

Pulse Contour Analysis and Transpulmonary Thermodilution

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“The pulse ranks first among our guides; no surgeon can despise its counsel, no physician shut its ears to its appeal. Since then, the information the pulse affords is of so great importance ... surely it must be to our advantage to appreciate fully what it tells us, and to draw from it all that it is capable of imparting.”

— (Dr Mohammed. *Turn of the century*)



INTRODUCTION

The measurement of cardiac output and assessment of a patient's volume status is clearly a useful aim for many critically ill patients and for a number of patients undergoing major surgery, particularly cardiac procedures. While bedside clinical methods of assessing organ perfusion will not be replaced, in certain situations more advanced monitoring is nevertheless required to assess the effects of potent vasoactive agents and monitor the progression of serious illnesses.

While debate over the benefits and risks of the pulmonary artery catheter (PAC) remains unresolved after 30 years, a new generation of hemodynamic monitors have evolved and are ready to compete for the attention of sceptical clinicians throughout the world. Expenditure on these devices in the US has increased from \$6.3 million in 1999 to \$32.9 million in 2002. By 2006, this is expected to reach \$61.5 million. Concerns about the safety and accuracy of the PAC and perhaps the unfair pressure of expectation placed on the monitor to alter outcome has led to its gradual fall from grace. This article will look at the alternative technique of pulse contour analysis combined with transpulmonary thermodilution (TPTD) using the PiCCO device (Pulsion Medical Systems, Munich, Germany). The basic principles involved will be explained and its application in clinical practice both in anaesthesia and intensive care will be assessed.

HISTORICAL PERSPECTIVE

Since the discovery of circulation by Harvey in 1616, theorists, mathematicians, physicists, physiologists and, of course, doctors have been developing methods to measure cardiac output and have yet to reach a consensus. Adolf Fick first proposed a method to measure cardiac output in 1870, the principles of which still apply today. In 1897, Stewart introduced indicator dilution theory but the first attempt at analysing the *pulse* to yield information on cardiac output was ascribed to a German physicist-mathematician turned physiologist, Otto Frank in 1899. A few years later in 1904,

Erlanger published a study on the relationship between blood pressure and pulse pressure. While work on pulse contour analysis lost momentum thereafter, indicator dilution techniques were developed by Hamilton and colleagues over the next 25 years. Thermodilution was subsequently introduced as a method of measuring blood flow by Fegler in 1954. At the time the idea that heat could serve as an indicator was received with scepticism. In the same year Isaac Starr performed experiments on cadavers simulating systole and studied the relationship between pulse pressure and stroke volume.¹ A simple formula was derived whereby the stroke volume could be calculated from the blood pressure and age of the patient. Comparisons with other contemporary methods were surprisingly good. This was one of the earlier demonstrations of the non-linearity of aortic compliance with age.

It was not until the 1960s, however, that practical results from pulse contour analysis began to appear. Formulae derived by Herd, Warner, Kouchoukos and Remington were studied in animals initially, and usually compared to a direct form of cardiac output monitoring using electromagnetic flow measurement.² While reasonable correlation figures were obtained, they lacked precision. A factor common to these earlier formulae was a lack of correction for individual aortic impedance. Subsequent work by Wesseling and colleagues in the 1970s set about correcting for this and has continued until the present day.³

THE THEORY OF PULSE CONTOUR ANALYSIS

The basic algorithm for the determination of cardiac output from the pulse contour was developed by Wesseling. In a complex 37 page document, published in 1983, paradoxically entitled "A *simple* device for continuous measurement of cardiac output", Wesseling describes the mathematical principles involved in great detail.⁴

Put more simply, the arterial pressure waveform is a result of the interaction between the heart and the vascular tree. Left ventricular ejection creates a wave that travels through the arteries (~6-10 m/s) and is reflected from the periphery. This reflection of the arterial pressure wave, known as the Wetterer hypothesis, is a summation of reflected waves arising at bifurcations near the heart and reflected waves from the peripheral part of the system.⁵ The forward wave in turn may be divided into a wave that is set up by the heart (the primary wave), and a wave that is the backward wave reflected at the heart. Theoretically if these reflected waves were absent then the pressure and flow contours would be identical, the size of the wave being related to aortic impedance. Differences between pressure and flow contours in the aorta occur because the reflected waves cause an increase in the pressure but a decrease in flow. A simple analogy is a wave reflected from a cliff causing incoming waves to increase in height but lose some power.

According to Wesseling's algorithm, the left ventricular stroke volume (SV) is computed by measuring the area under the systolic portion of the arterial pressure waveform, which is then divided by the aortic impedance (Figure 1). The SV is multiplied by heart rate to give the cardiac output. To calculate for individual aortic impedance, an arterial thermodilution measurement is performed simultaneously to calibrate the system.

The calculation as utilised by the PiCCO system (Pulsion Medical Systems, Munich, Germany) for continuous cardiac output incorporates a patient specific calibration factor, the heart rate, the area under the pressure curve, and finally the compliance and shape of the pressure curve (Figure 2).

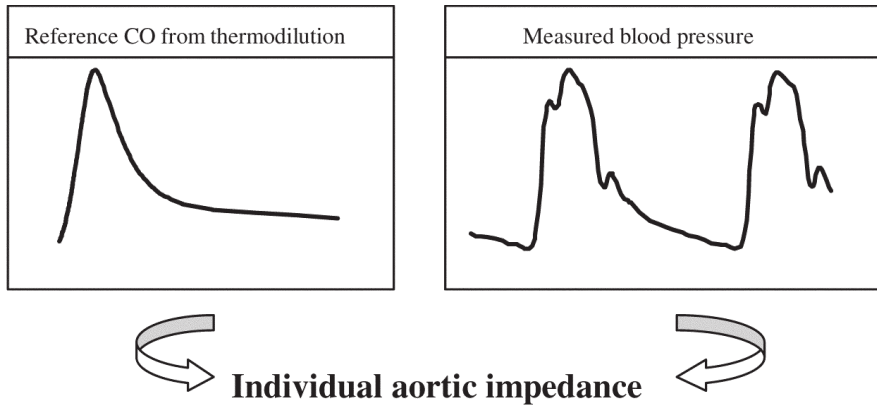


Figure 1. Typical thermodilution and arterial blood pressure curves from which individual aortic impedance is derived (see text for explanation).

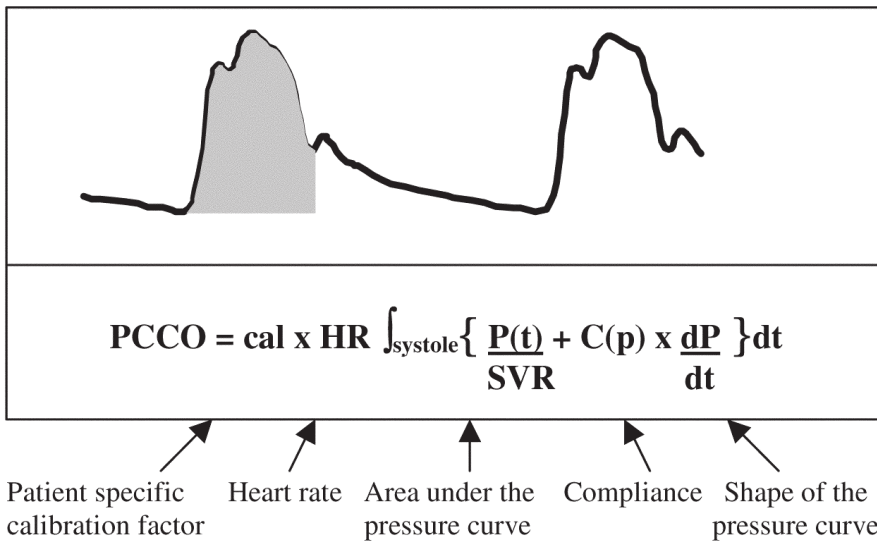


Figure 2. Calculation used by the PiCCO for measurement of continuous cardiac output.

TRANSPULMONARY THERMODILUTION (TPTD)

The thermodilution technique of the PiCCO system requires a standard central venous catheter (CVC) and a 4F thermistor tipped femoral (or axillary) artery catheter. Based on the same principle of pulmonary thermodilution, a cold indicator is injected into the CVC and the temperature change is detected at the femoral artery catheter. The cardiac output is calculated in the usual manner using the Stewart-Hamilton algorithm. This technique differs to pulmonary thermodilution in some respects. The longer distance to travel results in a longer, flatter curve and is thus more sensitive to baseline thermal variations. To reduce the signal to noise ratio, the injectate is cooled to ~4°C and the volume injected can be increased depending on the

size of the patient. The reading however is less affected by variations in respiration, slowing of the heart rate, and tricuspid regurgitation, which have been shown to affect the PAC readings. It is also noted that en route to the femoral artery thermistor the indicator will have simultaneously flowed into other vascular beds (cerebral, upper limb, gut, kidneys). This does not alter the validity of the result, however, as the ratio of local blood flow (in the distal aorta) and local recovery of indicator is equal at all sites of detection, as is the area under the thermodilution curve.⁶

ASSESSMENT OF INTRAVASCULAR VOLUME BY INDICATOR DILUTION

In addition to the cardiac output result, a measure of the volume status of the patient can be obtained by analysing characteristic transit times of the indicator. After injection of the indicator, the particles mix thoroughly with the flowing blood but do not reach the point of detection (femoral artery) simultaneously. Rather, each particle has its own particular transit time. **The Mean Transit Time (MTt)** is taken as the time for the first particle to be detected plus the mean time difference between the detection of the first particle and all the following particles⁷ (Figure 3).

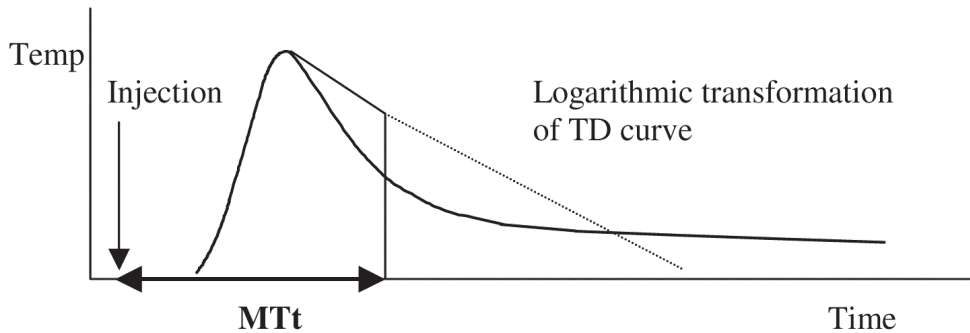


Figure 3. Estimation of mean transit time (MTt) using logarithmic transformation of the thermodilution (TD) curve.

Given that we have measured the flow between the two points, the cardiac output (CO), which represents volume per unit time, and we have also determined the time taken for the indicator to travel the distance, we can estimate the volume by multiplying the CO by the transit time.⁸

$$\text{CO} \times \text{MTt} = \text{Volume}$$

Where CO=cardiac output and MTt=mean transit time

For an indicator that remains in the intravascular space, such as indocyanine green (ICG) this represents the blood volume from the point of injection to the point of detection and is termed the **Intrathoracic Blood Volume (ITBV)**.⁹

thus for ICG:

$$\text{CO} \times \text{MTt} = \text{ITBV}$$

Note: The volume between the point of injection and the point of detection is not a closed circuit and clearly some indicator has flowed elsewhere (into the cerebral, upper limb and splanchnic circulation), which has not been detected by the thermistor. While this has not been clearly explained by most investigators, it has to be assumed that the transit time we are measuring relates only to the indicator particles which have taken

the direct route to the femoral artery and thus, this is the volume which it reflects. By the same logic we can place the catheter in the axillary artery and get a result, which is essentially the same but does not include the descending aortic volume.

We know that a thermal indicator, however, rapidly equilibrates between the intra and extravascular space ($\sim \times 100$ times faster than molecular diffusion) so the total volume measured in this way is termed the **Intrathoracic Thermal Volume (ITTV)**¹⁰ (Figure 4).

for a thermal indicator:

$$\text{CO} \times \text{MTt} = \text{ITTV}$$

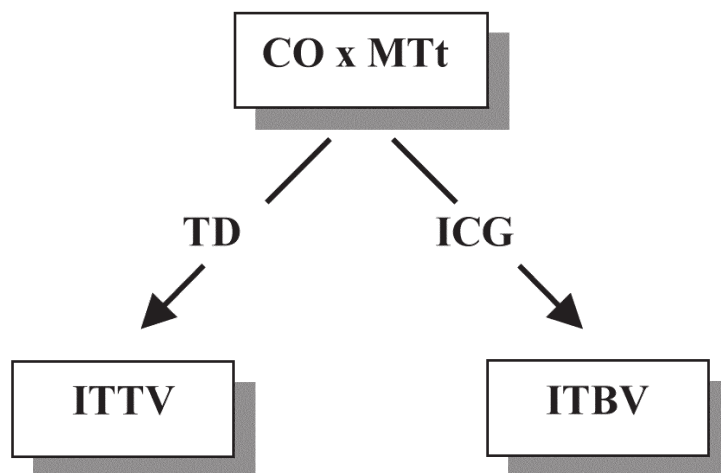


Figure 4. Depending on the indicator used for the estimation of MTt (ie thermodilution, TD, or indocyanine green, ICG) the derived volume will be either intrathoracic thermal volume (ITTV) or intrathoracic blood volume (ITBV).

The **ITBV** is composed of the volume of blood in the heart, or **Global End-Diastolic Volume (GEDV)**, the **Pulmonary Blood Volume (PBV)**, and the volume of blood in the aorta to the point of detection.

$$\text{ITBV} = \text{GEDV} + \text{PBV}$$

Where **ITBV**=intrathoracic blood volume, **GEDV**=global end-diastolic volume, and **PBV**=pulmonary blood volume.

The **ITTV** is composed of the **ITBV** (as above) plus the extravascular compartment, termed **Extravascular Lung Water (EVLW)** (Figure 5).

$$\text{ITTV} = \text{GEDV} + \text{PBV} + \text{EVLW}$$

Where **ITTV**=intrathoracic thermal volume, **GEDV**=global end-diastolic volume, **PBV**=pulmonary blood volume, and **EVLW**=extravascular lung water.

MEASUREMENT OF EXTRAVASCULAR LUNG WATER

Depending on the type of indicator used either the **ITBV** or the **ITTV** can be measured. If both indicators are used simultaneously, as previous monitors used to do (COLD medical systems, Munich, Germany), then simply by subtracting the **ITBV** from the **ITTV**, the resulting volume is the **EVLW**.

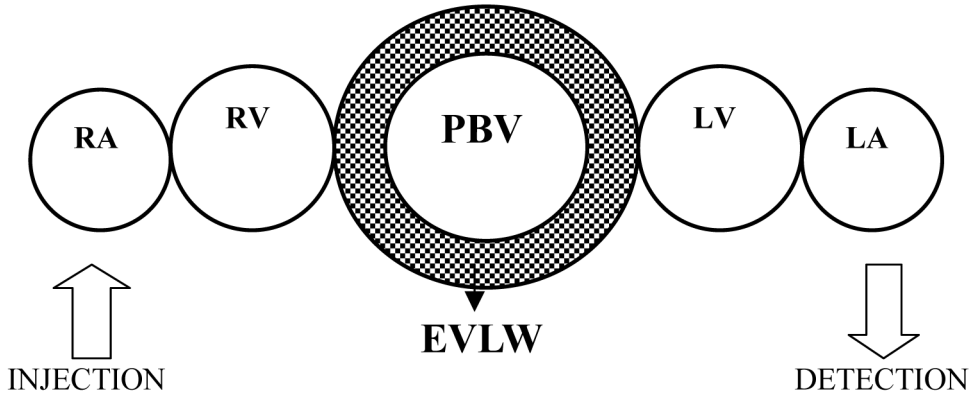


Figure 5. Diagrammatic representation of extravascular lung water (EVLW). Global end-diastolic volume (GEDV)=sum of right atrial (RA), right ventricular (RV), left ventricular (LV), and left atrial (LA) end-diastolic volumes. Intrathoracic thermal volume (ITTV)=GEDV+pulmonary blood volume (PBV)+EVLW.

$$\text{EVLW} = \text{ITTV} - \text{ITBV}$$

As the ICG techniques were time consuming and more expensive, the PiCCO monitor was developed to use only thermodilution. How then does it give us all of the information? As explained above it can tell us the ITTV by multiplying the CO by the MTt. Using one more characteristic transit time, termed the **Exponential Downslope Time (DSt)**, the **Pulmonary Thermal Volume (PTV)** can be measured. PTV is the sum of PBV and the EVLW.

$$\text{PTV} = \text{PBV} + \text{EVLW}$$

This is explained by Newman's theory that an indicator will always mix evenly, and in a series of chambers the dilution curve of the indicator will depend on the largest mixing chamber which will be reflected by an exponential decay curve.¹¹ Although the pulmonary thermal volume is not actually the *largest* chamber by volume, for the purposes of thermal exchange, it is the most significant given the surface area involved. Hence by the same principles as above, by multiplying the CO by the DSt, we can measure the PTV.

$$\text{CO} \times \text{MTt} = \text{ITTV}$$

$$\text{CO} \times \text{DSt} = \text{PTV}$$

By subtracting the PTV from the ITTV, we are left with the GEDV.

$$\text{GEDV} = \text{ITTV} - \text{PTV}$$

In the final calculation, by using a structural regression analysis, the mathematical relationship between GEDV and ITBV has been established in patient population studies.¹² This regression equation is used to estimate ITBV from GEDV.

$$\text{ITBV} = 1.25 \times \text{GEDV}$$

Using the estimated ITBV, an estimated EVLW can be calculated also.

$$\text{EVLW} = \text{ITTV} - \text{ITBV}$$

There are additional derived variables the PiCCO monitor also displays, the **systemic vascular resistance (SVR)** and the **stroke volume variation (SVV)**. The latter has been used as a measure of volume responsiveness, which may be of particular use in patients who are on fully controlled mechanical ventilation.

DISCUSSION

Pulse contour analysis provides a **continuous measurement of cardiac output**. A continuous rather than an intermittent measure of cardiac output may be more useful in patients who experience sudden changes in haemodynamic state that you would wish to recognise and treat without delay, such as during “off-pump” cardiac revascularisation, aortic cross clamping for aneurysm repair, and other major vascular procedures in patients with cardiac disease. In the intensive care unit, the unstable patient with septic shock is the most obvious example especially as more potent vasoactive agents such as vasopressin, are increasingly being used. There are many other patients who might also benefit from this form of monitoring including patients with severe burns, cardiogenic shock post-myocardial infarction, and labile cardiothoracic surgery patients in the early post operative period. Critically ill paediatric patients who are either too small or in whom it is too difficult to place a PAC may also benefit from this form of monitoring.

The **Intrathoracic Blood Volume (ITBV)** is a measure of **cardiac preload**. This can be indexed against body surface area and is usually about one third of the blood volume, with a normal range of 850-1000 ml/m². This has been compared to CVP and pulmonary capillary wedge pressure (PCWP) as an indicator of preload in animal experiments by Pfeiffer.¹³ A quote from the author “...*The results of this study demonstrate that the interpretation of PCWP as an indicator of circulating volume could be complete nonsense.*” Similar studies performed by Bindels¹⁴ and Sakka¹⁵ in humans comparing ITBVI to CVP and PCWP in critically ill ICU patients revealed good correlation between ITBV and aortic stroke volume but poor correlation between PCWP and stroke volume. Hinder assessed volume status by transoesophageal echocardiography and indicator dilution techniques in 15 patients undergoing cardiac surgery.¹⁶ He concluded that although CVP and PCWP correlated with each other, they did not correlate with either left ventricular end-diastolic area (LVEDA) nor ITBVI, while the latter two, given certain conditions were essentially interchangeable. Several other studies looking at ITBV as a marker of preload seem to suggest reliability.

Extravascular Lung Water (EVLW) can be used as a measure of **fluid overload**. In patients with acute respiratory distress syndrome, and many forms of respiratory failure, the EVLW indices may prove very useful. The normal range is ~5-7 ml/kg. Greater than 10 ml/kg may predict fluid overload. In general terms this may be more useful to intensivists than anaesthetists as the former group often has to rescue near drowning victims from the latter! Clearly, this is one area of intensive care where we can be more scientific. Beyond our clinical assessment and fluid balance indices, other common markers of fluid overload such as worsening pulmonary compliance and oxygenation are perhaps “too little, too late”. Although there are scoring systems for grading pulmonary oedema on a CXR, the usual comments on the morning X-ray rounds, such as ...“*it looks a little wet*” seems to lack scientific rigour. A number of studies have looked at the relevance and accuracy of EVLW measurements. The

Table 1
Studies comparing pulmonary artery thermodilution cardiac output (COTDpa) vs transpulmonary thermodilution cardiac output (COTDa)

Author	patients (n)/ observations	COTDa-COTDpa (bias±SD, l/min/m ²)	Correlation (r)
McLuckie et al, 1996 ²²	9/162	0.19±0.21	—
Goedje et al, 1998 ²³	30/150	0.16±0.31	0.96
Goedje et al, 1998 ²⁴	30/810	0.26±0.7	0.96
Goedje et al, 1999 ²⁵	24/216	-0.29±0.66	0.93
Sakka et al, 1999 ²⁶	37/449	0.68±0.62	0.97
Sakka et al, 2000 ²⁷	12/51	0.73±0.38	0.98
Zöllner et al, 2000 ²⁸	19/76	0.21±0.73	0.96
Bindels et al, 2000 ²⁹	45/283	0.49±0.45	0.95

original paper by Lewis in 1979 pointed out potential for error with asymmetric lung disease and macroscopic pulmonary embolisation.¹⁷ Also pointed out by Bock was the issue that EVLW measurements have tended to slightly overestimate lung water.¹⁰ This could be due to loss of thermal indicator, although this was an inconsistent finding in other studies,¹⁸ or more likely is due to heat exchange with non-pulmonary extravascular structures, pulmonary perfusion defects or recirculation of indicator. On the last issue, recirculation of indicator is generally assumed to be accounted for by monoexponential extrapolation of indicator dilution curves. More importantly, Mitchell looked at how strategies aimed at managing EVLW compared to wedge pressure driven fluid management was associated with improved outcome in terms of ICU stay and ventilation days in a prospective randomised trial involving 101 patients.¹⁹ Other data from Sturm has shown a positive correlation between mortality and increased EVLW.²⁰ This is an interesting area of research which certainly warrants further appraisal.

Is this technology accurate? I have not attempted to do a meta-analysis of the published data but there appears to be reasonable evidence to suggest that this technology is accurate within the limits of clinical acceptability. The results of some of the studies comparing this form of CO monitoring to traditional PAC derived CO are displayed in Table One. Mostly, the PiCCo monitor has been compared to the PAC in terms of cardiac output data. As pointed out by Bland and Altman, good correlation does not necessarily imply good agreement between the two variable monitoring techniques.²¹ This is particularly the case when you consider that the clinical gold standard to which the PiCCo has been compared (PAC) has many inherent inaccuracies itself. Incidentally, the manufacturers of the **lithium dilution monitor** (LIDCo, Cambridge, UK) claim that their monitor is three times more accurate than thermodilution methods. It involves injecting a dose of lithium (~240-fold lower than the standard dose for bipolar affective disorder) into a central venous line and the dilution curve is measured by means of an ion-sensitive electrode sensor in the radial arterial line.

Is this technology safe? It is less invasive than a PAC but still requires central venous access and large bore arterial access, which are not without risk. Femoral artery catheterisation resulting in injury necessitating surgical repair has been estimated at 0.28% in one large series.³⁰ Is it expensive? The femoral artery catheter costs about

\$250.00 (Australian) and the additional hardware costs are approximately \$17,500 (Australian).

CONCLUSION

Pulse contour analysis is an exciting new form of haemodynamic monitoring, which shows considerable promise, and which has the potential to extend the amount of physiological information available to guide therapy in critically ill patients. There are already over 70 such monitors in use in Australasia. Having a clearer understanding of how it works is likely to further increase its acceptance into clinical practice. However, further studies are required to examine its cost-benefit and risk-benefit ratios, and to demonstrate its influence, if any, on patient outcome.

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