What Is the Best Way To Measure Cardiac Output?

Who Cares, Anyway?

Despite recent controversies regarding its safety and efficacy, pulmonary artery catheterization (PAC) remains a widely used tool for the management of patients with cardiovascular instability. In addition to providing measurements of cardiac output (CO), several other potentially useful pieces of data can be obtained, including estimates of preload, afterload, and oxygen utilization. However, many practitioners feel that CO is the most useful parameter obtained with PAC.

The desire to measure CO without the risks of PAC has driven the search for other, less invasive measurement methods, such as esophageal Doppler measurements, lithium dilution, and carbon dioxide-based techniques. Esophageal Doppler monitoring involves inserting a flexible probe, similar to an esophageal stethoscope, into the midthoracic esophagus. A pulse-wave Doppler transducer in the probe tip calculates blood flow velocity from the Doppler frequency shift of RBCs in the descending aorta. By entering the age, gender, height, and weight of the patient, the aortic diameter can be estimated. From this and the blood flow velocity, aortic blood flow is calculated, representing approximately 70% of the total CO. Estimates of preload and afterload can be derived from the shape of the velocity waveforms. Modifications of this technique allow for the actual measurement of aortic diameter using M-mode ultrasound, eliminating the error associated with nomogram-based estimates. The resulting values for aortic blood flow correlate well with those of thermodilution CO.

Lithium dilution CO, a relatively new technique, is less invasive than PAC but requires central venous and intra-arterial catheters. This method involves the injection of a small dose of the indicator lithium chloride through a central venous catheter. The arterial plasma concentration curve then is measured by a specialized sensor connected to the arterial line, and the CO is calculated. Comparing lithium dilution and thermodilution with electromagnetic flowmetry as the “gold standard,” lithium dilution showed higher correlation with electromagnetic flowmetry as well as better limits of agreement when compared with thermodilution. Although the accumulation of lithium with repeated dosing is a potential concern, a once-daily lithium dilution may be used with pulse contour analysis to allow the continuous beat-to-beat analysis of CO, stroke volume, and systemic vascular resistance.

CO2-based techniques provide a noninvasive measure of CO in patients receiving mechanical ventilation. This method, which is based on the Fick principle, involves transient partial rebreathing of CO2 and the measurement of changes in CO2 elimination and end-tidal CO2 (a measure of arterial CO2). Based on these values, the CO component participating in gas exchange is calculated. Total CO then is calculated by estimating the shunt fraction (based on pulse oximetry and inspired oxygen concentration) and by adding this value to the initial value obtained. The CO2 technique has been shown to be quite accurate when compared to thermodilution CO. Like other noninvasive techniques, the CO2 Fick method does not provide for the measurement of preload indexes.

In this issue of CHEST (see page 990), Dhingra and colleagues compare CO obtained using oxygen consumption (VO2), which is called the oxygen Fick method, with the method of thermodilution. By measuring VO2 through indirect calorimetry and dividing this value by the arteriovenous oxygen content difference (obtained by the analysis of arterial and mixed venous samples), the CO is derived. The group found that the accuracy of the oxygen Fick method was fair only when using thermodilution as the standard, limiting the usefulness of the method. Their approach also is limited by the need to measure mixed venous oxygen saturation. As opposed to CO2 Fick methods, using easily measured expired CO2 values, the oxygen Fick method requires the sampling of mixed venous blood, necessitating the insertion of a PAC. This defeats the major purpose of most alternative methods of measuring CO, which is to use a less invasive method than the pulmonary artery catheter. However, the authors are to be applauded both for the study and for their statistical analysis of the technique. Instead of using a correlation coefficient to show the agreement between the two methods, the authors measured the bias and precision of the Fick method compared to thermodilution. This approach gives a much more discriminating evaluation of the new method, as two methods can have a high correlation coefficient but can have limited agreement between sets of measurements.

However, several other factors may have explained their findings. The improved agreement between the
oxygen Fick method and the thermodilution method in patients with lower CO (ie, < 50% of the patients studied in this series) is not surprising. Patients with higher CO or severe liver dysfunction often present with an altered oxygen extraction ratio (O_2ER) from a lack of O_2 utilization or severe systemic/pulmonary shunts, narrowing the arterial-mixed venous oxygen content difference. In this situation, any errors in the calculation of the concentration and arterial O_2 content (\( \text{CaO}_2 \)) or the concentration and mixed venous O_2 content (\( \text{CvO}_2 \)) will result in a larger error in CO that is calculated with the oxygen Fick equation, when compared with thermodilution, than in patients with a low CO state. Furthermore, previous studies confirm the limitations of the \( \text{VO}_2 \) Fick method compared to \( \text{VO}_2 \) calorimetry, with an estimated error of up to 31%.

In the “Materials and Methods” section of the article by Dhingra et al, withdrawal of care was performed first with the removal of pressors. It is not clear whether this process was gradual or abrupt. A thermogenic effect of catecholamine has been described in animals as well as in human volunteers. The importance of the effect of withdrawing treatment with vasopressors and inotropes on metabolic rate could be particularly important in critically ill patients, in whom a complete exhaustion of endogenous catecholamines is likely to occur.

Finally, it is difficult to estimate the degree of error that results from lung metabolic activity in the group of patients with sepsis and multisystem organ failure because the intensity of lung inflammation does not correlate with lung \( \text{VO}_2 \). Today, therefore, CO calculation by thermodilution catheter remains the clinical “gold standard.” An additional advantage of PAC over other methods of measuring CO is the ability to assess pulmonary pressures and preload. As is known, the pulmonary capillary wedge pressure is not a measure of preload (ie, left ventricular end-diastolic volume) but, instead, is a pressure measurement. The relationship between the pressure and volume is defined by compliance and will vary from patient to patient. Indeed, in the critically ill patient, pulmonary capillary wedge pressure correlates poorly with CO. This raises obvious questions about, for example, our consensus definition of ARDS, with which we cannot deal here. Newer catheters that allow the calculation of right ventricular end-diastolic volume demonstrate a better correlation between preload (ie, right ventricular end-diastolic volume) and CO, and, more importantly, between preload and preload-recruitable stroke work.

Instead of asking which monitor is best for measuring CO, we might query why, in any event, CO is important to measure. CO is used in critical care medicine to calculate the amount of oxygen delivered to the tissues per minute, using the following formula:

\[
\text{DO}_2 = \text{CO} \times \text{O}_2\text{content (\text{CaO}_2)}
\]

where \( \text{CaO}_2 = \text{hemoglobin (g/L)} \times 1.39 \times \text{SaO}_2 + (0.003 \times \text{PaO}_2) \) [where \( \text{SaO}_2 \) is arterial oxygen saturation]. \( \text{VO}_2 \) represents a global measurement of tissue aerobic generation of adenosine triphosphate and can be measured by indirect calorimetry or calculated using the following formula:

\[
\text{VO}_2 = \text{CO} \times (\text{Hgb} \times 1.39 \times [\text{SaO}_2 - \text{SvO}_2])
\]

where Hgb is hemoglobin and \( \text{SvO}_2 \) is mixed venous saturation.

In a normal situation, the ratio between \( \text{VO}_2 \) and \( \text{DO}_2 \), the O_2ER ([\( \text{VO}_2 \) \( \div \) \( \text{DO}_2 \) \( \times \) 100]), is between 25% and 30%. Thus, the progressive reduction of \( \text{DO}_2 \) and changes in O_2ER can be measured in the ICU and can be secondary to ischemic hypoxia (ie, decreased CO), hypoxic hypoxia (ie, decreased PaO_2), anemic hypoxia (ie, decreased hemoglobin), or distributive hypoxia (ie, increased O_2ER) with decreased oxygen utilization, a condition that is commonly called dyoxia. In an anesthetized healthy animal, the reduction of \( \text{DO}_2 \) from a baseline of 25 mL/kg/min to approximately 10 mL/kg/min increases the O_2ER by approximately 100%, to 50 to 60%. Below this level of \( \text{DO}_2 \), O_2ER cannot increase further, and \( \text{VO}_2 \) decreases. This level of oxygen delivery is called \( \text{DO}_2 \) critical and generally correlates well with the anaerobic metabolism and systemic lactic acidosis. However, when dyoxia, or the primary alteration of O_2ER, is present, the level of \( \text{DO}_2 \) critical cannot be identified easily. The measurement of \( \text{DO}_2 \) presents several other limitations. While \( \text{DO}_2 \) defines the bulk movement of oxygen to the tissues in general, in many critically ill patients, cellular oxygen delivery is affected by complex interactions of neurohumoral, anatomic, and pharmacologic factors, and typically is subjected to maldistribution among different organ districts.

Data obtained from critically ill patients during the discontinuation of life support, and from Jehovah’s Witnesses, show the \( \text{DO}_2 \) critical level to be approximately half (ie, 2 to 3 mL/kg/min) that of healthy animals (4 to 5 mL/kg/min). However, these data differ remarkably from previous studies of healthy anesthetized and critically ill patients in which data were obtained from multiple patients that identified \( \text{DO}_2 \) critical as being between 8 and 21 mL/kg/min.

It is, therefore, no surprise that data comparing the “coupling” of \( \text{DO}_2 \) with \( \text{VO}_2 \) below \( \text{DO}_2 \) critical in both animal and human studies are discordant,
especially when $DO_2$ and $VO_2$ are measured by independent methods (ie, thermodilution and indirect calorimetry). This controversial issue remains unclear due to the lack of controlled experiments in humans and the difficulty in obtaining multiple data points over a wide range of $DO_2$ values while maintaining a constant oxygen demand. Dhingra and colleagues obtained patient data during the withdrawal of care. Although the authors satisfied the requirements of obtaining multiple data points on both the oxygen delivery and oxygen dependence curves, their patients may not represent the pathophysiology of a hyperdynamic critically ill patient, in whom $DO_2$ critical seems to be set at a point higher than that in healthy patients. Finally, despite the widespread use of invasive monitoring in the ICU, which allows the easy measurement of $DO_2$, $VO_2$, and $O_2$ER in critically ill patients, none of these parameters have been reliable in predicting outcome.

Are there any alternatives to the hemodynamic and oximetric measurement in critically ill patients? Conventional clinical parameters of resuscitation (eg, BP, heart rate, and urine output) seem to be generally unreliable. Nonconventional blood markers have been extensively studied as resuscitation end points in critically ill patients. Lactic acid level correlates well with insufficient oxygen delivery beyond $DO_2$ critical in animal models of hemorrhagic shock. Remarkably, 48-h lactate level trends have been considered to be superior to measurements of oxygen delivery and $VO_2$ in determining outcome in patients with septic shock.

A base deficit $> -4$ is correlated with the onset of multiorgan system failure and mortality in several models of trauma. Venoarterial $CO_2$ gap has also been correlated with poor outcome in patients after they experience cardiac arrest and in those being resuscitated from hemorrhagic shock. The production of $CO_2$ by the gut (intramural pH [pHi]) recently has been proposed as an early marker of regional dysoxia. The distribution of flow away from the gut when oxygen delivery is insufficient represents a compensatory mechanism to maintain oxygen delivery to more essential organs. Therefore, dysoxia of the gastric mucosa can represent an earlier estimate of global tissue dysoxia. A pHi of $< 7.32$ has been associated with a statistical increase in mortality in a heterogeneous group of critically ill patients and trauma patients. Furthermore, a pHi of $< 7.35$ has been a better predictor of sepsis and mortality than $DO_2$ and $VO_2$.

More recently, a noninvasive, sublingual electrode that is capable of measuring mucosal $CO_2$ has been studied as an index of proper resuscitation and correlated to gastric tonometry. A sublingual $CO_2$ of 70 mm Hg has been noted as a critical value that is significant for survival (sensitivity, 0.73; specificity, 1.0) in a subset of critically ill emergency department patients. While all these methods aim to indirectly evaluate critical end points of resuscitation, a direct measurement of oxygen transport at the “ultimate frontier” level (ie, mitochondrial oxidative phosphorylation) is now available. Near-infrared light spectroscopy is the only technology allowing the continuous monitoring of cytochrome aa3 redox status, a reliable index of cell hypoxia. Unfortunately, at the time of this writing its use is only experimental and its cost is prohibitive.

While the utility of invasive cardiac monitoring to improve outcome in critically ill patients is still subject to verification, we note that there are at least two studies and suprapharmacologic studies have added anything to that understanding. While we applaud the attempt of Dhinga and colleagues to deal with this question in a forthright and innovative manner, the increased potential for inaccuracies in patients with high or very low CO makes the calculation of CO by the Fick method in critically ill patients impractical and of questionable use. Finally, the utility of the data extrapolated from terminally ill patients just before death should be carefully considered before applying any conclusions to critically ill patients.

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REFERENCES

4. Guzzi L, Jaffe MB, Orr JA. Clinical evaluation of a new noninvasive method of cardiac output measurement: prelimi-
inary results in CABG patients [abstract]. Anesthesiology 1998; 89:A543
10 deBoisblanc BP, McClarity E, Lord K. Oxygen consumption in the intensive care unit: indirect calorimetry is the way to go, but where? Crit Care Med 1999; 26:1153–1154
33 Mark PJ. Sublingual capnometry: a clinical validation study. Chest 2001; 120:923–927
37 Connors AF, Speroff T, Dawson NY, et al. The effectiveness of right heart catheterization in the initial care of critically ill patients. JAMA 1996; 276:889–897

A Waist Is a Terrible Thing to Mind

Central Obesity, the Metabolic Syndrome, and Sleep Apnea Hypopnea Syndrome

In this issue of CHEST (see page 829), Schäfer and colleagues report on a consecutive sample of men who had been referred for suspected sleep apnea hypopnea syndrome (SAHS) and were subjected to overnight polysomnography, anthropomorphic measurements reflecting obesity and body fat distribution, and blood testing for various cardiovascular risk factors as well as the measurement of serum leptin levels. They found significant associations between...