Transpulmonary Thermodilution for Advanced Cardiorespiratory Monitoring

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Introduction

Since the introduction of the pulmonary artery catheter (PAC) into clinical practice in the 1970s, this device has been considered to be the gold standard for cardiac output measurement and advanced hemodynamic monitoring. Nevertheless, in the last 10 years, its risk-to-benefit ratio has become a subject of controversy. One recent meta-analysis on the impact of the PAC in critically ill patients [1] has presented conclusive results showing that the PAC does not bring any clinical benefit, although its use does not prolong hospital length of stay or increase the mortality rate, as was previously claimed by Connors et al. [2]. Another recent prospective multicenter study on 1041 critical patients came to the same conclusions as the meta-analysis [3]. Finally, in a randomized trial comparing hemodynamic management guided by a PAC with hemodynamic management guided by a central venous catheter (CVC), using an explicit management protocol in 1000 patients with established acute lung injury (ALI), PAC-guided therapy did not improve survival or organ function, but was associated with more complications than the CVC-guided therapy. The authors concluded that these results, when considered with those of previous studies, suggested that the PAC should not be routinely used for the management of patients with ALI [4]. The negative results of the PAC studies have led to a gradual decrease in the use of this monitoring modality. In fact, a survey in Germany in 2006 showed that, in a population of 3877 critically ill patients, less than 15% of patients with the criteria of severe sepsis or septic shock were monitored with a PAC [5].

However, a recent retrospective study in a population of 53,000 critically ill trauma patients demonstrated that the use of the PAC, in contrast to conventional hemodynamic monitoring, was associated with a decreased mortality rate [6]. Proponents of the PAC still claim that it is a powerful tool that suffers from gross misinterpretation of data and from routine use without any specific indication, and that there is currently no evidence from randomized, controlled trials that any diagnostic or monitoring tool used in intensive care patients improves outcomes [7].

As a result of the decline in the use of the PAC, we have been witnessing the development of less invasive techniques of hemodynamic monitoring in recent years [8]. These 'less invasive monitoring techniques', which are capable of monitoring cardiac output, include transesophageal echocardiography (TEE), Doppler ultrasonography, thoracic bioimpedance, partial rebreathing of CO_2, pulsed dye densitometry, lithium dilution, pulse contour analysis, and transpulmonary thermodilution. An experimental study that evaluated the reliability of cardiac output measurement by partial rebreathing of CO_2, pulmonary arterial thermodilution, transpulmonary thermodilution, and Doppler ultrasonography, used the periaortic flow as the refer-

ence measurement for cardiac output and concluded that only the pulmonary artery thermodilution (r=0.93) and the transpulmonary thermodilution (r=0.95) could be considered as interchangeable with the method of reference, even in situations of hemodynamic instability [9].

However, although many studies have dealt with the accuracy of cardiac output measurement by various new monitoring technologies, monitoring cardiac output by itself is frequently insufficient for the complex hemodynamic management of critically ill patients. The PiCCO monitor (Pulsion, Germany), which uses the transpulmonary thermodilution technique, offers complete hemodynamic monitoring, including an integrated pulse contour method for continuous cardiac output measurement, while other measured and derived parameters enable the simultaneous estimation of the cardiac preload, afterload, contractility, and extravascular lung water (EVLW) at the bedside. The monitoring of cardiac output by means of transpulmonary thermodilution is considered to be minimally invasive since it requires only an arterial (thermistor-tipped) catheter and a central venous pressure (CVP) line.

Technical Considerations with Transpulmonary Thermodilution

The transpulmonary thermodilution technique begins with the injection of an ice-cold (<8 °C) or ambient temperature (<24°) bolus of saline [10] through a temperature sensor placed in a central venous line. The change in temperature of the injectate is sensed by a thermistor that is embedded in the femoral (or axillary) arterial catheter (catheter 5F, 20 cm long). However, the technique has been recently validated using longer catheters (4F, 50 cm long) placed in the radial artery with the thermistor tip located at the axilary artery level [11]. The direct axillary or radial artery approaches serve as alternatives to the femoral route in those patients in whom femoral cannulation is contraindicated or is technically complex (aortic-femoral bypass, femoral arteriopathy, morbid obesity, etc).

The cardiac output is calculated by the analysis of the thermodilution curve in the usual way using the Stewart-Hamilton algorithm. From this, preload indices (intrathoracic blood volume (ITBV) and global end-diastolic volume (GEDV), and EVLW are calculated. The continuous measurement of cardiac output by the pulse contour method of the PiCCO is based on Wesseling's method, which determines the area underneath the systolic portion of the arterial pulse. An initial cardiac output has to be measured for the calibration process, in which the aortic impedance is calculated by dividing the cardiac output by the area under the systolic portion of the pulse contour. The calculated impedance is used for the continuous derivation of the cardiac output from the arterial pressure waveform.

The measurement of cardiac output using this techique has been validated by several clinical studies summarized in a recent paper [12]. Additionally, other studies appear to confirm the fact that the continuous cardiac output measurements from pulse contour analysis are accurate, remain reliable during significant hemodynamic changes, and are not influenced by the use of drugs that change the blood pressure and/or the systemic vascular resistance [12]. In addition, the use of intra-aortic balloon counterpulsation does not contraindicate the use of the PiCCO monitor, since hemodynamic information from transpulmonary thermodilution is not affected whilst on this device [13]. It has also been shown that the precision of cardiac output, ITBV, and EVLW measurements are maintained during continuous veno-venous therapies of renal replacement [14] and during hypovolemic shock [15].

Hemodynamic Monitoring by Means of Transpulmonary Thermodilution

Cardiac Output

Acute circulatory failure is often due to a fall in blood pressure and/or cardiac output, because both pressure and flow are major determinants of organ function. However, hypotension can be due to a low cardiac output, but may also result in systemic vasodilation. In this sense, the measurement of cardiac output might be useful to differentiate between high and low flow states and, therefore, to discriminate between patients who will benefit from vasopressors (high cardiac output and low arterial pressure) and those who will benefit from fluids and/or inotropes (low cardiac output). In addition the measurement of cardiac output is important to identify those patients whose low flow state cannot be identified by clinical examination alone.

Preload

The evaluation of preload in low flow states is the most useful tool to identify those patients who would benefit from volume loading. Although cardiac filling pressures (CVP and pulmonary artery occlusion pressure [PAOP]) are often still used for the assessment of preload, these parameters have been repeatedly shown to reflect preload poorly. The reasons for the inadequacy of filling pressures to assess preload include erroneous readings from the pressure waveforms, discrepancies between measured pressures and transmural pressures (especially at high levels of positive end-expiratory pressure [PEEP] or with dynamic hyperinflation) [16], and simply because the physiological relation between the ventricular end-diastolic pressure and its volume depends on the distensibility and compliance of the cardiac chambers (e.g., high PAOP due to left ventricular hypertrophy, high CVP due to *cor pulmonale*, etc.).

Several other parameters have been proposed to evaluate preload at the bedside. These include the right ventricular end-diastolic volume (RVEDV) measured by a special PAC; the left ventricular end-diastolic area (LVEDA) measured by echocardiography; the ITBV evaluated by the double indicator dye-cold dilution technique; and more recently the GEDV obtained by transpulmonary thermodilution. It has been demonstrated that the changes in the GEDV induced by a volume load have a good correlation with changes in stroke volume and, therefore, in cardiac output [17]. This is consistent with the physiological relationship between preload and stroke volume. Both ITBV and GEDV have been shown to be more reliable indicators of preload than the cardiac filling pressures [18, 19]. In contrast with the measurement of the RVEDV, the determination of the GEDV does not require a PAC. Compared with the echocardiographic measurement of the LVEDA, the GEDV is not dependent on operator skills or on the presence of a 24 hour echo service, and its measurement can be repeated easily with each cardiac output determination at the bedside.

Nevertheless, both GEDV and ITBV must be interpreted along with the patient's clinical status and other hemodynamic variables. Sakka and Meier-Hellmann [20] published a case report of a patient with pulmonary embolism in whom the ITBV was low, the CVP high, and the cardiac output did not increase after a volume load. The authors suggested that in these patients, other causes that can reduce the central blood volume (for example, pulmonary embolism, tension pneumothorax, etc) should be ruled out.

Prediction of the Response to a Fluid Challenge

One of the most frequent challenges for the intensivist is the prediction of the response of the cardiac output to fluid loading. This is especially true since most studies show that only 50 % of critically ill patients respond favorably to fluid loading, and since fluid loading may have a detrimental effect on pulmonary and other organ function. Because the slope of the relationship between preload and stroke volume depends on ventricular contractility, the isolated evaluation of ventricular preload is not enough to predict the response to volume loading [21]. Although volumetric indicators of preload are useful in the prediction of the response to volume expansion when their values are high or low, they are not conclusive when they are in the intermediate range [21]. A series of dynamic parameters have, therefore, been proposed in order to predict the hemodynamic effects of fluid loading mainly in mechanically ventilated patients, using the influence of the positive pressure breath on the stroke volume [22]. In sedated patients on mechanical ventilation, the intrathoracic inspiratory positive pressure produces a stroke volume variation (SVV). The SVV informs us about the sensitivity of the heart to a potential volume load. In the same way, because the pulse pressure (systolic less diastolic blood pressure) is directly proportional to the left ventricular stroke volume, variations in pulse pressure (PPV) induced by ventilation are well correlated with those in stroke volume, and consequently can predict the response to a volume load (Fig. 1) [23]. The PiCCOplus monitor automatically calculates the PPV and the SVV on a beat-to-beat basis using the pulse contour analysis. As with the PPV, the SVV has been demonstrated to be a precise predictor of volume responsiveness in patients submitted to neuro- [24] and cardiac surgery [25]. However, it is important to remember that the PPV and SVV are affected by the size of the tidal volume. For example, it has been shown recently that the SVV may show values compatible with hypovolemia even during hypervolemic situations when very high ventilatory tidal volumes (>15 ml/kg) are employed [26]. Reuter et al. [27] demonstrated the validity of these parameters also in patients with an open thorax following midline sternotomy. In a later study in a similar patient population, it was demonstrated that "responders" to a volume load became "non-responders" after sternotomy [28]. According to the authors, opening of the thorax may cause the heart to function on the plateau portion of the Frank-Starling curve, turning these patients into "non-responders".

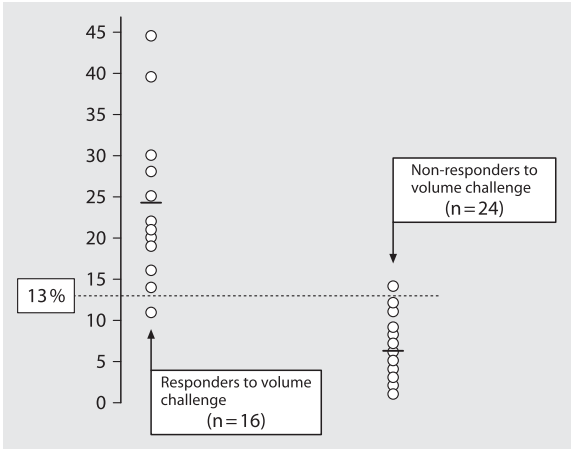

Fig. 1. Variations in pulse pressure (PPV) due to mechanical ventilation. PPV induced by the ventilation correlated well to stroke volume variations (SVV), and consequently can predict the response to a volume load. Patients with a PPV above 13 % will have a good response to volume loading. From [50] with permission.

Evaluation of Cardiac Contractility/Function

In low flow states, evaluation of cardiac contractility/function can be useful to identify those patients who may benefit from the administration of inotropic agents. The precise evaluation of cardiac contractility at the bedside is not straightforward because, amongst other reasons, it is dependent on preload and/or afterload. The ventricular ejection fraction is the parameter most frequently used to evaluate the ventricular function, being the ratio of the stroke volume to the ventricular end-diastolic volume. Transpulmonary themodilution measures the GEDV, which constitutes the blood volume of four cardiac chambers at the end of diastole [12]. Therefore, the quotient between the stroke volume and one-fourth of the GEDV can estimate the global ejection fraction (GEF) of the heart. This parameter is calculated automatically by the PiCCOplus and can be used to identify patients with ventricular dysfunction. In addition, the PiCCOplus monitor provides a continuous assessment of left ventricular contractility by measurement of the dP/dtmax, which is derived from the maximum speed of the arterial pressure curve during the ejection phase. A good correlation has been demonstrated between the dP/dtmax estimated from the pressure curve of the femoral artery and that obtained directly from the left ventricle [29].

Respiratory Monitoring by Means of Transpulmonary Thermodilution

Detection of Pulmonary Edema

Although chest radiography and arterial blood gases are the main components of the international definition of ALI and acute respiratory distress syndrome (ARDS), these parameters have been demonstrated to be of little value in the identification of patients with pulmonary edema [30]. Because of this, several techniques have been proposed to evaluate lung edema (EVLW) in humans. The double indicator dye, cold dilution technique has been one of the most frequently used methods for this purpose in critically ill patients [31], and stands in contrast to other techniques that cannot be performed at the bedside (computerized axial tomography, magnetic nuclear resonance, positron emission tomography). However, this technique is not frequently used nowadays because it is cumbersome and costly, and because it has been suggested that although the technique is useful to evaluate interstitial edema in cases of indirect ALI/ARDS, it is less accurate in cases of direct ALI/ARDS [32].

The transpulmonary thermodilution technique, which is based on the injection of cold solution only (single indicator), is much simpler, yet offers similar results in the measurement of EVLW when compared with both the double indicator technique [33] and the 'gold standard' gravimetric method [34]. Additionally, the EVLW calculated by the PiCCO has been used, along with the PAOP, as a reference parameter for validation of lung ultrasound for the diagnosis of pulmonary edema [35]. This EVLW measurement has been shown to be able to detect even small increases (10 – 20 %) in EVLW, indicating the presence of incipient edema in the absence of other clinical and diagnostic signs [36].

Monitoring EVLW can also be useful as a guide for fluid therapy, especially in patients with increased pulmonary microvascular permeability (e.g., sepsis). In view of the recent findings that fluid restriction and negative fluid balance may improve the evolution of ALI/ARDS [37], EVLW measurement may have special importance as it can be used to identify those patients with high EVLW who would benefit from

such a therapeutic approach. In other words, the measurement of EVLW could be the response to the current controversy between the 'dry or wet' therapy of patients with ARDS [38]. It is, however, important to note that the benefit of fluid restriction must be balanced against the risk of possible hemodynamic deterioration. By measuring EVLW simultaneously with cardiac output, preload (GEDV) and fluid responsiveness (PPV and SVV), the PiCCO monitor is capable of guiding fluid therapy and solving therapeutic dilemmas.

Theoretically, the measurement of EVLW may be less accurate in patients undergoing pulmonary resection (lobectomy, pneumonectomy), due to the changes in gas volume and pulmonary blood flow that occur during and after these surgical procedures. However, Roch et al. [39] and Kuzkov et al. [40] have found that both the double indicator dilution technique and transpulmonary thermodilution may be useful for EVLW monitoring after pneumonectomy, although, when compared with lung gravimetry, both methods, and especially transpulmonary thermodilution, tended to overestimate the measurement of EVLW under these circumstances [39]. Clinical studies have not yet been performed to test the prognostic value of EVLW measurement in these patients.

Calculation of the Pulmonary Vascular Permeability

By definition, EVLW may increase with hydrostatic (cardiogenic) pulmonary edema or in edema due to disturbances in pulmonary vascular permeability. In the former, the increase in EVLW stems from an increase in pulmonary blood volume (PBV) and pressure, leading to a low ratio of EVLW to PBV. However, in the presence of permeability pulmonary edema, the EVLW to PBV ratio is expected to be much higher. By being able to measure both parameters, the PiCCO monitor offers an automatic calculation of the EVLW and the PBV, termed the pulmonary vascular permeability index (PVPI). This parameter may be useful not only to discriminate between cardiogenic and permeability pulmonary edema, but also to evaluate the effects of several illnesses and treatments on pulmonary vascular permeability. In this way, Morisawa et al. [41] suggested that the PVPI can be useful in determining the origin of ALI/ARDS. This study demonstrated that the PVPI, ITBV, and EVLW values were significantly higher in direct lung injury (aspiration, pneumonia) than in indirectly induced ALI/ARDS (e.g., sepsis).

Two recent studies from the same group examined the correlation of EVLW and PVPI with the lung injury score (LIS) and produced discordant results. In the first study, by Groeneveld et al. [42], EVLW was measured by the double dye-dilution technique in 16 patients after major vascular surgery, and PVPI was found to be significantly higher in patients with an LIS>1 compared to those with an LIS equal to or lower than 1. In the second study, Verheij et al. [43] studied 67 patients after cardiac and major vascular surgery. Using the same technique, they concluded that the changes in both PVPI and EVLW were not correlated to the LIS. Comparisons of the PVPI with the LIS should be interpreted with caution, because the parameters included in the LIS may not be the most appropriate for the evaluation of pulmonary injury, and are confounded by objective and subjective multi-factorial factors (e.g., lung compliance depends on lung recruitment, applied-PEEP can be very variable, and the evaluation of the affected lung quadrants depends on the quality of the X-ray image).

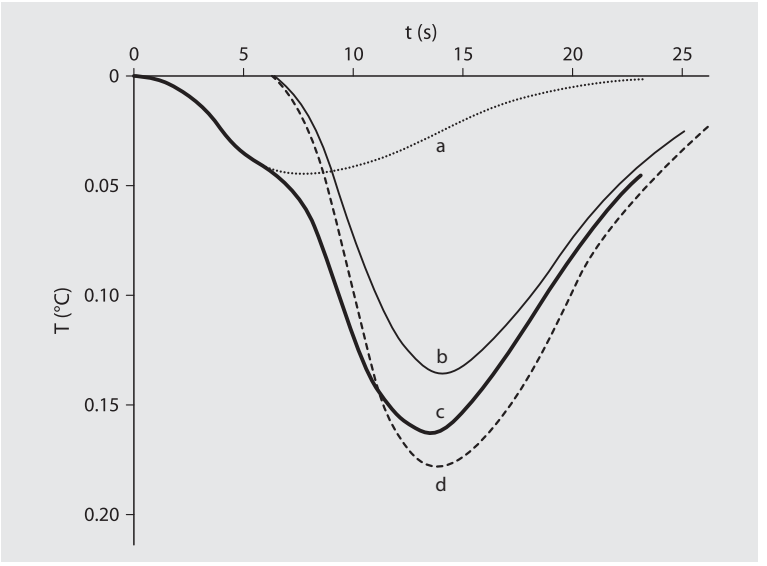

Fig. 2. Intracardiac right to left shunt detection by transpulmonary thermodilution. The cold indicator goes through the foramen ovale and reaches the arterial temperature sensor much more rapidly creating a characteristic 'hump' in the curve. a: 'shunt' curve; b: normal curve; c: effective curve (a+b); d: curve in absence of 'shunt'. From [50] with permission.

Causes of Hypoxemia

Arterial hypoxemia is mainly due to ventilation-perfusion mismatch and/or intrapulmonary shunting. Occasionally arterial hypoxemia may be caused by an anatomic intra-cardiac right-to-left shunt across an open foramen ovale which is present in 20–34% of autopsies in the general population [44]. The prevalence of intracardiac right to left shunt is around 25% in patients with pulmonary hypertension [45], ARDS [46], and positive pressure ventilation [47], while in liver cirrhosis its incidence can be as high as 70% [48]. The occurrence of such a shunt may also increase with the application of PEEP [49]. Color-Doppler and contrast echocardiography can be used to diagnose an intracardiac right to left shunt [50] but are not routinely used in patients with ARDS. However, a right to left shunt can be easily identified by simple observation of the thermodilution curve, since part of the cold indicator goes through the foramen ovale and reaches the arterial temperature sensor much more rapidly, creating a characteristic 'hump' in the curve (Fig. 2). The early diagnosis of such a shunt can have important therapeutic implications, such as the administration of inhaled nitric oxide (NO) [49] or reduction of the PEEP level [50]. The efficacy of these therapeutic maneuvers can be seen immediately by the disappearance of the two-phase morphology of the thermodilution curve.

Last but not least, the transpulmonary thermodilution technique may help in the prediction of potential PEEP-induced hemodynamic instability. Although the application of PEEP may improve gas exchange, it can, nevertheless, also cause a decrease in the cardiac output, preventing the expected benefits of oxygen delivery. These cardiovascular adverse effects of the PEEP cannot usually be predicted by conventional static hemodynamic parameters. However, the presence of high PPV and SVV values has good correlation with the percentage of reduction in cardiac output in

response to the application of PEEP and is an indication for a very cautious application or increase in the PEEP level [50].

Conclusion

The transpulmonary thermodilution technique, which is the mainstay of the PiCCO monitoring system, constitutes a minimally invasive, simple and effective monitoring method, which offers integrated and comprehensive hemodynamic and pulmonary information. Such a combined monitoring of hemodynamic and pulmonary parameters is essential for decision-making and problem-solving in the care of the critically ill.

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