

Review

Equipment review: New techniques for cardiac output measurement – oesophageal Doppler, Fick principle using carbon dioxide, and pulse contour analysis

Christine Berton and Bernard Cholley

Department of Anesthesiology and Intensive Care, Hôpital Lariboisière, Paris, France

Correspondence: Bernard Cholley, bernard.cholley@lrb.ap-hop-paris.fr

Published online: 25 April 2002

Critical Care 2002, 6:216-221

© 2002 BioMed Central Ltd (Print ISSN 1364-8535; Online ISSN 1466-609X)

Abstract

Measuring cardiac output is of paramount importance in the management of critically ill patients in the intensive care unit and of 'high risk' surgical patients in the operating room. Alternatives to thermodilution are now available and are gaining acceptance among practitioners who have been trained almost exclusively in the use of the pulmonary artery catheter. The present review focuses on the principles, advantages and limitations of oesophageal Doppler, Fick principle applied to carbon dioxide, and pulse contour analysis. No single method stands out or renders the others obsolete. By making cardiac output easily measurable, however, these techniques should all contribute to improvement in haemodynamic management.

Keywords cardiac output, Fick principle, monitoring, oesophageal Doppler, pulse contour analysis, stroke volume, thermodilution

Intensive and perioperative care share a common goal, namely to maintain 'adequate' organ perfusion throughout the body during the time course of critical illness or surgery. Adequate organ perfusion implies two different physical properties: perfusion pressure that is sufficiently high to force blood into the capillaries of all organs; and sufficient flow to deliver oxygen and substrates, and to remove carbon dioxide and other metabolic byproducts. However, in many instances the only aspect of perfusion that is carefully monitored is pressure, whereas flow is simply ignored. One of the reasons for this may be related to the difficulties encountered in obtaining flow measurements. Indeed, in many centres the only way to obtain a measure of cardiac output is to use the thermodilution technique through a pulmonary artery catheter. The difficulties and risks associated with pulmonary artery catheter insertion may account, in part, for the lack of routine cardiac output monitoring in every patient. New emerging techniques can provide a measure of cardiac output less invasively than is the case with a pulmonary artery catheter.

The purpose of the present review is to provide an overview of the new cardiac output measurement techniques, with an emphasis on their principles of operation and their respective

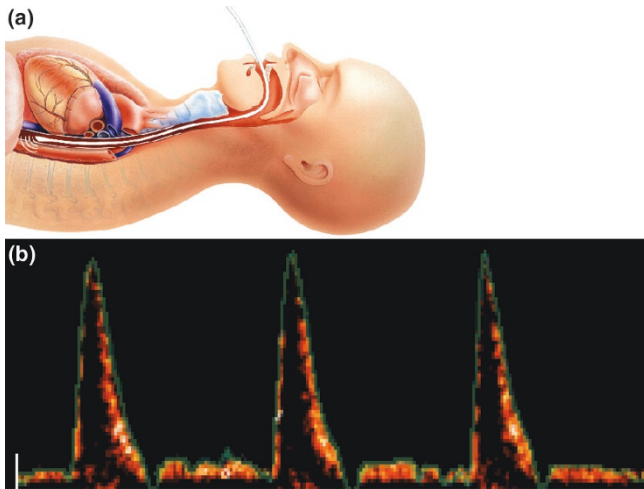
limitations. We review methods based on Doppler velocimetry of the descending aorta, the Fick principle applied to carbon dioxide, and arterial pulse contour analysis.

Oesophageal Doppler

The oesophageal Doppler technique is based on measurement of blood flow velocity in the descending aorta by means of a Doppler transducer (4 MHz continuous or 5 MHz pulsed wave, according to the type of device) at the tip of a flexible probe. The probe may be introduced orally in anaesthetized, mechanically ventilated patients. Following introduction of the probe, it is advanced gently until the tip is located approximately at the mid-thoracic level; it is then rotated so that the transducer faces the aorta and a characteristic aortic velocity signal is obtained (Fig. 1). Probe position is optimized by slow rotation in the long axis and alteration of the depth of insertion to generate a clear signal with the highest possible peak velocity. Gain setting is adjusted to obtain the best outline of the aortic velocity waveform.

Measurement of stroke volume using oesophageal Doppler is derived from the well established principles of stroke volume

Figure 1

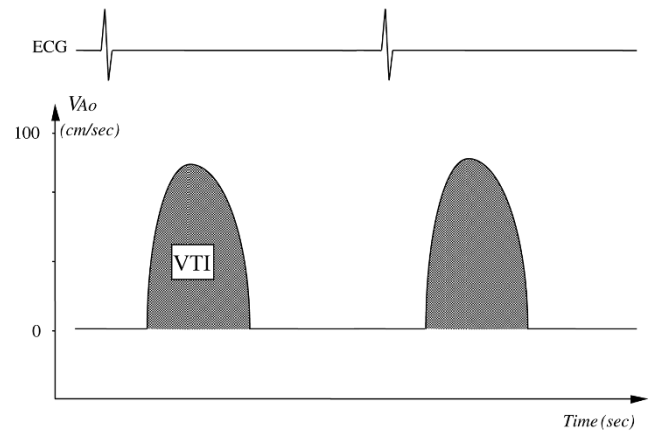


Oesophageal Doppler. **(a)** Schematic representation of oesophageal Doppler probe in a patient, demonstrating the close relation between oesophagus and descending thoracic aorta. **(b)** Characteristic velocity waveform obtained in the descending aorta. The spectral representation shows that most red blood cells (orange-white color) are moving at the maximum velocity (close to the green envelope) during systole, and that diastolic flow is minimal.

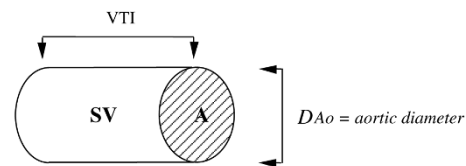
measurement in the left ventricular outflow tract using transthoracic echo and Doppler (Fig. 2) [1]. Several assumptions are required for transposition of this algorithm from the left ventricular outflow tract to the descending aorta: accurate measurement of descending aortic blood flow velocity; a 'flat' velocity profile in the descending aorta; an estimated aortic cross-sectional area close to the mean value during systole; a constant division of blood flow between the descending aorta (70%) and the brachiocephalic and coronary arteries (30%); and, finally, a negligible diastolic flow in the descending aorta.

Accurate velocity measurement requires good alignment between the Doppler beam and blood flow, and knowledge of the angle at which the blood flow is insonated. Alignment is optimal where the signal is the brightest on the spectral representation (CardioQ, Deltex Medical Ltd, Chichester, UK; and Waki, Atys Medical, Soucieu en Jarrest, France) or when the aortic walls are well defined on M-mode echocardiography (HemoSonic, Arrow International, Reading, PA, USA), and when peak velocity is maximum (all devices). The angle between the Doppler beam and the flow is presumed to be the same as that between the transducer and the probe (45° or 60°, depending on the device), because the oesophagus and aorta are usually parallel in the thorax. A discrepancy between the true and the theoretical angle is more problematic when the inclination of the transducer is 60°. Indeed, a discrepancy of 10° will result in an error ranging between +28% and -32% for a 60° transducer (5 MHz) but only +16% to -19% for a 45° transducer (4 MHz).

Figure 2



■ = VTI = Velocity x Time integral = (cm/sec) x sec = cm
= stroke distance



▨ = A = aortic cross sectional Area = $(\pi \times DAo^2)/4$

□ = SV = Stroke Volume = VTI x A

Principle of stroke volume calculation from aortic velocity (V_{Ao}) measurements. The area under the maximum aortic velocity envelope (VTI) represents the stroke distance. Assuming that all red blood cells are moving at maximum velocity and that aortic cross-sectional area is constant during systole, stroke volume is obtained by multiplying stroke distance by aortic cross-sectional area.

The assumption regarding the velocity profile is that all red blood cells are moving at approximately the same speed.

The cross-sectional area of the descending aorta can be measured at the bedside by using transoesophageal echocardiography; however, this technique is not available in all centres. The manufacturers of oesophageal Doppler devices have solved this problem either by incorporating an M-mode echo transducer into their probe in order to measure aortic diameter instantaneously (HemoSonic, Arrow) or by providing a nomogram to estimate the cross-sectional area of the descending aorta based on the patient's age, weight and height (CardioQ, Deltex Medical Ltd; and Waki, Atys Medical). Systematic errors due to a discrepancy between the actual area and the estimated value would not affect the trend of cardiac output variation over time [2]. A large variation in cardiac output can only be underestimated by failing to take into account the concomitant change in aortic diameter, which is necessarily in the same direction.

Finally, some manufacturers of oesophageal Doppler devices provide measures of systemic cardiac output rather than of descending aortic blood flow. They calculate the systemic values by assuming a constant partition of blood between cephalic (30%) and caudal (70%) territories. Although this may be valid in healthy, resting persons, the partition may vary depending on haemodynamic conditions, reflex activation, or metabolic activity within different organs. Therefore, the assumed constant ratio between cephalic and caudal territories (7:3) may become inaccurate under a variety of pathophysiological conditions [2–4].

Learning curve and reproducibility

Oesophageal Doppler is a simple technique, and most users acknowledge that it is fairly easy to achieve adequate probe positioning and to obtain reproducible results [5,6]. Investigators who studied the learning curve with the technique [7,8] noted a dramatic improvement in the skills of untrained operators after performing only 10 or 12 probe placements. Inter-observer variability has been shown to be less than 10% and intraobserver variability is only 8% – a figure that is closer to 12% for thermodilution [2,5,9,10].

Probe displacement can occur during prolonged monitoring as a result of various factors (nursing procedures, deglutition and gravity, among others), and results in a poorly defined velocity envelope or loss of signal. It is therefore mandatory to recheck the signal quality, on a systematic basis, before acquiring and interpreting Doppler-derived data. Failure to reposition the probe before each measurement may lead to grossly erroneous cardiac output values.

Validation of cardiac output measurement using oesophageal Doppler

'Gold standard' techniques for cardiac output measurement, such as aortic electromagnetic or ultrasound transit time flowmetry, are highly invasive and cannot be used in patients. Clinically available techniques include the Fick principle, dye dilution, thermodilution and transthoracic echo Doppler. These techniques are less accurate and reproducible, and none of them has ever been validated in comparison with a 'gold standard' technique in critically ill, mechanically ventilated patients. The widespread use of thermodilution in intensive care units has made it a 'reference' technique, despite its well-known pitfalls [11]. Therefore, all trials aimed at validating cardiac output measurement using oesophageal Doppler have compared this technique with thermodilution. Such studies [2,5,7,9,12] generally found a rather poor agreement between the two techniques, but suggested that the difference in measures of cardiac output was consistent (i.e. a change in cardiac output with one technique was matched by a proportionate change with the other technique).

More recently, a multicentre study compared multiple techniques with oesophageal Doppler [10]. Patients from three different intensive care units underwent paired cardiac output

measurements using thermodilution and oesophageal Doppler. In addition, simultaneous suprasternal Doppler and indirect calorimetry (Fick principle) were used to measure cardiac output in some patients from one centre. Good correlation was found between thermodilution and oesophageal Doppler ($r=0.95$), with a small systematic underestimation (bias 0.24 l/min) using oesophageal Doppler. The limits of agreement between thermodilution and oesophageal Doppler were +2 l/min to –1.5 l/min. Variations in cardiac output between two consecutive measurements using either oesophageal Doppler or thermodilution techniques were similar in direction and magnitude (bias 0 l/min; limits of agreement ± 1.7 l/min; Fig. 3). Suprasternal Doppler and indirect calorimetry yielded similar correlations and agreement in the subset of patients in which they were used. These findings confirmed that oesophageal Doppler can provide a noninvasive, clinically useful estimate of cardiac output, and may detect haemodynamic changes in mechanically ventilated, critically ill patients.

Methods using Fick Principle

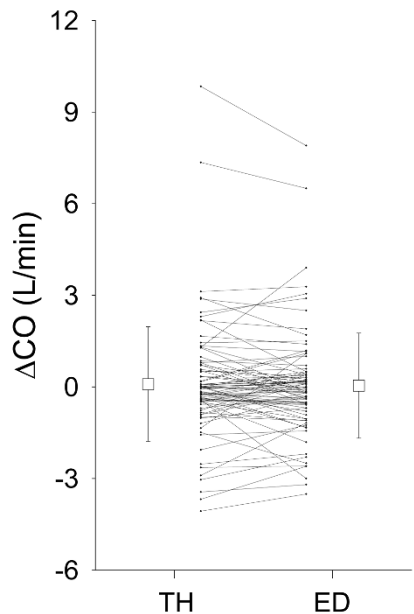
In 1870, Fick described the first method to estimate cardiac output in humans. Fick postulated that oxygen uptake in the lungs is entirely transferred to the blood. Therefore, cardiac output can be calculated as the ratio between oxygen consumption (VO_2) and arteriovenous difference in oxygen ($AVDO_2$).

$$\text{Fick equation: Cardiac output (CO)} = \frac{VO_2}{AVDO_2} \quad (1)$$

This estimation is accurate when the haemodynamic status is sufficiently stable to allow constant gas diffusion during the mean transit time of blood through the lungs.

Devices that measure VO_2 , such as the Delta-Trach (Datex, Helsinki, Finland) indirect calorimetry monitor, can be used to calculate cardiac output. However, this technique has a number of practical limitations: it requires central venous and arterial catheters for mixed venous and arterial blood sampling in order to compute $AVDO_2$; and it cannot be used in patients ventilated with a fractional inspired oxygen (FiO_2) greater than 60% because of the poor accuracy of the paramagnetic oxygen sensors that measured inspired and expired fractions of oxygen [13]. Therefore, this technique is often not applicable in critically ill patients, because they require extreme ventilatory conditions with high FiO_2 or because their haemodynamic status is unstable.

The Fick principle can be applied to any gas diffusing through the lungs, including carbon dioxide. A new monitor called NICO (Novamatrix Medical Systems, Inc., Wallingford, CT, USA) is based on application of the Fick principle to carbon dioxide in order to estimate cardiac output noninvasively, using intermittent partial rebreathing through a specific disposable rebreathing loop. The monitor consists of a carbon dioxide sensor (infrared light absorption), a disposable airflow sensor

Figure 3

Eighty-eight paired measurements of cardiac output (CO) variations between two time-points obtained simultaneously using thermodilution (TH) with a pulmonary artery catheter and oesophageal Doppler (ED). Ideal agreement is represented by a horizontal line. Contradictory information with the two techniques was observed in only three cases [10]. The open boxes and vertical bars indicate mean and standard deviation, respectively.

(differential pressure pneumotachometer) and a pulse oxymeter. VCO_2 is calculated from minute ventilation and its carbon dioxide content, whereas the arterial carbon dioxide content ($CaCO_2$) is estimated from end-tidal carbon dioxide ($etCO_2$), with adjustments for the slope of the carbon dioxide dissociation curve and the degree of dead space ventilation. The partial rebreathing reduces carbon dioxide elimination and increases $etCO_2$. Measurements under normal and rebreathing conditions allow one to omit the venous carbon dioxide content ($CvCO_2$) measurement in the Fick equation (see below), and therefore the need for a central venous access is eliminated. The principle used by the NICO monitor is as follows.

Fick equation applied to carbon dioxide:

$$CO = \frac{VCO_2}{CvCO_2 - CaCO_2} \quad (2)$$

Assuming that cardiac output remains unchanged under normal (N) and rebreathing (R) conditions:

$$CO = \frac{VCO_{2N}}{CvCO_{2N} - CaCO_{2N}} = \frac{VCO_{2R}}{CvCO_{2R} - CaCO_{2R}} \quad (3)$$

By subtracting the normal and rebreathing ratios, the following differential Fick equation is obtained:

$$CO = \frac{VCO_{2N} - VCO_{2R}}{(CvCO_{2N} - CaCO_{2N}) - (CvCO_{2R} - CaCO_{2R})} \quad (4)$$

Because carbon dioxide diffuses quickly in blood (22 times faster than oxygen), one can assume that $CvCO_2$ does not differ between normal and rebreathing conditions, and therefore the venous contents disappear from the equation.

$$CO = \frac{\Delta VCO_2}{\Delta CaCO_2} \quad (5)$$

The delta in $CaCO_2$ can be approximated by the delta in $etCO_2$ multiplied by the slope (S) of the carbon dioxide dissociation curve. This curve represents the relation between carbon dioxide volumes (used to calculate carbon dioxide content) and partial pressure of carbon dioxide. This relation can be considered linear between 15 and 70 mmHg of partial pressure of carbon dioxide [14].

$$CO = \frac{\Delta VCO_2}{S \times \Delta etCO_2} \quad (6)$$

Because changes in VCO_2 and $etCO_2$ only reflect the blood flow that participates in gas exchange, an intrapulmonary shunt can affect estimation of cardiac output using the NICO device. To take this into account, the monitor estimates the shunting fraction using a measured peripheral oxygen saturation of haemoglobin combined with the FiO_2 and the arterial oxygen tension measured in arterial blood gases, according to Nunn's iso-shunt tables [15].

Increased intrapulmonary shunt and poor haemodynamic stability (which are not uncommon in critically ill patients) are likely to alter the precision of cardiac output estimation by the NICO monitor. The first published clinical and experimental validation studies [16–18] reported a relatively loose agreement (bias ± 1.8 l/min) between cardiac output measured using thermodilution and NICO (this is similar to standard observations whenever a technique is compared with thermodilution). Those investigators therefore concluded that the technique is not yet ready to be substituted to thermodilution. However, comparable limits of agreements have been observed in many studies that compared cardiac output measurement techniques with thermodilution, including 'bolus' versus 'continuous' thermodilution [10,19,20]. Bland and Altman [21] asserted that tight agreement is impossible to obtain when the method used for reference is not very precise itself. In our opinion, such limits of agreement do not preclude the potential usefulness of cardiac output measurement using NICO, although the above-mentioned limitations must be kept in mind and the technique is to be used in only the most appropriate patients.

It is also important to note that the patient must be under fully controlled mechanical ventilation if the NICO monitor is to be used. In addition, arterial blood samples are required to enter arterial oxygen tension values for shunt estimation, which somewhat tempers the noninvasive nature of this technique.

Pulse contour cardiac output

The first attempt to determine stroke volume from the shape of the arterial pulse curve can be tracked as far back as 1904 [22]. The aortic pressure waveform results from the interaction between stroke volume and the mechanical characteristics of the arterial tree. Many models have been proposed to describe the physical properties of the arterial tree. The simplest model, which is used routinely in clinical practice, consists of a single resistance (peripheral resistance) to represent arteriolar tone (i.e. the degree of vasoconstriction of the small arteries); this determines the value of mean arterial pressure for a given flow. However, peripheral resistance alone cannot account for the shape of the arterial pulse curve (Fig. 4, first model). In order to improve the arterial model with respect to its ability to reproduce the shape of the aortic pressure waveform, other elements must be incorporated. For example, adding a capacitance element allows one to generate a more physiological pulse pressure wave (Fig. 4, second model), and an additional resistance that represents the characteristic aortic impedance renders the predicted waveform very similar to its measured counterpart (Fig. 4, third model) [23].

In contrast to the concept presented in Fig. 4, pulse contour methods use the pressure waveform as an input for a model of the systemic circulation in order to predict instantaneous flow. The pressure waveform is not obtained from the aorta itself but rather from a peripheral artery (radial or femoral), which requires assumptions to be made regarding the changes in pulse shape between these different locations. The models used to represent the systemic circulation may vary according to specific pulse contour device, and include the following: the three-element 'Windkessel' model (as in the example presented in Fig. 4) [24,25], or more sophisticated models that allow one to account for finite pulse wave velocity and wave reflection phenomena [26]. The values attributed to model parameters (resistance, compliance and characteristic impedance) are initially estimated according to the patient's sex and age, and from the pressure waveform. They are then refined following a calibration of mean cardiac output using an indicator dilution technique: transpulmonary thermodilution for the PiCCO (Pulsion Medical Systems, Munich, Germany) [27] or lithium chloride dilution for the PULSECO (LiDCO Ltd, Cambridge, UK) [28].

Regardless of the model used, the accuracy of flow prediction is greatly increased after initial calibration [25]. By providing a reference value for peripheral resistance (ratio of mean arterial pressure to mean systemic flow), this calibration allows the system to compute more precisely the other parameters that represent arterial mechanical properties and to obtain a better estimation of cardiac output. Recalibrating every 4 hours (or at least before any important data acquisition) may augment the accuracy of pulse contour estimated cardiac output in critically ill patients, who are likely to exhibit frequent changes in degree of arteriolar vasoconstriction [26].

Figure 4

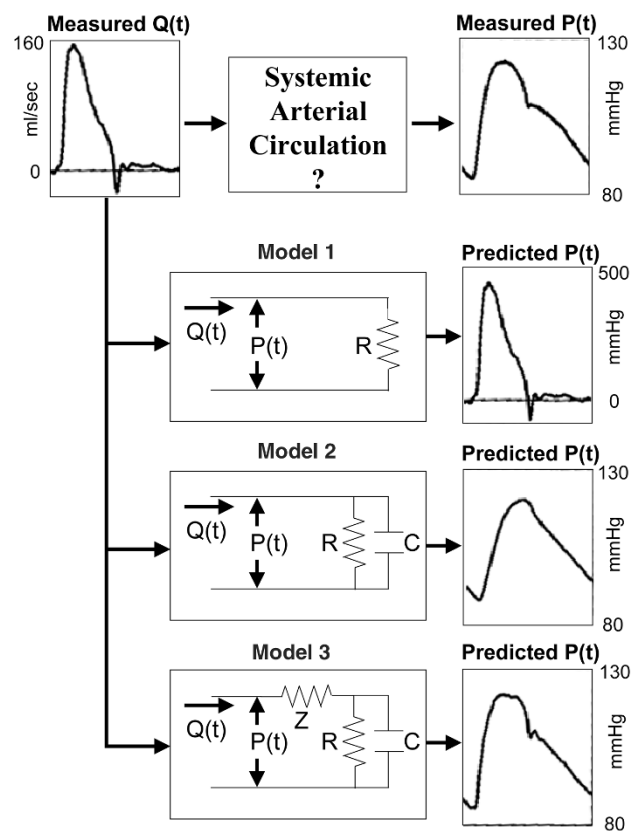


Illustration of the importance of various arterial mechanical properties in generating the aortic pressure waveform. With the measured instantaneous flow $Q(t)$ as an input, a single resistance (R) model of the circulation (model 1) would generate a pressure waveform $P(t)$ with morphology identical to that of the flow waveform, differing only in magnitude by a factor of R . When arterial compliance, represented by a capacitance element (C), is incorporated (model 2), the predicted pressure waveform begins to exhibit many of the morphological characteristics of its measured counterpart. If a third element representing characteristic impedance (Z) is introduced (model 3), the morphologies of the predicted and measured pressure waveforms become very similar [23].

Several studies have compared cardiac output as measured using thermodilution and pulse contour [26,29,30], and found fair agreement between values obtained using the two techniques. However, patients who had poorly defined arterial waveforms or who presented with arrhythmia were always excluded because pulse contour methods cannot provide reliable results in such conditions. The limits of agreement are always quite loose (close to ± 1.5 l/min), as is usual when thermodilution is used as a reference method. A similar agreement was found in a group of patients with septic shock and who were receiving catecholamines [25], indicating that this technique appears quite robust in critically ill patients.

Conclusion

Several 'new' techniques are now available that provide easier cardiac output measurement. None of them emerges as more accurate than the others, although no formal comparisons have yet been attempted. They are still relatively invasive, requiring either sedation and mechanical ventilation for oesophageal Doppler and Fick/carbon dioxide methods, or arterial and central venous access for pulse contour techniques. Oesophageal Doppler is operator dependent, training is required to obtain 'optimal' aortic velocity signals, and probe repositioning is mandatory if reliable results are to be obtained. The pulse contour methods also require frequent calibration, and the need for both arterial and central venous catheters preclude their routine use in the operating room. Unlike Doppler and pulse contour, the Fick/carbon dioxide method does not provide an instantaneous measure of cardiac output, but rather a mean value every 3 min. No visible, real-time signal allows the operator to make a critical judgement based on the cardiac output values obtained. This promising technique still requires more extensive validation in critically ill patients, who are haemodynamically unstable and who have lung disease with increased shunt.

These techniques do not exclude each other because their advantages and limitations are quite different. They also are not intended to replace the pulmonary artery catheter, which remains quite unique in providing pressures (right atrial, pulmonary artery and pulmonary 'wedged' pressures) as well as venous oxygen saturation, in addition to cardiac output. These parameters are still extremely useful in the management of some of the most severely ill patients.

Competing interests

None declared.

References

- Huntsman LL, Stewart DK, Barnes SR, Franklin SB, Colocousis JS, Hessel EA: **Noninvasive Doppler determination of cardiac output in man: clinical validation.** *Circulation* 1983, **67**:593-602.
- Mark JB, Steinbrook RA, Gugino LD, Maddi R, Hartwell B, Shemin R, DiSesa V, Rida WN: **Continuous noninvasive monitoring of cardiac output with esophageal Doppler ultrasound during cardiac surgery.** *Anesth Analg* 1986, **65**:1013-1020.
- Perrino AC, Fleming J, LaMantia KR: **Transesophageal Doppler cardiac output monitoring: performance during aortic reconstructive surgery.** *Anesth Analg* 1991, **73**:705-710.
- Cariou A, Monchi M, Joly LM, Bellenfant F, Claessens YE, Thebert D, Brunet F, Dhainaut JF: **Noninvasive cardiac output monitoring by aortic blood flow determination: evaluation of the Sometek Dynemo-3000 system.** *Crit Care Med* 1998, **26**:2066-2072.
- Singer M, Clarke J, Bennett ED: **Continuous hemodynamic monitoring by esophageal Doppler.** *Crit Care Med* 1989, **17**:447-452.
- Gan TJ, Arrowsmith JE: **The esophageal Doppler monitor: a safe means of monitoring the circulation.** *BMJ* 1997, **315**:893-894.
- Freund PR: **Transesophageal Doppler scanning versus thermodilution during general anesthesia. An initial comparison of cardiac output techniques.** *Am J Surg* 1987, **153**:490-494.
- Lefrant JY, Bruelle P, Aya AG, Saissi G, Dauzat M, de La Coussaye JE, Eledjam JJ: **Training is required to improve the reliability of esophageal Doppler to measure cardiac output in critically ill patients.** *Intensive Care Med* 1998, **24**:347-352.
- Lavandier B, Cathignol D, Muchada R, Bui Xuan B, Motin J: **Non-invasive aortic blood flow measurement using an intra-oesophageal probe.** *Ultrasound Med Biol* 1985, **11**:451-460.
- Valtier B, Cholley BP, Belot J, de la Coussaye J, Mateo J, Payen D: **Noninvasive monitoring of cardiac output in critically ill patients using transesophageal Doppler.** *Am J Respir Crit Care Med* 1998, **158**:77-83.
- Cholley BP: **Benefits, risks and alternatives of pulmonary artery catheterization.** *Curr Opin Anaesthesiol* 1998, **11**:645-650.
- Schmid ER, Spahn DR, Tornic M: **Reliability of a new generation transesophageal Doppler device for cardiac output monitoring.** *Anesth Analg* 1993, **77**:971-979.
- Ultman JS, Bursztein S: **Analysis of error in the determination of respiratory gas exchange at varying FIO₂.** *J Appl Physiol* 1981, **50**:210-216.
- McHardy GJ: **The relationship between the differences in pressure and content of carbon dioxide in arterial and venous blood.** *Clin Sci* 1967, **32**:299-309.
- Benatar SR, Hewlett AM, Nunn JF: **The use of iso-shunt lines for control of oxygen therapy.** *Br J Anaesth* 1973, **45**:711-718.
- van Heerden PV, Baker S, Lim SI, Weidman C, Bulsara M: **Clinical evaluation of the non-invasive cardiac output (NICO) monitor in the intensive care unit.** *Anaesth Intensive Care* 2000, **28**:427-430.
- Nilsson LB, Eldrup N, Berthelsen PG: **Lack of agreement between thermodilution and carbon dioxide-rebreathing cardiac output.** *Acta Anaesthesiol Scand* 2001, **45**:680-685.
- Maxwell RA, Gibson JB, Slade JB, Fabian TC, Proctor KG: **Noninvasive cardiac output by partial CO₂ rebreathing after severe chest trauma.** *J Trauma* 2001, **51**:849-853.
- Monchi M, Thebert D, Cariou A, Bellenfant F, Joly LM, Brunet F, Dhainaut JF: **Clinical evaluation of the Abbott Qvue-OptiQ continuous cardiac output system in critically ill medical patients.** *J Crit Care* 1998, **13**:91-95.
- Burchell SA, Yu M, Takiguchi SA, Ohta RM, Myers SA: **Evaluation of a continuous cardiac output and mixed venous oxygen saturation catheter in critically ill surgical patients.** *Crit Care Med* 1997, **25**:388-391.
- Bland MJ, Altman DJ: **Statistical methods for assessing agreement between two methods of clinical measurement.** *Lancet* 1986, **1**:307-310.
- Erlanger J, Hooker DR: **An experimental study of blood pressure and of pulse pressure in man.** *Johns Hopkins Hosp Rep* 1904, **12**:145-378.
- Cholley BP, Shroff SG, Sandelski J, Korcarz C, Balasia BA, Jain S, Berger DS, Murphy MB, Marcus RH, Lang RM: **Differential effects of chronic oral antihypertensive therapies on systemic arterial circulation and ventricular energetics in African-American patients.** *Circulation* 1995, **91**:1052-1062.
- Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, Peterson E, Tomlanovich M: **Early goal-directed therapy in the treatment of severe sepsis and septic shock.** *N Engl J Med* 2001, **345**:1368-1377.
- 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.
- 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.
- Sakka SG, Reinhart K, Meier-Hellmann A: **Comparison of pulmonary artery and arterial thermodilution cardiac output in critically ill patients.** *Intensive Care Med* 1999, **25**:843-846.
- Linton R, Band D, O'Brien T, Jonas M, Leach R: **Lithium dilution cardiac output measurement: a comparison with thermodilution.** *Crit Care Med* 1997, **25**:1796-1800.
- Goedje O, Hoeke K, Lichtwarck-Aschoff M, Faltchauser A, Lamm P, Reichart B: **Continuous cardiac output by femoral arterial thermodilution calibrated pulse contour analysis: comparison with pulmonary arterial thermodilution.** *Crit Care Med* 1999, **27**:2407-2412.
- Zollner C, Haller M, Weis M, Morstedt K, Lamm P, Kilger E, Goetz AE: **Beat-to-beat measurement of cardiac output by intravascular pulse contour analysis: a prospective criterion standard study in patients after cardiac surgery.** *J Cardiothorac Vasc Anesth* 2000, **14**:125-129.