reflects circulatory volume status in critically ill patients with mechanical ventilation. *Intensive Care Med* 1992; 18:142–147
47. Sakka SG, Bredle DL, Reinhart K, et al: Comparison between intrathoracic blood volume and cardiac filling pressures in the early phase of hemodynamic instability of patients with sepsis or septic shock. *J Crit Care* 1999; 14:78–83
48. Pfeiffer UJ, Lichtwarch-Aschoff M, Beale R: Single thermodilution monitoring of global end-diastolic volume, intrathoracic blood volume and extravascular lung water. Abstr. *Clin Intensive Care* 1994; 5(Suppl):38–39
49. Oppenheimer L, Elings VB, Lewis FR: Thermal-dye lung water measurements: Effects of edema and embolization. *J Surg Res* 1979; 26:504–512
50. Linton R, Band D, O'Brien T, et al: Lithium dilution cardiac output measurement: A comparison with thermodilution. *Crit Care Med* 1997; 25:1796–1800
51. Young CC, Garcia-Rodriguez CR, Cassell C, et al: Lithium dilution versus thermodilution cardiac output measurement in cardiac surgery patients. Abstr. ASA Meeting, 2000, A-586
52. Linton RA, Jonas MM, Tibby SM, et al: Cardiac output measured by lithium dilution and transpulmonary thermodilution in patients in a paediatric intensive care unit. *Intensive Care Med* 2000; 26:1507–1511
53. 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
54. Garcia-Rodriguez C, Cassell C, Young C, et al: Cardiac output measurement without pulmonary artery or central venous catheterization: A clinical assessment of the lithium dilution method. Abstr. ASA Meeting, 2000, A-587
55. Holm C, Melcer B, Horbrand F, et al: Intrathoracic blood volume as an endpoint in resuscitation of the severely burned: An observational study of 24 patients. *J Trauma* 2000; 48:728–734

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