Transpulmonary thermodilution in the critically ill

Transpulmonary thermodilution (TPD) was introduced into clinical practice over a decade ago as an integral component of the COLD system of haemodynamic monitoring (Pulsion Medical Systems). With this system, following central injection of cold indicator, cardiac output is determined from the area under the cold washout-curve recorded by a thermistor-tipped catheter in the femoral artery. When used in conjunction with transpulmonary indocyanine green (ICG) dye dilution (double indicator dilution), values for intrathoracic blood volume (ITBV), extravascular lung water (EVLW) and plasma disappearance rate of ICG (PDRdyce) can also be obtained.

Despite the availability of the technology, the COLD system has remained predominantly a research tool, due to the cost of ICG and the cumbersome nature of the equipment. However, further refinement of the transpulmonary thermodilution technique has resulted in the development of the PiCCO system (Pulsion Medical Systems), a relatively user-friendly machine that combines measurement of cardiac output, by TPD and pulse contour analysis, with estimation of ITBV and EVLW from single indicator dilution alone. In addition, the PiCCO has the capacity to monitor the variation in stroke volume with respiration (SVV), giving clinicians a new and potentially valuable index of volume responsiveness.

THE PICCO SYSTEM

The essential components of the PiCCO monitoring system are a central venous catheter (CVC), placed in either the internal jugular or subclavian vein, and a thermistor-tipped femoral arterial catheter (Figure 1).

**TPD measurement of cardiac output, intrathoracic thermal volume and pulmonary thermal volume**

To measure a TPD cardiac output (COart), 15 ml of cold 5% dextrose is injected into the CVC and the area under the femoral arterial cold washout curve is calculated using the Stewart Hamilton formula.

Several studies have validated COart measurements against those obtained with a pulmonary artery catheter (PAC, COPac) and the direct Fick method. In these studies, COart values are consistently higher than those obtained with the PAC, although the differences are not large enough to be of clinical significance. Loss of thermal indicator during its passage through the lungs, left heart and aorta may explain this phenomenon. Alternatively, transient slowing of the heart at the time of cold injection will clearly reduce COPac to a greater extent than COart.

In addition to allowing intermittent measurement of COart by thermodilution, the PiCCO system displays a continuous cardiac output value (CCO), derived from pulse contour analysis. To ensure accuracy, the CCO must be recalibrated against COart at least every 8 hours, or more often in situations where the haemodynamic status of the patient is changing rapidly.

Intrathoracic thermal volume (ITTV), the volume of distribution of the injected 5% dextrose, is given by the product of cardiac output and the mean transit time of the thermal indicator. Pulmonary thermal volume (PTV), being the largest mixing chamber in the series through which the indicator travels, can be calculated according to the theory of Newman from the slope of the downstroke section of the thermodilution curve. Global end-diastolic volume (GEDV), the volume of blood inside the heart, is obtained by subtracting PTV from ITTV (see Table 1 and Figure 2).

**Estimation of intrathoracic blood volume and extravascular lung water**

With single indicator dilution, intrathoracic blood volume and extravascular lung water are not measured, but calculated using an equation derived from double indicator dilution that describes the relationship between GEDV and ITBV.

\[ \text{ITBV} = [1.25 \times \text{GEDV}] - 28.4 \text{ml} \]

Normal range = 850-1000ml/m²

Extravascular lung water is obtained by subtracting the calculated ITBV from the measured ITTV (Figure 3).

\[ \text{EVLW} = \text{ITTV} - \text{ITBV} \]

Normal range = 3-7ml/kg

When single indicator derived ITBV (ITBV_s) is compared with double indicator measured ITBV (ITBV_d), good agreement is observed, with a bias of 7.6 ml/m² (standard deviation 57.4 ml/m²). Single indicator values for EVLW tend to overestimate EVLW at low values and underestimate EVLW at high values (above 12 ml/kg), with a bias of −0.2 ml/kg (standard deviation 1.4 ml/kg), but overall are well correlated (\( r = 0.87 \)). Animal studies have also confirmed the close
relationship between gravimetrically determined EVLW and that measured by single indicator transpulmonary dilution with the PiCCO.8

**CLINICAL USE OF TRANSPULMONARY THERMODILUTION**

**Identification of volume responsiveness**

In critically ill patients with hypotension and/or low cardiac output states, optimisation of cardiac filling is a prime goal, and the clinician must try to determine whether a patient will benefit or deteriorate with further fluid administration.

Measurement of intracardiac filling pressures (CVP and PAOP) are not particularly helpful in this regard, since in ventilated critically ill patients they are also influenced by changes in intrathoracic pressure, ventricular compliance and afterload, and often lead to an overestimation of end-diastolic ventricular volume. Furthermore, following a fluid challenge changes in filling pressures (CVP and PAOP) are poorly correlated with changes in stroke volume. In contrast, intrathoracic blood volume, a central blood volume closely related to global end-diastolic volume, has been shown to be a better measure of cardiac filling and a better indicator of ‘volume responsiveness’ than either CVP or PAOP.9,10 The suggestion that ‘mathematical coupling’ of ITBV and cardiac output (CO) might explain the close relationship observed between ITBV and stroke volume is refuted by a study demonstrating that, under euvolaemic conditions, CO can be increased significantly with dobutamine whilst ITBV remains unchanged.11

Monitoring of stroke volume variation (SVV) with mechanical ventilation may also help the clinician identify patients whose stroke volume is likely to increase with fluid administration.12,13,14 During early inspiration, systolic blood pressure increases due to compression of the pulmonary vessels and/or a decrease in left ventricular afterload. In contrast, during late inspiration and early expiration, systolic blood pressure falls to a level below its initial value due to a decrease in venous return and right ventricular stroke output. The difference between the maximal and minimal values is termed the systolic pressure variation (SPV), and is associated with corresponding changes in stroke volume. In studies of graded hypovolaemia, the degree of volume depletion is closely linked to the magnitude of rise in SPV and SVV.

The stroke volume variation continuously displayed by the PiCCO represents the % change between maximum and minimum stroke volume divided by the average of the minimum and maximum over a floating period of 30 seconds. Patients with an SVV <5% are generally not ‘volume responsive’, whilst those with a value >9.5% will get at least a 5% increase in stroke volume with a 100 ml volume load.15 Although stroke volume variation provides the clinician with a new, dynamic measure of volume responsiveness, interpretation of the parameter remains problematic in patients with arrhythmias such as atrial fibrillation that produce variation in stroke volume.

**Prevention of inappropriate fluid administration**

Whilst it is important to identify patients who will benefit from fluid administration, it is
equally important to determine which patients will deteriorate with further fluid. This is particularly so in patients with acute lung injury (ALI) and systemic inflammatory response syndrome (SIRS), due to either an infectious or non-infectious cause, who have increased pulmonary capillary permeability and are prone to develop pulmonary oedema with injudicious fluid administration.

A number of recent studies have highlighted the increased mortality associated with the use of pulmonary artery catheters to guide fluid and inotropic therapy in critically ill patients.\textsuperscript{16,17} It is postulated that, armed with the information provided by the PAC, the physician embarks on an overly-aggressive style of fluid and inotropic therapy that is ultimately deleterious to the patient.\textsuperscript{18} This theory is supported by the findings of a study carried out by Sandison,\textsuperscript{17} where patients undergoing non-elective abdominal aortic aneurysm in two different centres were compared. In one centre PACs were inserted in 96% of cases vs. 18% in the other. The patients in the centre with higher PAC usage also received more crystalloid, colloid and inotropes. Their incidence of renal failure was noted to be higher as were their lengths of stay in both ICU and hospital.

Mitchell \textit{et al.} demonstrated that outcome can be improved in critically ill patients when fluid therapy is guided by measurement of EVLW rather than pulmonary artery occlusion pressure (PAOP).\textsuperscript{19} The patients in the EVLW-guided treatment group were observed to have a less positive cumulative fluid balance, and a shorter duration of mechanical ventilation and ICU stay.

\textbf{Outcome prediction}

Elevated EVLW is an independent predictor of poor outcome in critically ill patients, with mortality increasing from 33\% when EVLW is <10 ml/kg to 67\% with values >15 ml/kg.\textsuperscript{20}

\textbf{Limitations of transpulmonary thermodilution}

As with any thermodilution technique, intracardiac shunts and valvular insufficiencies may affect absolute cardiac output values. In left to right shunts, recirculation of the indicator spays out the thermodilution curve and cardiac output is underestimated. Conversely, right to left shunts result in overestimation due to premature delivery of the indicator. The direction and magnitude of the error introduced by valvular regurgitation is more difficult to predict, and will depend on several factors including the site and severity of the regurgitation and the actual cardiac output. Intra-thoracic blood volume is noted to be spuriously high in patients with large aortic aneurysms or very peripherally placed catheters. Care should also be taken in interpreting ITBV and EVLW measurements in patients with severely reduced pulmonary perfusion.

\begin{figure}[h]
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\includegraphics[width=0.5\textwidth]{fig3.png}
\caption{Figure 3.}
\end{figure}

\textbf{SUMMARY}

Transpulmonary thermodilution has superseded pulmonary thermodilution as the mainstay of advanced haemodynamic monitoring in many intensive care units. It enables intermittent thermodilution measurements of cardiac output to be obtained without the need for pulmonary artery catheterisation. When used in conjunction with pulse contour analysis, as in the PiCCO system, cardiac output can be monitored continuously and facilitates the optimisation of fluid and inotropic therapy.

The determination of intrathoracic blood volume index by transpulmonary thermodilution provides the clinician with a more accurate estimate of cardiac preload than measurement of either CVP or PAOP in ventilated critically ill patients. Furthermore, continuous display of stroke volume variation with the PiCCO system may help to identify those patients whose stroke volume will increase in response to a volume challenge.

The use of fluid and inotrope treatment algorithms based on EVLW measurements rather than PAOP have been shown to improve outcome.\textsuperscript{13} With transpulmonary thermodilution now available at the bedside, it may be time to revisit our targets for fluid administration in the critically ill.

\textbf{REFERENCES}


4. Harris AP \textit{et al.} The slowing of sinus rhythm during thermodilution cardiac output determination and the


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