Cardiac output measurement

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Abstract

Cardiac output measurement has become increasingly important in anaesthesia and critical care, particularly with the growing emphasis on perioperative medicine. Flow cannot be measured by any direct means and therefore models are employed to deduce useful information from other parameters. Numerous techniques are available, each with advantages and disadvantages in terms of invasiveness and validity. Often a balance is struck between invasiveness and validity of the measurements, with acceptance of trends monitoring in some cases, rather than absolute values of cardiac output.

Keywords Aortic Doppler; bioimpedance; cardiac output; indicator dilution; oesophageal Doppler; pulse contour analysis; pulse power analysis; pulse waveform analysis; thermodilution

Royal College of Anaesthetists CPD Matrix: 1A03, 2A04

Learning objectives

After reading this article, you should understand:
- the relevance of cardiac output measurement
- underlying principles of different methods of cardiac output measurement and their limitations
- limitations and validity of commonly used methods of cardiac output monitoring

The importance of cardiac output measurement

In perioperative and critical care, techniques are used to estimate the overall state of organ function. These vary in sophistication, with the most simple means utilizing clinical observation of conscious level, skin colour and urine output. These observations provide a crude but useful estimation. Other methods include measurement of core peripheral temperature difference, central venous oxygen saturations and serum lactate. Arterial pressure is related to organ perfusion, usually by an autoregulatory mechanism and is therefore also useful. These methods attempt to approximate end-organ function by estimation of oxygen delivery or perfusion, but they yield only an indication of function and so more sophisticated means have been developed in an attempt to address this problem.

Surgery or critical illness precipitates an inflammatory response with an increase in oxygen demand to facilitate energy production. Proper organ function relies on maintenance of aerobic metabolism requiring adequate oxygen delivery, which is the product of oxygen content and cardiac output:

$$\begin{aligned} DO_2\,[\mathrm{ml\,min^{-1}}] &= \text{cardiac output}\,[\mathrm{l\,min^{-1}}] \\ &\quad \times \text{arterial oxygen content}\,[\mathrm{ml\,dl^{-1}}] \times 10. \end{aligned}$$

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Cardiac output is a measure of flow defined as the volume of blood ejected from the left or right ventricle per unit time, with the units of litres per minute. It can be expressed as the product of heart rate and stroke volume:

$$\text{cardiac output}\,[\mathrm{l\,min^{-1}}] = \text{stroke volume}\,[\mathrm{l}] \times \text{heart rate}$$

Monitoring techniques attempt to derive the cardiac output by employing models that yield an estimate of the stroke volume. Approaches range from ultrasonography and Doppler techniques, indicator dilution, utilizing the pressure flow relationship and detection of electrical bioimpedance.

The Fick principle

The Fick principle states that the blood flow to an organ can be calculated using a marker substance if the uptake of the marker is known. Using oxygen as the marker, whole body blood flow or cardiac output can be calculated (Figure 1).

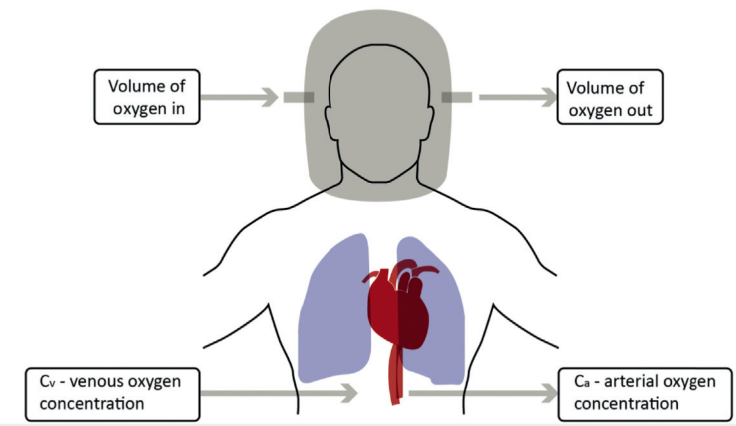
Using a pulmonary artery catheter (PAC), central venous oxygen saturations can be measured and combined with arterial oxygen saturations are used to calculate cardiac output. Limitations of the method include inaccuracy due to the assumption that pulmonary and systemic blood volume are equal and that no pulmonary or cardiac shunt is present. Measurement of oxygen uptake from respiratory gasses in a closed system, such as a sealed hood, is more accurate and can be used for experimental purposes but is impractical in a clinical setting.

Indicator dilution techniques

Indicator dilution techniques utilize the principle that if a substance is injected into the circulatory system, its change in concentration over time is related to the rate of flow in the system. If a known indicator is introduced into the system and is measured by a detector, a curve of indicator change over time can be plotted. Flow or cardiac output can be found by the amount of indicator, divided by the integral, of the area under this curve. For a fixed amount of indicator, the cardiac output is inversely proportional to the area under the curve. Values for cardiac output can be gained in this way using the modified Stewart–Hamilton equation (Figure 2). Indicator dilution can be performed using a PAC to yield right ventricular output, or by a transpulmonary technique (Figure 3).

The Fick Principle

$$\text{Cardiac output} = \frac{\text{oxygen flux}}{\text{arterio-venous oxygen difference}} \qquad CO = \frac{VO_2}{C_a - C_v}$$



Cardiac output can be determined by this method using oxygen as a marker of uptake. This can be achieved by either measurement of respiratory gases in a closed system, or by measurement of the partial pressure of dissolved oxygen in arterial and mixed venous blood.

Figure 1

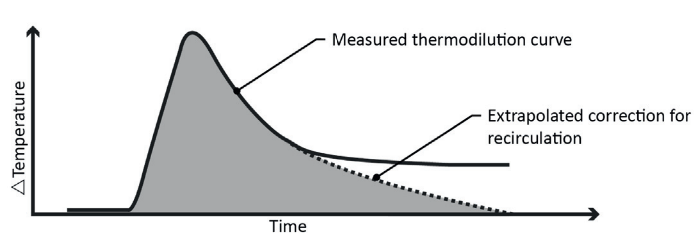
Indocyanine green is a dye with some favourable characteristics which may be used as an indicator. It is highly albumin bound, remaining in the intravascular space and has a maximal light absorption spectroscopy value of 800nm which is close to the isobestic point for haemoglobin. Photometric detection is therefore unaffected by variations in haemoglobin oxygen saturation.

Lithium is an indicator utilized in systems such *LiDCO* to monitor cardiac output. Circulating lithium ions cause a detectable change in current at a lithium sensitive electrode which is plotted against time. This method can only be used intermittently due to accumulation leading to artefact and toxicity. It is therefore generally used in combination pulse contour analysis, where

The Stewart-Hamilton equation

$$\dot{Q} = \frac{V \times (Tb - Ti)\ K1 \times K2}{Tb(t)\ dt}$$

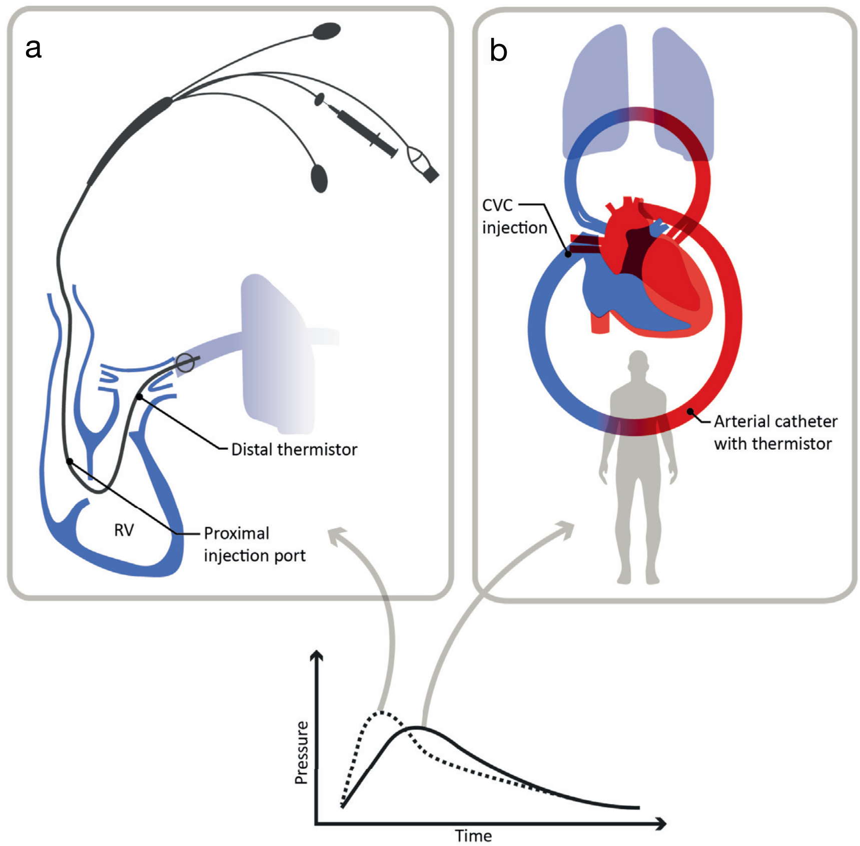
Q = cardiac output
V = injected volume
Tb = blood temperature
Ti = injectate temperature
K1 and K2 = corrections for specific heat and density of the injectate and for blood and dead space volume
Tb(t)dt = change in blood temperature as a function of time



Indicator change is plotted against time and the area under an extrapolated curve is calculated. Cardiac output is inversely proportional to the area under the curve.

Figure 2

Indicator dilution by pulmonary artery catheter and transpulmonary techniques



Indicator dilution using a pulmonary artery catheter is still considered the gold standard technique. The newer transpulmonary technique has been well validated against the gold standard. A central venous catheter and modified arterial cannula are utilized. Pressure time plots differ between the two with a lower and wider peak seen in the transpulmonary technique due to the greater distance between injection and detector.

Figure 3

intermittent lithium dilution measurements are used to calibrate continuous pulse waveform analysis readings.

Thermodilution utilizes temperature change in an indicator to estimate cardiac output. This can be achieved using room temperature or colder saline. Were a PAC is used, saline is injected into the right atrium and a distal thermistor detects temperature change, yielding an estimate of right ventricular output. By convention, temperature change (dT) is plotted rather than actual temperature, which would be displayed as a negative deflection.

Transpulmonary thermodilution is performed in systems where cold saline in administered via standard central venous access. This is combined with a modified arterial line which incorporates a thermistor. *PiCCO* is an example of a system utilizing this technique, and in common with *LiDCO*, requires another form of analysis for continuous readings which are calibrated according to intermittent thermodilution.

Continuous cardiac output monitoring can be achieved by thermodilution where a proximal heating coil and a distal thermistor are incorporated into a PAC. Right atrial blood is heated intermittently to a small but detectable degree and time averaged values of cardiac output are given at 5−10 minute intervals. As the temperature change is small, values may be inaccurate in comparison to other techniques in some circumstances, such as high cardiac output states.

Limitations and validity

Various sources of potential error exist with these systems. For example, since PAC indicator dilution measures right heart cardiac output, the presence of intra cardiac or pulmonary shunt leads to inaccuracy. There is a theoretical chance of loss of indicator into extravascular lung water in transpulmonary thermodilution, especially in the presence of pulmonary oedema. Indicator recirculation, especially after repeated injections, can lead to error although this can generally be corrected for by extrapolation. In the use of lithium as an indicator, allowances must be made for patients on long term lithium therapy or medications which interact with lithium such as non-depolarizing muscle relaxants.

A major limitation in the case of PAC-derived cardiac output is the known association with complications such as pneumothorax, infection, pulmonary artery rupture, arrhythmias, valve injury, thrombosis and embolism. Failure to demonstrate survival benefit in light of these complications has led to a significant decline in their use although they are still generally considered the gold standard against which other methods are measured.[1] Inaccuracy can also occur due to methodical error and significant variation is seen in results when injectate is administered at differing times in the respiratory cycle. Tricuspid regurgitation also contributes to error and is seen consistently, to a variable degree, in critically ill patients.

As previously stated, PAC indicator dilution is considered the gold standard technique in cardiac output estimation. Transpulmonary indicator dilution has shown good correlation with PAC derived indicator dilution and is generally considered reliable.[2]

Pressure waveform analysis

The first observations intimating the utility of arterial waveforms in cardiac output estimation were made by Otto Frank. It was noted that aortic pulse pressure was closely related to stroke volume. The initial observation assumed that ventricular ejection occurs instantaneously whereas it actually takes place over a period of time between opening and closure of the aortic valve. During this period, elements such as ventricular compliance and arterial resistance have important effects on the pressure. Frank addressed this problem, describing the circulation with a 'Windkessel model'. Progress was hindered for some time by problems including two particularly challenging issues. Firstly, it was known that although the relationship between pulse pressure and stroke volume was proportional, calibration was required and it was some time before the introduction of transpulmonary indicator dilution. Secondly the non-linear relationship between pressure and volume due to compliance (the Windkessel element) required a correction factor that was not known. Sufficient data to overcome this problem was not available until 1948.[4] Following the resolution of the aforementioned problems, it became possible to move from simple pulse pressure measurements to measuring the systolic area. This is commonly referred to as pulse contour analysis and forms the basis of many modern systems still in use.

Windkessel model and pulse contour analysis

The Windkessel model described by Frank was based upon the observation that the elasticity or compliance of the large arteries acts in a similar way to a pneumatic air chamber used in fire engines of the period (Figure 4). This was the first element of the model. The second element represented resistance in the smaller peripheral arteries and arterioles, together making up Frank's two-element model. In this model there is a characteristic exponential decay of aortic pressure in diastole. With the diastolic pressure waveform and an independent estimate of compliance, resistance could be calculated. Cardiac output can then be gained by dividing the mean aortic pressure by resistance. The two-element model suffered from a problem in that resistance was well represented but compliance was not accurately reproduced.

As technology improved and new measurement techniques became available, it was possible to improve the correlation between pressure and flow. When Fourier analysis became available it was possible to isolate the individual pressure waves contributing to the inaccuracy. Three and four element models were developed to correct for phenomena, including wave travel characteristics of the arterial system such as reflected waves. The three-element model introduced arterial impedance, an oscillatory phenomenon acting like a resistor. The modelling of this oscillation as a resistor produced error in the low frequency range and the addition of a fourth element was introduced to address this, in the form of total arterial inertance.[4]

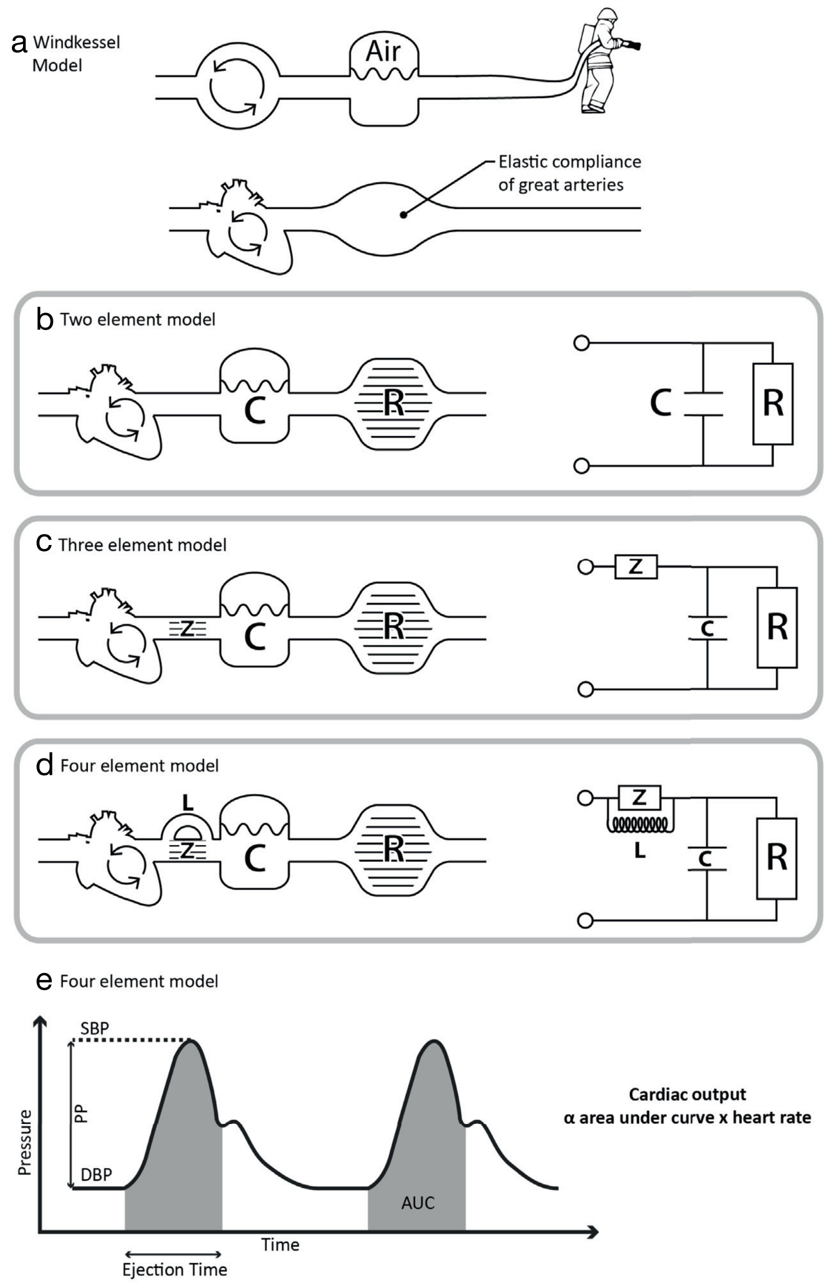
These models can be used in various ways to derive the cardiac output. Current technology employs methods using area under the curve (AUC) or systolic area calculations, commonly known as pulse contour analysis. The calculated area is integrated from the pressure waveform up to the point of aortic valve closure. The *PiCCO* system is an example of one such system and is calibrated using transpulmonary thermodilution (Figure 4).

Empirical approach and pulse power analysis

Based on the Frank's initial observation, stroke volume could be determined from pulse pressure readings transduced from the aorta. In practice, pulse pressure readings are derived from a peripheral systemic arterial pressure transducer. The waveform used has undergone some transformation during travel from the central to peripheral arteries meaning that peripheral arterial pulse pressure may not correlate well with the aortic waveform. As an alternative to the Windkessel models, pulse power analysis attempts to eliminate error associated with systolic area analysis by avoiding the use of the waveform and instead using net power from the stroke volume. The *LiDCOplus* system works in this way using the principle of conservation of mass or power. After application of correction factors and following calibration, a linear relationship between power and flow can be found. This is an example of a non-morphology based approach. The theoretical advantages of this approach are that a peripheral site can be used for blood pressure measurement and it is proposed that issues affecting peripheral waveform morphology become less important.[3]

Another method of obtaining stroke volume data with a non-morphological approach is to calculate the standard deviation of the arterial pressure. A correction factor is then applied to account for compliance and resistance via a multivariate polynomial equation. Variables in the pressure/time plot such as skewness and kurtosis are accounted for. Skewness, a measure of lack of asymmetry, can indicate a change in vascular tone. For example, where data points increase quickly and decrease slowly. Kurtosis, a measure of how peaked or flat a waveform is, relates to large vessel compliance. A high kurtosis value is seen in a peaked wave, whereas a low kurtosis value may be seen with decreased central tone such as in the neonatal circulation. The *FloTrac* system is able to function without need for calibration based on this feature, avoiding the need for central venous access required for transpulmonary indicator dilution.[5]

The Windkessel model



a The concept proposed by Frank that pulse pressure was proportional to stroke volume was describes initially according to the Windkessel model, named after the air chamber used in fire engines of the period.

b The original two-element model accounted for compliance of the great arteries (C) and resistance of the vascular system, principally in the arterioles (R). An equivalent electrical circuit with corresponding components is displayed as a useful analogy.

c The three-element model introduced arterial impedance (Z). This oscillatory phenomenon led alteration of the pressure wave by phenomena including reflected waves.

d The four-element model introduces arterial inertance (L). Modelled as an inductor, new data allowed correction factors to be applied, with the aim of improving accuracy of arterial impedance at low readings.

e Cardiac output estimation by AUC calculation. This method of pulse contour analysis integrates the area up to the dicrotic notch and is used in systems such as *PiCCO*.

Figure 4

Vascular unloading or Peňáz technique

This method represents a useful tool as demand for less invasive cardiac output monitoring devices increases. This is particularly true in the perioperative population where longer term monitoring is not required. The Peňáz, volume clamp, or vascular unloading technique as it may be known, uses a finger cuff which is variably pressurised over time. An infrared light source is shone through the finger and absorption indicates the artery's diameter. The absorption signal is used to control inflation of the cuff so that the artery's volume is kept constant. Thus, the cuff pressure required to maintain the artery's volume is proportional to the arterial pressure and an arterial pressure waveform can be derived. The term vascular unloading refers to the fact that since arterial pressure subtracted from cuff pressure is zero, there is no wall tension in the artery and it can therefore be considered unloaded. The waveform gained can be further analysed by empirical or Windkessel models to determine values for cardiac output.

Limitations and validity

All devices rely on accurate reproduction of the arterial waveform. Over- and under-damping can lead to problems, although some systems based on the empirical approach are designed to limit this factor. Various mathematical correction factors are used to account for issues such as compliance, resistance and reflected waves. These mathematical models are based on data which may not closely apply to outliers, with inaccuracy occurring in some patients. In addition, arrhythmias, aortic regurgitation and intra-aortic balloon pump devices all affect accuracy.

Devices employing pressure waveform analysis have been extensively studied. Modern devices such as *LiDCO* and *PiCCO* have stood up well to scrutiny. Other devices such as *FloTrac/Vigileo* have had less consistent validation. The less invasive nature and lack of calibration may account for these findings, but also makes the device appealing in some cases, particularly when they are used to measure trends rather than absolute values.[2]

Stroke volume variation (SVV) is a useful parameter available with these systems. It is found by measuring the difference between the largest and smallest stroke volumes measured over the respiratory cycle. A SVV of >10% is considered indicative of potential fluid responsiveness.

Aortic Doppler

Cardiac output values can be derived using Doppler ultrasound to determine aortic blood velocity and estimate flow. A Doppler probe can be inserted into the oesophagus and is oriented towards the descending aortic blood flow. The probe emits ultrasonic waves at a frequency of 4−5 Hz. When the waves come into contact with an interface between media of differing densities, some of the waves are reflected. If the waves are reflected by an object moving relative to the source, a frequency shift will occur in accordance with the Doppler principle. In this case, moving red blood cells reflect the ultrasound waves and the waves' rarefaction can be detected (Figure 5). Pulsed or continuous ultrasound can be used. The continuous system is able to measure high velocities taking an average of frequency shifts along the length of the descending aorta. This presents an issue where variation in cross sectional area may exist at different levels. The advantage of a pulsed system is that the beam can be focused and the operator can determine the precise depth that the data is taken from. The disadvantage of this system is that it is less able to measure high velocities so is less useful in high cardiac output states.

Red blood cell velocity can be calculated using the Doppler equation. Velocity (V) is given when transmitted (Ft) and detected (Fd) frequencies are known along the speed of sound within tissue and plasma (C) of 1540 ms^{-1} and a correction factor (Cosθ) for the incident angle of the transmitted waves or angle of insonation. This correction factor is required as it is not feasible to place a probe inside the aorta and orient the transmitted ultrasound waves along the same axis as aortic blood flow. The greater the angle, the greater the apparent change in frequency shift. Angles of up to 20^o can be compensated for accurately. When an angle of 90^o is reached, no Doppler shift can be detected. Two frequency shifts occur; one in the transmitted waves, and one in the reflected waves. Only the reflected frequency shift should be taken into account for the velocity calculation so a term is included to halve the detected value.

$$\mathrm{Fd} = \frac{2\mathrm{FtVCos}\theta}{\mathrm{C}}$$

To estimate flow, the cross-sectional area of the aorta must be determined. This can be achieved by the use of M-mode ultrasonography or alternatively, a value can be estimated based on normograms using patient demographics such as height, weight and age.

Stroke distance (SD) can be inferred from the calculated velocity by finding the integral of the blood velocity/ejection time curve. Stroke volume is found by multiplying stroke distance by the cross sectional area of the aorta. Cardiac output is yielded by multiplying this value by the heart rate, which is determined by the time between adjacent flow/time ejection peaks.

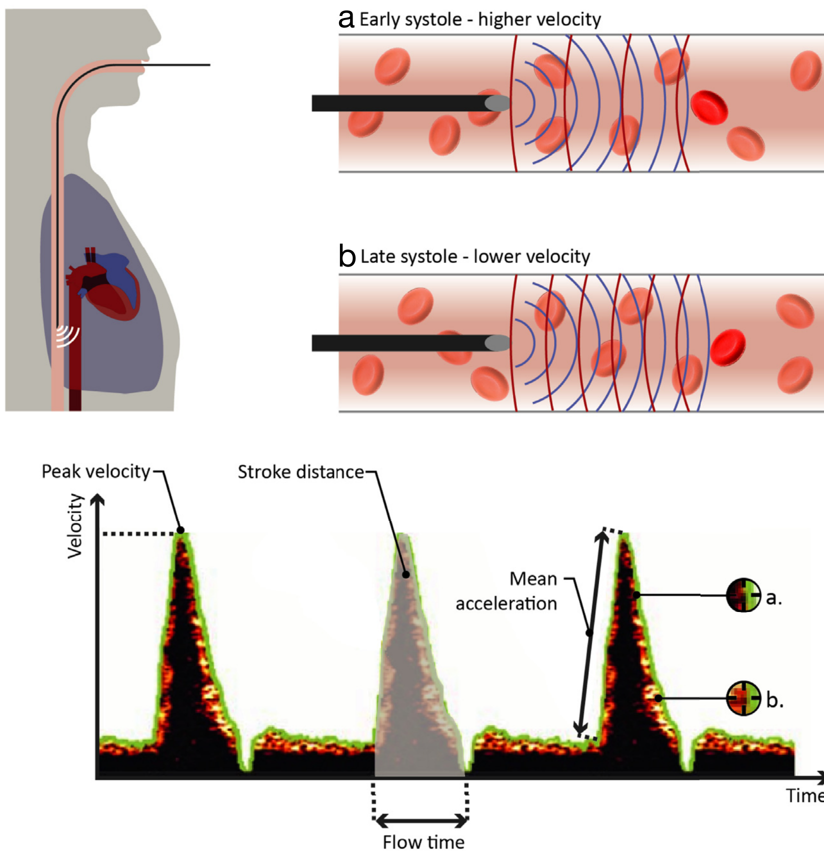
Mean acceleration (MA) reflects contractility. This value is the mean upslope of the velocity time peak. It is independent of changes in vascular tone so is more a reproducible and useful parameter than peak velocity.

Flow time corrected (FTc) reflects preload. It represents the time from beginning to end of a flow/time ejection peak. This is corrected for heart rate to give a value normalized to 60 beats per minute. A value of <450 is considered to indicate inadequate filling and can be used to guide fluid therapy.

Limitations and validity

Estimation of cross sectional area of the aorta is a problem for this method of cardiac output estimation. In systems where the value is measured, small differences in probe position can produce large differences in the measured value. Similarly, velocity measurements can vary significantly over time due to movement of the probe and are thus highly operator dependent. An additional consideration is that the prediction of flow from the product of cross sectional area and stroke distance is only valid

Oesophageal Doppler



Peak velocity and mean acceleration can be used to indicate contractility. Flow time is used as a measure of preload. Stroke distance (SD) = area under the curve (AUC) x heart rate (HR). SV = SD x aortic cross sectional area.

a Frequency shift occurs due to relative movement of erythrocytes in relation to the ultrasound source. Early in systole, a larger frequency shift is detected due to high velocity of the erythrocytes.

b Later in systole lower frequency shift detected due to lower velocity of erythrocytes.

Figure 5

where flow is laminar. In a large vessel such as the aorta, turbulent flow may occur, and the variable direction of flow may invalidate the Cosθ correction factor.

This technology has been well studied and meta-analysis has been performed. Correlation between oesophageal Doppler and PAC thermodilution was good, although comparison with absolute cardiac output measures was less convincing.[6]

Bioimpedance

Thoracic electrical bioimpedance (TEB) cardiac output monitoring was first developed and used by astronauts in the 1960s. The technology is based on the principle that an electrical current can be conducted through organic tissue due to the presence of charged particles in the form of ions. When a current is passed through a structure, the potential difference can be measured between electrodes and the resistance can be determined using Ohm's law.

Potential difference (V) $=$ current (I) $\times$ resistance (R)

Cardiac output can be expressed as proportional to the mean pressure drop over the systemic circulation and is inversely proportional to the systemic vascular resistance. An analogous relationship of flow, resistance and potential difference (or pressure) is observed in ohms law, governing the flow of electrical current. This forms the basis of the bioimpedance model:

$$\text{Cardiac output} = \frac{\text{Mean arterial pressure} - \text{Central veous pressure}}{\text{Systemic vascular resistance}}$$

$$\text{CO} = \frac{\text{MAP} - \text{CVP}}{\text{SVR}} \sim \text{I} = \frac{\text{V}}{\text{R}}$$

Impedance can be defined as a combination of Ohmic resistance and reactance, or resistance to alternating current, and is denoted by the symbol Z. In an alternating current circuit R is substituted for Z. If current remains constant, then changes in resistance lead to equivalent changes in voltage:

$$\Delta Z \approx \Delta V$$

Different tissues have varying impedance properties; for example, blood and plasma have the lowest impedance of 150 $\Omega\ cm^{-1}$ and 63 $\Omega\ cm^{-1}$, respectively and air and cardiac muscle have the highest impedances at 1275 $\Omega\ cm^{-1}$ and 750 $\Omega\ cm^{-1}$, respectively. Systems using the bioimpedance principle employ a model where tissues are separated broadly into high and low impedance compartments. The thorax is viewed as a cylinder where blood is represented by a smaller, inner low impendence compartment and the larger outer compartment represents the rest of the thoracic tissue (Figure 6). This model was first introduced by Kubicek in 1966 and later modified by Bernstein to account for the truncated cylindrical shape of the thorax, improving accuracy.[7,8]

A high frequency, low amplitude current is passed between the electrodes and the potential difference is measured. Electrodes are placed on either side of the thorax at the neck (thoracic inlet) and diaphragm or xiphoid sternum. A total of eight electrodes including inner and outer pairs are used. The outer pairs are the source and sink of the applied current. The inner pair constitutes the transducing electrodes used for sensing the TEB signal and ECG waveforms. The mean signal between the left and right pairs is used to give an overall value (Figure 6).

Current passed between the outer electrodes finds the path of least resistance through the low impedance compartment, made up of the blood filled spaces. During systole, blood is ejected from the ventricle and the aorta distends transiently, increasing the volume of the low impedance compartment and increasing the electrical conductivity of the thorax. The baseline impedance (Z_0) and change in impedance (ΔZ) are measured by the inner transducing electrodes and are used to calculate haemodynamic parameters.[9] Baseline impedance is inversely proportional to the volume of conducting fluid in the thorax and thoracic conductivity is proportional to thoracic fluid content. Change in impedance is measured from the baseline impedance and its cardiac origin is apparent when compared to the corresponding ECG waveform (Figure 7).

The maximum negative slope of the bioimpedance signal ($(dZ/dt)_{max}$) is multiplied by total fluid conductivity to give the ejection phase contractility index. This value can be used to estimate stroke volume using the equation:[10]

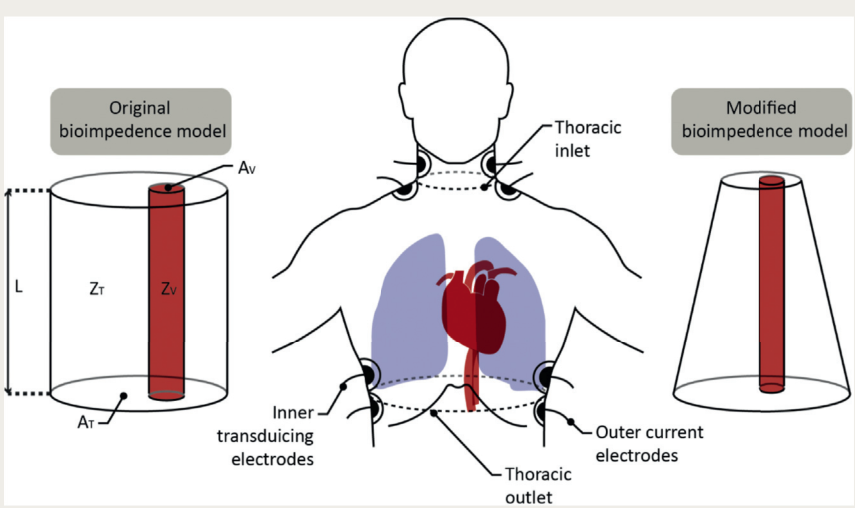
$$SV = VEPT \times VET \times EPCI$$

VEPT = volume of electrically participating tissue.
VET = ventricular ejection time taken from the R−R interval.
EPCI = ejection phase contractility index which is indirectly proportional to TEB.

Several assumptions must be made when deriving the SV in this way:

- The change in bioimpedance is due to aortic blood flow.
- Changes in capacitance vessel blood and microcirculation vary little with respiration.
- $(dZ/dt)_{max}$ corresponds to peak aortic blood volume.
- Systolic ejection time can be measured from the ECG R−R interval.

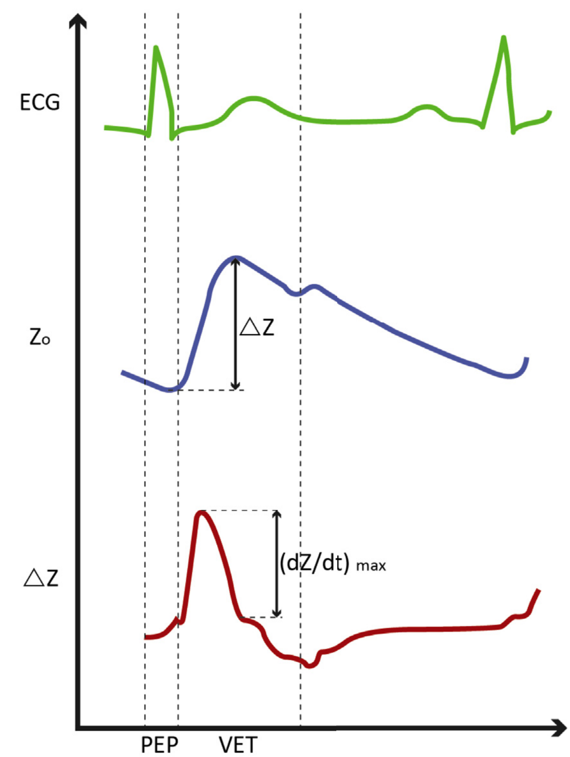
Thoracic electrical bioimpedance



Original bioimpedance model viewed the chest as a cylinder containing high and low impedance compartments spanning the length of the thorax (L). A newer model accounted for the cylindrical shape of the thorax, increasing accuracy. A_V = area of great vessels with low impedance. A_T = the remaining thoracic contents with high impedance. Z_A = low impedance compartment. Z_T = High impedance compartment. Four pairs of electrodes are used. Two pairs at the thoracic inlet and two pairs at the thoracic outlet. The outer electrodes are the source and sink of the current. The inner electrodes detect the current.

Figure 6

Bioimpedance signal



PEP = pre-ejection period. VET = ventricular ejection time.
Z_0 = baseline impedance. ΔZ = change in bioimpedance.
The TEB signal increases after ventricular depolarization is seen on the ECG trace and the low impedance compartment expands during ventricular ejection.

Figure 7

- EPCI is equal to $(dZ/dt)_{max}$ multiplied by total fluid conductivity.
- Finally that VEPT can be predicted using patient demographics of gender, height and weight.

Limitations and validity

Practical issues include the fact that validity of measurements rely on correct placement of electrodes and lack of electrical interference. Interference can be encountered from diathermy circuits and movement artefact. Changes to assumed VEPT can occur due to the presence of abnormal fluid composition of the thoracic complement such as in the presence of pleural effusion, cardiac tamponade and pulmonary oedema. Assumptions based on patient demographics fail to take into account morphological outliers.

Initial studies suggested poor correlation with cardiac output when compared to other established methods. Later validation studies based on improved technology provided promising data but results still suffered from inconsistent outcomes, lack of agreement on reference techniques and ability to predict cardiac output trends. Bioreactance was a modification of this technology introduced to improve accuracy, an example being the *CHEETAH NICOM* system. This system has been more successfully validated with a large multicentre study comparing data to PAC derived readings. Another study found comparable results compared to transpulmonary thermodilution and pressure waveform analysis.[6] ◆

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