Transpulmonary Thermodilution:
Its Role in Assessment of Lung Water and Pulmonary Edema

Abstract:

Tissue edema, and in particular pulmonary edema, is increasingly recognized as a perioperative complication impacting outcome. Management strategies directed at avoiding excessive fluid administration, reducing inflammatory response and decreasing capillary permeability are commonly advocated in perioperative care protocols.

In this review, we examine transpulmonary thermodilution (TPTD) as a bedside tool to quantitatively monitor lung water accumulation and optimize fluid therapy. We explore its roles as an early detector of fluid accumulation prior to the development of overt pulmonary edema and in risk stratification. In addition, the ability of TPTD to provide insight on the etiology of pulmonary edema, specifically differentiating hydrostatic versus increased pulmonary capillary permeability, is emerging as an aid in therapeutic decision-making. The combination of hemodynamic and lung water data afforded by TPTD offers unique benefits for the care of high-risk perioperative patients.

Introduction:

The clinical manifestation of excessive accumulation of extravascular lung water (EVLW) is pulmonary edema. In normal circumstances, a tight balance between the net fluid filtered from the pulmonary circulation and fluids absorbed by the lymphatic system ensures only a small volume of fluid in the interstitial space. Excessive accumulation of fluid in the extravascular space results from either an increase in the amount of filtered fluid secondary to marked increases in pulmonary hydrostatic pressure or an increase in the pulmonary capillary permeability, which causes water and proteins extravasation[1] or from interruption of the lymphatic drainage as in lung resection surgery[2].

The perioperative period represents a well-known trigger for edema, and in particular pulmonary edema, where factors such as fluid overload, systemic inflammatory response to surgery, myocardial ischemia, blood product transfusion, and others contribute to increased fluid transudation from capillary to interstitium and alveoli. The resultant fluid accumulation in the lung impairs respiratory gas exchange resulting in respiratory distress and the need for mechanical ventilation. This is increasingly recognized as a perioperative complication impacting outcome and management strategies directed at avoiding excessive fluid administration (e.g. goal directed fluid therapy) or reducing inflammatory response and capillary permeability (e.g. protective lung ventilation to avoid ventilator induced lung injury) are commonly advocated in perioperative care protocols[1, 3-5].

The impact of postoperative pulmonary edema both in respect of patient harm and healthcare resources is alarming. A review of 8195 patients who underwent major inpatient operations in 2 university teaching hospitals revealed an incidence of pulmonary edema of 7.6% with an associated in hospital mortality rate of 11.9%[6]. Pulmonary edema is associated with higher morbidity rates and prolonged intensive care (ICU) stay, in which 15% will require mechanical ventilation[7]. Further, the addition of mechanical ventilation will extend the length of stay in the ICU from 6 days to 11 days[8]. As such this complication adds an enormous burden on healthcare costs[9].

Auscultation and chest radiography have been the mainstays for clinicians to diagnose pulmonary edema and monitor response to therapy. Recognition of limitations in accuracy and sensitivity of these methods and the desire for detection of early lung water changes to assist in guidance of fluid therapy are leading to the adoption of newer technologies[10]. Of these, lung ultrasound and transpulmonary thermodilution methods have now entered the clinical arena. The aim of this review is to examine the role of quantitative EVLW to perioperative medicine. We will emphasize the emerging role of TPTD quantitative EVLW measurements in the perioperative period as a new tool to guide fluid therapy and provide early diagnosis of pulmonary edema.

The Indicator Dilution Technique of lung water measurement:

Transpulmonary Indicator Dilution: Anesthesiologists are most familiar with indicator dilution as a technique to measure cardiac output (CO). In common practice a bolus of cold saline (i.e. thermodilution such that the 'indicator' is temperature) is injected into the central circulation and its passage is detected at a point downstream either in the pulmonary artery (trans-cardiac thermodilution, TCTD), or in the distal aorta (trans-pulmonary thermodilution, TPTD). The principles developed by Stewart and Hamilton provide the calculation of cardiac output by examining the passage of the indicator against time with the subsequent generation of an indicator dilution curve (concentration vs. time)[11]. In clinical practice, TPTD utilizes a central venous catheter inserted into the superior vena cava through either the internal jugular or subclavian veins for injection and a thermistor tipped catheter placed in the femoral or axillary artery for detection.

There is a good association between TPTD and TCTD in measurement and detection of changes in CO with a correlation coefficient of >0.9 and bias <10%[12]. The TPTD was found to have a systematic, yet, clinically acceptable overestimation of CO. This overestimation is widely thought to result from the loss of the indicator due to thermal transfer from the intravascular compartment between injection and detection sites[13, 14]. This thermal transfer can be capitalized upon to measure intrathoracic volumes and most importantly extravascular lung water (EVLW).

Transpulmonary Double Indicator Technique: The volume of distribution of a dye indicator during TPTD measurement consists of the blood volume between the site at which the bolus is delivered and the site at which passage of indicator is detected. Accordingly, the combined volumes of a portion of the superior vena cava, that of all four cardiac chambers, and the pulmonary blood volume as well as the aorta are included and is conventionally referred to as the intrathoracic blood volume (ITBV). Unlike dye techniques where the indicator is restricted to the vascular space, part of the thermal indicator escapes due to heat transfer to the vessel walls and the surrounding lung parenchyma. Thus the volume of distribution for a thermal indicator is significantly greater than the ITBV and is referred to as the intrathoracic thermal volume (ITTV). The extravascular lung water can be estimated by the difference between the ITTV and ITBV.

Historically, measurement of EVLW relied upon the simultaneous injection of both cold saline and indicator dye ("double-indicator technique"), with the volume of distribution of each indicator calculated as the product of flow (CO) and the mean transit time (MTt) for the indicator. ITTV and ITBV are thus determined as the volumes of distribution of the cold and dye indicator (commonly indocyanine green) respectively and from the difference, EVLW is estimated.

Unfortunately, the technique of 'double-indicator' TPTD is time consuming, cumbersome and expensive, and despite promise failed to become established in routine clinical practice[13, 15, 16]. Fortunately, a more clinically suitable alternative was developed utilizing a 'single' bolus thermal indicator that by a series of calculations and assumptions provided determination of EVLW.

Transpulmonary Thermodilution EVLW: Figure 1 demonstrates the single indicator TPTD method to calculate EVLW. Whilst ITTV can be determined as the product of CO and MTt; ITBV cannot be directly measured and must be derived by an alternative mechanism. Newman et al[17] using a dye indicator demonstrated that the down-slope of the indicator dilution curve is determined solely by the volume of the pulmonary circulation which acts as the largest "chamber" in the series. For TPTD with a thermal indicator, the pulmonary thermal volume (PTV) can thereby be determined as the product of CO and down-slop time (DSt). ITTV is greater than PTV by an amount, which is approximately equivalent to the thermal volume of the non-pulmonary chambers, i.e. the blood volumes of the cardiac chambers. As these are largest at end-diastole, this volume has by convention become known as the global end-diastolic volume (GEDV).

To progress from the calculation of ITTV and GEDV to the determination of EVLW, Sakka et al[13, 18] demonstrated and subsequently validated with thermo-dye double indicator technique that there is a constant and linear relationship between intrathoracic blood volume (ITBV) and GEDV that is well maintained even in conditions associated with hypovolemic shock[19] such that:

$$ITBV = (1.25 \text{ x GEDV}) \qquad [1]$$

Once ITBV has been determined by this method, it is a simple step to derive EVLW from the difference of ITTV (calculated from mean transit time) and ITBV. As shown below, conditions associated with independent changes in GEDV from PBV will subsequently lead to errors in EVLW estimations.

Validations of TPTD Derived EVLW Measurements:

In the absence of a gold standard *in-vivo* measure of pulmonary edema, the validity of EVLW using single thermal indicator technique has been demonstrated in a variety of animal models by comparison to *ex-vivo* gravimetric techniques[20, 21]. In combination, these studies demonstrate good agreement between TPTD EVLW and laboratory techniques, albeit with a systematic overestimation by TPTD EVLW. Notably in humans, Tagami et al also observed good association between EVLW and post-mortem lung weight (r=0.90; p<0.001) in 30 human lung specimens harvested at autopsy[16]. In ARDS patients, EVLW was shown to correlate well with quantitative computed tomography[22]. Further 'face' and 'construct' validity of EVLW measurement in a clinical setting has been demonstrated by numerous studies observing association between EVLW and clinical findings suggestive of increased lung water such as: oxygenation[16, 23-26], chest X-ray scores[23, 25, 27, 28], lung injury score[16, 23-26, 29], and pulmonary compliance[25, 26]. TPTD showed high accuracy in detecting small changes in EVLW of as little as 10-20% from baseline[30].

Limitations of the single thermal indicator technique

TPTD is an invasive modality requiring central venous access and a central arterial thermistor tipped catheter commonly inserted in a femoral or axillary artery. The central venous access is achieved through the superior vena cava via a catheter placed into either the internal jugular or subclavian veins. Catheters placed in the inferior vena via the femoral vein led to unacceptable percentage errors in calculating EVLW[31] and underestimation of pulmonary vascular permeability index.

Currently two proprietary TPTD systems are commercially available (PiCCO$_2$ System (Pulsion Medical Systems SE, Munich, Germany) and VolumeView/EV1000 system, (Edwards Lifesciences, Irvine CA, USA) (Figure 2). The main differences between the 2 systems are shown in table 1. In brief, both systems rely on the Stewart-Hamilton equation to calculate the thermodilution derived cardiac output but they use different algorithms to calculate GEDV. The $PiCCO_2$ system use the mean transit time (MTt) and the downslope time (DSt) according to the paradigm, while the VolumeView system applies a newly developed algorithm using the maximum up-slope and down-slope of the thermodilution curve. The algorithm for EVLW calculation is the same between both systems. However, EVLW calculation relies on GEDV that is calculated differently between both systems according to the following formulas:

$$EVLW_{PiCCO} = CO \cdot DSt - (0.25 \cdot GEDV_{PiCCO}) \quad [2]$$

$$EVLW_{VolumeView} = CO \cdot DSt - (0.25 \cdot GEDV_{VolumeView}) \quad [3]$$

As they are based on the same underlying principles, it is not surprising the resulting data appear comparable[32]. Similarly, both systems share common limitations which we briefly describe following.

Ventilation-perfusion relationships: TPTD methods for measuring EVLW can only measure lung water in perfused areas of lung and so rely upon a homogeneous distribution of pulmonary perfusion in order to accurately determine EVLW; a large perfusion deficit will lead to underestimation of EVLW. Regional pulmonary perfusion is influenced by many factors pertinent to the critically ill population; hypoxic pulmonary vasoconstriction[33], lung injury[34], vascular obstruction[35] and positive end-expiratory pressure[36, 37] can all influence ventilation-perfusion relationships and so lead to errors in the estimation of EVLW.

Systemic-venous circulatory shunt represents another source of erroneous measurements. In fact, overestimation of EVLW in the absence of gas exchange abnormalities can be used as an indicator suggesting circulatory shunt[38].

Independent changes in GEDV or PBV***:*** The assumption of a constant and linear relationship between ITBV and GEDV (Equation 1) is fundamental to EVLW measurement by the single-dye technique. As such, any circumstance in which GEDV and/or PBV may change independently of one-another could lead to error in the estimation of EVLW. This is of particular importance in the context of mechanical ventilation. The original observations made by Sakka et al[13, 18] was made in critically ill patients undergoing positive pressure ventilation. During mechanical ventilation, increases in intra-thoracic pressure result in reduced inferior vena caval blood flow and a reduction in pre-load to the right ventricle[39]. Reduced preload (and consequently reduced GEDV) in the context of an unchanged pulmonary blood volume would result in an increase in the ITBV:GEDV ratio; Kirov et al[40] demonstrated a significantly increased ITBV:GEDV in mechanically ventilated sheep when compared to those spontaneously breathing. Clinicians must therefore be cautious in making direct comparison of (for example) baseline values of EVLW made ventilated intraoperatively with post-operative estimates made whilst spontaneous breathing; potentially leading to a relative underestimation of EVLW post-operatively.

Lung resection is a unique situation in which PBV may be reduced independently of GEDV; it seems implausible that PBV can remain constant when a significant portion of the pulmonary circulation has been resected. A single human study exploring changes in the ITBV:GEDV relationship in humans demonstrated that there are large and inconsistent changes in ITBV:GEDV following lung resection[41]. It has been suggested that adjustment of the GEDV/ITBV relationship might improve the validity of TPTD monitoring following lung resection[42], but this approach (though built into some commercially available monitors) has not been validated.

Application of EVLW in Clinical Practice

The application of EVLW measurement in perioperative practice has focused on its use to guide fluid management in major surgeries and critical care settings and as means by which to objectively quantify and track changes in lung water in response to therapy (Table 2). Quantitative EVLW measurements are also showing value in several additional domains including as a predictor of outcome and for the early detection of lung water accumulation prior to clinical manifestations, In addition, TPTD, as it offers both hemodynamic and lung water assessments, provides promise as an effective means to differentiate hydrostatic versus high permeability pulmonary edema and identify appropriate therapy for the given situation (Table 3).

EVLW as a Prognostic Tool

The use of EVLW as an early marker for postoperative pulmonary complications and prolonged mechanical ventilation in patients post major surgery was studied in a group of patients undergoing esophagectomy. Elevated EVLW 12 hours post surgery was shown to be a marker for pulmonary complications, which had an incidence of 33% in this group [43]. In a study of patients undergoing orthotopic liver transplant, the development of elevated EVLW at the end of surgery was associated with prolonged mechanical ventilation[44]. In lung transplant, immediate post reperfusion elevation of EVLW (optimal cut off: 13.7 ml/kg) was shown to be an early predictor of pulmonary graft dysfunction and may trigger early therapeutic interventions[45]. Similar findings were observed in a prospective study of patients undergoing high-risk cardiac or aortic vascular surgery. Intraoperative and early postoperative monitoring of EVLW effectively predicted postoperative pulmonary edema and outcome. These patients faced increased incidence of hypoxia, prolonged mechanical ventilation, intensive care stay and hospital stay[46].

In a study of 29 patients at risk to develop adult respiratory distress syndrome (ARDS), the use of cutoff for EVLW index of 10ml/kg was associated with high sensitivity and specificity to predict the development of ARDS. The elevation preceded the clinical and radiological signs of ARDS by 2.6 $\pm$ 0.3 days[47].

The persistence of elevated EVLW beyond 48 hours from initial resuscitation in septic patients was associated with an odds ratio of mortality of

2 - 4.7 [48, 49]. In contrast, a drop in the EVLW after 48 hours was associated with a higher 28-day survival[50]. A meta-analysis of diagnostic tests confirms EVLW measures as a good predictor of mortality in critically ill patients[51]. Indexing EVLW to predicted body weight instead of actual body weight was shown to improve the predictive value of EVLW for survival and correlation with markers of disease severity in a study of patients with ARDS[24].

These studies lead to the recommendation of EVLW exceeding 10 ml/kg is an early marker for at risk patients. As such, EVLW monitoring can provide an opportunity for more prompt and appropriate early therapy in surgical patients.

Use of EVLW to Guide Fluid Therapy

One of the difficult questions anesthesiologists and intensivists face regarding fluid management is *how much is enough but not too much.* Inadequate fluid administration risks tissue hypoperfusion and end organ damage, while excessive fluids risk tissue edema including pulmonary edema. The challenge of appropriate fluid management is further complicated in the perioperative period due to the potential for injury of the endothelial glycocalyx layer resulting in increased permeability and edema formation[52]. This was shown in a study of patients undergoing orthognathic surgery where the volume of infused fluid failed to increase the intravascular volume; instead, it resulted in an increase in the amount of fluid leakage into the interstitial space[53]. In these circumstances, small increases in intravascular volume may result in amplified increases in the EVLW.

Anesthesiologists have been early adopters of sophisticated hemodynamic monitors such as central venous pressure, pulmonary artery catheters, as well as echocardiography to guide the fluid management. In clinical practice, however, these modalities fall short as none measure EVLW directly. The clinician is left to rely on surrogate measures such as pulmonary capillary occlusion pressure (PAOP) and cardiac chamber dimensions. In addition, alterations in pulmonary capillary permeability in the perioperative period further limit the utility of hemodynamic based assessments. Although firm evidence is lacking to support its use at this time, the potential benefit to the technique and its impact on clinical management has been demonstrated in several studies as we discuss in the following sections.

Hydrostatic Pulmonary Edema: The challenges of fluid management in the operating room and ICU provide an ideal domain to take advantage of the benefits of EVLW measurement in patients at risk for hydrostatic pulmonary edema from overly aggressive fluid loading. In a study of patients suffering from vasospasm following subarachnoid hemorrhage (SAH), fluid loading guided with pulmonary artery catheter derived indices resulted in greater fluid administration and a higher incidence of pulmonary edema compared to TPTD guided fluid loading[54]. In patients with Takostubo cardiomyopathy who suffered SAH, serial cardiac output measurements and EVLW determinations provided an easy bedside method to detect early changes in cardiopulmonary function and directing proper post SAH treatment[55]. The benefit of EVLW guided fluid therapy was shown in 101 patients with pulmonary edema randomized to receive a fluid protocol based on EVLW or PAOP using pulmonary artery catheter. The EVLW group received lesser amounts of fluids and resulted in shorter ventilator days and intensive care stay with no clinically significant adverse effect [56]. The utility of EVLW monitoring in pediatric populations was shown in burn patients where excessive fluid resuscitation was detected and shown to be associated with poor survival[57]. Furthermore, the use of TPTD in this patient population was shown to accurately reflect the severity of the hyperdynamic state when compared to transthoracic echocardiography[58].

The benefits of EVLW measurement as a complement to echocardiographic evaluation in guiding fluid therapy were evaluated by using an algorithm that provided a safe and practical framework for fluid administration in the critically ill patients. This algorithm utilized lung ultrasound as means to assess lung water and ultrasound of the inferior vena cava as means to assess fluid status[59].

The addition of EVLW monitoring provides new insights to clinical management of patients susceptible to fluid overload and hydrostatic pulmonary edema with potential to improve case management. For example, hypotension/low CO in the context of elevated EVLW > 10 ml/kg suggests the use of vasopressors/inotropes and restriction of volume expansion. Conversely in the normotensive patient diuresis and vasodilators are indicated (Figure 3).

TPTD monitoring, providing parameters of CO and GEDV in conjunction with lung water, has also been extended into the intraoperative period. Surgical patients with major comorbidities and undergoing procedures where the possibility of major cardiorespiratory insult or hemorrhage is a concern are those where TPTD monitoring may provide the greatest benefit.

In a study of patients undergoing coronary artery bypass grafting (CABG) under cardiopulmonary bypass (CPB), randomized to receive either hydroxyethyl starch 200/0.5 (HES) or 0.9%NaCl at a dose of 4 ml/kg 30 minutes after induction of anesthesia. There was no difference between the 2 groups in the fluid management in the intraoperative or postoperative periods. EVLW was significantly lower in the HES group on the first postoperative day, which was associated with significantly higher PaO_2/FiO_2 ratio and significantly lower alveolar arterial O_2 difference [60]. These benefits on pulmonary functions were seen also in patients undergoing CABG under CPB randomized to receive combined general anesthesia with epidural anesthesia/analgesia (EA) versus general anesthesia (GA) alone. In the GA group, the EVLW was significantly higher, while, in the EA group, there was no significant increase in intrathoracic blood volume and no increase in EVLW. This was associated with shorter mechanical ventilation duration in the EA group [61].

Permeability Pulmonary Edema: In patients at risk for high permeability pulmonary edema, such as patients with sepsis or ARDS, fluid management represents a particular challenge as conventional hemodynamic monitors fall short in monitoring EVLW accumulation. The limitations of PAOP were highlighted in a study of 102 mechanically ventilated patients where pulmonary edema was detected over a wide range of PAOP values, including low to normal values[62]. In a study of ARDS and/or sepsis patients who were thought to be euvolemic under conventional parameters (e.g. central venous pressure), the implementation of EVLW based protocol in the therapeutic management resulted in a change in original treatment plan in 52% of the patients (Figure 4). This clinical protocol was effective in 82% of the patients[63].

In a study of fluid protocol based on EVLW (using double-indicator technique) versus pulmonary artery catheter in patients presenting with permeability pulmonary edema (15 patients), the EVLW fluid protocol reduced the mortality rate from 100% to 33%[64]. These findings offered a preliminary signal that EVLW assessment to guide fluid management in patients with increased capillary permeability might be useful.

Lung resection surgery carries a high risk for postoperative complications of increased capillary permeability and ARDS with an incidence varying between 0.9% for sublobar resection up to 8% for pneumonectomy[65]. ARDS has multiple etiologies post thoracic surgery, including excessive fluid administration; ventilator induced lung injury and other inflammatory conditions and has led to the long-term practice of restrictive fluid therapy. This practice comes with a risk of tissue hypoperfusion and acute kidney injury[66].

EVLW monitoring provides a unique opportunity to closely track the balance between hemodynamic optimization and lung water accumulation during lung resection surgery. Our group published an observational study of patients undergoing lung resection surgery who received a fluid protocol targeting normovolemia. EVLW was monitored for 3 postoperative days together with hemodynamic indices and tissue perfusion biomarkers. Using protective lung ventilation together with normovolemia resulted in improvement in cardiac index, favorable tissue perfusion markers, and no elevation in EVLW [67].

Haas et al. studied the use of stroke volume variation (SVV) and EVLW to guide fluid therapy in patients undergoing lung resection or esophagectomy under protective lung ventilation. This resulted in optimized cardiac performance without pulmonary fluid overload[68]. These studies support a new paradigm for fluid management in high-risk patients such that cardiac and pulmonary functions can be optimized.

Extravascular lung water measurement is useful beyond fluid management during lung resection as a means to guide ventilation strategies and pharmacologic interventions. EVLW was employed to monitor the resolution of pulmonary edema from treatment with aerosolized salbutamol in high-risk patients following lung resection surgery [69].

The use of EVLW was also extended to monitor the effect of different ventilation strategies and recruitment maneuvers during the one-lung ventilation on the lung water accumulation. In patients undergoing video-assisted thoracic surgery ventilation during OLV with a tidal volume of 4 ml kg^{-1} was associated with lower EVLW accumulation than ventilation with 6 ml kg^{-1} or 8 ml kg^{-1} of ideal body weight[70]. The safety of intermittent reinflation of the deflated lung to improve oxygenation during OLV for thoracic surgery was also addressed using

EVLW measurements. Here the beneficial effects of reinflation on oxygenation were established without adverse increases in EVLW[71].

Differentiating Hydrostatic Vs. Permeability Pulmonary Edema

Pulmonary edema is a result of either an increase in pulmonary hydrostatic pressure or an increase in pulmonary permeability or both. The ability to differentiate between the two causes is of utmost importance in management yet remains a diagnostic dilemma. In an attempt to provide an estimate of pulmonary vascular permeability ratios of EVLW to TPTD derived blood volumes have been utilized. These ratios are intended to reflect EVLW in the context of, or indexed to preload, and were first described in 2001 by Honore et al [72]. The concept is intuitive; a high EVLW in a hypovolemic patient (and therefore an elevated ratio) would suggest capillary permeability is the primary pathology whilst low EVLW in a patient with elevated preload (and therefore a low ratio) would suggest capillary permeability to be intact. Similarly the diagnosis of hydrostatic pulmonary edema is suggested by high EVLW in a patient with high preload and therefore a normal ratio of EVLW to preload. Intrathoracic blood volume (ITBV)[72-74] global end-diastolic (GEDV)[73, 75] and pulmonary blood volume (PBV)[73-75] are indices of cardiac preload derived from TPTD to which EVLW has been indexed in the derivation of 'pulmonary vascular permeability indices' (PVPIs).

Attempts to establish the validity of PVPIs are challenged by the technical complexities involved in determining a 'gold standard' measure of pulmonary vascular permeability. PVPIs have however, been shown to agree well with radio-isotope derived pulmonary leak index [73, 74], to be strongly associated with clinically and radiographically derived measures of lung injury[25, 75], and have high sensitivity and specificity in distinguishing patients with ALI/ARDS from controls, in fact, a PVPI >/= 3 allowed the diagnosis of ALI/ARDS with a sensitivity of 85% and specificity 100%[75,76].

Whilst determination of PVPIs offers much promise in aiding clinicians to distinguish between hydrostatic and permeability induced pulmonary edema, these techniques are far from mature. Additional work, such as defining ‘normal’ PVPI values and the ideal preload parameter to which EVLW should be indexed, will advance its utility as a clinical monitor.

Conclusion: TPTD is a major advancement in our monitoring armamentarium, offering a quantitative, bedside means to monitor EVLW and the development of pulmonary edema. Its sensitivity provides both early detection of lung water accumulation prior to overt pulmonary edema and offers new approaches to more optimally guide perioperative fluid therapy. In addition, the ability to provide insight on the etiology of pulmonary edema, specifically hydrostatic versus increased pulmonary capillary permeability, is emerging as an aid in therapeutic decision-making. Whilst the technique is not without limitations, both on technical and physiologic grounds, the combination of hemodynamic and lung water data afforded has unique benefits for the care of perioperative patients.

Figure Legends:

Figure 1: Schematic representation of the determination of extravascular lung water (EVLW) from 'single indicator' transpulmonary thermodilution curve using Stewart-Hamilton, Newman and Sakka principles. EVLW is calculated from the difference between the ITTV and ITBV. Additional hemodynamic parameters provided include CO and GEDV, a preload measure consisting of the combined volumes of the RA, RV, LA, & LV in diastole.

ITTV: Intrathoracic thermal volume, ITBV: intrathoracic blood volume, CO: cardiac output, GEDV: cardiac global end diastolic volume, RA: right atrium, RV: right ventricle, LA: left atrium, LV: left ventricle, PBV: pulmonary blood volume.

Figure 2. Displays from two proprietary TPTD systems commercially available (PiCCO$_2$ System (Pulsion Medical Systems SE, Munich, Germany) and VolumeView/EV1000 system (Edwards Lifesciences, Irvine CA, USA).

Figure 3. Proposed algorithm for hemodynamic management based on transpulmonary thermodilution parameters. (Adapted from Pulsion Medical Systems).

GEDI: global end diastolic index. EVLW: extravascular lung water.

Figure 4. Hemodynamic protocol in sepsis/ARDS patients based on EVLW determination. (Protocol adapted from Pino-Sanchez F, et al.: Influence of

extravascular lung water determination in fluid and vasoactive therapy. J Trauma. 67:1220-1224, 2009).

EVLW: extravascular lung water ml/kg. ARDS: acute respiratory distress syndrome.

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