VIA MEDICA

ORIGINAL AND CLINICAL ARTICLES

Anaesthesiology Intensive Therapy
2015, vol. 47, no 2, 89–116
ISSN 0209–1712
10.5603/AIT.a2014.0068
www.ait.viamedica.pl

Common pitfalls and tips and tricks to get the most out of your transpulmonary thermodilution device: results of a survey and state-of-the-art review

Pieter-Jan Hofkens[1], Anton Verrijcken[1], Kelly Merveille[1], Stef Neyrinck[1], Niels Van Regenmortel[1], Inneke De laet[1], Karen Schoonheydt[1], Hilde Dits[1], Berthold Bein[2], Wolfgang Huber[3], Manu L.N.G. Malbrain[1]

[1]*Intensive Care, Ziekenhuis Netwerk Antwerpen, ZNA Stuivenberg, Antwerp, Belgium*
[2]*Department of Anaesthesia, ASKLEPIOS Hospital St. Georg, Hamburg, Germany*
[3]*II Department of Internal Medicine, "Klinikum rechts der Isar", Technical University Munich, Munich, Germany*

Abstract

Background: Haemodynamic monitoring with transpulmonary thermodilution (TPTD) is less invasive than a pulmonary artery catheter, and is increasingly used in the Intensive Care Unit and the Operating Room. Optimal treatment of the critically ill patient demands adequate, precise and continuous monitoring of clinical parameters. Little is known about staff knowledge of the basic principles and practical implementation of TPTD measurements at the bedside. The aims of this review are to: 1) present the results of a survey on the knowledge of TPTD measurement among 252 nurses and doctors; and 2) to focus on specific situations and common pitfalls in order to improve patient management in daily practice.

Methods: Web-based survey on knowledge of PiCCO technology (Pulsion Medical Systems, Feldkirchen, Germany), followed by PubMed and Medline search with review of the relevant literature regarding the use of TPTD in specific situations.

Results: In total, 252 persons participated in the survey: 196 nurses (78%) and 56 medical doctors (22%) of whom 17 were residents in training. Knowledge on the use of TPTD appears to be suboptimal, with an average score of 58.3%. Doctors performed better than nurses (62.7% vs 57.0%, $P = 0.012$). About 190 out of 252 (75.4%) scored at least 50% but only 45 respondents (17.9%) obtained a score of 70% or more. Having five years of PiCCO experience was present in 15.8% of the participants and this was correlated to passing the test, defined as obtaining a test result of ≥ 50% ($P = 0.07$) or obtaining a test result of ≥ 70% ($P = 0.05$). There were no other parameters significantly predictive for obtaining a result above 50% or above 70% such as gender or doctor versus nurse or Belgian versus Dutch residency, or years of ICU experience. High quality education of nursing and medical staff is necessary to perform the technique correctly and to analyse and interpret the information that can be obtained. Visual inspection of thermodilution curves is important as this can point towards specific pathology. Interpretation of the parameters that can be obtained with TPTD in specific conditions is discussed. Finally, a practical approach is given in ten easy steps for nurses and doctors.

Conclusion: TPTD has gained its place in the haemodynamic monitoring field, but, as with any technique, its virtue is only fully appreciated with correct use and interpretation.

Key words: transpulmonary thermodilution, PiCCO, haemodynamic monitoring, cardiac output, pulse contour analysis, calibration, pitfalls, tips and tricks, survey, knowledge, critical care

Any measurement that we perform on a daily basis in the Intensive Care Unit (ICU) stands or falls on its accuracy, reproducibility and correct interpretation of the data derived [1, 2]. No monitoring device, no matter how simple or sophisticated, will improve patient-centred outcomes unless coupled with a treatment protocol that, itself, improves outcomes [2–4].

The pulmonary artery catheter (PAC) is still considered to be the clinical gold standard, but its use is declining due to the absence of a convincing outcome benefit and the development of less invasive haemodynamic monitoring methods such as transpulmonary thermodilution (TPTD) [3, 5–7].

As of today, two haemodynamic monitoring devices using single indicator TPTD with a cold fluid bolus as indicator are commercially available, the PiCCO (Pulsion Medical Systems, Feldkirchen, Germany) and more recently also the VolumeView/EV1000 (Edwards Lifesciences, Irvine, CA, USA) [8–12].

In this review, we will focus on the PiCCO system because it has been in use for several years and has been validated in numerous studies and clinical situations [10, 13–19]; as such the recommendations regarding TPTD presented herein can be extrapolated to other devices using the same technique. The PiCCO is a haemodynamic monitoring device that combines continuous measurement of the cardiac output (CO) using pulse contour analysis with intermittent volumetric measurement of cardiac preload like global end-diastolic volume (GEDV) and extravascular lung water (EVLW) using TPTD amongst other haemodynamic parameters [2, 10, 20–22]. With each TPTD measurement (and its associated CO value) the continuous CO measurement (CCO) of the PiCCO device is calibrated. PiCCO stands for 'pulse contour, intermittent and continuous cardiac output' or just Pulse Contour Cardiac Output with the 'i' there to facilitate pronunciation.

A detailed description of the principles, measurements and calculations can be found in the manufacturer's manual and has also been described elsewhere [2, 12, 23–28]. A brief summary will be given below because this knowledge helps the correct interpretation of the derived parameters.

The aims of this review are to: 1) present the results of a survey on the knowledge of TPTD measurement among nurses and doctors; and 2) to focus on specific situations, common pitfalls, tips and tricks. After learning these, we hope the reader can get more information out of the device, which would ultimately lead to better patient management in daily practice.

DESCRIPTION OF THE TRANSPULMONARY THERMODILUTION TECHNIQUE

RATIONALE

During a TPTD cardiac output CO measurement, a known volume of a cold indicator, typically 0.9% saline, injected via a central vein, mixes with the ambient circulation as it travels through the right heart, pulmonary circulation, left heart, and aorta. A thermistor-tipped catheter in a central (femoral, brachial, axillary) artery or a long radial artery catheter records the surrounding blood temperature and generates a thermodilution curve qualitatively similar to the one generated by a pulmonary artery catheter (PAC). The main difference from PAC is a time delay caused by the longer travel time between injection site and temperature recording site, rendering it less affected by arrhythmias, changes in intrathoracic pressures (e.g. during mechanical ventilation) and timing of injection in the respiratory cycle [25, 29–32].

The CO can then be calculated from the area under the thermodilution curve using the classic Stewart-Hamilton formula:

$$CO = \frac{K \times (T_b - T_i)}{\int \Delta T_b \times dt}$$

with K = computation constant adjusting for the injectate volume and physical characteristics of the catheter and injectate; T_b = blood temperature; T_i = injectate temperature;= integral of temperature change over time (reflecting area under the thermodilution curve)

INTERMITTENT MEASUREMENTS

The TPTD CO measurement serves as calibration for the CO derived from the arterial pulse contour waveform, which then allows continuous (beat-to-beat) CO monitoring [2, 20, 25, 33–35]. The mean transit time (MTt) is the mean time required for the indicator to reach the detection point at the tip of the PiCCO catheter (mostly positioned in the femoral artery) and the downslope time (DSt) is the exponential downslope time of the thermodilution curve (Fig. 1). In addition to CO, based on the mean transit time (MTt) of the cold indicator and the exponential downslope time (DSt) of the thermodilution curve, several other clinical variables can be readily measured and calculated: the intrathoracic thermal volume (ITTV) as the product of CO and MTt and the pulmonary thermal volume (PTV), which includes the pulmonary blood volume (PBV) and the extravascular lung water (EVLW), as the product of CO and DSt. Subsequently,

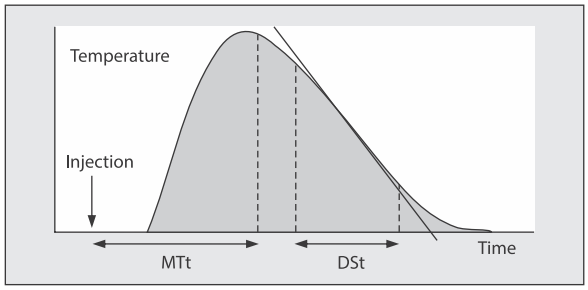


Figure 1. Logarithmic extrapolation of a transpulmonary thermodilution curve with identification of mean transit time (MTt) and downslope time (DSt). See text for explanation

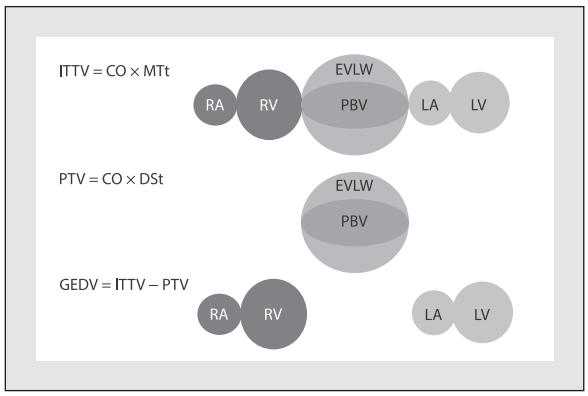


Figure 2. Schematic representation of volumetric monitoring. Intrathoracic thermal volume (ITTV) is derived from cardiac output (CO) and mean transit time (MTt). The largest mixing chamber is the pulmonary thermal volume (PTV) which is derived from CO and downslope time (DSt). The preload parameter global enddiastolic volume can then be calculated as ITTV minus PTV). RA — right atrium; RV — right ventricle; LA — left atrium; LV — left ventricle; EVLW — extravascular lung water; PBV — pulmonary blood volume; PTV — pulmonary thermal volume (= EVLW + PBV)

two volumetric measures of cardiac preload, the global end-diastolic volume (GEDV) and the intrathoracic blood volume (ITBV), are calculated by respectively subtracting the PTV from the ITTV (for GEDV) and, based on a linear relation, by multiplying the GEDV by 1.25 [2, 36]. This is illustrated in Figure 2. Moreover, the unique and important parameter extravascular lung water (EVLW) as a measure of pulmonary oedema is estimated by subtracting ITBV from ITTV [37, 38]. Derived from these measurements, the device will calculate different parameters of myocardial performance: stroke volume (SV) as: CO/heart rate (HR), global ejection fraction (GEF) as: (4 × SV)/GEDV, cardiac function index (CFI) as: CO/GEDV and a parameter of alveolar-capillary barrier permeability, the pulmonary vascular permeability index (PVPI) as the ratio of EVLW to PBV [37, 39–47].

PULSE CONTOUR ANALYSIS

Besides CO, the following parameters can be calculated (continuously) from the arterial pulse contour on a continuous basis: SV calculated as area under the arterial pulse contour, systemic vascular resistance (SVR) as: 80 × (mean arterial pressure (MAP) – central venous pressure (CVP))/CO, stroke volume variation (SVV) in % as: 100 × (SV_{max} – SV_{min}) /(SV_{mean}) over a period of time (12 seconds), pulse pressure variation (PPV) in % as: 100 × (PP_{max} – PP_{min})/(PP_{mean}), maximum left ventricular contractility (dPmax): as the rate of increase in blood pressure and cardiac power output (CPO) in watts as: MAP × CO/451 [48–51].

All values are indexed for body weight or surface area; the $PiCCO_{Plus}$ with software version 7.1 or higher and $PiCCO_2$ use predicted body weight (PBW) and body surface area (BSA) for the volumetric preload parameters and the extravascular lung water: The GEDV values are usually indexed to BSA (m^{-2}) while EVLW is indexed to PBW.

The new $PiCCO_2$ monitor can also measure central venous oxygen saturation ($S_{cv}O_2$) continuously using spectrophotometry, after calibration with a central venous blood gas analysis (CeVox). Table 1 lists the range of normal values for the different intermittent and continuous parameters that can be obtained with the TPTD technique.

Table 1. Normal values and ranges of haemodynamic parameters. Values for intermittent (#) and continuous parameters that can be obtained with transpulmonary thermodilution

I. Oxygenation
• Central Venous Oxygenation ($S_{cv}O_2$): 70–80%
• Oxygen Delivery Index (DO_2I): 400–650 mL min^{-1} $m^{-2\#}$
• Oxygen Consumption Index (VO_2I): 125–175 mL min^{-1} $m^{-2\#}$
II. Flow*
• Cardiac Output (CO): 5.0–7.0 L $min^{-1\#}$
• Cardiac Index (CI): 3.0–5.0 L min^{-1} $m^{-2\#}$
• Pulse contour cardiac index (PCCI): 3.0–5.0 L min^{-1} m^{-2}
III. Cardiac Preload
• Global Enddiastolic Volume Index (GEDVI): 680–800 mL $m^{-2\#}$
• Intrathoracic Blood Volume Index (ITBVI): 850–1,000 mL $m^{-2\#}$
• Central venous pressure (CVP): 5–7 mm Hg
IV. Volume Responsiveness
• Stroke Volume Variation (SVV): ≤ 10%
• Pulse Pressure Variation (PPV): ≤ 10%
V. Afterload
• Systemic Vascular Resistance Index (SVRI): 1,700–2,400 dyn s cm^{-5} m^{-2}
VI. Cardiac Contractility
• Cardiac Function Index (CFI): 4.5–6.5 L $min^{-1\#}$
• Global Ejection Fraction (GEF): 25–35% #
• Index of Left Ventricular Contractility (dPmax): 1,200–2,000 mm Hg sec^{-1}
• Cardiac Power Index (CPI): 0.5–0.7 W m^{-2}
VII. Pulmonary Oedema
• Extravascular Lung Water Index (EVLWI): 3.0–7.0 mL kg^{-1} PBW #
• Pulmonary Vascular Permeability Index (PVPI): 1.0–3.0 #

these parameters can only be obtained intermittently by performing a TPTD as calibration
* values for cardiac output are also dependent on age and gender

Table 2. Necessary equipment for PiCCO measurement

- Central venous catheter, preferably right internal jugular (or subclavian) vein
- PiCCO arterial catheter with thermistor, preferably femoral (or axillary/brachial/long radial), pressurised bag (up to 300 mm Hg) of normal saline
- PiCCO monitoring kit (includes disposable pressure transducer)
- Cold injectate (saline, three boluses of 0.2 mL kg^{-1} BW, < 8°C) and injectate sensor housing
- PiCCO monitor

The specially designed arterial catheters exist in 3F to 5F and from 7 cm to 22 cm long (or even 50 cm for the long radial) and also allow use in the paediatric population as opposed to the pulmonary artery catheter [52, 53]. The equipment necessary for setup is listed in Table 2. The manufacturer recommends that the maximum placement period for the PiCCO catheter is ten days.

SURVEY ON KNOWLEDGE OF TRANSPULMONARY THERMODILUTION

We present herein the results of a survey on knowledge of PiCCO technology among healthcare providers working in the ICU. The survey was conducted among mainly nurses from Belgium and the Netherlands.

SURVEY BACKGROUND

Optimal treatment of the critically ill patient demands precise and continuous monitoring of clinical parameters. Recent studies show that the application of haemodynamic monitoring can improve outcomes [54, 55]. As explained above, CO monitoring with TPTD combined with pulse contour analysis obtained with the PiCCO system provides information on fluid status, fluid responsiveness, CO, contractility of the myocardium and severity of the pulmonary oedema. The PiCCO is considered a less invasive haemodynamic monitoring device compared to the PAC, and is increasingly being used as a haemodynamic monitoring tool to guide management in critically ill patients. No research has been previously performed on staff knowledge of the basic principles and practical implementation of TPTD measurements at the bedside.

SURVEY METHODS

We set up a descriptive study in which medical and paramedical ICU personnel were asked to participate in a survey that consisted of 25 questions based upon the information found in the manual of the PiCCO system (www.pulsion.com). During a six month period in 2009, we performed the survey among nursing and medical staff from different ICUs in Belgium and the Netherlands on their knowledge of the basic principles and practical use of the PiCCO haemodynamic monitoring system. Participants were asked to complete an online questionnaire with one open and 24 multiple-choice questions. An English translation of the questionnaire, originally in Dutch, with correct answers, is available in Appendix 1. Statistical analysis was performed with SPSS software. Results are expressed as mean with standard deviation, a *P*-value below 0.05 was considered to be statistically significant.

SURVEY RESULTS

In total, 252 persons participated: 196 nurses (78%) and 56 medical doctors (22%) of whom 17 were residents in training. 78.6% of the respondents knew that a PiCCO CO measurement is performed intermittently by TPTD and on a continuous basis by arterial pulse contour analysis. About 43% were convinced that a PiCCO measurement is an invasive procedure, while in fact it is considered less invasive. The basic knowledge on CO calibration appeared to be insufficient: 59 respondents (23.3%) did not know that the temperature of the bolus injectate (T_i) should best be below 8°C. Regarding the volume of the injectate (V_i), only 55 (21.8%) correctly stated that it should be adjusted according to body weight (0.2 mL kg^{-1}), with a maximum of 20 mL. About 162 (64.3%) of the participants knew that the cold injectate needs to be administered within seven seconds (or thus 2.5 mL sec^{-1}) and 153 (60.7%) erroneously believed that the patient needs to be in supine position while performing the TPTD measurement. 138 persons (54.8%) stated correctly that the PiCCO needs to be calibrated only once every nursing shift (thus 3–4 times per day), but only 91 (36.1%) knew that a rapid flush test should be performed before each measurement. A further 65.5% of the participants recognised the curve of a correct rapid flush test, while 36.9% did not know why there is a need to perform the rapid flush test. 41.7% of the participants knew that stroke volume variation (SVV) and pulse pressure variation (PPV) are unreliable if the patient is not in sinus rhythm, whereas 26.6% didn't recognise atrial fibrillation as an underlying rhythm stated in question 24.

A total of 178 (70.6%) stated correctly that the placement of the venous and arterial femoral catheters is important for the interpretation of the obtained values. Table 3 lists the distribution of correct answers to the different questions.

The overall score with correct answers was poor, and around 58.3 ± 15.1% (Fig. 3). The doctors performed better than the nurses (62.7% vs 57.0%, $P = 0.012$); no difference was found between male and female respondents (59.4% vs 57.6%, P = NS), nor between Belgian and Dutch respondents (57.3% vs 59.5%, P = NS). 190 out of 252 (75.4%) scored at least 50%, whereas only 45 respondents (17.9%) obtained a score of 70% or more. The number of years of ICU experience was inversely related to the knowledge on

Table 3. Questions with correct answers and percentage of correct answers, sorted by highest percentage of correct answers (see addendum for full length MCQs and accompanying figures)

Question	Correct answer	Correct answers (%)
23B — Look at the following thermodilution curve and state if it is performed correctly	Correct	220 (87.3%)
9 — Is it important to enter information like weight and height of the patient?	Yes, to display the indexed values correctly (latest software uses predicted body weight)	218 (86.5%)
3 — What does PiCCO measure besides cardiac output?	Preload, contractility, extravascular lung water, filling status, afterload and fluid responsiveness	208 (82.5%)
23A — Look at the following thermodilution curve and state if it is performed correctly	False	205 (81.3%)
2 — What principles are used with PiCCO measurements?	Intermittent thermodilution and continuous arterial pulse contour analysis	198 (78.6%)
6 — What specifically do we need to perform a PiCCO measurement?	Central venous line, PiCCO catheter and a PiCCO kit	196 (77.8%)
7 — What is the correct T_i?	< 8°C	193 (76.6%)
24 — Determine the underlying rhythm	Atrial fibrillation or irregular rhythm	185 (73.4%)
18A — Is the placement of the catheters important for the interpretation of the obtained values?	Yes	178 (70.6%)
23C — Look at the following thermodilution curve and state if it is performed correctly	False	174 (69.0%)
17A — Interpret the following rapid flush test	Normal signal	165 (65.5%)
11 — How many bolus injections must at least be done to obtain a correct value?	Three	165 (65.5%)
19 — The injectate should be injected	In less than seven seconds (< 2.5 mL sec^{-1})	162 (64.3%)
20 — What to do if the delta T° is less than 0.2°C?	Use cooler injectate or increase injectate volume	161 (63.9%)
15 — Why do we perform a rapid flush test?	To determine whether there is damping of the curve or to check if the pressurised bag is sufficiently inflated	159 (63.1%)
17C — Interpret the following rapid flush test	Overdamped	155 (61.5%)
13 — What values should be noted for volumes and extravascular lung water?	The indexed values	141 (56%)
14 — How many times does the arterial pressure curve needs to be zeroed?	Once every nursing shift	138 (54.8%)
17B — Interpret the following rapid flush test	Underdamped	128 (50.8%)
25 — Which PiCCO measurements are not reliable if the patient is not in sinus rhythm?	SVV and PPV are unreliable (however, if they are low the patient is probably not fluid responsive)	105 (41.7%)
10 — Should the patient be supine for a measurement?	No, it does not matter	99 (39.3%)
18B — Which of the following would be the ideal catheter position?	Right internal jugular vein in combination with left or right femoral artery	94 (37.3%)
21 — What happens if the injectate volume is less than the amount entered on the PiCCO (this is the amount the device expects)?	False increase in CO or false increase in CI (also the GEDVI and EVLWI will be falsely increased)	93 (36.9%)
16 — When do we perform a rapid flush test?	Before each measurement	91 (36.1%)
22 — Should the CVP repeatedly be entered?	Yes, for the calculation of the SVR (practically this is done at each TPTD)	91 (36.1%)
5 — In which patients is the use of PiCCO appropriate?	All of the above	84 (33.3%)
8 — Is the V_i dependent on the body weight?	Yes, with a maximum of 100 kg (0.2 mL kg^{-1})	55 (21.8%)
12 — Which deviation from the mean CO is allowed for a thermodilution CO measurement?	15% (and this also holds true for GEDVI and EVLWI)	49 (19.4%)

PiCCO. Persons who had more than ten years of ICU experience scored less (54.5%) on the knowledge questions than personnel with 5–10 years (60.5%) and those with less than five years' ICU experience (59.8%) respectively, with no significant difference between doctors and nurses except for those with more than ten years' experience (Fig. 4). Doctors (72.4%) performed better than nurses (54.5%) in the group of personnel with more than five years of PiCCO experi-

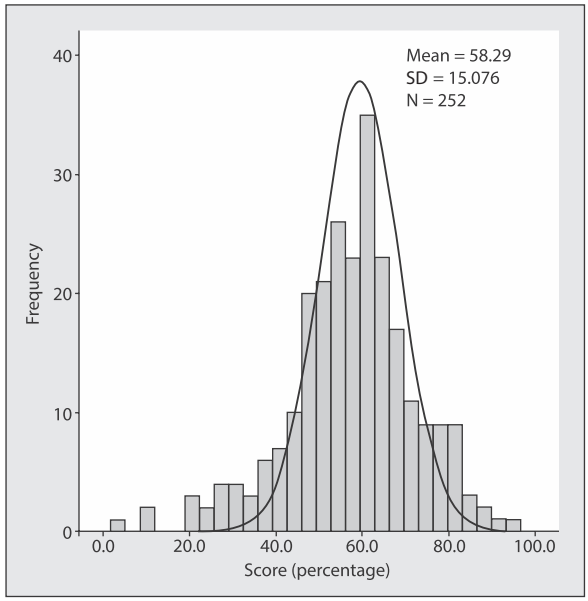


Figure 3. Histogram displaying the frequency of average scores (in percentage) on the knowledge questions

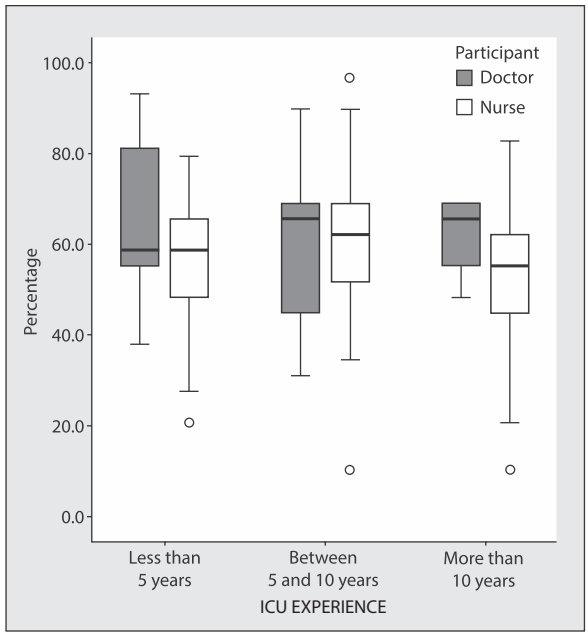


Figure 4. Boxplots showing median scores (as percentage) for doctors as compared to nurses according to the number of years of ICU experience. The *P*-values were NS except for the group with more than 10 years ICU experience ($P = 0.05$)

ence (Fig. 5). Figure 6 shows the different scores in men compared to women with regard to years of ICU experience, while Figure 7 show the same results in relation to years of PiCCO experience. In the group of respondents having more than five years of PiCCO experience, men (64.0%) showed significantly better results than women (54.3%). There was no significant difference in the results related to gender in the group with less than five years of PiCCO experience.

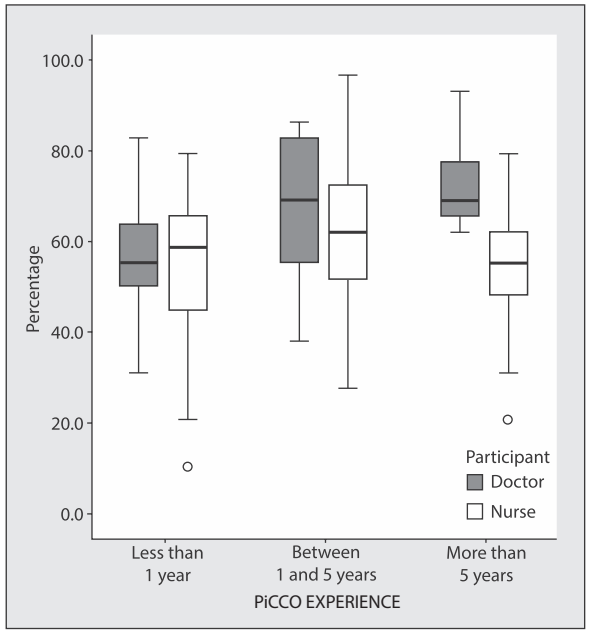


Figure 5. Boxplots showing median scores (as percentage) for doctors as compared to nurses according to the number of years of PiCCO experience. The *P*-values were NS except for the group with more than 5 years PiCCO experience ($P < 0.0001$)

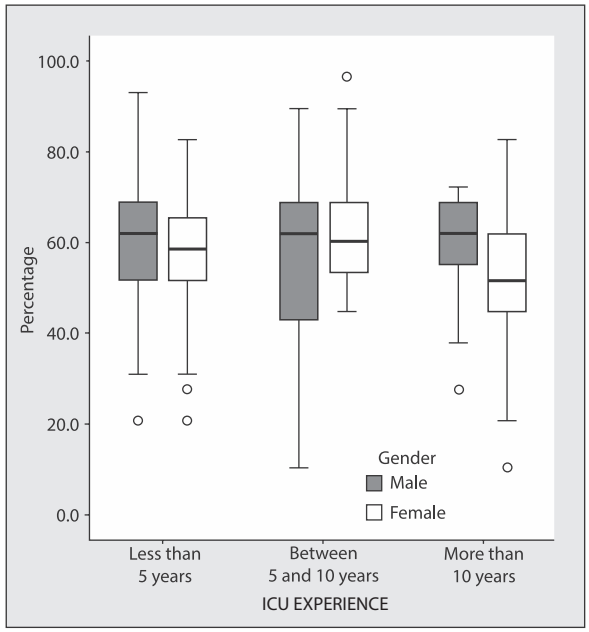


Figure 6. Boxplots showing median scores (as percentage) for men as compared to women according to the number of years of ICU experience. All the *P*-values were NS

Having five years of PiCCO experience was present in 15.8% of the total number of participants and this was correlated to passing the test (obtaining ≥ 50%) ($P = 0.07$) or obtaining a test result of ≥ 70% ($P = 0.05$). There were no other parameters significantly predictive for obtaining a result above 50% or above 70% such as gender, doctor

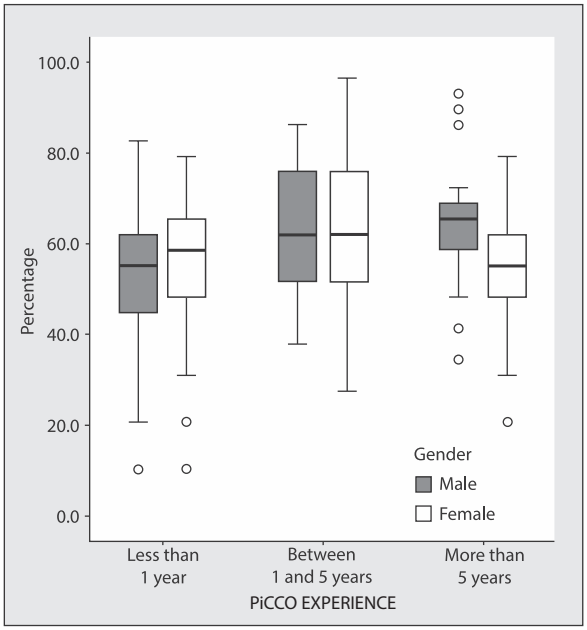


Figure 7. Boxplots showing median scores (as percentage) for man as compared to woman according to the number of years of PiCCO experience. The *P*-values were NS except for the group with more than 5 years PiCCO experience ($P = 0.012$)

versus nurse, Belgian versus Dutch residency, or years of ICU experience.

SURVEY CONCLUSIONS

PiCCO has gained its place in the haemodynamic monitoring field, but as with any technique, its usefulness and virtue is only fully appreciated with correct understanding of the principles, a flawless measurement technique, and a correct interpretation of the obtained values in different scenarios. We can conclude from the results of this survey that the knowledge on the measurement technique and interpretation of the PiCCO, although being used regularly, was suboptimal among the ICU personnel. From our survey among ICU personnel, it appears that knowledge on TPTD appears to be suboptimal. High quality and repeated education of ICU staff is necessary to exploit the information that can be obtained. This education can be facilitated by a good measurement (TPTD calibration) protocol that can be implemented by nurses and doctors at the bedside to avoid human error. Specific thermodilution curves can point towards specific diagnoses, and an interpretation of acquired parameters in specific conditions is suggested.

PRACTICAL APPROACH

In the following section, we will guide the reader through four important aspects of correct TPTD measurement and interpretation: 1) when to perform a TPTD calibration; 2) how to obtain a correct TPTD measurement; 3) how to learn from the intermittent readings obtained with TPTD; and finally 4) how to interpret the continuous haemodynamic parameters.

WHEN TO PERFORM TPTD

In general, TPTD is performed for two purposes: first it provides volumetric TPTD parameters such as CI, EVLWI and GEDVI. The frequency of TPTD measurements of CI, EVLWI and GEDVI predominantly depends on the clinical situation of the individual patient: in a case of shock, repeated measurements within minutes can be useful. Furthermore, repeated TPTD might be required before and after interventions, e.g. probatory fluid application ('volume challenge') requires TPTD before and after the volume challenge within 30 minutes.

The second purpose of TPTD is to (re-)calibrate pulse contour derived CI (PCCI) to ensure accurate beat-by-beat estimation of CI by PCCI. Only a few studies have investigated predictors of inaccuracy of PCCI. As a minimal consensus, a re-calibration of PCCI should be performed within eight hours after the previous TPTD. However, there is limited evidence that 'time since last TPTD' is an independent predictor of the inaccuracy of PCCI [56]. There are several hints that changes in vascular tone measured by TPTD-derived SVRI are associated with inaccuracy of PCCI [56]. Since changes in SVRI can only be demonstrated by a new TPTD, they are *explanatory* but not *predictive* for inaccuracy of PCCI.

From a practical viewpoint, changes in continuously provided pulse-contour parameters might be more appealing as *predictors* of inaccuracy of PCCI. Although in part preliminary and not fully published, there is evaluation and validation data indicating that changes of PCCI compared to the previous TPTD obtained CI are predictive for the inaccuracy of PCCI compared to the next TPTD derived CI [57, 58]. Based on this data, the manufacturer of the PiCCO-device (Pulsion Medical Systems, Feldkirchen, Germany) implemented a 'trend-alarm' indicating a > 15% deviation of PCCI compared to the previous CI obtained with TPTD. In the V3.1 algorithm, this 'calibration-index' can be activated with different cut-offs (15%, 25%, 35%).

HOW TO OBTAIN A GOOD MEASUREMENT IN TEN SIMPLE STEPS FOR NURSES

STEP 1. LOOK AT ARTERIAL PRESSURE CURVE AND PERFORM THE RAPID FLUSH TEST

Simple visual evaluation and inspection of the arterial waveform should be done before performing a TPTD measurement and the nurse should obtain an idea on the arterial waveform and confirm if the signal is correct (see Fig. 8) [59]. The square waveform and oscillations generated

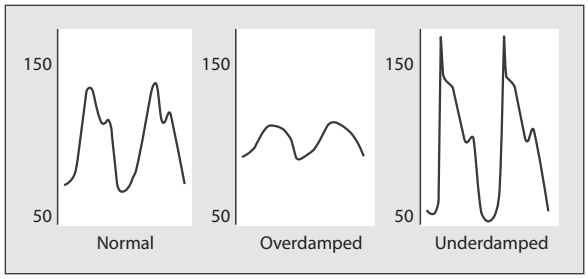


Figure 8. Visual inspection of the arterial curve can identify dynamic response properties

by a rapid flush have been suggested as a suitable method for determining the dynamic response characteristics of a monitoring system (Fig. 9). The system is overdamped if the rapid flush produces sluggish or no oscillations. If the square wave shows undulations or if ringing occurs after the release of the rapid flush device, the system is most likely underdamped. Overdamping and underdamping both indicate that the dynamic response characteristics of the monitoring system are unsatisfactory. A rapid flush test needs to be performed before each TPTD in order to calculate the intrinsic resonance frequency of the transducer system.

STEP 2. ZERO THE PRESSURE SYSTEM

As a general rule in invasive haemodynamic monitoring, the pressure transducer needs to be levelled at the phlebostatic axis (at the level of the right atrium) and the system needs to be zeroed against atmospheric pressure. This should be done at least once every nursing shift. An incorrect zeroing will lead to false MAP readings and therefore false SVR calculations. An easy solution is the use of a dedicated zeroing line fixed at the theoretical zero reference point midaxillary line 5 cm under the sternal notch of Louis (Fig. 10).

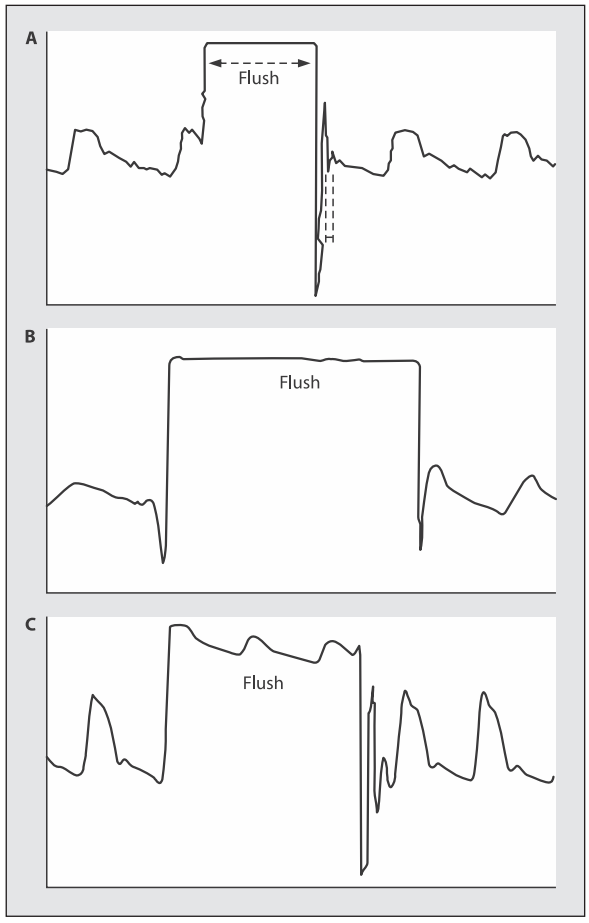


Figure 9. Rapid flush test. Adapted from Marino, Paul L, the ICU Book, 3rd Edition, Lippincott Williams & Wilkins ISBN — 0-7817-4802-X; **A** — normal curve; **B** — overdamped curve; **C** — underdamped curve

STEP 3. CHECK AND ENTER CORRECT DEMOGRAPHIC DATA

Most human mistakes are probably made before performing the actual TPTD measurement. As mentioned, entering appropriate and accurate patient data is of para-

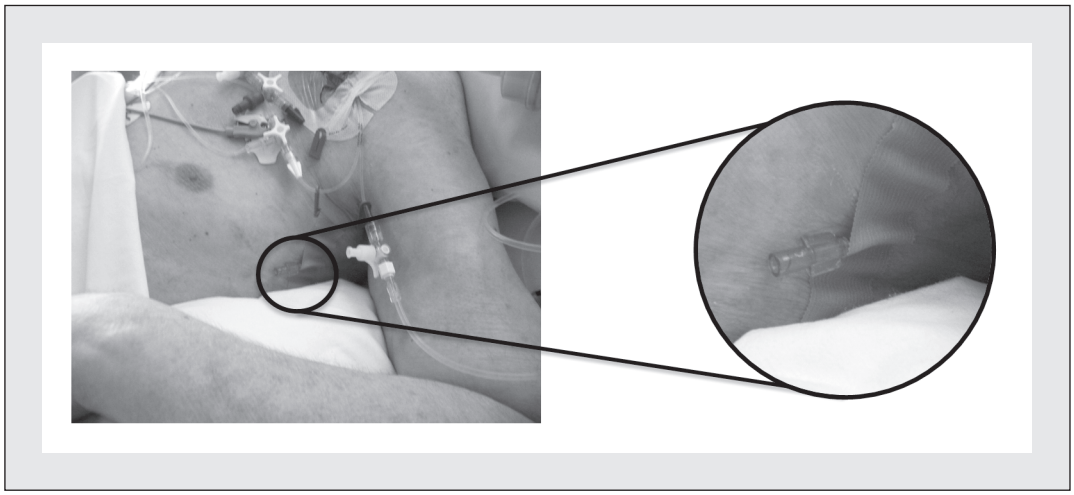


Figure 10. Zero calibration line fixed at the level of the theoretic zero reference level of the phlebostatic axis (circle) allowing repeated calibration regardless of patient position

Figure 11. Practical position of inline sensor. The inline temperature sensor should be placed as close as possible to the distal lumen of the central venous catheter but outside the infusion lines via a stopcock

mount importance for correct TPTD. This pertains to biometric data such as height, weight and gender, injectate volume, as well as to the relative positions of the arterial and central venous catheters.

STEP 4. CORRECT BOLUS PREPARATION: VOLUME AND TEMPERATURE

The manufacturer recommends using 0.9% saline. Because the PiCCO can also be used in a paediatric population, it is important to adjust the volume according to body weight. A volume of 0.2 mL kg^{-1} is recommended with a maximum of 20 mL. This amount is standard practice for all adult patients in our institution. It is important to inject the exact amount that was pre-set on the PiCCO monitor; if the injected volume is smaller than that expected by the device, a false increase in CO, GEDV and EVLW reading is the result and vice versa. For instance, if the 20 mL pre-set on the PiCCO monitor is injected and values obtained for CI, GEDVI and EVLWI are 3.3 L min^{-1} m^{-2}, 839 mL m^{-2} and 9 mL kg^{-1} respectively, then injecting only 10 mL will give falsely increased values of 7, 1862, and 19 respectively. If the Philips® Intellivue module is used, a maximum of 30 mL can be given. This can be useful in situations where the change in temperature at the thermistor level (Δt°) is small or when EVLWI is high.

The manufacturer recommends using an injectate temperature of < 8 °C. Theoretically, room temperature injectate can be used, but this will lead to a systematic overestimation of CO, GEDVI and EVLWI [60, 61]. Therefore the colder the injectate, the better.

STEP 5. INJECTION SITE

The most distal lumen of the central venous catheter is preferred and the connection should be as close to the patient as possible (see Fig. 11). The effect of catheter position is discussed below.

STEP 6. INJECTION SPEED

A fast and steady injection is recommended at a speed of > 2.5 mL sec^{-1}, the whole bolus hence should be injected < 8 for a 20 mL bolus or < 6 sec for a 15 mL bolus. A slow or interrupted bolus will cause a deformed TPTD curve. The device will give an error message if the injection is performed too slowly.

STEP 7. OBSERVE THE TPTD CURVE

It is important to check the morphology and the time intervals on the TPTD curve (see Fig. 12). A typical TPTD curve has a flat portion which reflects the transit time of the cold injectate from injection site to thermistor, followed by a rise and fall in ΔT° with an exponential decrease, ending in a plateau due to physiological recirculation of the indicator. In patients with normal cardiac function, the mean appearance time should be less than 5 seconds (i.e. the start of cooling), the mean transit time around 10 seconds (point of maximal cooling), and the point of recirculation around 15 seconds. If the transit and downslope times are increased, the value of CO can be expected to be low. So it is all about identifying the correct TPTD curve and this demands repeated education for the nurses. Some examples of 'bad' TPTD curves are shown in Figure 13.

STEP 8. CHECK THE NUMBERS

At least three cold boluses are necessary to obtain acceptable precision [62] and any measured CO should not deviate by more than 15% from the mean value (Fig. 12). The same holds true for GEDVI and EVLWI. Certain 'abnormal'

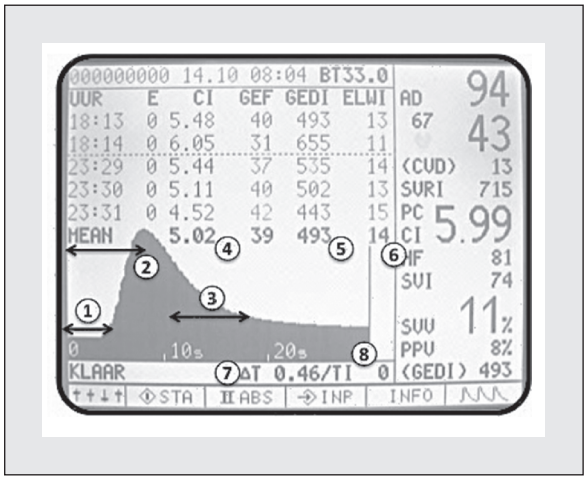


Figure 12. The ideal transpulmonary thermodilution curve

Sample TPTD curve obtained with PiCCO$_{plus}$ monitor

1) the mean appearance time should occur within 5 seconds

2) the mean transit time should occur within 10 seconds

3) the downslope time should occur around 15 seconds

4) each individual TPTD CI measurement should not differ more than 15% from the mean CI

5) each individual TPTD GEDVI measurement should not differ more than 15% from the mean GEDVI

6) each individual TPTD EVLWI measurement should not differ more than 15% from the mean EVLWI

7) the cooling (or thus Δt°) should be more than 0.2°C

8) the injectate temperature should be below 8°C

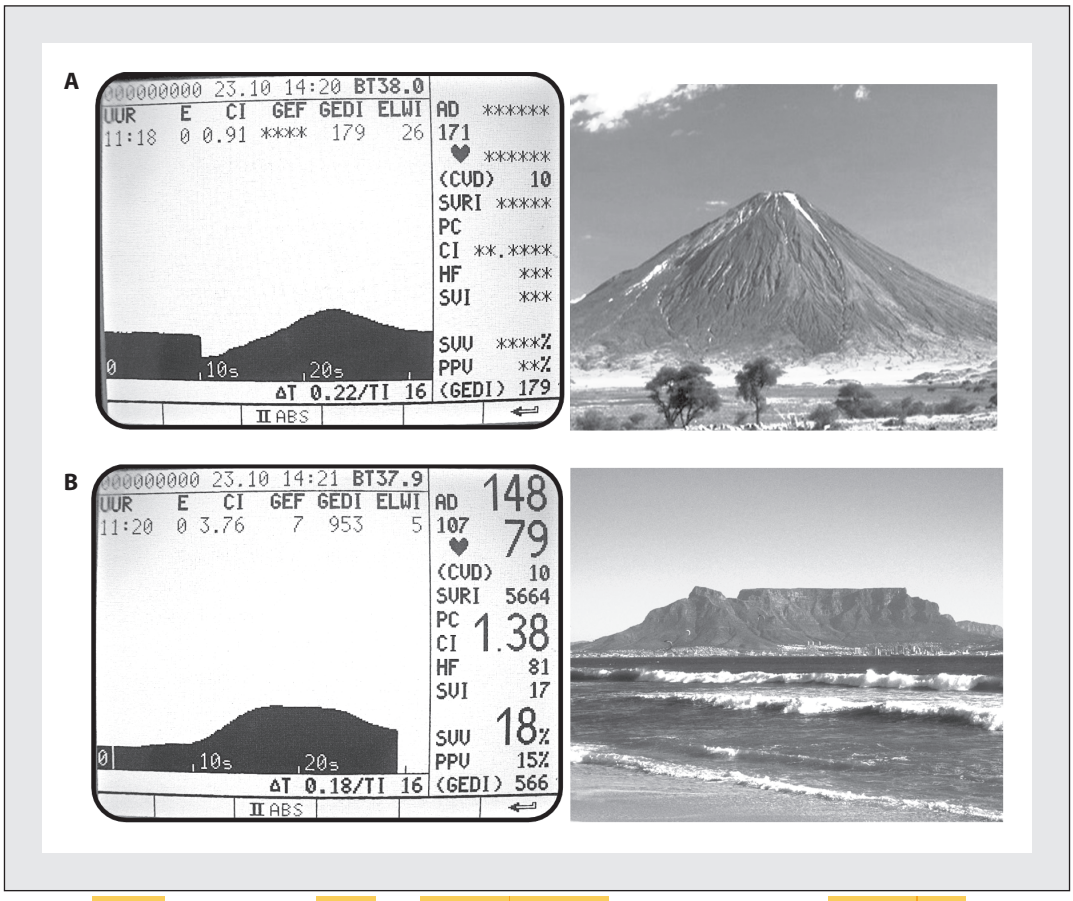


Figure 13. Analysis of thermodilution curves. **A** — erroneous Kilimanjaro mountain type TPTD; **B** — erroneous Table mountain type TPTD, probably caused by a decrease in injection speed of the thermal bolus

curves can point towards a specific condition (discussed further).

STEP 9. CHECK ΔT°

The minimum ΔT° to ascertain correct CO measurement is 0.2°C. The accuracy of PiCCO measurements in accidental or therapeutic hypothermia, regularly used after cardiac arrest, and during hypothermic cardiopulmonary bypass, has not been studied extensively although case reports suggest a poorer reproducibility because of thermal noise [63, 64]. However, if necessary, a colder or higher volume bolus can be tried in order to obtain a ΔT° > 0.2°C. Tagami

et al. performed TPTD in patients under therapeutic hypothermia and found that the measurements were not only feasible but also precise [65, 66].

STEP 10. ENTER THE CVP

It is a misconception among nurses that entering the CVP is necessary for the calculation of the TPTD parameters; the sole purpose is for the calculation of the SVR, and as such the CVP can be entered at the very end of the procedure.

HOW TO INTERPRET TRANSPULMONARY THERMODILUTION CORRECTLY IN TEN SIMPLE STEPS FOR DOCTORS

STEP 1. OBSERVE THE TPTD CURVE AND VERIFY CORRECT INJECTION METHOD

An interrupted injection can cause the thermodilution curve to be bifid with over- or underestimation of the volumetric indices (depending on where the curve is cut off by the software algorithm) while the cardiac output, derived from the area under the curve, may still be relatively correct (see Fig. 14). Bolus mixing can occur when the injection is given through a three-way stopcock where another infusion is running simultaneously and when the stopcock is placed in a 45° position after bolus injection. This should obviously be avoided (see Fig. 15). Moreover, the TPTD curve can also point to specific diagnoses, as will be discussed further.

STEP 2. SHUNTS

A right-to-left shunt as occurs in patent foramen ovale, through which moderate to large shunting is documented in up to 19% of ARDS patients [67], typically gives a premature hump on the thermodilution curve caused by passage of a portion of the indicator through the defect, reaching the thermistor more rapidly than the portion that goes through the pulmonary circulation [68]. This has been termed 'camel curve'. The disappearance of this shunt during treatment of such a patient with inhaled NO has been illustrated nicely in case reports [69, 70]. In a case of an anatomical substrate for intracardiac shunting, right-to-left shunting will become clinically significant if shunting is aggravated by pulmonary hypertension, positive pressure ventilation, positive end-expiratory pressure (PEEP) and hypovolemia shifting zones of West. The mechanism of right-to-left shunt in a case of hypovolemia and addition of PEEP is illustrated in Figure 16. It is possible to quantify the shunt with TPTD [68]. Figure 17 shows an example of right-to-left shunt in an extreme hypovolemic patient under mechanical ventilation with high PEEP and in a young girl suffering from 35% TBSA burns developing ARDS, acute right heart failure with pulmonary hypertension (PAP pressures up to 65 mm Hg).

A left-to-right shunt on the other hand, is characterised by an early recirculation of the cold indicator responsible for a premature flattening of the descending portion of the curve, resulting in an increased mean transit time (with 25%) and increased downslope time (with 50%) and hence affecting EVLW [18, 71–74] (Fig. 18). High EVLW in the absence of gas exchange abnormalities suggests a left-to-right shunt [18].

In conclusion, by looking at TPTD curves, it is possible to detect a wide variety of shunts (intracardiac, arteriovenous fistula) and it has been suggested that TPTD curves could also be useful during surgery to evaluate the success of intra-cardiac shunt closure [75].

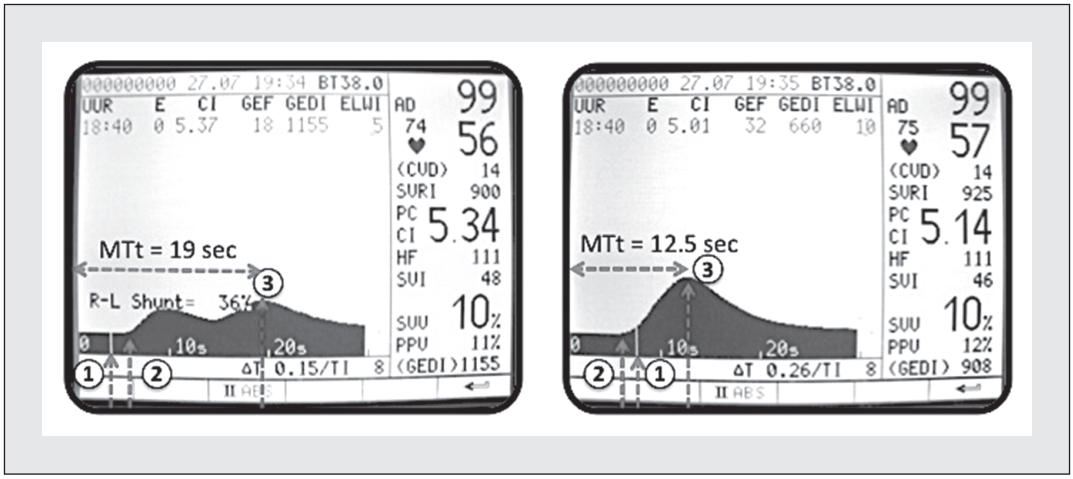


Figure 14. Analysis of thermodilution curves — interrupted bolus. Sample TPTD curves obtained with PiCCO$_{plus}$ monitor. Bolus interrupted on the left-hand side (showing a premature hump and camel-like curve indicated by number 3) and normal TPTD curve on right-hand side in the same patient. Mean appearance time is equal in both curves (indicated by number 2), note that the value for CI is similar and around 5 L m^{-2}, however the value for GEDVI is higher (1155 vs 660 mL m^{-2}) when the bolus was interrupted due to longer mean transit time of 19 sec vs 12.5 sec (horizontal dashed line). The number 1 indicates the end of the injection period

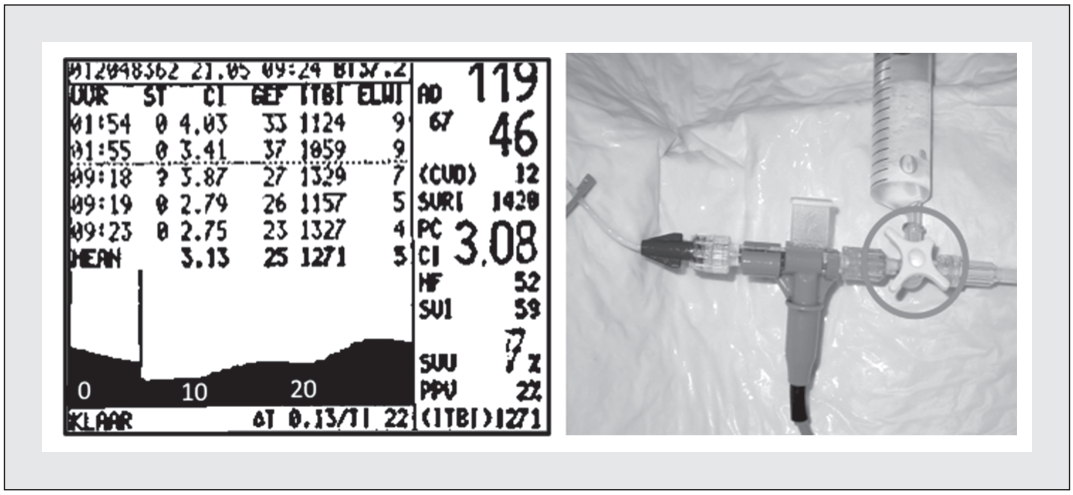


Figure 15. Analysis of thermodilution curves — bolus mixing. Example of TPTD obtained with a $PiCCO_{classic}$ monitor with a premature hump and camel-like curve (left-hand side) caused by bolus mixing with maintenance infusion of parenteral nutrition as a result of incomplete closure of 3 way stopcock after bolus injection (right-hand side)

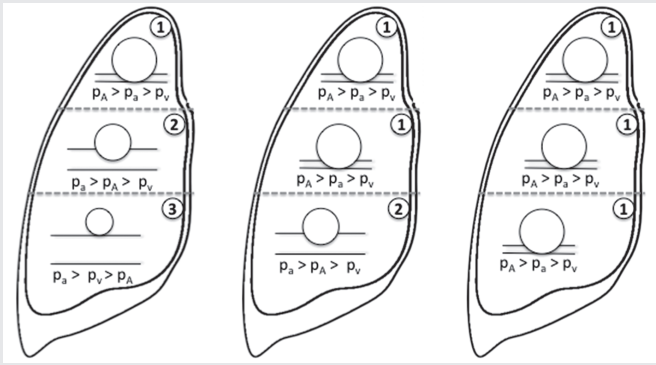


Figure 16. Evolution of West zones during hypovolemia and PEEP. Left panel shows normal West zone distribution. Middle panel shows the situation in a patient under mechanical ventilation and hypovolemia where zone 1 conditions ($p_A > p_a > p_v$) expand to zone 2 ($p_a > p_A > p_v$) and zone 2 conditions to zone 3 ($p_a > p_v > p_A$). With p_a arterial capillary pressure, p_A alveolar pressure and p_v venous capillary pressure. Right panel shows the situation in a hypovolemic patient with excessive PEEP causing further excursion of zone 1 conditions to zone 3 resulting in a right-to-left shunt explaining the premature hump seen on the TPTD curve (Fig. 17A)

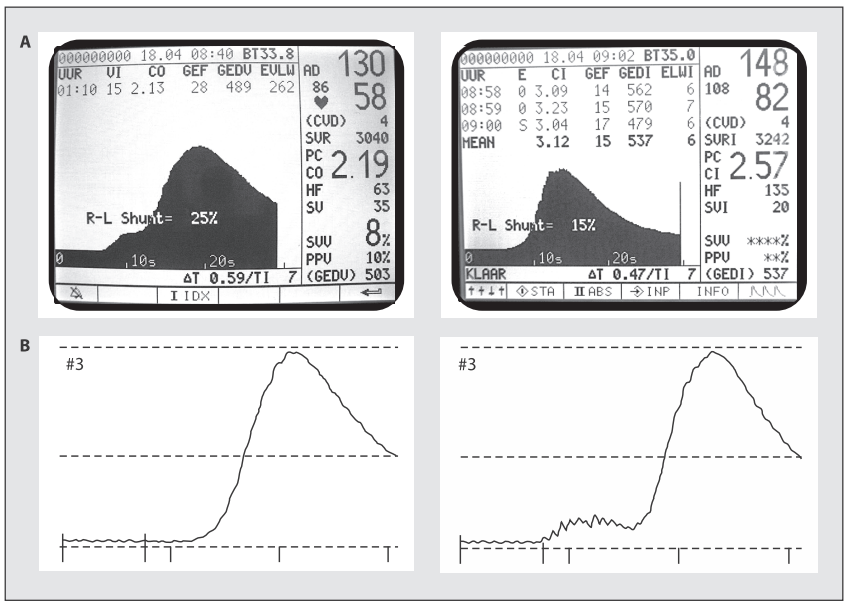


Figure 17. Analysis of thermodilution curves — right-to-left shunt. **A** — example of TPTD obtained with $PiCCO_{plus}$ monitor in a patient with extreme hypovolemia and under positive pressure ventilation with a PEEP of 12 cm H_2O. Because of Zone 1 of West excursions to position 3 a right-to-left shunt became apparent as evidenced by the premature hump on the left-hand side. The GEDV was 489 mL giving a GEDVI of 245 mL m^{-2} before and 537 mL m^{-2} 20 minutes later after adminstration of 1000 mL of voluven and PEEP reduction to 5 cm H_2O (TPTD at right-hand side). After fluid administration the premature hump disappeared. See text for explanation; **B** — example of a TPTD curve obtained with $PiCCO_2$ monitor in a 19 year old burn victim (TBSA 35%) at baseline (left-hand side) and during an episode of acute right heart failure in relation to ARDS (right-hand side). Pulmonary artery pressures measured via transthoracic cardiac ultrasound were 65 mm Hg at that moment. The TPTD is indicative for a right-to-left shunt

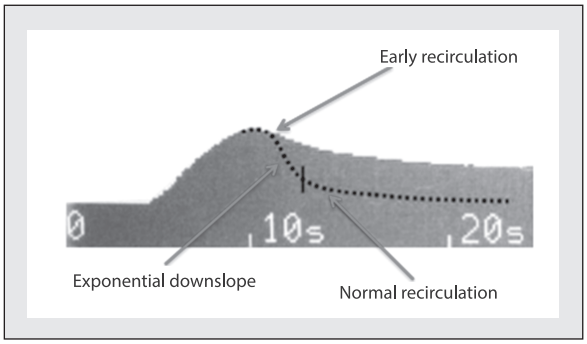


Figure 18. Analysis of thermodilution curves — left-to-right shunt. Sample TPTD curve obtained in a patient with left-to-right shunt. Adapted from Giraud et al. [186]

STEP 3. EFFECT OF CATHETER POSITION

■ *VENOUS CATHETER POSITION*

Often, a femoral central venous catheter is in place. It has been shown that all TPTD values like CI, GEDVI and EVLWI obtained through femoral injection are increased, which is logical due to the longer transit time of the indicator and the augmented volume participating in thermodilution [76, 77]. Saugel et al. proposed a correction formula for jugular GEDVI after TPTD via femoral injection was calculated [78]. Based on this data, the manufacturer of the PiCCO device (Pulsion Medical Systems, Feldkirchen, Germany) implemented a new software version 3.1 requiring the information about CVC site (femoral or jugular/subclavian). This suggests that GEDVI is corrected in a case of femoral injection.

If both the venous and arterial femoral lines are inserted on the same side and have the same length, a premature hump, similar to that in a right-to-left shunt, can be seen due to local changes in temperature sensed by the thermistor on the arterial catheter tip, a phenomenon that has been termed 'cross-talk' [79] as shown in Figure 19. This effect is more pronounced in low CO states [80, 81] and has also been reported when equally long femoral venous and arterial lines are inserted on the opposite side due to anatomical contiguity of the large vessels. A practical approach could be to draw back the arterial catheter if they are located near each other and an early and biphasic thermodilution curve is derived [76, 82–84].

■ *ARTERIAL CATHETER POSITION*

The PiCCO thermistor-equipped arterial lines are designed for use in a central artery; but it is widely accepted that the femoral artery provides more accurate readings. Especially in critically ill patients, where TPTD will be used, a femoral-to-radial pressure gradient often exists [85]. Alternative insertion sites are the axillary or brachial artery and also a long (50 cm) radial catheter has been used successfully [29, 86]. A central arterial catheter insertion site seems to have a low complication rate and is considered to be safe. Therefore, PiCCO can be seen as a minimally invasive form of haemodynamic monitoring [87].

STEP 4. EFFECT OF EXTRACORPOREAL CIRCUIT

Continuous renal replacement therapy (CRRT) seems to have no major clinical impact with a small (albeit statistically significant) decrease in CI and GEDVI and a small increase in EVLWI [77, 88–90]. This effect will be more pronounced when the central venous and dialysis catheter are in the femoral and subclavian/internal jugular position respectively, a constellation that is best avoided. Or stated otherwise "when the dialysis catheter is placed in between the bolus injection site and the central blood temperature

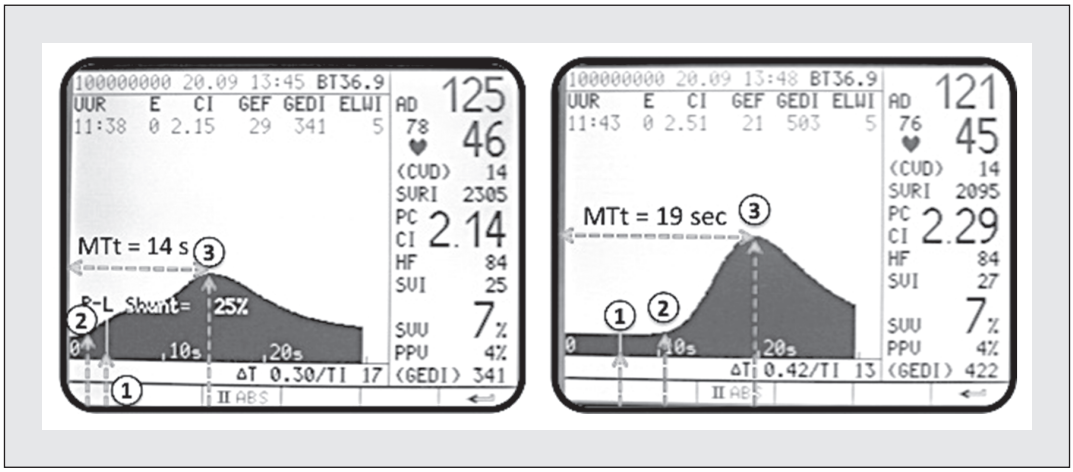


Figure 19. Analysis of thermodilution curves — cross-talk phenomenon. Example of cross-talk phenomenon as shown on TPTD curves obtained with $PiCCO_{plus}$ monitor. On the left-hand side injection and detection are at the femoral site while in the TPTD curve on the right-hand side the injection was via subclavian vein and detection was femoral. When there is a crosstalk phenomenon the cooling will take place immediately and already during the injection period (the end of the injection is indicated by number 1, while 2 indicates mean appearance time and start of cooling and number 3 the mean transit time)

measurement site (tip of PiCCO catheter)" [77]. The extent to which blood flow, filtration rate and temperature contribute to this has not been determined.

Observations suggest that the influence of extracorporeal circuit on the reliability of the TPTD measurements is related to the ratio of the cardiac output and the extracorporeal flow rate. It also has been suggested to wait with TPTD measurements when CRRT is stopped or started until blood temperature has reached a steady state. In extracorporeal lung assist systems, due to indicator loss in the extracorporeal circuit, cardiac output measurement as assessed by TPTD has been reported to be erroneously high, especially when high extracorporeal blood flows are applied [91, 92]. However, some reports suggest that EVLWI measurement is reliable if extracorporeal blood flow does not exceed 20% of cardiac output [91, 93]. The effects of an extracorporeal circuit are probably more pronounced if CO is low and the blood flow over the circuit is high (blood flow during continuous veno-venous haemofiltration (CVVH) is generally around 150–180 mL min^{-1}, compared to 450 mL min^{-1} during dialysis and 3 or more L min^{-1} during extracorporeal membrane oxygenation (ECMO). Furthermore other aspects may also play a role such as the amount of ultrafiltration and the blood temperature. Normally the use of CVVH causes a drop in baseline temperature; stopping the CVVH momentarily may give a rise in central temperature after the inflow of colder fluids coming from the CVVH stops as suggested previously [88]. The effect of rising and falling baseline temperatures is illustrated in Figure 20.

STEP 5. EFFECT OF VALVULOPATHY AND HEART FUNCTION

Little literature is available in patients with valvulopathy with conflicting data: a small study in 18 patients undergoing transcatheter aortic valve implantation (TAVI) for severe aortic stenosis (AS) suggests that stroke volume measurements derived by TPTD are accurate — compared to transoesophageal echocardiography — during all investigated haemodynamic situations (AS, AI [aortic insuffciency], after TAVI), as were measurements by calibrated pulse contour in AS and after TAVI. In contrast, pulse contour (calibrated and uncalibrated) was not accurate in severe AI [25, 94]. Trending ability seems to be acceptable for each measurement modality [94, 95]. Regurgitation of the thermodilution injectate can prolong the transit time of the indicator or interfere with the thermodilution curve. However, where a thermodilution curve is possible, the calculation of the cardiac output is correct. The long and flat running of the TD curve may result in an overestimation in the GEDVI and EVLWI. Mitral regurgitation (MR) gives a consistent increase in the volumetric parameters while aortic stenosis gives an inconsistent increase (see Fig. 21). The same holds true when using a Swan-Ganz catheter in patients with severe tricuspid regurgitation [96–99]. In a case of right ventricular failure, CFI and GEF underestimate left ventricular function,

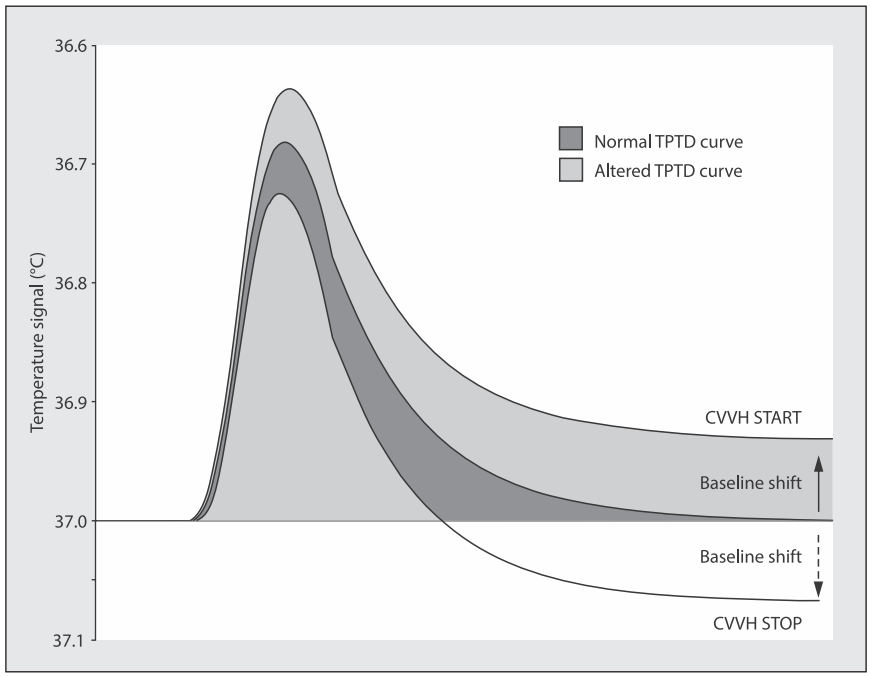


Figure 20. Effect of CVVH on baseline temperature and TPTD curves (adapted from [88]). During starting of CVVH cold blood flows from the CVVH machine into the central circulation and the baseline temperature drops (full arrow) resulting in an increased area under the curve and a decrease in TPTD cardiac output. Vice versa, during stopping of CVVH the baseline temperature rises (dotted arrow) resulting in a diminished area under the curve and an increase in TPTD cardiac output

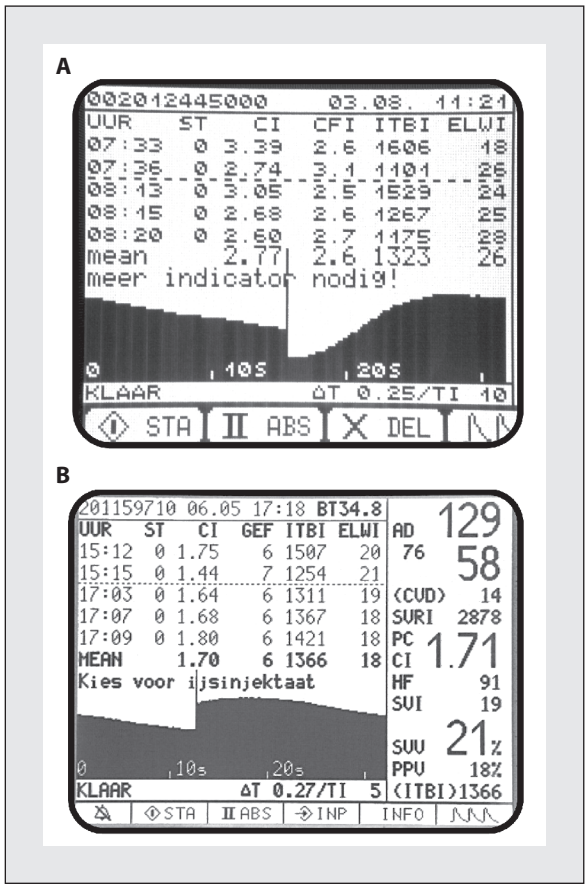


Figure 21. Transpulmonary thermodilution in valvulopathy. **A** — TPTD results obtained with $PiCCO_{classic}$ monitor in a patient with aortic stenosis (valve surface area 0.8 cm^{-2} and peak gradient 88 mm Hg) showing inconsistently increased values (with huge variations) of GEDVI (ranging from 1101 to 1606 mL m^{-2}) and EVLWI (ranging from 18 to 28 mL kg^{-1}); **B** — TPTD results obtained with $PiCCO_{classic}$ monitor in a patient with severe mitral regurgitation showing consistently increased (close to each other) values of GEDVI (ranging from 1311 to 1421) and EVLWI (ranging from 18 to 19)

as these represent global myocardial contraction. On the other hand, if these parameters are normal, left ventricular function is preserved [43]. In our institution, we perform an echocardiography in all haemodynamically unstable patients at least once [17, 96, 97, 100]. Larger studies are warranted to examine the magnitude of influence of valvular and cardiac function on TPTD [25].

STEP 6. CORRECTION FOR GEF

Static monitoring of the volumetric parameters (GEDV) has not consistently been shown to be able to predict

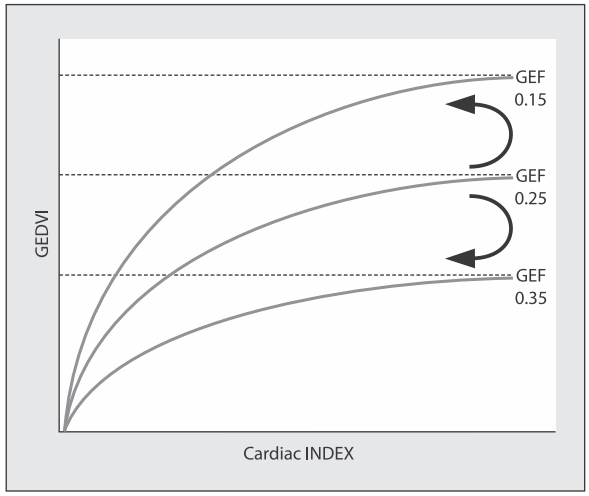


Figure 22. Ventricular function curves by GEF. GEDVI must be interpreted in conjunction with the patient's GEF (GEF — global ejection fraction, GEDVI — global end-diastolic volume index)

changes in CI. For any patient admitted to the ICU who becomes haemodynamically unstable, it is important to know what the Frank-Starling curve looks like and where the patient is situated on the curve (Fig. 22).

After correction for ejection fraction, correlation between the corrected GEDVI (cGEDVI) and CI becomes better and statistically significant [22, 101, 102]. We suggest a 'GEF-corrected' GEDVI; assuming a normal GEF of approximately 0.30 in critically ill patients, the cGEDVI would then be 625 mL m^{-2}. The formula to calculate cGEDVI is given below:

$$cGEDVI = \frac{GEDVI}{exp\,(2.74 \times (0.3 - GEF))}$$

According to that approach, patients with a lower contractile reserve, as estimated by GEF, would then have a goal for resuscitation to proportionally higher GEDVI values. Table 4 lists GEF-adjusted target values based on this approach, in normal and critically ill conditions, while Figure 23 shows an EF-nomogram for GEDVI resuscitation target values related to GEF values. A patient with a GEF of 0.25 might have a *target* GEDVI value of 775 mL m^{-2}, whereas a patient with a GEF of 0.15 might have a *target* GEDVI of 950 mL m^{-2}. However, target values for corrected GEDVI represent at this stage only a proposal which needs to be evaluated by future studies.

Table 4. Global ejection fraction corrected volumetric target values

Ejection Fraction	5%	10%	15%	20%	25%	30%	35%	40%	45%	50%	55%
GEDVI-target (normal)	1,175	1,050	950	850	775	700	625	575	525	475	435
GEDVI-target (critically ill)	1,450	1,300	1,150	1,025	925	825	750	675	600	550	500

critically ill — refers to an unstable patient with clinical diminished preload; GEDVI — global enddiastolic volume index; normal — refers to a stable patient

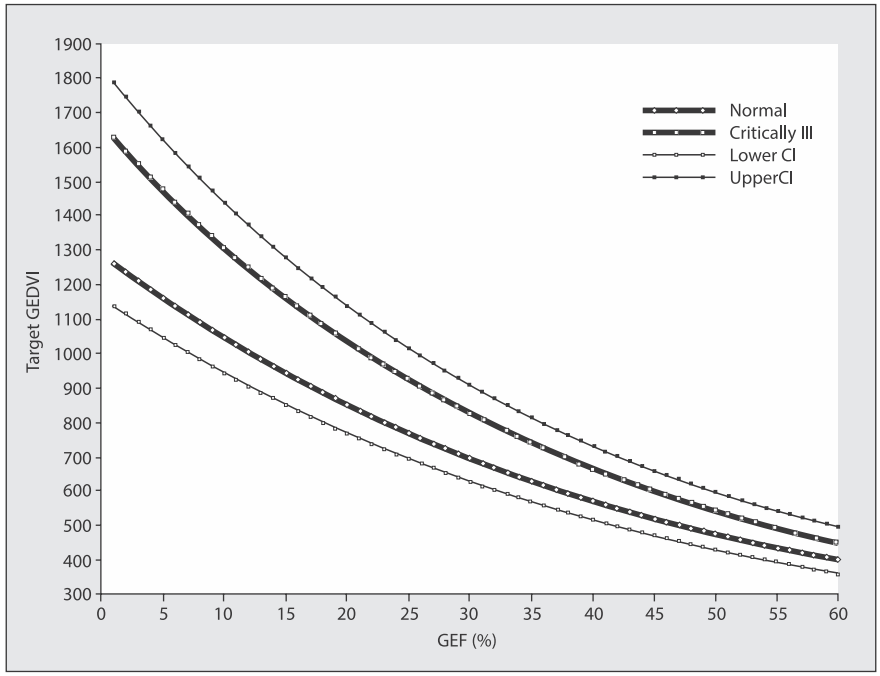


Figure 23. Ejection fraction (EF)-nomogram for global enddiastolic volume index (GEDVI) resuscitation target values in relation to observed global ejection fraction (GEF) values

STEP 7. EFFECT OF PLEURAL EFFUSION

The aetiology of pulmonary opacities, especially when bilateral, can be heterogeneous. EVLW has shown a good correlation with the degree of pulmonary oedema which can be cardiogenic or non-cardiogenic [45]. The PVPI may help to differentiate between hyperpermeability versus hydrostatic oedema in a case of increased EVLWI [103]. Pleural effusions do not contribute to the dilution of the thermal indicator in single transpulmonary thermodilution measurements and consequently do not increase TPTD-derived EVLW [20, 104]. Therefore, if EVLWI is normal (EVLW ≤ 10 mL kg^{-1}), the presence of a 'white' chest X-ray may prompt the clinician to perform a thorax ultrasound to look for a pleural effusion.

STEP 8. NORMAL VALUES AND INDEXATION

With the first PiCCO devices, actual body weight and derived body surface area were used for indexing of output and volumetric parameters. Later software versions, the Philips® module but also the latest PiCCO$_2$ device, allow using predicted rather than actual body weight and the derived predicted body surface area for indexing the volumetric parameters (GEDVI, ITBVI) and the extravascular lung water (EVLWI). This improves accuracy in obese patients and improves correlation with severity of illness and survival in acute lung injury patients [105–107]. Recent data shows that no indexation at all or indexation related to height is better [108], as suggested by others [109, 110]. The problem is that there are no good ranges for normal values and such algorithms and decision trees should be used with caution [21, 111].

STEP 9. WHAT AFTER PNEUMONECTOMY? AORTIC ANEURYSM? PULMONARY EMBOLISM?

Limited data is available but it is believed that TPTD could be useful to detect postpneumonectomy pulmonary oedema early on by looking at trend of cardiac index and EVLW [16, 112, 113]. Correct calculation of the CO and GEDVI is possible in patients after pneumonectomy. The under-estimation of the EVLWI is dependent on the amount of lung resected, whereas the trend of the EVLWI remains accurate. Other conditions such as pulmonary embolism, aortic or left ventricular aneurysm (hidden volumes) or cardiac tamponade may also affect TPTD values [114–116]. If the patient is known with an aortic aneurysm and a femoral arterial catheter is used, GEDVI and ITBVI are overestimated due to the volume of the aneurysm, so a brachial, a long radial or axillary catheter is recommended [117]. When there is an obstruction of the pulmonary vasculature, in a case of pulmonary embolism or acute respiratory distress syndrome (ARDS) due to microthrombi and/or high levels of PEEP, the GEDVI will be overestimated while the EVLWI will be underestimated [23, 114, 116]. In a surgical intensive care unit population, the estimation of EVLW by was influenced by the amount of EVLW, the PaO_2/FiO_2 ratio, the tidal volume, and the level of positive end-expiratory pressure [114].

Oedematous lung areas may compress pulmonary vessels and enhance pulmonary vasoconstriction; both of these are factors that may reduce pulmonary blood volume and hence lead to overestimation of GEDVI and underestimation of EVLWI. However, compared to the double indicator method, transpulmonary thermodilution estimation remains clinically acceptable even in patients with severe lung disease.

STEP 10. INFLUENCE OF MODE OF VENTILATION: PEEP, BODY POSITIONING (PRONE POSITIONING) AND ONE-LUNG VENTILATION

One study in patients with acute lung injury suggests that EVLWI and cGEDVI increase in the prone position, due to an improved equilibration of the thermal indicator, but that the differences are small and presumably of no clinical significance [102]. Cardiac output with uncalibrated pulse contour on the other hand seems not to be reliable [24, 118]. Because of the small sample sizes in the studies, further research is warranted.

In a case of one–lung ventilation, the area under the thermodilution curve will not change and consequently the CO is reliable, however the MTt and DSt derived from the contour of the thermodilution curve and associated volumetric variables are affected and not correct [26, 119, 120]. The effect of PEEP on EVLW measurement is controversial as discussed by Michard in a nice review [116]. On one hand, the use of high levels of PEEP may be responsible for pulmonary vascular defects resulting in a decrease in EVLWI. On the other hand, by recruiting the lungs, PEEP may induce a redistribution of pulmonary blood flow toward previously excluded areas and hence artificially 'increase' EVLWI. Importantly, PEEP may have an effect not only on the measurement of EVLW by dilution methods but also on the real amount of EVLW. Indeed, PEEP may decrease EVLW by decreasing pulmonary capillary pressure (if cardiac output drops during PEEP application). In contrast, PEEP may increase EVLW by reducing lymph flow (PEEP does increase central venous pressure, the backward pressure for the lymphatic ducts) and by increasing lung volume (i.e. by decreasing the pulmonary interstitial pressure).

HOW TO INTERPRET FUNCTIONAL HAEMODYNAMICS IN TEN SIMPLE STEPS

The issues related to functional haemodynamics and the analysis of the continuous parameters are nicely reviewed elsewhere [121–123].

STEP 1. EFFECT OF SPONTANEOUS BREATHING

SVV and PPV are functional haemodynamic indices of fluid responsiveness that are continuously displayed on a beat-to-beat basis. Functional haemodynamics cannot be used if the patient is not intubated and mechanically ventilated or if the patient is breathing spontaneously on an assisted mode (ASB) [124, 125].

STEP 2. VENTILATOR SETTINGS: TIDAL VOLUME

Conditions that are necessary for correct interpretation are: controlled mechanical ventilation (i.e. no spontaneous breaths) and tidal volume ≥ 8 mL kg^{-1}. The latter can be a problem with a low tidal volume strategy in ARDS patients [126], but this is less problematic in stable postoperative patients [127]. Recent data shows that also lower tidal volumes are sufficient [128, 129].

STEP 3. VENTILATOR SETTINGS: RESPIRATORY RATE AND COMPLIANCE

Also high respiratory rates and low compliance of the respiratory system appear to reduce the ability for functional haemodynamic parameters like PPV and SVV to predict fluid responsiveness [130]. In those circumstances, passive leg raising or a tele-expiratory occlusion test may perform better [131]. Transmission of alveolar pressure to the vasculature is dependent on the compliance of the respiratory system. Teboul developed an index of transmission (IT) looking at the difference between end-inspiratory (ei) and end-expiratory (ee) CVP or PAOP values and calculated as:

$$IT = (CVP_{ei} - CVP_{ee})/(P_{plat} - PEEP)$$

$$IT = (PAOP_{ei} - PAOP_{ee})/(P_{plat} - PEEP)$$

Transmural CVP and PAOP can then be calculated as follows:

$$CVP_{tm} = CVP_{ee} - IT \times PEEP$$

$$PAOP_{tm} = PAOP_{ee} - IT \times PEEP$$

The index of transmission is higher the better the compliance (e.g. lung emphysema) [132]. As such in ARDS compliance is poor and so no huge impact is to be expected. Conversely, if blood pressure drops dramatically during a recruitment manoeuvre (e.g. low flow PV loop) in an ARDS patient and PPV increases, this always suggests low preload and fluid responsiveness.

STEP 4. WHAT IF PEEP IS HIGH OR DURING HIGH FREQUENCY VENTILATION?

The influence of high levels of PEEP is still unclear [133–135]. However some animal data suggests that in the setting of high PEEP levels, SVV may be a better predictor for fluid responsiveness, although the mechanism is

still unclear [135]. Because functional haemodynamics are based on cyclic changes in intrathoracic pressure induced by mechanical ventilation, SVV and PPV are not usable if the patient is under High Frequency Oscillatory Ventilation (HFOV) (CareFusion, San Diego, CA, USA) while it can still be used in patients undergoing High Frequency Percussive Ventilation (HFPV)(VDR4, Percussionnaire, Sagle, ID, USA) [136]. This can be explained by the fact that during HFPV tidal excursions are observed as with conventional positive pressure ventilation, in contrast to HFOV where only small oscillations are present.

STEP 5. EFFECT OF RIGHT HEART FUNCTION

Right ventricular dysfunction is a possible cause for an absent response to fluid loading when SVV or PPV are high. Peak tricuspid annulus systolic (TA Sa) velocity, with a proposed cut off value of 0.15 m sec^{-1}, and tricuspid annular plane systolic excursion (TAPSE) as echocardiographic measures of right ventricular systolic function can predict false-positive increase in SVV and PPV [137].

STEP 6. EFFECT OF ARRHYTHMIA

Another condition is that the patient must have a regular sinus rhythm, although some less invasive devices provide algorithms to correct for extrasystoles occurring at a low frequency. The pulse contour analysis may be correct in mild to moderate rhythm disturbances (normal rate atrial flutter (AFL) or fibrillation (AF), bigeminal, trigeminal or incidental extrasystoles). In severe cardiac rhythm disturbances (tachyarrhythmias, supraventricular tachycardia), pulse contour analysis may be inaccurate. Hence, in a case of AF with irregular ventricular response, the PPV and SVV values will be erroneously increased. It should be pointed out that the thermodilution parameters are measured correctly in the presence of severe arrhythmia (a common misunderstanding among nurses). On the other hand, if PPV is low and the patient has AF, then this surely means he/she is not fluid responsive. So in a case of low CO dobutamine should then be given instead of fluids.

STEP 7. WHAT IS BEST: SVV OR PPV?

Dynamic changes of arterial waveform-derived variables during mechanical ventilation are highly accurate in predicting volume responsiveness in critically ill patients, with an accuracy greater than that of traditional static indices of volume responsiveness. PPV seems to have the highest correlation with response to volume loading [33, 123, 138]. Even in the presence of large pleural effusions, functional haemodynamic parameters and volumetric preload indicators can reliably predict fluid responsiveness, as illustrated in an animal study [139].

STEP 8. WHAT IF INTRA-ABDOMINAL PRESSURE OR INTRATHORACIC PRESSURE IS HIGH OR LOW?

Evidence from several animal studies shows that intra-abdominal hypertension (IAH) can increase the values for SVV and PPV, an effect that seems to be proportional to the degree of IAH [138, 140, 141]. This can be observed in patients with severe acute pancreatitis [142]. This could lead to the false assumption that the patient is volume-responsive. In this respect, it is worth noting that the passive leg raising (PLR) manoeuvre needs to be performed differently in the presence of IAH, i.e. in the Trendelenburg position [131, 143], as the PLR can be false negative in situations of increased IAP [144]. On the other hand, when intrathoracic pressure (ITP) is low, as in patients after sternotomy, functional haemodynamics should be interpreted with caution as some studies have shown a good [145, 146] while others have shown a poor [147, 148] predictive value for predicting fluid responsiveness under open chest or open pericardium conditions. The same may hold true in patients under ECMO where the ventilator is set at minimal tidal volume excursions: in those patients, PLR based on changes in SVV performed better than PPV [149].

STEP 9. CATHETER WHIP ARTEFACT AND USE OF INTRA-AORTIC BALLOON COUNTERPULSATION

Occasionally, in a situation of hyperdynamic circulation such as aortic regurgitation, severe sepsis, or any condition associated with high output cardiac failure (thiamine deficiency, thyreotoxicosis, burns, severe acute pancreatitis, chronic anaemia, AV fistula, multiple myeloma, Morbus Paget) catheter whip artefact can be mistaken for a true signal and included in the pulse contour analysis by the software algorithm (our own observations, unpublished). This may result in it being impossible to measure continuous cardiac output, or in a CO value that is erroneously low. An example is given in Figure 24 [150]. A similar issue can occur during the use of an intra-aortic balloon pump (IABP). It should be noted that the use of continuous CO measurement based on the principle of pulse contour analysis is not a viable option during IABP [151]. The intermittent transpulmonary thermodilution derived parameters on the other hand remain accurate. The reason for this discrepancy is the alteration of the aortic pressure curve caused by the inflation and deflation of the intra-aortic balloon resulting in a double-peaked pressure curve (diastolic augmentation) for every heart cycle. As a simple rule of thumb, in order to obtain a correct value, the following adjustment needs to be considered for the pulse contour-derived cardiac output (PCCO), depending on the counterpulsation ratio: for a 1:1 ratio divide the PCCO by 2; for a 1:2 ratio, divide by 3 and multiply by 2; in a case of 1:3 augmentation, correct CO can be calculated by

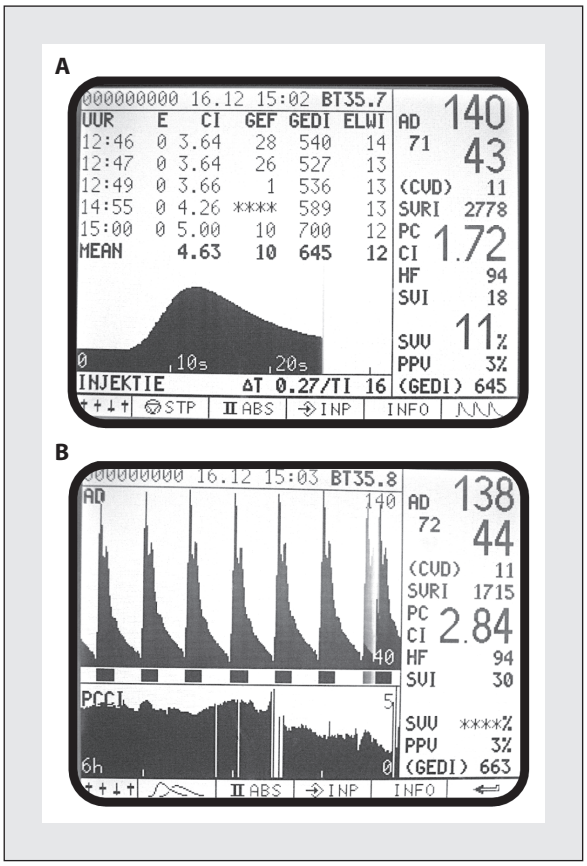


Figure 24. Catheter whip artefact. **A** — TPTD calibration in patient with catheter whip artefact. Note the difference between the intermittent and pulse contour cardiac output and the false extremely low GEF; **B** — Underdamped arterial pressure curve showing presystolic augmentation

dividing PCCO by 4 and multiplying by 3, etc. Alternatively, the use of a CCO PAC may provide continuous cardiac output measurements during counterpulsation, although this has not been validated yet.

STEP 10. EFFECT OF VASOMOTOR TONE

Because the accuracy of the arterial pulse contour is dependent on different variables (e.g. arterial compliance), the PiCCO device has to be calibrated every eight hours (in practice this corresponds to once every nursing shift). However, whenever a significant change occurs in the patient's afterload (vasopressor use), preload (fluid therapy) or contractility (catecholamine requirements), earlier recalibration may be recommended [56, 152–157]. Systolic and pulse pressures depend not only on stroke volume, but also on arterial compliance. Thus, PPV could vary from one patient to another according to the arterial compliance. Therefore, if arterial compliance is low (e.g. patients with significant peripheral vascular disease or atherosclerosis), this can be translated to large changes in arterial pressure despite small changes in stroke volume. Conversely, if arterial compliance is high (e.g. young patients without vascular disease), small changes in arterial pressure could be seen despite large changes in stroke volume. This explains why some patients only respond with an increase in systolic pressure during PLR, while others have an increase in both stroke volume and systolic arterial pressure [158, 159].

DISCUSSION

The PiCCO haemodynamic monitoring system has been in clinical use since 1997 (PiCCO *Classic*) in Europe and received FDA approval in 2000 in the United States. An updated version named PiCCO *Plus* was launched in 2002; in 2005, a software update (version 7.0) was introduced and since 2007 the software has been updated to use PBW (7.1). Around the same time, the PiCCO$_2$ was introduced to intensive care physicians. An overview of the patient monitors that can be linked to the PiCCO system is given in Table 5 and the parameters obtained with PiCCO technology can be imported directly to several Patient Data Management Systems (PDMS).

The PiCCO has gained a place in the field of haemodynamic monitoring in critically ill patients admitted to the Intensive Care Unit (ICU) or Operating Room (OR), which was ruled by the pulmonary artery catheter for decades. Compared to the PAC, its major advantages are that it is less invasive and is independent of the respiratory cycle, allows beat-to-beat analysis, gives additional information on volumetric preload and extravascular lung water, and no loss of indicator in case of a right-to-left shunt. On the other hand, PiCCO cannot measure pulmonary artery pressures, but with the advent of transthoracic and transoesophageal echocardiography as a readily available tool in the modern ICU, these can also be estimated non-invasively [160–163].

Mixed venous oxygen saturation monitoring is also confined to the PAC, but with the PiCCO2 being able to continuously measure central venous oxygen saturation, closely related to mixed venous oxygen saturation in the majority of patients, this advantage of the PAC has also become a relative one [2]. Haemodynamic monitoring should be individualised and dependent on the underlying disease, keeping in mind the strengths, weaknesses, advantages, disadvantages and limitations of the method chosen [2, 10, 101, 162, 164–177].

Table 5. Availability of PiCCO modules with different monitoring companies

• Spacelabs Monitoring Systems (Issaquah, WA, USA)
• GE Healthcare`s Monitoring Systems (London, UK)
• Philips Healthcare (Eindhoven, the Netherlands)
• Draeger Medical (Lubeck, Germany)
• Nihon Kohden (Tokyo, Japan)
• Mindray (Nanshan, Shenzhen, P. R. China)

As suggested before [123], the combination of the PiCCO technology and echocardiography seems to be an all-encompassing and powerful method for monitoring haemodynamically unstable patients. The results of recent studies in patients with subarachnoid bleeding (at risk for neurogenic oedema) and severe burn injury have shed new light on the use, usefulness and indications for TPTD monitoring beyond the classical patients with cardiogenic or septic shock or those presenting with hydrostatic vs permeability pulmonary oedema [19, 35, 178–181]. But as with any technology, it stands or falls on the accuracy and reproducibility of the parameters collected. Moreover, no parameter has ever improved outcomes, only a good protocol can do that [2, 182]. These haemodynamic treatment algorithms should follow physiology or they may also fail to improve outcomes [111, 162].

The PiCCO has been extensively validated with the PAC as comparator and new devices using the TPTD method are promising [2, 10]. Some authors have raised concerns about the mathematical analysis of the thermodilution curve and the physiological significance of the two parameters GEDV and EVLW as they are mathematically coupled with CO [183]. The fact that these volumetric haemodynamic indices are clinically applicable and useful, however, has been extensively demonstrated and in this regard we agree with Della Rocca and Teboul in their response to Bigatello [184]. Michard also nicely showed that fluid loading increases both GEDVI and CI while dobutamine only increased CI, hence confirming the fact that both parameters are not mathematically coupled at the bedside [36]. To confuse things further, a recent publication claimed again the presence of mathematical coupling [185]. However, this was only a small study in 17 patients where dobutamine administration significantly increased CI by 48 ± 35%, whereas the average increase in GEDVI was only 8.2 ± 12.3%. The change in GEDVI was statistically significant ($P < 0.0001$), but clinically probably not relevant [185].

As with all technologies, the usefulness relies on correct understanding of the principles, a flawless measurement technique, and a correct interpretation of the obtained values in different scenarios.

From our survey among ICU personnel, it appears that knowledge on the PiCCO is far from optimal. We have tried to give the reader a guide for correct use of the device with hints for specific situations and a few caveats. The protocol used in our unit to obtain a good TPTD calibration is shown in Figure 25.

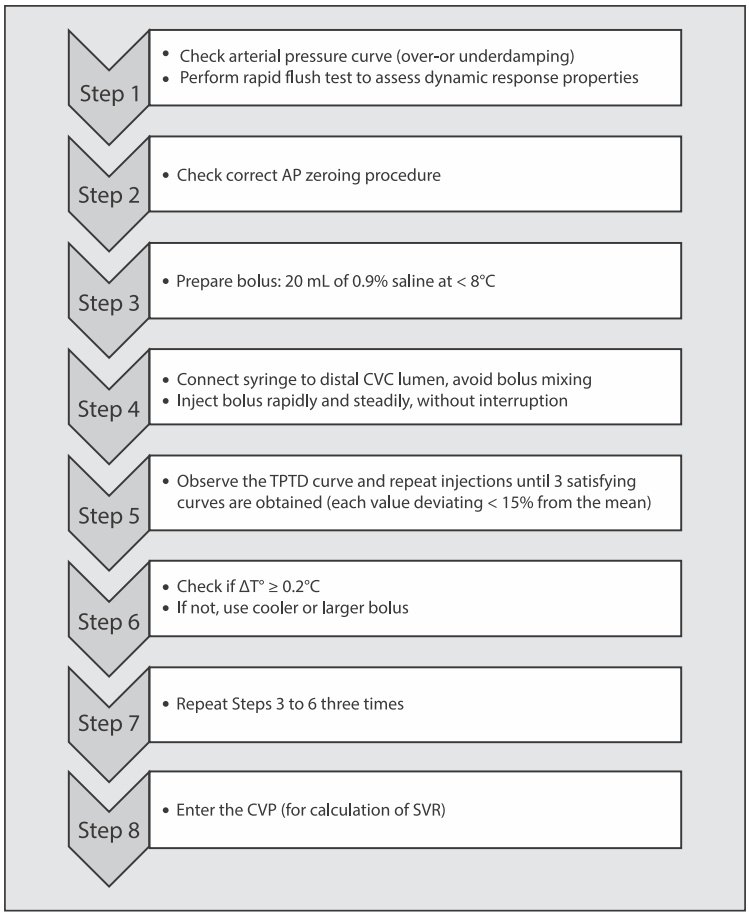


Figure 25. Standard TPTD measurement protocol (see text for details)

CONCLUSION

From our survey, we can conclude that knowledge on the use and interpretation of the PiCCO, although being used regularly, is suboptimal among ICU personnel. This triggered our ambition to review the available published literature on the use of PiCCO technology in specific circumstances. Based on this, and on the long experience we have in our institution, we have tried to give the interested reader a schematic overview on how to use the device and how to interpret the obtained parameters correctly at the bedside.

References:

1. *Cecconi M, Dawson D, Casaretti R, Grounds RM, Rhodes A:* A prospective study of the accuracy and precision of continuous cardiac output monitoring devices as compared to intermittent thermodilution. Minerva Anestesiol 2010; 76: 1010–1017.
2. *Malbrain ML, De Potter P, Deeren D:* Cost-effectiveness of minimally invasive hemodynamic monitoring. Yearbook of Intensive Care and Emergency Medicine 2005: 603–618.
3. *Pinsky MR, Vincent JL:* Let us use the pulmonary artery catheter correctly and only when we need it. Crit Care Med 2005; 33: 1119–1122.
4. *Cecconi M, Rhodes A, Poloniecki J, Della Rocca G, Grounds RM:* Bench-to-bedside review: The importance of the precision of the reference technique in method comparison studies — with specific reference to the measurement of cardiac output. Crit Care 2009; 13: 201.
5. *Vincent JL, Pinsky MR, Sprung CL et al.:* The pulmonary artery catheter: in medio virtus. Crit Care Med 2008; 36: 3093–3096.
6. *Harvey S, Harrison DA, Singer M et al.:* Assessment of the clinical effectiveness of pulmonary artery catheters in management of patients in intensive care (PAC-Man): a randomised controlled trial. Lancet 2005; 366: 472–477.
7. *Connors AF, Jr., Speroff T, Dawson NV et al.:* The effectiveness of right heart catheterization in the initial care of critically ill patients. SUPPORT Investigators. JAMA 1996; 276: 889–897.
8. *Kiefer N, Hofer CK, Marx G et al.:* Clinical validation of a new thermodilution system for the assessment of cardiac output and volumetric parameters. Crit Care 2012; 16: R98.
9. *Bendjelid K, Giraud R, Siegenthaler N, Michard F:* Validation of a new transpulmonary thermodilution system to assess global end-diastolic volume and extra-vascular lung water. Crit Care 2010; 14: R209.
10. *Palmers PJ, Vidts W, Ameloot K et al.:* Assessment of three minimally invasive continuous cardiac output measurement methods in critically ill patients and a review of the literature. Anaesthesiol Intensive Ther 2012; 44: 213–224.
11. *Hamzaoui O, Monnet X, Teboul JL:* Transpulmonary thermodilution. In: *Ehrenfeld JM, Cannesson M (ed:)* Monitoring technologies in acute care environments. Springer Science + Business Media, New York 2014.
12. *Litton E, Morgan M:* The PiCCO monitor: a review. Anaesth Intensive Care 2012; 40: 393–409.
13. *Duan J, Cong LH, Wang H, Zhang Y, Wu XJ, Li G:* Clinical evaluation compared to the pulse indicator continuous cardiac output system in the hemodynamic assessment of critically ill patients. Am J Emerg Med 2014; 32: 629–633.
14. *Meybohm P, Gruenewald M, Renner J et al.:* Assessment of left ventricular systolic function during acute myocardial ischemia: a comparison of transpulmonary thermodilution and transesophageal echocardiography. Minerva Anestesiol 2011; 77: 132–141.
15. *Sakka SG, Ruhl CC, Pfeiffer UJ et al.:* Assessment of cardiac preload and extravascular lung water by single transpulmonary thermodilution. Intensive Care Med 2000; 26: 180–187.
16. *Hofmann D, Klein M, Wegscheider K, Sakka SG:* Extended hemodynamic monitoring using transpulmonary thermodilution influence of various factors on the accuracy of the estimation of intrathoracic blood volume and extravascular lung water in critically ill patients. Anaesthesist 2005; 54: 319–326.
17. *Lenkin AI, Kirov MY, Kuzkov VV et al.:* Comparison of goal-directed hemodynamic optimization using pulmonary artery catheter and transpulmonary thermodilution in combined valve repair: a randomized clinical trial. Crit Care Res Pract 2012; 2012: 821218.
18. *Keller G, Desebbe O, Henaine R, Lehot JJ:* Transpulmonary thermodilution in a pediatric patient with an intracardiac left-to-right shunt. J Clin Monit Comput 2011; 25: 105–118.
19. *Sanchez M, Garcia-de-Lorenzo A, Herrero E et al.:* A protocol for resuscitation of severe burn patients guided by transpulmonary thermodilution and lactate levels: a 3-year prospective cohort study. Crit Care 2013; 17: R176.
20. *Deeren DH, Dits H, Daelemans R, Malbrain ML:* Effect of pleural fluid on the measurement of extravascular lung water by single transpulmonary thermodilution. Clin Intensive Care 2004; 15: 119–122.
21. *Eichhorn V, Goepfert MS, Eulenburg C, Malbrain ML, Reuter DA:* Comparison of values in critically ill patients for global end-diastolic volume and extravascular lung water measured by transcardiopulmonary thermodilution: a metaanalysis of the literature. Med Intensiva 2012; 36: 467–474.
22. *Malbrain ML, De Potter TJ, Dits H, Reuter DA:* Global and right ventricular end-diastolic volumes correlate better with preload after correction for ejection fraction. Acta Anaesthesiol Scand 2010; 54: 622–631.
23. *Oren– Grinberg A:* The PiCCO Monitor. Int Anesthesiol Clin 2010; 48: 57–85.
24. *Sakka SG, Reuter DA, Perel A:* The transpulmonary thermodilution technique. J Clin Monit Comput 2012; 26: 347–353.
25. *Reuter DA, Huang C, Edrich T, Shernan SK, Eltzschig HK:* Cardiac output monitoring using indicator-dilution techniques: basics, limits, and perspectives. Anesth Analg 2010; 110: 799–811.
26. *Haas SA, Trepte CJ, Nitzschke R et al.:* An assessment of global end-diastolic volume and extravascular lung water index during one-lung ventilation: is transpulmonary thermodilution usable? Anesth Analg 2013; 117: 83–90.
27. *Hewitt NA, Braaf SC:* The clinical application of pulse contour cardiac output and intrathoracic volume measurements in critically ill patients. Aust Crit Care 2006; 19: 86–94.
28. *Isakow W, Schuster DP:* Extravascular lung water measurements and hemodynamic monitoring in the critically ill: bed-side alternatives to the pulmonary artery catheter. Am J Physiol Lung Cell Mol Physiol 2006; 291: 1118–1133.
29. *Segal E, Katzenelson R, Berkenstadt H, Perel A:* Transpulmonary thermodilution cardiac output measurement using the axillary artery in critically ill patients. J Clin Anesth. 2002; 14: 210–213.
30. *Giraud R, Siegenthaler N, Bendjelid K:* Transpulmonary thermodilution assessments: precise measurements require a precise procedure. Crit Care 2011; 15: 195.
31. *Huang CC, Chen NH, Li LF et al.:* Effects of cardiac output levels on the measurement of transpulmonary thermodilution cardiac output in patients with acute respiratory distress syndrome. J Trauma Acute Care Surg 2012; 73: 1236–1241.
32. *Sakka SG, Reinhart K, Meier-Hellmann A:* Comparison of pulmonary artery and arterial thermodilution cardiac output in critically ill patients. Intensive Care Med 1999; 25: 843–846.
33. *Wiesenack C, Fiegl C, Keyser A, Prasser C, Keyl C:* Assessment of fluid responsiveness in mechanically ventilated cardiac surgical patients. Eur J Anaesthesiol 2005; 22: 658–665.
34. *Muller L, Candela D, Nyonzyma L et al.:* Disagreement between pulse contour analysis and transpulmonary thermodilution for cardiac output monitoring after routine therapeutic interventions in ICU patients with acute circulatory failure. Eur J Anaesthesiol. 2011; 28: 664–669.
35. *Mutoh T, Kazumata K, Terasaka S, Taki Y, Suzuki A, Ishikawa T:* Impact of transpulmonary thermodilution-based cardiac contractility and extravascular lung water measurements on clinical outcome of patients with Takotsubo cardiomyopathy after subarachnoid hemorrhage: a retrospective observational study. Crit Care 2014; 18: 482.
36. *Michard F, Alaya S, Zarka V, Bahloul M, Richard C, Teboul JL:* Global end-diastolic volume as an indicator of cardiac preload in patients with septic shock. Chest 2003; 124: 1900–1908.
37. *Dres M, Teboul JL, Guerin L et al.:* Transpulmonary thermodilution enables to detect small short-term changes in extravascular lung water induced by a bronchoalveolar lavage. Crit Care Med 2014; 42: 1869–1873.
38. *Jozwiak M, Silva S, Persichini R et al.:* Extravascular lung water is an independent prognostic factor in patients with acute respiratory distress syndrome. Crit Care Med 2013; 41: 472–480.
39. *Friesecke S, Heinrich A, Abel P, Felix SB:* Comparison of pulmonary artery and aortic transpulmonary thermodilution for monitoring of cardiac output in patients with severe heart failure: validation of a novel method. Crit Care Med 2009; 37: 119–123.

40. *Nirmalan M, Willard TM, Edwards DJ, Little RA, Dark PM:* Estimation of errors in determining intrathoracic blood volume using the single transpulmonary thermal dilution technique in hypovolemic shock. Anesthesiology 2005; 103: 805–812.
41. *Kushimoto S, Taira Y, Kitazawa Y et al.:* The clinical usefulness of extravascular lung water and pulmonary vascular permeability index to diagnose and characterize pulmonary edema: a prospective multicenter study on the quantitative differential diagnostic definition for acute lung injury/acute respiratory distress syndrome. Crit Care 2012; 16: R232.
42. *Perel A:* Extravascular lung water and the pulmonary vascular permeability index may improve the definition of ARDS. Crit Care 2013; 17: 108.
43. *Aguilar G, Belda FJ, Ferrando C, Jover JL:* Assessing the left ventricular systolic function at the bedside: the role of transpulmonary thermodilution-derived indices. Anesthesiol Res Pract 2011; 2011: 927421.
44. *Sakka SG:* Extravascular lung water in ARDS patients. Minerva Anestesiol 2013; 79: 274–284.
45. *Tagami T, Kushimoto S, Yamamoto Y et al.:* Validation of extravascular lung water measurement by single transpulmonary thermodilution: human autopsy study. Crit Care 2010; 14: R162.
46. *Belda FJ, Aguilar G, Jover JL, Ferrando C, Postigo S, Aznarez B:* Clinical validation of minimally invasive evaluation of systolic function. Rev Esp Anestesiol Reanim 2010; 57: 559–564.
47. *De Iaet I, Deeren D, Schoonheydt K, Van Regenmortel N, Dits H, Malbrain ML:* Renal replacement therapy with net fluid removal lowers intra-abdominal pressure and volumetric indices in critically ill patients. Ann Intensive Care 2012; 2 (Suppl 1): S20.
48. *Michard F:* Changes in arterial pressure during mechanical ventilation. Anesthesiology 2005; 103: 419–428; quiz 49–55.
49. *Benington S, Ferris P, Nirmalan M:* Emerging trends in minimally invasive haemodynamic monitoring and optimization of fluid therapy. Eur J Anaesthesiol 2009; 26: 893–905.
50. *Michard F, Chemla D, Richard C et al.:* Clinical use of respiratory changes in arterial pulse pressure to monitor the hemodynamic effects of PEEP. Am J Respir Crit Care Med 1999; 159: 935–939.
51. *Wang XT, Li SW, Chai WZ et al.:* Clinical role of evaluating vascular paralysis in septic shock patients. Zhonghua Yi Xue Za Zhi 2013; 93: 2778–2781.
52. *Proulx F, Lemson J, Choker G, Tibby SM:* Hemodynamic monitoring by transpulmonary thermodilution and pulse contour analysis in critically ill children. Pediatr Crit Care Med 2011; 12: 459–466.
53. *Gergely M, Ablonczy L, Kramer S et al.:* Comparison of transpulmonary thermodilution, transthoracic echocardiography and conventional hemodynamic monitoring in neonates and infants after open heart surgery: a preliminary study. Minerva Anestesiol 2012; 78: 1101–1108.
54. *Trepte CJ, Bachmann KA, Stork JH et al.:* The impact of early goal-directed fluid management on survival in an experimental model of severe acute pancreatitis. Intensive Care Med 2013: 39: 717–726.
55. *Salzwedel C, Puig J, Carstens A et al.:* Perioperative goal-directed hemodynamic therapy based on radial arterial pulse pressure variation and continuous cardiac index trending reduces postoperative complications after major abdominal surgery: a multi-center, prospective, randomized study. Crit Care 2013; 17: R191.
56. *Hamzaoui O, Monnet X, Richard C, Osman D, Chemla D, Teboul JL:* Effects of changes in vascular tone on the agreement between pulse contour and transpulmonary thermodilution cardiac output measurements within an up to 6-hour calibration-free period. Crit Care Med 2008; 36: 434–440.
57. *Huber W, Koenig J, Saugel B, Schuster T, Schmid R, Mair S:* Accuracy of the $PiCCO_2$-derived pulse contour cardiac index (CIpc): development and validation of a calibration index in two independent collectives. Crit Care 2012; 16 (Suppl 1): P222.
58. *Huber W, Waldleitner K, Mair S, Saugel B, Schmid RM:* Evaluation of a new calibration index suggesting recalibration of the pulse contour cardiac index by transpulmonary thermodilution: a prospective study. Crit Care 2013; 17 (Suppl 2): P188.
59. *King D, Price A:* Measuring cardiac output using the PiCCO system. British Journal of Cardiac Nursing 2008; 3: 512–519.
60. *Faybik P, Hetz H, Baker A, Yankovskaya E, Krenn CG, Steltzer H:* Iced versus room temperature injectate for assessment of cardiac output, intrathoracic blood volume, and extravascular lung water by single transpulmonary thermodilution. J Crit Care 2004; 19: 103–207.
61. *Huber W, Kraski T, Haller B et al.:* Room-temperature vs. iced saline indicator injection for transpulmonary thermodilution. J Crit Care 2014; 29: 1133.e7–1133.e14.
62. *Monnet X, Persichini R, Ktari M, Jozwiak M, Richard C, Teboul JL:* Precision of the transpulmonary thermodilution measurements. Crit Care 2011; 15: R204.
63. *Sami A, Sami A, Rochdil N, Hatem K, Salah BL:* PiCCO monitoring accuracy in low body temperature. Am J Emerg Med 2007; 25: 845–856.
64. *Ong T, Gillies MA, Bellomo R:* Failure of continuous cardiac output measurement using the PiCCO Device during induced hypothermia: a case report. Crit Care Resusc 2004; 6: 99–101.
65. *Tagami T, Kushimoto S, Tosa R et al.:* The precision of PiCCO(R) measurements in hypothermic post-cardiac arrest patients. Anaesthesia 2012; 67: 236–243.
66. *Holm C, Mayr M, Horbrand F et al.:* Reproducibility of transpulmonary thermodilution measurements in patients with burn shock and hypothermia. J Burn Care Rehabil 2005; 26: 260–265.
67. *Mekontso Dessap A, Boissier F, Leon R et al.:* Prevalence and prognosis of shunting across patent foramen ovale during acute respiratory distress syndrome. Crit Care Med 2010; 38: 1786–1792.
68. *Michard F, Phillips C:* The camel curve: the icing on the transpulmonary thermodilution cake. Crit Care Med 2011; 39: 611–612.
69. *Hermans GM, Wilmer A, Knockaert DC, Bobbaers H:* Acute intracardiac right-to-left shunt in a patient with acute respiratory distress syndrome and shock successfully treated with nitric oxide. Br J Anaesth 2006; 96: 268–269.
70. Michard F, Alaya S, Medkour F. Monitoring right-to-left intracardiac shunt in acute respiratory distress syndrome. Crit Care Med 2004; 32: 308–309.
71. *Schwarzkopf K, Simon S, Preussler NP, Huter L:* Measurement of cardiac output in ventricular rupture following acute myocardial infarction — pulmonary artery catheter vs transpulmonary thermodilution — a case report. Middle East J Anaesthesiol 2009; 20: 105–106.
72. *Suga Y, Uchino S, Saito K et al.:* Arterio-vena caval fistula detected by monitoring of transpulmonary thermodilution curves. J Anesth 2014; 28: 794–795.
73. *Nusmeier A, van der Hoeven JG, Lemson J:* Interpretation of the transpulmonary thermodilution curve in the presence of a left-to-right shunt. Intensive Care Med 2011; 37: 550–551.
74. *Nusmeier A, de Boode WP, Hopman JC, Schoof PH, van der Hoeven JG, Lemson J:* Cardiac output can be measured with the transpulmonary thermodilution method in a paediatric animal model with a left-to-right shunt. Br J Anaesth 2011; 107: 336–343.
75. *Bendjelid K:* Monitoring intra-cardiac shunts correction with transpulmonary thermodilution curve: the best is yet to come! J Clin Monit Comput 2011; 25: 89–90.
76. *Schmidt S, Westhoff TH, Hofmann C et al.:* Effect of the venous catheter site on transpulmonary thermodilution measurement variables. Crit Care Med 2007; 35: 783–786.
77. *Van Craenenbroeck A, Van Ingelgem A, Palmers PJ et al.:* Influence of continuous venovenous hemofiltration (CVVH) and catheter position on transpulmonary thermodilution derived parameters with PiCCO. Intensive Care Med 2010; 36 (Suppl. 2): S294.
78. *Saugel B, Umgelter A, Schuster T, Phillip V, Schmid RM, Huber W:* Transpulmonary thermodilution using femoral indicator injection: a prospective trial in patients with a femoral and a jugular central venous catheter. Crit Care 2010; 14: R95.
79. *Michard F:* Looking at transpulmonary thermodilution curves: the cross-talk phenomenon. Chest 2004; 126: 656–657.
80. *Lemson J, van der Hoeven JG:* The 'cross-talk phenomenon' in transpulmonary thermodilution is blood-flow dependent. Neth J Crit Care 2009; 13: 311–314.
81. *Lemson J, Eijk RJ, van der Hoeven JG:* The 'cross-talk phenomenon' in transpulmonary thermodilution is flow dependent. Intensive Care Med 2006; 32: 1092.
82. *Keller R, Goettel N, Bendjelid K:* Transpulmonary thermodilution curve and the cross-talk phenomenon. Med Intensiva 2012; 36: 446–448.
83. *Schmidt S, Westhoff TH, Compton F, Zidek W, van der Giet M:* Avoiding the cross-talk phenomenon when assessing cardiac output using the transpulmonary thermodilution technique via the femoral vein access. Crit Care Med 2007; 35: 2670.
84. *Bendjelid K:* Avoiding the cross-talk phenomenon when assessing cardiac output using the transpulmonary thermodilution technique via the femoral vein access. Crit Care Med 2007; 35: 2670.

85. *Galluccio ST, Chapman MJ, Finnis ME:* Femoral-radial arterial pressure gradients in critically ill patients. Crit Care Resusc 2009; 11: 34–38.
86. *Orme RM, Pigott DW, Mihm FG:* Measurement of cardiac output by transpulmonary arterial thermodilution using a long radial artery catheter. A comparison with intermittent pulmonary artery thermodilution. Anaesthesia 2004; 59: 590–594.
87. *Belda FJ, Aguilar G, Teboul JL et al.:* Complications related to less-invasive haemodynamic monitoring. Br J Anaesth 2011; 106: 482–486.
88. *Heise D, Faulstich M, Morer O, Brauer A, Quintel M:* Influence of continuous renal replacement therapy on cardiac output measurement using thermodilution techniques. Minerva Anestesiol 2012; 78: 315–321.
89. *Dufour N, Delville M, Teboul JL et al.:* Transpulmonary thermodilution measurements are not affected by continuous veno-venous hemofiltration at high blood pump flow. Intensive Care Med 2012; 38: 1162–1168.
90. *Sakka SG, Hanusch T, Thuemer O, Wegscheider K:* The influence of venovenous renal replacement therapy on measurements by the transpulmonary thermodilution technique. Anesth Analg 2007; 105: 1079–1082.
91. *Sakka SG:* Influence of an extracorporeal lung assist system on transpulmonary thermodilution-derived variables. Br J Anaesth 2010; 104: 664–665.
92. *Mross M, Sakka SG:* Influence of different blood flows through a pumpless lung assist system on transpulmonary thermodilution-derived variables. Intensive Care Med 2010; 36: 369–370.
93. *Haller M, Zollner C, Manert W et al.:* Thermodilution cardiac output may be incorrect in patients on venovenous extracorporeal lung assist. Am J Respir Crit Care Med 1995; 152: 1812–1817.
94. *Petzoldt M, Riedel C, Braeunig J et al.:* Stroke volume determination using transcardiopulmonary thermodilution and arterial pulse contour analysis in severe aortic valve disease. Intensive Care Med 2013; 39: 601–611.
95. *Cecconi M, Malbrain ML:* Cardiac output obtained by pulse pressure analysis: to calibrate or not to calibrate may not be the only question when used properly. Intensive care medicine 2013; 39: 787–789.
96. *Nishikawa T, Dohi S:* Errors in the measurement of cardiac output by thermodilution. Can J Anaesth 1993; 40: 142–153.
97. *Breukers RM, Groeneveld AB, de Wilde RB, Jansen JR:* Transpulmonary versus continuous thermodilution cardiac output after valvular and coronary artery surgery. Interact Cardiovasc Thorac Surg 2009; 9: 4–8.
98. *Spinale FG, Mukherjee R, Tanaka R, Zile MR:* The effects of valvular regurgitation on thermodilution ejection fraction measurements. Chest 1992; 101: 723–731.
99. *Balik M, Pachl J, Hendl J:* Effect of the degree of tricuspid regurgitation on cardiac output measurements by thermodilution. Intensive Care Med 2002; 28: 1117–1121.
100. *Combes A, Berneau JB, Luyt CE, Trouillet JL:* Estimation of left ventricular systolic function by single transpulmonary thermodilution. Intensive Care Med 2004; 30: 1377–1383.
101. *Trof RJ, Danad I, Reilingh MW, Breukers RM, Groeneveld AJ:* Cardiac filling volumes versus pressures for predicting fluid responsiveness after cardiovascular surgery: the role of systolic cardiac function. Crit Care 2011; 15: R73.
102. *Brücken U, Grensemann J, Wappler F, Sakka S:* Influence of prone positioning on the measurement of transpulmonary thermodilution--derived variables in critically ill patients. Acta Anaesthesiol Scand 2011; 55: 1061–1067.
103. *Monnet X, Anguel N, Osman D, Hamzaoui O, Richard C, Teboul JL:* Assessing pulmonary permeability by transpulmonary thermodilution allows differentiation of hydrostatic pulmonary edema from ALI/ARDS. Intensive Care Med 2007; 33: 448–453.
104. *Saugel B, Phillip V, Ernesti C et al.:* Impact of large-volume thoracentesis on transpulmonary thermodilution-derived extravascular lung water in medical intensive care unit patients. J Crit Care 2013; 28: 196–201.
105. *Phillips CR, Chesnutt MS, Smith SM:* Extravascular lung water in sepsis--associated acute respiratory distress syndrome: indexing with predicted body weight improves correlation with severity of illness and survival. Crit Care Med 2008; 36: 69–73.
106. *Craig TR, Duffy MJ, Shyamsundar M et al.:* Extravascular lung water indexed to predicted body weight is a novel predictor of intensive care unit mortality in patients with acute lung injury. Crit Care Med 2010; 38: 114–120.
107. *Wolf S, Riess A, Landscheidt JF, Lumenta CB, Friederich P, Schuerer L:* Global end-diastolic volume acquired by transpulmonary thermodilution depends on age and gender in awake and spontaneously breathing patients. Crit Care 2009; 13: R202.
108. *Huber W, Hollthaler J, Schuster T et al.:* Association between different indexations of extravascular lung water (EVLW) and PaO_2/FiO_2: a two--center study in 231 patients. PLoS ONE 2014; 9: e103854.
109. *Huber W, Mair S, Gotz SQ et al.:* Extravascular lung water and its association with weight, height, age, and gender: a study in intensive care unit patients. Intensive Care Med. 2013; 39: 146–150.
110. *Wolf S, Riess A, Landscheidt JF, Lumenta CB, Schurer L, Friederich P:* How to perform indexing of extravascular lung water: a validation study. Crit Care Med 2013; 41: 990–998.
111. *Malbrain MLNG, Reuter D:* Hemodynamic treatment algorithms should follow physiology or they fail to improve outcome. Crit Care Med 2012; 40: 2923–2924.
112. *Roch A, Michelet P, D'Journo B et al.:* Accuracy and limits of transpulmonary dilution methods in estimating extravascular lung water after pneumonectomy. Chest 2005; 128: 927–933.
113. *Leo F, Tullii M, Della Grazia L et al.:* What happens after pneumonectomy? A prospective study using the transpulmonary thermodilution method. J Thorac Cardiovasc Surg 2008; 135: 210–211.
114. *Michard F, Schachtrupp A, Toens C:* Factors influencing the estimation of extravascular lung water by transpulmonary thermodilution in critically ill patients. Crit Care Med 2005; 33: 1243–1247.
115. *Michard F, Phillips C:* Measuring extravascular lung water (and derived parameters) in patients with acute respiratory distress syndrome: what's right, what's wrong, and what's ahead? Crit Care Med 2009; 37: 2118–2119.
116. *Michard F:* Bedside assessment of extravascular lung water by dilution methods: temptations and pitfalls. Crit Care Med 2007; 35: 1186–1192.
117. *Antonini M, Meloncelli S, Dantimi C, Tosti S, Ciotti L, Gasparetto A:* The PiCCO system with brachial-axillary artery access in hemodynamic monitoring during surgery of abdominal aortic aneurysm. Minerva Anestesiol 2001; 67: 447–456.
118. *Grensemann J, Bruecken U, Treszl A, Wappler F, Sakka SG:* The influence of prone positioning on the accuracy of calibrated and uncalibrated pulse contour-derived cardiac index measurements. Anesth Analg 2013; 116: 820–826.
119. *Huter L, Schwarzkopf K, Preussler NP et al.:* Measuring cardiac output in one-lung ventilation: a comparison of pulmonary artery and transpulmonary aortic measurements in pigs. J Cardiothorac Vasc Anesth 2004; 18: 190–193.
120. *Trepte CJ, Haas SA, Nitzschke R, Salzwedel C, Goetz AE, Reuter DA:* Prediction of volume-responsiveness during one-lung ventilation: a comparison of static, volumetric, and dynamic parameters of cardiac preload. J Cardiothorac Vasc Anesth 2013; 27: 1094–100.
121. *Saugel B, Kirsche SV, Hapfelmeier A et al.:* Prediction of fluid responsiveness in patients admitted to the medical intensive care unit. J Crit Care 2013; 28: 537 e1– 9.
122. *Sakka SG, Becher L, Kozieras J, van Hout N:* Effects of changes in blood pressure and airway pressures on parameters of fluid responsiveness. Eur J Anaesthesiol 2009; 26: 322–327.
123. *Marik PE, Cavallazzi R, Vasu T, Hirani A:* Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: A systematic review of the literature. Crit Care Med 2009; 37: 2642–2647.
124. *Perner A, Faber T:* Stroke volume variation does not predict fluid responsiveness in patients with septic shock on pressure support ventilation. Acta Anaesthesiol Scand 2006; 50: 1068–1073.
125. *De Backer D, Pinsky MR:* Can one predict fluid responsiveness in spontaneously breathing patients? Intensive Care Med 2007; 33: 1111–1113.
126. *De Backer D, Heenen S, Piagnerelli M, Koch M, Vincent JL:* Pulse pressure variations to predict fluid responsiveness: influence of tidal volume. Intensive Care Med 2005; 31: 517–523.
127. *Rex S, Brose S, Metzelder S et al.:* Prediction of fluid responsiveness in patients during cardiac surgery. Br J Anaesth 2004; 93: 782–788.
128. *Freitas FG, Bafi AT, Nascente AP et al.:* Predictive value of pulse pressure variation for fluid responsiveness in septic patients using lung-protective ventilation strategies. Br J Anaesth 2013; 110: 402–408.
129. *Oliveira-Costa CD, Friedman G, Vieira SR, Fialkow L:* Pulse pressure variation and prediction of fluid responsiveness in patients ventilated with low tidal volumes. Clinics (Sao Paulo, Brazil) 2012; 67: 773–778.
130. *De Backer D, Taccone FS, Holsten R, Ibrahimi F, Vincent JL:* Influence of respiratory rate on stroke volume variation in mechanically ventilated patients. Anesthesiology 2009; 110: 1092–1097.
131. *Monnet X, Bleibtreu A, Ferre A et al.:* Passive leg-raising and end-expiratory occlusion tests perform better than pulse pressure variation

in patients with low respiratory system compliance. Crit Care Med 2012; 40: 152–157.
132. *Teboul JL, Pinsky MR, Mercat A et al.:* Estimating cardiac filling pressure in mechanically ventilated patients with hyperinflation. Crit Care Med 2000; 28: 3631–3636.
133. *Reuter DA, Felbinger TW, Schmidt C et al.:* Stroke volume variations for assessment of cardiac responsiveness to volume loading in mechanically ventilated patients after cardiac surgery. Intensive Care Med 2002; 28: 392–398.
134. *Benes J, Zatloukal J, Kletecka J, Simanova A, Haidingerova L, Pradl R:* Respiratory induced dynamic variations of stroke volume and its surrogates as predictors of fluid responsiveness: applicability in the early stages of specific critical states. J Clin Monit Comput 2014; 28: 225–231.
135. *Renner J, Gruenewald M, Meybohm P et al.:* Effect of elevated PEEP on dynamic variables of fluid responsiveness in a pediatric animal model. Paediatr Anaesth 2008; 18: 1170–1177.
136. *Angus DC, Lidsky NM, Dotterweich LM, Pinsky MR:* The influence of high-frequency jet ventilation with varying cardiac-cycle specific synchronization on cardiac output in ARDS. Chest 1997; 112: 1600–1606.
137. *Mahjoub Y, Pila C, Friggeri A et al.:* Assessing fluid responsiveness in critically ill patients: False-positive pulse pressure variation is detected by Doppler echocardiographic evaluation of right ventricle. Crit Care Med 2009; 37: 2570–2575.
138. *Malbrain ML, de laet I:* Functional hemodynamics and increased intra-abdominal pressure: same thresholds for different conditions...? Crit Care Med 2009; 37: 781–783.
139. *Broch O, Gruenewald M, Renner J et al.:* Dynamic and volumetric variables reliably predict fluid responsiveness in a porcine model with pleural effusion. PLoS ONE 2013; 8: e56267.
140. *Mahjoub Y, Touzeau J, Airapetian N et al.:* The passive leg-raising maneuver cannot accurately predict fluid responsiveness in patients with intra-abdominal hypertension. Crit Care Med 2010; 38: 1824–1829.
141. *Malbrain ML, De laet I:* Functional haemodynamics during intra-abdominal hypertension: what to use and what not to use. Acta Anaesthesiol Scand 2008; 52: 576–577.
142. *Huber W, Malbrain ML:* Goal-directed fluid resuscitation in acute pancreatitis: shedding light on the penumbra by dynamic markers of preload? Intensive Care Med 2013; 39: 784–786.
143. *Malbrain ML, Reuter DA:* Assessing fluid responsiveness with the passive leg raising maneuver in patients with increased intra-abdominal pressure: be aware that not all blood returns! Crit Care Med 2010; 38: 1912–1915.
144. *Marik PE, Monnet X, Teboul JL:* Hemodynamic parameters to guide fluid therapy. Ann Intensive Care 2011; 1: 1.
145. *Sander M, Spies CD, Berger K et al.:* Prediction of volume response under open-chest conditions during coronary artery bypass surgery. Crit Care 2007; 11: R121.
146. *Reuter DA, Goepfert MS, Goresch T, Schmoeckel M, Kilger E, Goetz AE:* Assessing fluid responsiveness during open chest conditions. Br J Anaesth 2005; 94: 318–323.
147. *Wyffels PA, Sergeant P, Wouters PF:* The value of pulse pressure and stroke volume variation as predictors of fluid responsiveness during open chest surgery. Anaesthesia 2010; 65: 704–709.
148. *Rex S, Schalte G, Schroth S et al.:* Limitations of arterial pulse pressure variation and left ventricular stroke volume variation in estimating cardiac pre-load during open heart surgery. Acta Anaesthesiol Scand 2007; 51: 1258–1267.
149. *Guinot PG, Zogheib E, Detave M et al.:* Passive leg raising can predict fluid responsiveness in patients placed on veno-venous extracorporeal membrane oxygenation. Crit Care 2011; 15: R216.
150. *Kleinman B, Frey K:* Artifact mistaken for electrical interference recorded from a pulmonary artery catheter. J Clin Monit Comput 1998; 14: 361–363.
151. *Janda M, Scheeren TW, Bajorat J et al.:* The impact of intra-aortic balloon pumping on cardiac output determination by pulmonary arterial and transpulmonary thermodilution in pigs. J Cardiothorac Vasc Anesth 2006; 20: 320–324.
152. *Monnet X, Jabot J, Maizel J, Richard C, Teboul JL:* Norepinephrine increases cardiac preload and reduces preload dependency assessed by passive leg raising in septic shock patients (R3). Crit Care Med 2011; 39: 689–694.
153. *Monnet X, Letierce A, Hamzaoui O et al.:* Arterial pressure allows monitoring the changes in cardiac output induced by volume expansion but not by norepinephrine. Crit Care Med 2011; 39: 1394–1399.
154. *Hadian M, Severyn DA, Pinsky MR:* The effects of vasoactive drugs on pulse pressure and stroke volume variation in postoperative ventilated patients. J Crit Care 2011; 26: 328 e1–8.
155. *Hamzaoui O, Georger JF, Monnet X et al.:* Early administration of norepinephrine increases cardiac preload and cardiac output in septic patients with life-threatening hypotension. Crit Care 2010; 14: R142.
156. *Johansson A, Chew M:* Reliability of continuous pulse contour cardiac output measurement during hemodynamic instability. J Clin Monit Comput 2007; 21: 237–242.
157. *Cottis R, Magee N, Higgins DJ:* Haemodynamic monitoring with pulse-induced contour cardiac output (PiCCO) in critical care. Intensive Crit Care Nurs 2003; 19: 301–317.
158. *Monge Garcia MI, Gil Cano A, Gracia Romero M:* Dynamic arterial elastance to predict arterial pressure response to volume loading in preload-dependent patients. Crit Care 2011; 15: R15.
159. *Monge Garcia MI, Gil Cano A, Diaz Monrove JC:* Arterial pressure changes during the Valsalva maneuver to predict fluid responsiveness in spontaneously breathing patients. Intensive Care Med 2009; 35: 77–84.
160. *Gassanov N, Caglayan E, Nia A, Erdmann E, Er F:* Hemodynamic monitoring in the intensive care unit: pulmonary artery catheter versus PiCCO. Dtsch Med Wochenschr 2011; 136: 376–380.
161. Gassanov N, Caglayan E, Nia A, Erdmann E, Er F: The PiCCO catheter. Dtsch Med Wochenschr 2010; 135: 2311–2314.
162. *Trof RJ, Beishuizen A, Cornet AD, de Wit RJ, Girbes AR, Groeneveld AB:* Volume-limited versus pressure-limited hemodynamic management in septic and nonseptic shock. Crit Care Med 2012; 40: 1177–1185.
163. *Hooper MH, Marik PE:* Transpulmonary thermodilution: the jury is out. Crit Care Med 2012; 40: 3109.
164. *Vernon C, Phillips CR:* Pulmonary artery catheters in acute heart failure: end of an era? Crit Care 2009; 13: 1003.
165. *De Backer D, Fagnoul D, Herpain A:* The role of invasive techniques in cardiopulmonary evaluation. Curr Opin Crit Care 2013; 19: 228–233.
166. *Fletcher AM, Andrews J, Frampton AE:* Individualizing hemodynamic optimization during the management of circulatory collapse. Expert review of cardiovascular therapy. 2012; 10: 1217–1220.
167. *Breukers RM, Trof RJ, de Wilde RB et al.:* Relative value of pressures and volumes in assessing fluid responsiveness after valvular and coronary artery surgery. Eur J Cardiothorac Surg 2009; 35: 62–68.
168. *Olmedilla L, Perez-Pena JM, Ripoll C et al.:* Early noninvasive measurement of the indocyanine green plasma disappearance rate accurately predicts early graft dysfunction and mortality after deceased donor liver transplantation. Liver Transpl 2009; 15: 1247–1253.
169. *Grigorov Tzenkov I, Arnal Velasco D, Perez Pena JM, Olmedilla Arnal L, Garutti Martinez I, Sanz Fernandez J:* Cardiac output by femoral arterial thermodilution-calibrated pulse contour analysis during liver transplantation: comparison with pulmonary artery thermodilution. Transplant Proc 2003; 35: 1920–1922.
170. *Vilchez-Monge AL, Tranche Alvarez-Cagigas I, Perez-Pena J et al.:* Cardiac output monitoring with pulmonary versus transpulmonary thermodilution during liver transplantation: interchangeable methods? Minerva Anestesiol 2014; 80: 1178–1187.
171. *Ameloot K, Van De Vijver K, Van Regenmortel N et al.:* Validation study of Nexfin(R) continuous non-invasive blood pressure monitoring in critically ill adult patients. Minerva Anestesiol 2014.
172. *Ameloot K, Van De Vijver K, Broch O et al.:* Nexfin noninvasive continuous hemodynamic monitoring: validation against continuous pulse contour and intermittent transpulmonary thermodilution derived cardiac output in critically ill patients. Scientific World Journal. 2013; 2013: 519080.
173. *Monnet X, Anguel N, Naudin B, Jabot J, Richard C, Teboul JL:* Arterial pressure- based cardiac output in septic patients: different accuracy of pulse contour and uncalibrated pressure waveform devices. Crit Care 2010; 14: R109.
174. *Ishihara H, Okawa H, Tanabe K et al.:* A new non-invasive continuous cardiac output trend solely utilizing routine cardiovascular monitors. J Clin Monit Comput 2004; 18: 313–320.
175. *Ishihara H, Hashiba E, Okawa H, Saito J, Kasai T, Tsubo T:* Neither dynamic, static, nor volumetric variables can accurately predict fluid responsiveness early after abdominothoracic esophagectomy. Perioper Med (Lond) 2013; 2: 3.
176. *Tagami T, Kuwamoto K, Watanabe A et al.:* Optimal range of global end-diastolic volume for fluid management after aneurysmal subarachnoid hemorrhage: a multicenter prospective cohort study. Crit Care Med 2014; 42: 1348–1356.

177. *Watanabe A, Tagami T, Yokobori S et al.:* Global end-diastolic volume is associated with the occurrence of delayed cerebral ischemia and pulmonary edema after subarachnoid hemorrhage. Shock 2012; 38: 480–485.
178. Mutoh T, Kazumata K, Ishikawa T, Terasaka S. Performance of bedside transpulmonary thermodilution monitoring for goal-directed hemodynamic management after subarachnoid hemorrhage. Stroke 2009; 40: 2368–2374.
179. *Mutoh T, Kazumata K, Ajiki M, Ushikoshi S, Terasaka S:* Goal-directed fluid management by bedside transpulmonary hemodynamic monitoring after subarachnoid hemorrhage. Stroke 2007; 38: 3218–3224.
180. *Csontos C, Foldi V, Fischer T, Bogar L:* Arterial thermodilution in burn patients suggests a more rapid fluid administration during early resuscitation. Acta Anaesthesiol Scand 2008; 52: 742–749.
181. *Bognar Z, Foldi V, Rezman B, Bogar L, Csontos C:* Extravascular lung water index as a sign of developing sepsis in burns. Burns 2010; 36: 1263–1270.
182. *Hadian M, Pinsky MR:* Evidence-based review of the use of the pulmonary artery catheter: impact data and complications. Crit Care 2006; 10 (Suppl. 3): S8.
183. *Bigatello LM, Kistler EB, Noto A:* Limitations of volumetric indices obtained by trans-thoracic thermodilution. Minerva Anestesiol 2010; 76: 945–949.
184. *Della Rocca G, Teboul JL:* Reply to: limitations of volumetric indices obtained by transthoracic thermodilution. Minerva Anestesiol 2011; 77: 754–755.
185. *Mallat J, Lemyze M, Salleron J et al.:* Mathematical coupling of data between global- end diastolic volume index and cardiac index calculated by the PiCCO device: myth or reality? Minerva Anestesiol 2014; 80: 996–1004.
186. *Giraud R, Siegenthaler N, Bendjelid K:* Impact of shunt on the transpulmonary thermodilution curve. Intensive Care Med 2011; 37: 552.

Corresponding author:
Manu LNG Malbrain, MD, PhD
Intensive Care Unit and High Care Burn Unit Director
Ziekenhuis Netwerk Antwerpen, ZNA Stuivenberg
Lange Beeldekensstraat 267
B-2060 Antwerp 6, Belgium
e-mail: manu.malbrain@skynet.be

Received: 24.09.2014
Accepted: 17.11.2014

APPENDIX 1. SURVEY ON THE KNOWLEDGE OF TRANSPULMONARY THERMODILUTION IN THE ICU

Questionaire about the use of PiCCO. More answers per question are possible

1. What does PiCCO mean? (open question)

2. What principles are used with PiCCO measurements?
   a) intermittent and continuous CO measurement by arterial pulse contour analysis
   b) intermittent by thermodilution and continuous by arterial pulse contour analysis
   c) intermittent and continuous measurements by thermodilution
   d) I have no idea

3. What does PiCCO measure besides cardiac output?
   a) preload
   b) contractibility
   c) extravascular lung water
   d) filling status
   e) wedge pressure
   f) afterload
   g) all answers are correct
   h) all answers are incorrect

4. Hemodynamic monitoring with the PiCCO is:
   a) invasive
   b) minimal invasive
   c) not invasive
   d) I have no idea

5. In which patients is the use of PiCCO appropriate?
   burned patients
   a) patients with septic shock
   b) patients undergoing major surgery that need cardiovascular monitoring
   c) patients with unknown filling status
   d) patients with kidney failure
   e) patients with respiratory failure
   f) all answers above
   g) I have no idea
   h) other:

6. What do we need to perform a PiCCO measurement?
   a) central venous catheter, PiCCO catheter, and a PiCCO kit
   b) arterial catheter, PiCCO catheter, and a PiCCO kit
   c) only a PiCCO kit
   d) Swan-ganz catheter
   e) I have no idea

7. What is the correct injectate temperature (Ti)?
   a) < 5°C
   b) < 8°C
   c) < 12°C
   d) ambient temperature
   e) I have no idea

8. Is the volume of the injectate (Vi) dependent on the body weight?
   a) yes
   b) no
   c) yes, with a maximum of 100 kg
   d) I have no idea

9. Is it important to enter information like weight and height of the patient?
   a) yes, jto present correctly the indexed values
   b) no, weight and height are not important
   c) only length is important because the PiCCO calculates the predicted body weight (PBW)
   d) I have no idea

10. Should the patient be supine during a TPTD measurement?
    a) yes
    b) no, it is of no importance
    c) head of bed should be elevated at 30–40°
    d) I have no idea

11. How many measurements must at least be done to obtain a correct value?

a) 2 measurements
b) 3 measurements
c) 4 measurements
d) I have no idea

12. Which deviation from the mean CO is allowed for a thermodilution CO measurement?
a) 10%
b) 15%
c) 20%
d) 25%
e) more than 25%

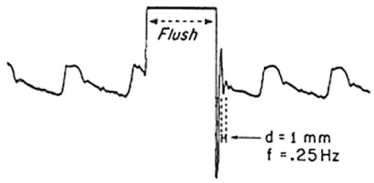
13. What values should be noted for volumes and extravascular lung water?
a) the indexed value
b) the absolute value
c) both are possible
d) I have no idea

14. How many times does the PiCCO arterial curve need to be zeroed/calibrated?
a) at least once a day
b) before each measurement
c) only when starting up the PiCCO
d) 1 ×/shift
e) 1 ×/week
f) 1 ×/month
g) I have no idea

15. Why do we perform a rapid flush test?
a) to check if the curve is damped
b) to see if there is a leak
c) to check if the pressure bag is sufficiently inflated
d) to measure the CO
e) I have no idea

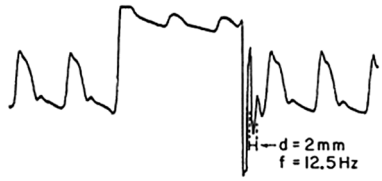
16. When do we perform a rapid flush test?
a) once a day
b) once per shift
c) before each TPTD measurement
d) I have no idea

17. Which of these rapid flush tests are correct or explain the pressure signal?
17A. CURVE 1



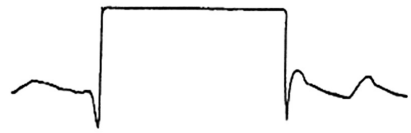
a) damped signal
b) normal signal
c) augmented signal

17B. CURVE 2



a) damped signal
b) normal signal
c) augmented signal

17C. CURVE 3



a) damped signal
b) normal signal
c) augmented signal

18. Question A: Is the placement of the catheters important for the interpretation of the obtained values?
a) yes
b) no
c) I have no idea
Question B: Which of the following is the ideal catheter position?
d) right jugular vein/left or right femoral artery
e) left femoral vein/right femoral artery
f) left subclavian vein/left or right femoral artery
g) I have no idea

19. The injectate should be injected:
a) in less than 7 sec
b) in less than 10 sec
c) in less than 12 sec
d) depending of the amount of injected volume, always 5cc/2 sec

20. What to do if the delta T° is less than 0.2 °C?
a) increase the cooling of the injectate
b) increase the speed of injection
c) increase the volume of the injectate
d) I have no idea

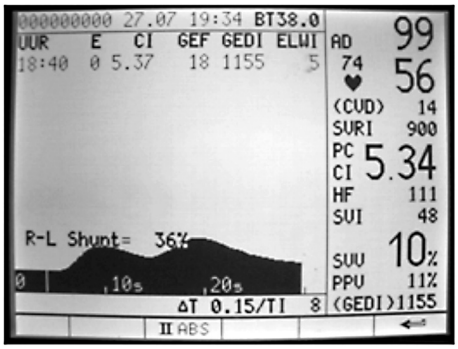
21. What happens if the injectate volume is less than the amount expected by the PiCCO?
a) false increase of the CO
b) false decrease of the EVLWi

c) false increase of the CI
d) false decrease of the GEDVi
e) I have no idea

22. Should the CVP be entered in the PiCCO?
a) no, it is calculated by PiCCO
b) yes, to calculate the cardiac output
c) yes, to calculate the systemic vascular resistance
d) I have no idea

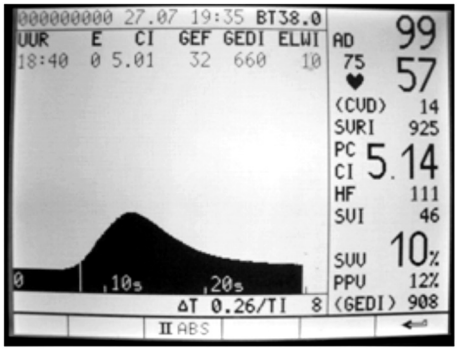
23. Look at the following thermodilution curves and state if correct

23A. CURVE 1



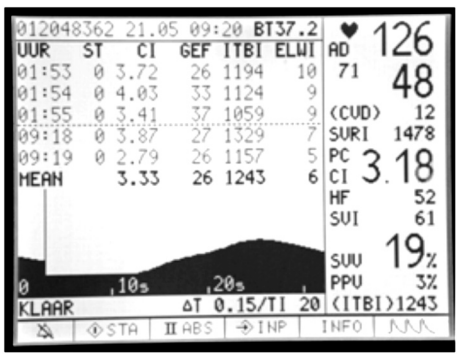
a) correct
b) incorrect
c) I have no idea

23B. CURVE 2



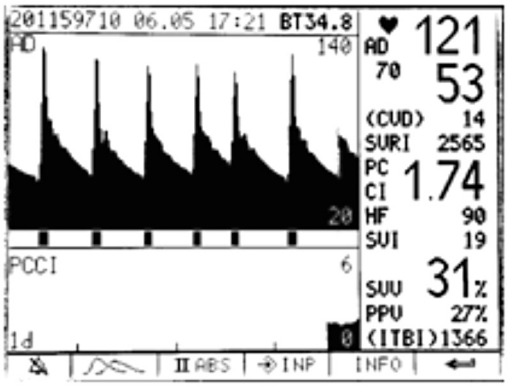
a) acorrect
b) incorrect
c) I have no idea

23C. CURVE 3



a) correct
b) incorrect
c) I have no idea

24. Determine the underlying rhythm



a) Regular sinus
b) atrial fibrillation
c) irregular
d) I have no idea

25. Which PiCCO measurements are not reliable if the patient is not in sinus rhythm?
a) all measurements are reliable
b) all measurements are unreliable
c) the pulse contour analysis is reliable
d) SVV and PPV are unreliable
e) the thermodilution measurements (GEDVi and EVLWi) are reliable
f) I have no idea

26. To finish this survey some questions about you :
a) What is your gender?
☐ Man
☐ Woman
b) Are you a doctor or a nurse?
☐ Doctor
☐ Trainee
☐ Nurse
c) In which country do you work?
☐ Belgium
☐ The Netherlands
☐ Other
d) In which city do you work?
e) On which ICU do you work?
☐ Medical ICU
☐ Surgical ICU
☐ Mixed ICU
☐ CCU
☐ Burn Unit
☐ Other
f) How many years do you work in the ICU?*
g) What is your experience (in years) with PiCCO?*