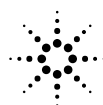


Hemodynamic Monitoring using the PiCCO Method

Application Note



Agilent Technologies

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Edition 1

Forward

This guide is intended as an introduction to the PiCCO concept and the interpretation of the hemodynamic parameters that the Agilent M1012A C#10 option (CCO) module provides. For a complete understanding of this subject area, further reading is necessary. The reference list provides an overview of some of the publications currently available.

The information in this guide is intended to support you with basic information on the interpretation of the received parameters for cardiovascular and volumetric management.

Therapeutic decisions based on this interpretation must always include considerations of the patient's medical history, drugs and medications used, an understanding of the monitoring methods used and, most important, your clinical findings and observations.

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Introduction

The Agilent CCO provides you with organ specific and clinically relevant parameters to assist in decision making regarding the patients treatment with cardiovascular drugs and volume management.

The PiCCO method is continuous pulse contour cardiac output with cardiac preload volume and lung water monitoring. It requires a central venous and an arterial access only.

The following parameters are continuously monitored:

- Pulse Contour Cardiac Output
- Stroke Volume
- Stroke Volume Variation
- Systemic Vascular Resistance
- Index of Left Ventricular Contractility (dpmax)*

The following parameters are quantified:

- Cardiac Output
- Intrathoracic Blood Volume
- Cardiac Function Index
- Extravascular Lung Water*

Combining all these variables results in the most complete picture of hemodynamic status and performance available is easily obtained from an inexpensive and quick measurement.

*Not Available in USA

Setup Configuration

The PiCCO method is a combination of transpulmonary thermodilution technique and arterial pulse contour analysis.

The transpulmonary thermodilution technique requires a central venous line and an arterial catheter placed in one of the bigger systemic arteries e.g. the femoral or the axillary artery to determine thermodilution cardiac output (CO), continuous cardiac output using the pulse contour method (CCO), intrathoracic blood volume (ITBV) and extravascular lung water (EVLW). The injectate is injected through the central venous line.

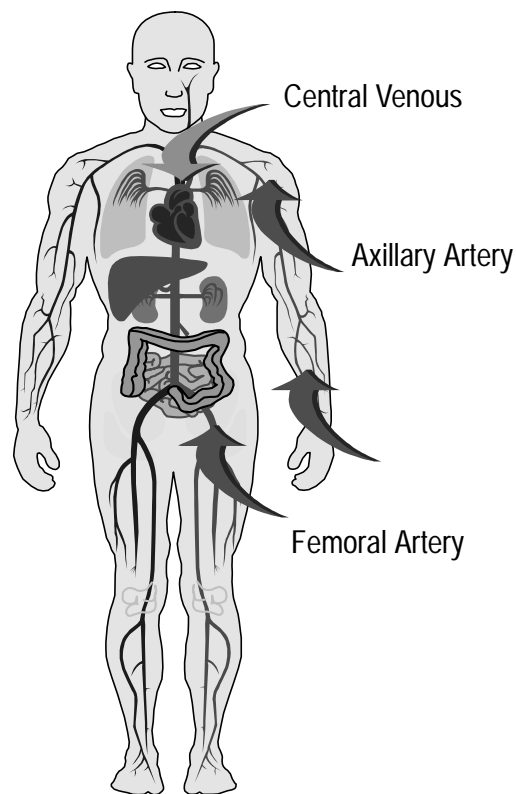
Transpulmonary thermodilution CO is used to calibrate the continuous cardiac output (CCO) derivation by means of pulse contour analysis.

The transpulmonary thermodilution and the CCO measurement require a special arterial catheter from PULSION Medical Systems. Only use this specific catheter and make sure that only the specified puncture locations for this catheter are used.

The arterial thermodilution catheters can only be used for transpulmonary thermodilution measurements with the M1012A Option C10 CO Parameter Module

All variables are easily obtained using any central venous line and an arterial thermodilution probe or catheter with the orifice of the distal lumen preferably placed in a large artery.

Catheter Positions



Catheters

Femoral artery PULSIOCATH PV2014L16 or compatible catheters from PULSION.

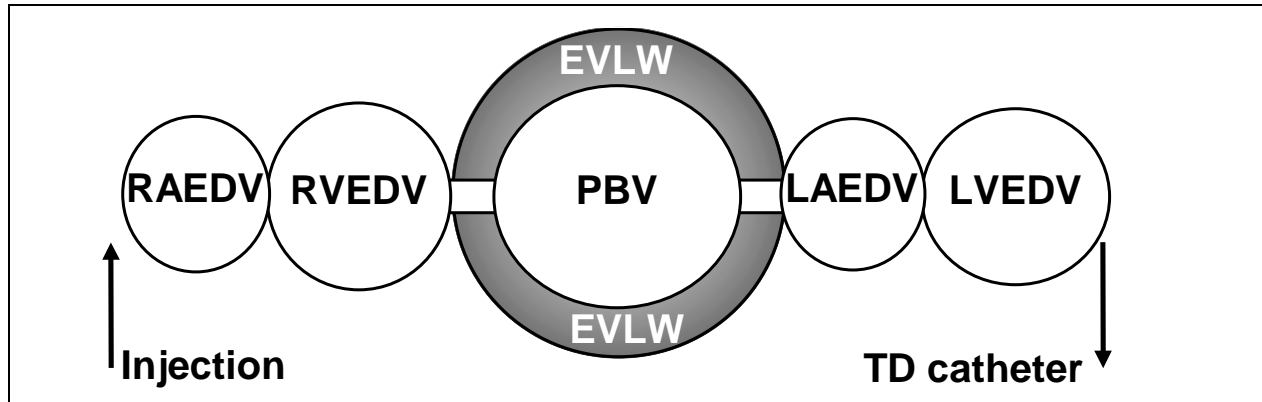
Application

1. Insert central venous catheter (CVC).
2. Insert the arterial PULSIOCATH catheter.
3. Connect the PULSIOCATH catheter to the cardiac output module with PiCCO (C10 option).
4. Perform three thermodilution measurements for calibration of pulse contour cardiac output determination.

Basics Information

Transpulmonary Indicator Dilution (TPID) Measurement

To an indicator injected in a central vein, the cardiopulmonary system represents a series of different mixing chambers.



Schematic description of the indicator mixing chambers of the cardiopulmonary system

- RAEDV = Right atrial end-diastolic volume
- RVEDV = Right ventricular end-diastolic volume
- PBV = Pulmonary blood volume
- EVLW = Extravascular lung water
- LAEDV = Left atrial end-diastolic volume
- LVEDV = Left ventricular end-diastolic volume

An injected indicator always mixes with the largest volume accessible - referring to the heart this volume is the combination of the end-diastolic volumes of the cardiac chambers. After dilution of the indicator in the respective volume, a reconcentration of the indicator is not possible.

Central venous injection of a bolus of cold injectate results in distribution of the thermal indicator in the intrathoracic thermal volume (ITTV). The ITTV consists of the intrathoracic blood volume (ITBV) and the extravascular lung water (EVLW) space. ITBV consists of the sum of all end-diastolic volumes, i.e. the global end-diastolic volume (GEDV), and pulmonary blood volume (PBV).

$$\begin{aligned} \text{GEDV} &= \text{RAEDV} + \text{RVEDV} + \text{LAEDV} + \text{LVEDV} \\ \text{ITBV} &= \text{GEDV} + \text{PBV} \end{aligned}$$

Cardiac output is calculated from an transpulmonary thermodilution curve in the usual way using the Stewart-Hamilton algorithm. Transpulmonary thermodilution curves are much longer and flatter compared to pulmonary artery thermodilution curves. Transpulmonary thermodilution is thus sensitive to thermal base line drift. However, transpulmonary thermodilution is not influenced by what ventilatory phase injection of indicator is performed. Special algorithms are used in the CCO module for analysis of the thermal base line drift and for calculation of true thermodilution curves. The transpulmonary thermodilution cardiac output (CO_{TDa}) measured with the PiCCO method compares favorably with the simultaneously determined pulmonary artery cardiac output (CO_{TDpa}) (see table). In addition, excellent correlation of CO_{TDa} with Fick was demonstrated by Tibby et al (Intensive Care Med 23: 987-991, 1997) and Sakka et al (J Cardiothorac Vasc Anesth 14: 119-124, 2000)

Table 1:

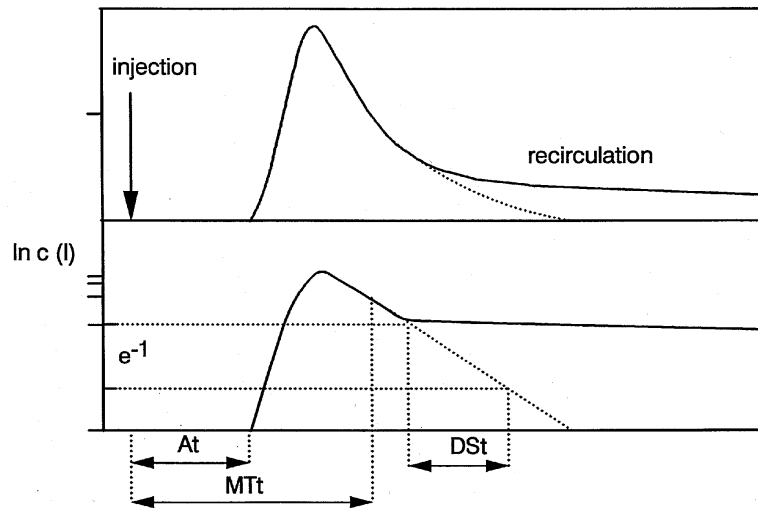
<i>Author</i>	<i>pat / obs</i>	$CO_{TDa} - CO_{TDpa}$ bias \pm SD	<i>r</i>
von Spiegel et al, 1996 Anaesthesist 45 (11)	21 / 48	- 4.7 \pm 1.5%	.97
McLuckie et al, 1996 Acta Paediatr 85	9 / ?	0.19 \pm 0.211/min/m ²	
Goedje et al, 1998 Chest 113 (4)	30/150(triple)	0.16 \pm 0.31 1/min/m ²	0.96
Goedje et al, 1998 Thorac Cardiovasc Surg 46	30 / 810	0.26 \pm 0.71 min	0.96
Zoolner et al, 1998 Anaesthesist 47 (11)	18/160 (131 double/29 triple)	0.03 l/min \pm 1.04	0.91
Goedje et al, 1999 Crit Care Med 27 (11)	24/216	-0.29 \pm 0.66 l/min	0.93
Sakka et al, 1999 Intensive Care Med 25	37 / 449	0.68 \pm 0.62 l/min	0.97
Sakka et al, 2000 J Cardiothorac Vasc Anesth 14 (2)	12 / 51 (triple)	0.73 \pm 0.38 l/min	0.98
Zollner et al 2000 J Cardiothorac Vasc Anesth 14 (2)	19/76 (triple)	0.21 \pm 0.73 l/min	0.96
Bindels et al, 2000 Crit Care 4	45/283	0.49 \pm 0.45 l/min/m ²	0.95

Pulmonary artery thermodilution cardiac output (CO_{TDpa}) vs. transpulmonary thermodilution cardiac output (CO_{TDa})

Detection of volumes

Specific volumes can be calculated by multiplying the cardiac output (CO_{TDa}) by characteristic transit times determined from the indicator dilution curves.

The CCO module calculates the mean transit time (MTt) and the exponential downslope time (DSt) of the thermodilution curve.



Schematic depiction of a dilution curve and definition of appearance time (At), mean transit time (MTt), and exponential downslope time (DSt)

MTt volume: The result of the product of CO and MTt is the volume through which the relevant indicator has travelled, i.e. the complete volume between the site of injection and the site of detection. For the thermal indicator this is total intrathoracic thermal volume (ITTV) which is composed of the global end-diastolic volume (GEDV), pulmonary blood volume (PBV), and extravascular lung water (EVLW).

$$ITTV = MTt_{TDa} * CO_{TDa} = GEDV + PBV + EVLW$$

DSt volume: The result of the product of CO and DSt is the largest individual mixing volume in a series of indicator dilution mixing chambers. For the thermal indicator this is the pulmonary thermal volume (PTV) which is composed of PBV and EVLW.

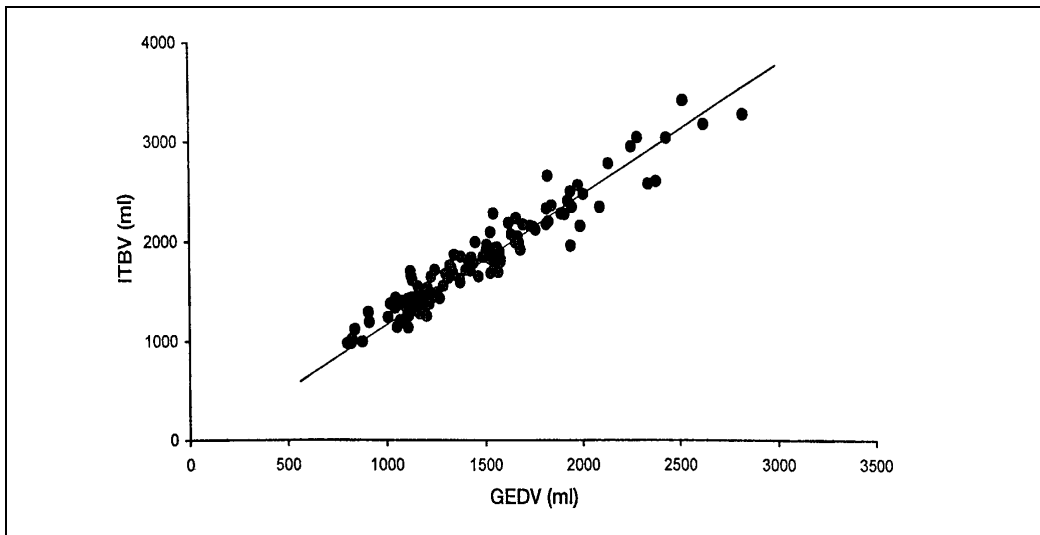
$$PTV = DSt_{TDa} * CO_{TDa} = PBV + EVLW$$

Application Note

By subtraction of PTV from ITTV a volume that represents the global end-diastolic volume is obtained.

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

In the CCO module the intrathoracic blood volume ITBV is estimated from the GEDV obtained by thermodilution measurement. GEDV correlates closely with ITBV in experimental and clinical studies (see figure). By using a structural regression analysis, the mathematical relationship between GEDV and ITBV has been established in a large patient population. This regression equation is used to estimate ITBV from GEDV.



Structural regression analysis between global end-diastolic volume (GEDV) and intrathoracic blood volume (ITBV) in 57 intensive care patients (Sakka et al; Intensive Care Med 26: 180-187, 2000)

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

Using the estimated ITBV an estimated EVLW can be calculated as well.

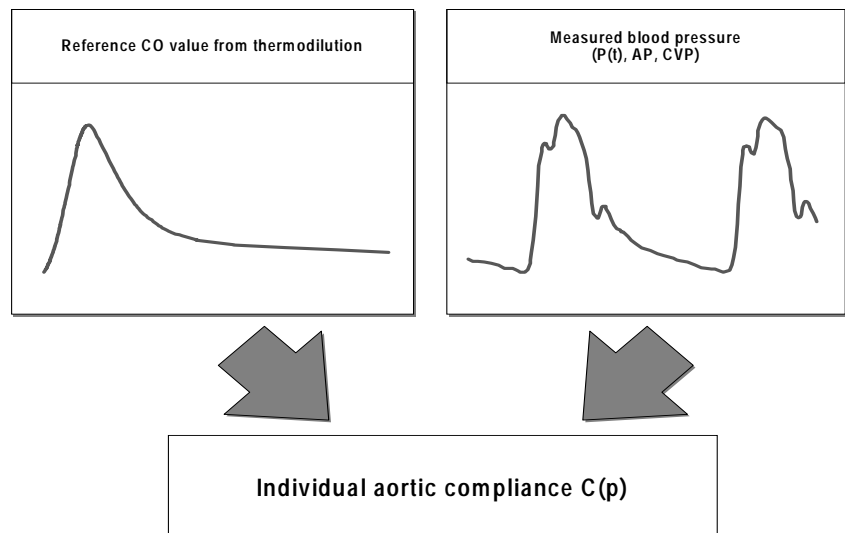
$$\text{EVLW} = \text{ITTV} - \text{ITBV}$$

Arterial Pulse contour cardiac output

The CCO module continuously determines CO by an improved arterial pulse contour analysis without the need of a more invasive pulmonary artery catheter. Pulse contour cardiac output

(CCO) is calibrated by means of a simple transpulmonary thermodilution measurement.

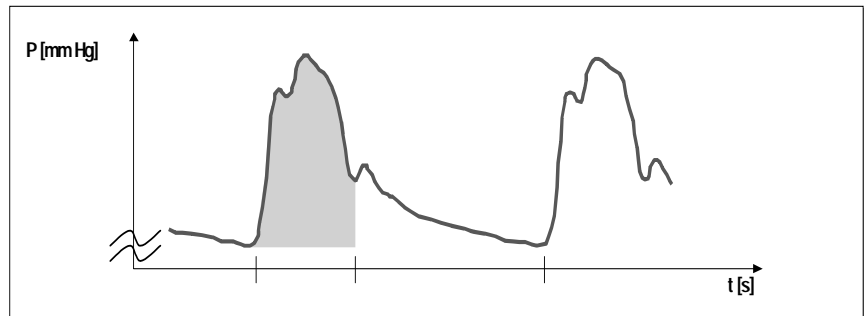
The relationship between blood flow out of the aorta and pressure measured at the end of the aorta (femoral artery or other large artery) is determined by the aortic compliance function. The aortic compliance function can therefore be characterized by measuring blood pressure and blood flow (cardiac output) simultaneously. Transpulmonary thermodilution cardiac output (C.O.) determined simultaneously with continuous arterial pressure (AP) measurement is utilized to calibrate the pulse contour analysis to each individual patient's aortic compliance function.



Determination of the individual aortic compliance

Application Note

For the continuous calculation of CCO the CCO method uses a calibration factor (cal) determined by thermodilution cardiac output measurement and the heart rate (HR), as well as the integrated values for the area under the systolic part of the pressure curve ($P(t)/SVR$), the aortic compliance ($C(p)$) and the shape of the pressure curve, represented by change of pressure over change of time (dP/dt).



$$PCCO = \text{cal} \cdot \text{HR} \cdot \int_{\text{Systole}} \left(\frac{P(t)}{\text{SVR}} + C(p) \cdot \frac{dP}{dt} \right) dt$$

Diagram illustrating the components of the PCCO equation:

- cal: Patient-specific calibration factor (determined with thermodilution)
- HR: Heart rate
- $\int_{\text{Systole}} \frac{P(t)}{\text{SVR}}$: Area under pressure curve
- $C(p)$: Compliance
- $\frac{dP}{dt}$: Shape of pressure curve

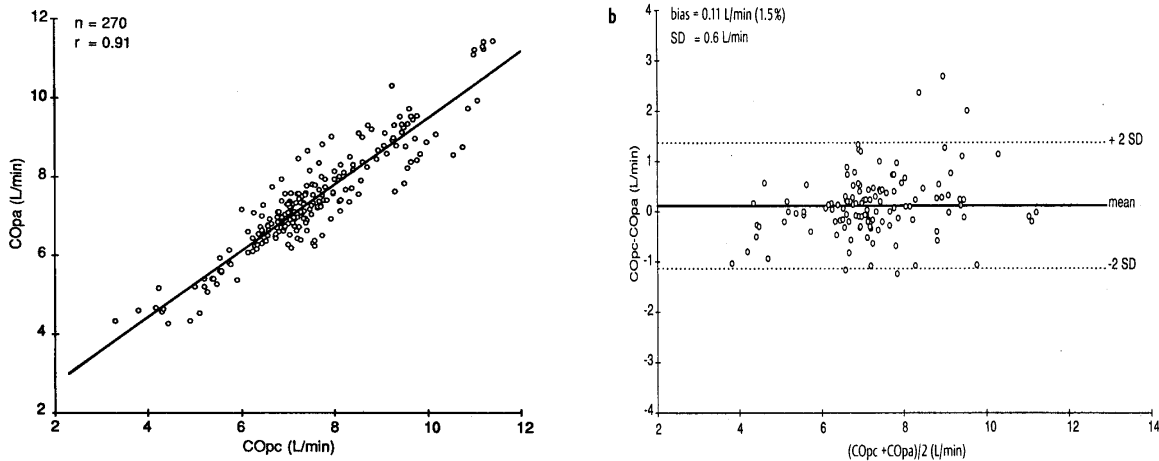
Calculation of pulse contour cardiac output (CCO)

The validity of the CCO derived from the improved arterial pulse contour analysis was demonstrated in clinical studies.

Table 2:

<i>Author</i>	<i>pat / obs</i>	$CO_{TDa} - CO_{TDpa}$ bias \pm SD	<i>r</i>
Goedje et al, 1998 Thorac Cardiovas Surg 46	30/ 270 (triple)	0.11 \pm 0.6 l/min	0.91
Goedje et al, 1999 Crit Care Med 27 (11)	24/216 (triple)	0.07 \pm 0.7 l/min	0.92
Buhre et al, 1999 J Cardiothorac Vasc Anesth 13 (4)	12 / 36 (triple)	0.003 \pm 0.63 l/min	0.94
Goedje et al, 1999 Ann Thorac Surg 68 (4)	20/192 (triple)	-01 \pm 0.42 l/min	0.91
Zollner et al, 2000 J Cardiothorac Vasc Anesth 14 (2)	19/76 (triple)	0.31 \pm 1.25 l/min	0.88

Pulmonary artery thermodilution cardiac output (CO_{TDpa}) vs. continuous pulse contour cardiac output (PCCO)



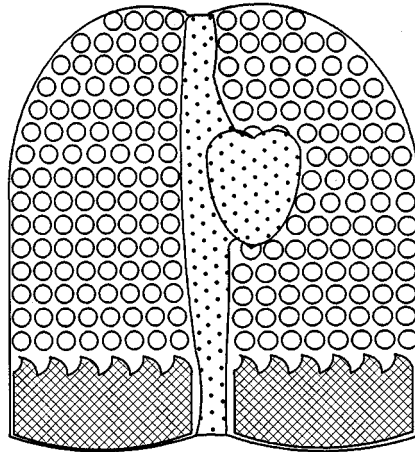
Standard pulmonary artery thermodilution cardiac output (CO_{TDpa} , in graphic as CO_{pa}) and arterial pulse contour cardiac output (PCCO, in graphic as CO_{pc}) calibrated with trans-cardiopulmonary thermodilution (initial calibration, data collection for 24 hours) in 30 cardiac surgery patients. (Gödjje et al, Thorac Cardiovasc Surg 46: 242-249, 1998)

The PiCCO method represents an inexpensive, less invasive technology for quantification of cardiac output, intrathoracic blood volume and extravascular lung water. CCO module requires a central venous and an arterial access. The CCO module represents for many fields of application an alternative to the pulmonary artery catheter and is also applicable in children and infants.

Clinical Application

Intrathoracic blood volume (ITBV):

The intrathoracic blood volume (ITBV) is composed of the global end-diastolic volume (GEDV, equals 2/3 to 3/4 of ITBV) and the pulmonary blood volume (PBV).

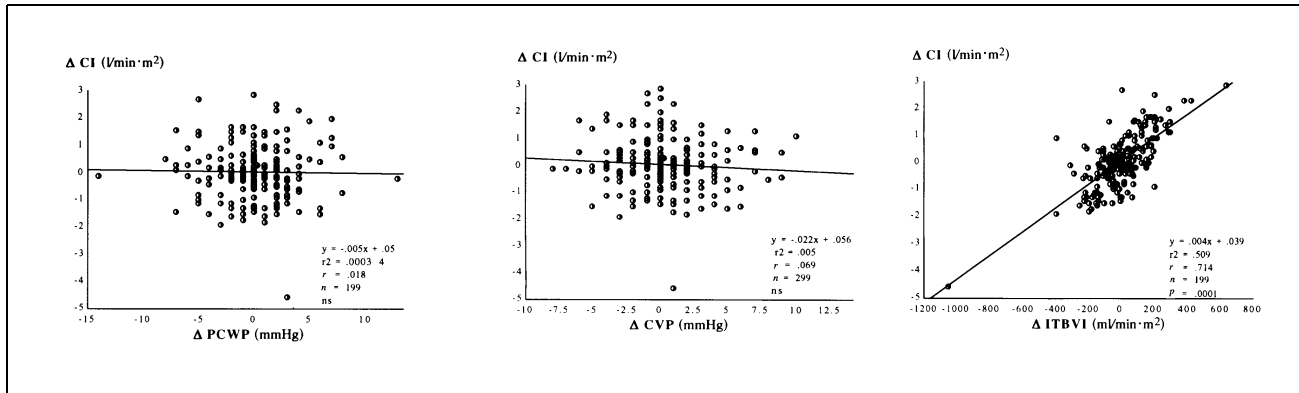


Three variable volumes are found in the chest that, due to the limited expansion ability of the chest, influence each other: the intrathoracic blood volume, the intrathoracic gas volume and the extravascular lung water. As a potential fourth compartment, space occupying lesions such as tumors or contusions could be an addition.

ITBV as a hemodynamic guide

In numerous experimental and clinical studies ITBV was shown to be a more sensitive indicator of cardiac preload compared to central venous pressure or pulmonary artery occlusion pressure. Also in direct comparison with the right ventricular end-diastolic volume ITBV proves to be the more sensitive parameter. Lichtwarck-Aschoff et al (1992) were able to show that ITBV reflects the status of the circulating blood volume of intensive care patients being artificially ventilated, whereas the clinical standard "cardiac filling pressures" like central venous pressure and the pulmonary artery occlusion pressure do not reflect cardiac preload.

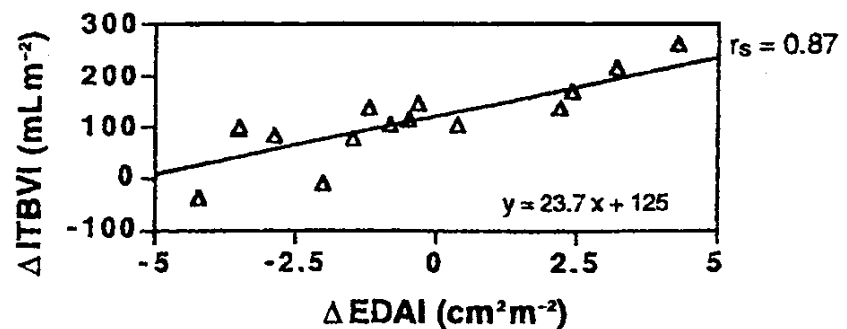
Application Note



Analysis of regression between CI and ITBV, CVP and PCWP, Lichtwarck-Aschoff et al.,; Intensive Care Med 18: 142-147,; 1992

In an experimental study Lichtwarck-Aschoff (1996) compared CVP, PAOP, RVEDV, and ITBV in a model with severe hypo- and hypervolemia. Again ITBV was the more sensitive. In addition, it was demonstrated, that ITBV is not mathematically coupled with cardiac output.

Transesophageal echocardiography (TEE) is a diagnostic method used for estimating the left ventricular end-diastolic volume through the left ventricular end-diastolic area (LVEDA). Though not being the same, Hinder et al. could demonstrate that changes of ITBV correlated closely with changes of LVEDA which demonstrates that both reflect cardiac preload.



Changes of intrathoracic blood volume index versus changes of left ventricular end-diastolic area index in cardiac surgical patients (Hinder et al; Eur J Anaesthesiol 15 (6): 633-640, 1998)

Conclusion

- CVP and PAOP are poor indicators for cardiac preload; they are the result of at least four components:
 - Vascular filling
 - Cardiac contractility
 - Vascular compliance
 - Intrathoracic pressure
- They have wide normal ranges, large interindividual scatter and low sensitivity for hypovolemia
- Measuring errors may result from:
 - Incorrect zero calibration, damping of pressure curve
 - Positioning of the patient
 - Ventilation (PEEP, ventilation phase, lung zone)
 - Positioning of the catheter

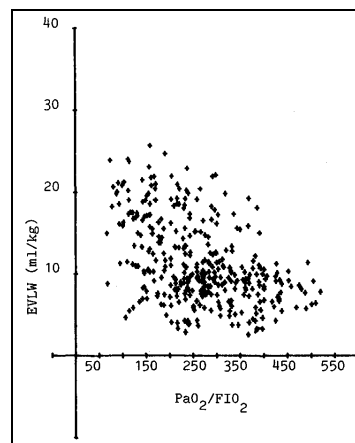
Management of circulating volume status is best done by measuring the volume which under normal circumstances is regulated physiologically by the body itself, i.e. intrathoracic blood volume. All physiological receptors taking part in volume regulation are located in the „ITBV-space“. There are no extrathoracic volume-receptors.

Cardiac preload is not a pressure but a volume. To guide volume you must measure volume.

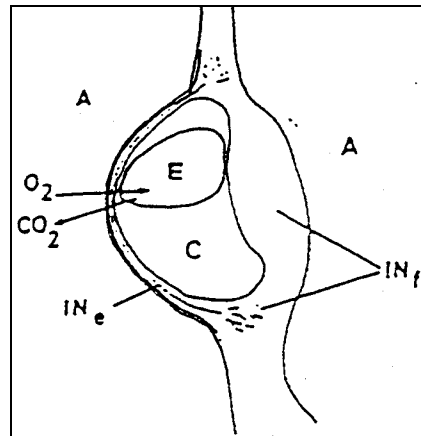
Extravascular lung water (EVLW)* (not available in USA)

EVLW and Oxygenation

There is poor correlation between extravascular lung water and oxygenation (Horowitz quotient) (Böck J, Lewis FR, In: Lewis FR and Pfeiffer UJ (Eds.): Practical Applications of Fiberoptics in Critical Care Monitoring. Springer-Verlag Berlin-Heidelberg-New York, pp 164-180, 1990).



Comparison of EVLW and the ratio of the arterial oxygen partial pressure and the inspiratory oxygen fraction (PaO_2/FiO_2)



Schematic cross-section through a septal lung capillary (IN_e = interstitium, which is limited in extension, IN_f = free interstitium, A = aperture of the alveolus, O_2 = oxygen, CO_2 = carbon dioxide, C = capillary volume, E = erythrocyte)

The poor correlation between the oxygenation (Horovitz coefficient) and the EVLW is primarily caused by the initial development of the interstitial edema into the free area of the interstitium. Through this process there is no immediate effect on the gas exchange between the alveolus and the blood vessel. Blood gases and lung function indices resulting from these are not organ specific, because they are not only dependent on the lung status but also on the lung perfusion and the quality of ventilation.

EVLW and Starling forces

Extravascular lung water does not correlate with the parameters used in the Starling equation, which also has been used for estimation of the pulmonary edema. The reasons for this are as follows: (1) the pulmonary capillary occlusion pressure is a poor indicator of the true capillary pressure, (2) the colloidosmotic pressure (COP) plays only a minor role in face of the increased permeability of the capillary membrane.

Table 3:

EVLW vs. COP	0.3152	p < 0.05
EVLW vs. PCWP	0.4199	p < 0.001
EVLW vs. Pmv	0.3944	p < 0.01
EVLW vs. COP-PCWP	-0.3285	p < 0.01
EVLW vs. COP-Pmv	-0.3457	p < 0.01

Poor correlation between EVLW and COP, PCWP, micro vascular pressure in the lungs (Pmv), COP-PCWP and COP-Pmv (Zadrobilek E et al, In: Lewis FR and Pfeiffer UJ (Eds.): Practical Applications of Fiberoptics in Critical Care Monitoring. Springer-Verlag Berlin-Heidelberg-New York, pp 140-142, 1990)

EVLW and X-ray score

There is only a poor correlation between extravascular lung water (EVLW) and estimation of pulmonary edema using x-ray scores.

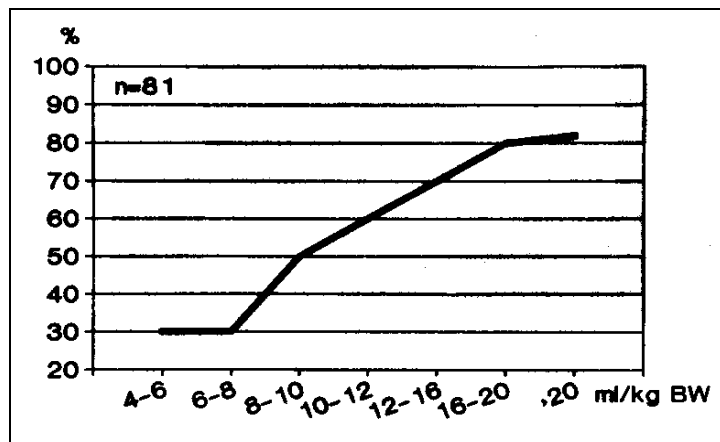
Table 4:

Reference	Comparison	Result
Halperin et al 1985 Chest 88: 649	X-ray score versus EVLW measurement	r = 0.51
Baudendistel et al 1982 J Trauma 22: 983	D X-ray score versus D EVLW measurement	77%
Sibbald et al 1983 Chest 83: 725	cardiac edema non cardiac edema	r = 0.66 r = 0.70
Sivak et al 1983 Crit Care Med. 11: 498	X-ray score vs EVLW D X-ray score vs. D EVLW	64% 42%
Laggner et al 1984 Intensive Care Med. 10: 309	X-ray score vs. EVLW	r = 0.84
Haller et al 1985 Fortschr. Röntgenstr. 142: 68	X-ray score vs. EVLW	66%
Eisenberg et al 1987 Am Rev Resp Dis 136: 662	X-ray score vs. EVLW	76%
Takeda et al 1995 J Vet Med Sci 57 (3): 481	X-ray score vs. EVLW	

The chest x-ray shows a density measurement of the total chest. This is why the chest x-ray is dependent on the air and blood content as well as extravascular lung water. Additionally, muscle and fat layers influence a quantitative density evaluation of a chest x-ray.

EVLW and mortality

The EVLW value is an indicator of the severity of illness. The relationship between the mortality of intensive care units patients with ARDS and the extravascular lung water was shown by J.A. Sturm (1990): Patients with increased EVLW need mechanical ventilation and intensive care and have a high risk of nosocomial infection. Therefore, any measure that reduces EVLW without decreased perfusion of e.g. splanchnic organs is likely to increase the chance of survival.



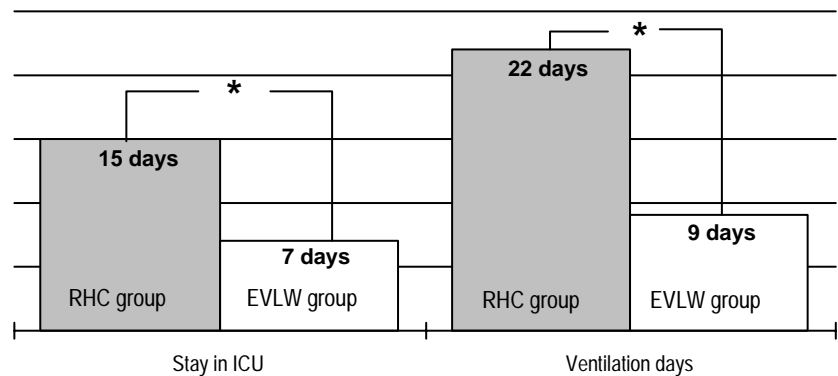
Close relationship between mortality and extravascular lung water in patients with multiple trauma (Sturm et al, In: Lewis FR and Pfeiffer UJ (Eds.): Practical Applications of Fiberoptics in Critical Care Monitoring. Springer-Verlag Berlin-Heidelberg-New York, pp 129-139, 1990)

The fluid content of the lung increases in left heart failure, pneumonia, sepsis, intoxications, burns, etc. EVLW increases through increased fluid transport to the interstitium as a result of either increased intravascular filtration pressure and vascular surface (left heart insufficiency, volume overload) or an increased pulmonary vascular permeability for plasma proteins. Protein pull water along with them corresponding to their colloid osmotic pressure (endotoxin, pneumonia, sepsis, intoxications, burns). Of course both mechanisms, the hydrostatic and increased permeability, may contribute to increased EVLW and it can become critical to separate one from each other.

EVLW is the only bedside parameter with which permeability damages can be quantified especially when the pulmonary edema has been caused by increased pulmonary vascular permeability. A clinically applicable guide for the pulmonary vascular permeability is the relationship of lung water to intrathoracic blood volume (EVLW/ITBV). The normal ratio is 0.25 and can go up as high as 1.5 indicating severe damage.

EVLW as a hemodynamic guide parameter

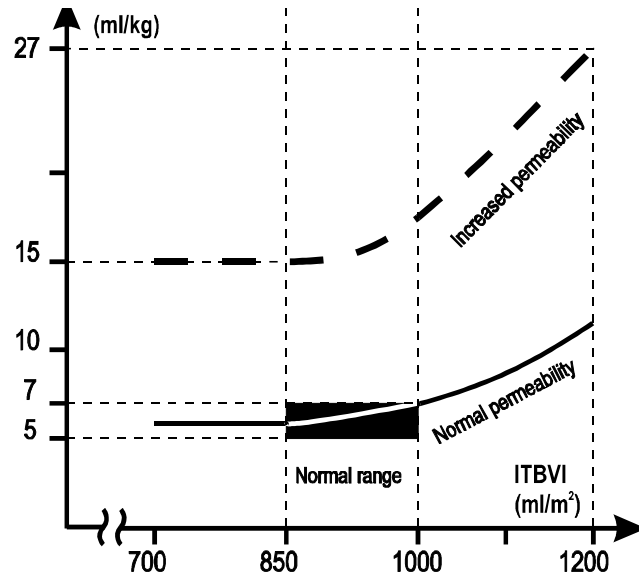
A prospective randomized study by Mitchell et al including over 100 intensive care patients concluded that hemodynamic management using EVLW, as opposed to the conventional pulmonary artery catheter (RHC) management using PAOP, significantly reduced ventilation days (Median: EVLW: 9 days, RHC: 22 days) as well as the length of ICU stay (Median: EVLW: 7 days, RHC: 15 days). The ICU mortality of the group guided by EVLW was 35% compared to 47% in the group guided by pulmonary artery catheter (RHC).



Mitchell JP, et al: Am Rev Resp Dis 145: 990-998, 1992

Relationship between intrathoracic blood volume and extravascular lung water

The level of EVLW correlates to patient outcome and measures to reduce EVLW are most likely to shorten ventilation days and stay in the ICU and reduce possible complications (pneumonia, pneumothorax, etc.).



Patient management by combined use of EVLW and ITBV

The hydrostatic component of increased EVLW can be reduced by volume restriction. In the lower portion of the diagram it is shown that below the “normal range” of ITBV, EVLW cannot be reduced. Thus, ITBV representing cardiac preload should not be driven below this level in order to avoid further reduction in cardiac output and hence oxygen supply to the body.

Conclusion

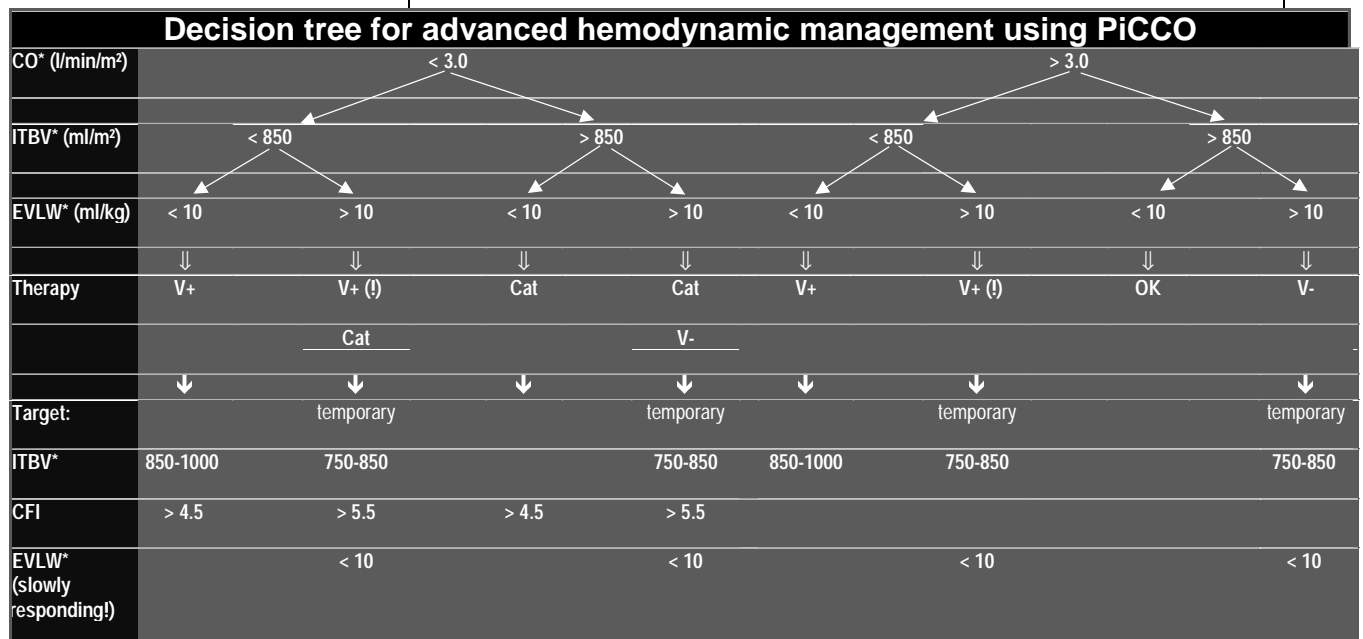
In conclusion transpulmonary physiological monitoring offers many advantages in comparison to the common hemodynamic monitoring with the pulmonary artery or right heart catheter:

- 1. A less invasive measurement with central venous and arterial access offers highly specific variables: continuous CCO and SV, CO, ITBV, EVLW.**
- 2. The technology has been successfully applied in babies and infants.**
- 3. Both, ITBV and EVLW are sensitive guides for hemodynamic management and may have the potential to increase effectiveness and decrease costs in therapy management of critically ill patients.**
- 4. Further analysis of the arterial pressure curve yields stroke volume variation which may offer additional valuable information.**

Decision Tree

The PiCCO method represents an inexpensive, less invasive technology for continuous quantification of cardiac output, intrathoracic blood volume and extravascular lung water. CCO module requires a central venous and an arterial access. The PiCCO method represents for many fields of application an alternative to the pulmonary artery catheter and is also applicable in children and infants.

The PiCCO method represents for many fields of application an alternative to the pulmonary artery catheter and is also applicable in children and infants.



V+ = volume loading (! = cautiously); V- = volume contraction; Cat = inotropic / vasoactive support instructions without guarantee

Normal Ranges

Variable	Normal Ranges	Unit
CI	3.0 - 5.0	l/min/m ²
ITBVI	850 - 1000	ml/m ²
EVLWI*	3.0 - 7.0	ml/kg
CFI	4.5 - 6.5	1/min
HR	60 - 90	1/min
CVP	2 - 10	mmHg
MAP	70 - 90	mmHg
SVRI	1200 - 2000	dyn ² sec ² cm ⁻⁵ m
SI	40 - 60	ml/m ²
SVV	£ 10	%

*Not available in the USA

Questions and Answers

Application Questions

General

1. What are the indications and contraindications for PiCCO method?

Indications:

Patients in whom cardiovascular and circulatory volume status monitoring is necessary. Such as patients in surgical, medical, cardiac and burn speciality units as well as other speciality units where cardiovascular monitoring is desired and patients undergoing surgical interventions of such magnitude that cardiovascular monitoring is necessary. In short, every patient who require a central venous and arterial catheter for monitoring.

Contraindications:

Arterial access restriction due to femoral artery grafting or severe burns in areas where the arterial catheter would normally have been placed. *Note: Axillary artery can be used as alternative site.*

The PiCCO method may give incorrect thermodilution measurements in patients with intracardiac shunts, aortic aneurysm, aortic stenosis, pneumonectomy, macro lung embolism and extracorporeal circulation (if blood is either extracted from or infused back into the cardiopulmonary circulation).

2. Which external factors influence the measured parameters in false direction and what kind of pathological situations and illnesses may result in incorrectly measured parameters?

Air bubbles in the arterial pressure monitoring kit will dampen the curve and possibly influence the pulse contour cardiac output. Inadequate amount of indicator (small volume or too high temperature) will influence thermodilution and volume calculations. However, the status line will alert you if the thermodilution is incorrect.

Clinical situations include arrhythmia (incorrect pulse contour cardiac output), large EVLW (more indicator necessary), aortic aneurysm (ITBV and GEDV will be overestimated if you use femoral arterial line), rapidly changing body temperature (malignant hyperthermia or rewarming influences blood temperature baseline) and intracardiac shunts (recirculation of indicator). In pediatric

patients you may encounter patent ductus botalli (recirculation of indicator).

3. How long can a CCO thermodilution catheter and other disposables be left in a patient?

In general the arterial line can be left for 10 days unless there are signs of infection around the catheter. Each hospital usually have protocols for indwelling catheters and what frequency they should be changed or removed. It is very rare that a patient will get a systemic infection from the arterial catheter. Systemic infections are more commonly associated with central venous catheters.

Depending on the hospital's policy the monitoring kit and the inline injectate sensor housing is changed approximately every 3-5 days.

4. Are there special recommendations for the use of the CCO in open-heart surgery?

The initial calibration of the CCO should be done by thermodilution measurements after induction of anaesthesia but before opening of the chest. During pulse contour calibration with thermodilution measurements the patient should be hemodynamically stable and have no significant change in body temperature. During extracorporeal circulation the CCO cannot give any valid results due to lack of arterial waveform. Thermodilution measurements are not useful during extracorporeal circulation. As soon as the heart is pumping again the CCO will show the cardiac output from pulse contour analysis. Immediate recalibration of pulse contour is usually not necessary.

5. Is it possible to use the CCO under the condition of intra-aortic balloon pump (IABP)?

The thermodilution measurement with the CCO is not influenced by IABP, but the pulse contour analysis is unable to provide valid continuous output.

6. Is it possible to use CCO in patients undergoing liver surgery?

The CCO can be used in any kind of surgery, including liver surgery.

Transpulmonary indicator dilution

1. Is it possible to use CCO in patients with important variations of blood temperature or with hypothermia?

The PiCCO compensates for baseline temperature drifts. If the baseline drift is higher than 0.05°C per minute, the display shows the message “Unstable baseline, injection not recommended” or Excessive baseline drift, don’t inject now”. Hypothermia does not cause any problems, if the CCO detects a stable baseline. However, room temperature injectate may not be used.

2. Is it possible to use the CCO in patients treated with continuous hemofiltration?

In patients with hemodialysis/hemofiltration the measurements with CCO will give accurate results as long as the hemodialysis catheter is not placed into the cardio-pulmonary circulation.

3. Is it possible to inject the cold bolus through a venous catheter placed in the right atria? Are the results obtained by this thermodilution exactly the same than those obtained by the bolus injection into the vena cava?

The catheter for indicator injection should be placed central venously, either directly before the right heart or into the right atrium to obtain correct volume measurements. For calibration of the pulse contour analysis injection of indicator in a peripheral vein is possible, as long as the arterial catheter can obtain a good quality thermal response curve. However, volume determinations are incorrect.

4. Is it possible to use a catheter placed into the Vena Basilica for the indicator injection?

Vena Basilica can be used for calibration of the pulse contour cardiac output as long as the thermodilution curve is within the time limits. However, the volumes (ITBV, GEDV, EVLW) will not be correct.

5. What is the effect of injecting the ice cold indicator for the PiCCO method into the femoral vein instead of the superior vena cava/right atrium. Does this make a clinically significant difference on the GEDV, ITBV and EVLW?

If the catheter for indicator injection is placed into the femoral vein, the CCO readings for ITBV and GEDV will be about 75 ml (as absolute values) higher than the volumes really are. Reason for this is, that the volume from the point of injection to the point of detection will be higher, because the catheter for indicator injection is not placed directly before or in the right atrium. The value for EVLW will be correct, because both, ITTV and ITBV will be about 75 ml higher than they really are and EVLW results from the formula $EVLW = ITTV - ITBV$.

The CCO reading for the index value ITBVI will accordingly be higher than it really is, based on the incorrect high absolute value and the body surface area of the patient. e.g. ITBVI measured through indicator injection into the femoral vein will be 840 ml/m^2 , whereas ITBVI through indicator injection directly before or into the right atrium will be 800 ml/m^2 .

6. Can temperature artifacts appear during baseline analysis?

Sometimes temperature artifacts can be visible, if the thermistor on the arterial thermodilution catheter is in contact with the vessel wall. The artefacts are more prominent if the artery is narrow. In general blood temperature does not change so fast that you will see spikes on the baseline.

7. What are the recommended volumes to be injected for arterial thermodilution measurement?

The injection volume is dependent on the body weight. If the patient has an increased amount of extravascular thermal volume (ETVI, more than 10 ml/kg body weight), the injection volume has to be increased.

Patient Weight	Cold Injectate		Room Temp Injectate	
	ETVI < 10	ETVI ≥ 10	ETVI < 10	ETV ≥10
< 3 kg	2ml	2ml	3ml	Use cold Injectate
< 10 kg	2ml	3ml	3ml	
< 25 kg	3ml	5ml	5ml	
< 50 kg	5ml	10ml	10ml	
< 100kg	10ml	15ml	15ml	
≥ 100 kg	15ml	20ml	20ml	

Iced = cold solution, RT = solution with room temperature

8. How many times is the injection of iced-cold injectate recommended to perform thermodilution measurements in a new patient?

Three times. Technically one time is enough. However, if the patient has large EVLW your first determination may be inaccurate and you have to adjust the amount of indicator given to the patient.

9. Is it detectable by M1012A C#10 cardiac output module (CCO) if the shape of the thermodilution curve is abnormal?

Yes, the M1012A C#10 Cardiac output module checks several parameters of the thermoldilution curve and uses them to derive several curve alerts.

Pulse contour analysis

1. The fact that all values are dependent on just "one" cal, what if cal is not properly done?

There are criteria that need to be met during calibration. Both the thermodilution curve and the arterial waveform must be considered technically acceptable before the CCO is calibrated.

2. Does the CCO give accurate values, when vasoconstrictors are used?

The CCO gives correct results as long as the vascular resistance does not change drastically. If there is a change of more than 20% in systemic vascular resistance, a recalibration is recommended. Additionally, we recommend a calibration by thermodilution every 8 hours. In the clinical situation, where vascular volume monitoring is performed, more frequent calibrations will usually be performed due to thermodilution measurements to obtain ITBV, GEDV and EVLW.

3. What are the time intervals or under what circumstances is it recommend to carry out new thermodilution measurements in order to keep the monitoring results from pulse contour analysis updated and more accurate to the patient status?

In general the CCO should be calibrated every 8 hours with a thermodilution determination. The time intervals are very patient dependent. If you are in the resuscitation phase when your patient is in shock maybe you have to determine ITBV every hour. When the patient is stabilized maybe you can decrease the frequency to once every 2 hours and if the patient remain stable decrease to every 4-6 hours. An other guide line would be to perform a thermodilution determination if the continuous cardiac output has changed consistently in the same direction for the past 15 minutes and of course if there are large and/or sudden changes in the patients clinical status.

Another helpful indicator in patients on mechanical ventilation is the Stroke Volume Variation (SVV). If the SVV increases to over 10%, without changes in ventilatory support, a thermodilution determination is in order to determine the

volume status of the patient.

4. What about pulse contour in case of arrhythmia?

In cases of severe arrhythmia (ventricular fibrillation, supra-ventricular tachycardia) the pulse contour cardiac output will not be accurate. However, in cases with mild to moderate arrhythmia (atrial flutter/fibrillation, bigemini, trigemini or occasional extra beats) the pulse contour will reflect current cardiac output. You have to calibrate the pulse contour more frequently as the arrhythmia changes and use 3-5 bolus injections each time.

5. What about Pulse Contour in case of changing pressure curves, tamponade, registration of bad quality curves etc.?

Each pulse waveform is analyzed to detect large variations in the shape. Certain criteria must be fulfilled for the waveform to be accepted. If the pulse contour is deemed not plausible no values will be displayed.

6. Pulse contour cardiac output shows vast differences compared to the cardiac output determined by arterial thermodilution. What are the possible reasons?

- a) Significant hemodynamic instability.
- b) Errors in detection of the arterial wave form and therefore errors in the wave form analysis.
- c) Extreme arrhythmia or frequent extrasystole.

PiCCO Technology

1. Does CCO measure or calculate volumes?

The PiCCO technology calculates the volumes based on the thermodilution curve using mean transit time and down slope time multiplied with cardiac output.

2. Why $ITTV = MTt * COa$? Why $PTV = DSt * COa$? So far we only know "what it is", but not "why it is". We only know that the results might be correct, but why they are correct? How are these two formulas developed and how to proof them to be accurate? Any clinical trials or experiments done to develop these two formulas?

The algorithm used is based on standard indicator dilution theory:

Mean Transit Time (MTt):

If you rapidly inject an indicator into a system of flowing liquid not all indicator will appear at the detection site at the same time. The concentration of the indicator will be distributed over time as a result of the volume of the system i.e. there is a given time for each indicator particle to traverse the distance between point of injection and point of detection. This time is called the transit time. No one transit time apply to all indicator particles rather there is a transit time for each particle. If you take the mean value of all these transit times you will get MTt.

The area under the dilution curve represents the flow of liquid through the system (volume/time) and the MTt how long it took the indicator to get through the system (time). If you multiply volume/time with time ($ml/min * min/1 = ml$) the result will be volume.

Down slope time (DSt):

DSt is a little more difficult to explain. The DSt is only dependent on the largest volume in a series of volumes. Think of DSt this way.

If you have four buckets and a bathtub and you place them in series with first two buckets, the bathtub and the remaining two buckets. Place some red dye in the first bucket and turn on the water. The first bucket will get filled and red water will overflow into the second bucket. When the second bucket is full all the red dye is gone from the first bucket (if the buckets are the same volume). Now the

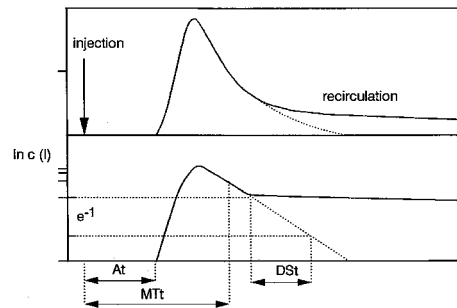
second bucket overflows into the bathtub. When the bathtub is full it will overflow into the third bucket. By this time there is no dye left in the first and second buckets. When the third bucket overflows into the fourth bucket there is still red dye in the bathtub and even when the fourth bucket overflows there is still red dye in the bathtub. It will take a large volume to clear the bathtub from dye, much larger than the four buckets individually or together. This is why the DSt is only dependent on the largest volume in a series of volumes and it does not matter where you place the bath tub in the series. Once again we are looking at a time relationship, how long time did it take to wash out the bath tub, and multiplying with the flow through the system ($\text{volume/time} * \text{time}/1 = \text{volume}$).

There are several published articles where ITBV have been compared to pressures obtained from the pulmonary artery catheter. All studies demonstrate the excellent correlation between changes in cardiac index and ITBV and very poor correlation between pressures and changes in cardiac index.

3. How is the exponential down-slope time (DSt) detected?

The down-slope time is detected by plotting the thermodilution curve with the temperature change (indicator concentration) on a logarithmic scale (ln) and time change on a linear scale (lin). When you plot the thermodilution curve as a lin-ln graph, the indicator decay approximates a linear function. Two points, the starting point located at 75% of the maximum temperature response and an end point defined as 45% of the maximum temperature response (see figure), are identified and the time difference is determined and is

labelled down-slope time..



4. We want to standardize pressure-monitoring kits, why do we have to use PULSION kits?

The PULSION kits have been tested for frequency response to give us the best fidelity and are matched to the algorithm used in the CCO. The most important factor to maintain fidelity is the connection tubing used with the PULSION transducer. This tubing is very stiff and with a certain length and inner diameter. If you use another pressure transducer and connection tubing the pulse contour cardiac output may not be correct.

Medical and Physiological Questions

1. Does the respiratory cycle influence the value of measured parameters?

No. The respiratory cycle does not influence our measurements since the thermodilution curve is at least 20 seconds long. You could fit at least 3 respiratory cycles under the curve.

2. Which cardiac output is more accurate, the one measured by PiCCO method or the one measured by pulmonary artery catheter?

This is a difficult question to answer since both methods are using the Stewart-Hamilton algorithm and thermodilution. In terms of accuracy the two methods are very comparable. However, our method has a much lower coefficient of variability that means that our method is less user dependent and gives more stable measurements. Compared to the gold standard (Fick method) the PiCCO CCO has excellent correlation ($r^2 = 0.9$ or better with bias of approximately 130 ml/min). Even the pulse contour cardiac output compares with high degree of correlation and low bias to the arterial thermodilution cardiac output.

3. Is the cardiac output measurement correct in case of aortic stenosis?

In aortic stenosis the arterial thermodilution accurately reflects the cardiac output. The arterial pressure waveform is basically normal with possibly reduced systolic and elevated diastolic pressures. The area under the arterial waveform still reflects the stroke volume.

4. Is the cardiac output measurement correct in case of aortic valve insufficiency?

In aortic insufficiency the aortic valve does not close correctly. The thermodilution curve will be affected since the indicator will be regurgitated which results in prolonged indicator decay time. In severe aortic insufficiency the curve may time out. However, if a thermodilution curve is obtained it accurately reflects the cardiac output. The arterial waveform may be distorted and the lack of dicrotic notch may influence the CCO accuracy.

In both cases, the pulmonary and arterial cardiac outputs are the same. However, in aortic insufficiency, if thermodilution cardiac output is compared to Doppler flow measurements, the Doppler measurements will show a higher cardiac output. The Doppler measures instantaneous forward flow that does not include the regurgitated blood. Thus a higher cardiac output is calculated based on forward flow.

5. In case of cardiac tamponade the thermodilution curve is very low. What is the reason?

One reason why the thermodilution curve is very long is that cardiac output is very low.

Cardiac tamponade is a situation where the pericardial sack is filled with fluid and/or blood clots. Since the pericardial sack completely envelopes the heart, any fluid in the sack will influence the function of the heart. If enough fluid is in the pericardial sack, the heart cannot fill and the cardiac output will drop. Another result of cardiac tamponade is that the arterial waveform is significantly dampened. When you see a very low heart rate during cardiac tamponade the situation is very critical and measurement of cardiac output is of no use. The patient needs a surgical procedure called pericardiocentesis to drain the fluid from the pericardial sack.

6. Is it possible to calculate the volume demand of a patient directly from values of the trans-pulmonary thermodilution measurement?

The intrathoracic blood volume (ITBV) is approximately 1/3 of total blood volume. Thus if you measure an intrathoracic blood volume index (ITBVI) of 650 ml/m², the normal value for ITBVI is 850 - 1000 ml/m², and the patient's body surface area is 1.8 m² you can calculate the amount of fluid necessary to restore normal ITBVI.

$$\text{Volume needed} = (850 - \text{ITBVI}_{\text{measured}}) * \text{body surface area} * 3$$

$$\text{In our example: } 1080 = (850 - 650) * 1.8 * 3$$

The patient needs approximately 1080 ml increase in vascular volume to return to normal ITBVI. If the doctor uses colloid solutions (blood, fresh frozen plasma, albumin,

hetastarch or dextran), 1080 ml is what is necessary. If however, crystalloid solution is used (Normal Saline, Ringers Lactate, 5% Dextrose I water or similar) you have to multiply the 1080 by 4 to reach the volume necessary. Of course a combination of crystalloid and colloid solutions may be used, remember that whatever portion of ITBVI that is replaced with crystalloid solution you have to multiply that portion by 4.

7. Cardiac preload volume of is not the equal to intrathoracic blood volume (ITBV). Why is ITBV a good indicator of cardiac preload? How is it possible to estimate cardiac preload from ITBV?

This raises the question: "What is preload?" Strictly defined, cardiac preload is the myocardial fibre stretch at the end of ventricular diastole. A parameter that accurately reflects preload in clinical practice is not yet available, however, studies have demonstrated, that:

1. ITBV is a reproducible and sensitive parameter for a close approximation of preload (Lichtwarck-Aschoff 1992, Preisman 1997, Hedenstierna 1992)
2. The so-called filling pressures (central venous pressure, pulmonary artery occlusion pressure), nor right ventricular end-diastolic volume reflects cardiac preload (Lichtwarck-Aschoff 1996, Pfeiffer 1990, Sakka 1999)

8. What is the level of error in case of aortic aneurysm?

It is very hard to predict the amount of error in ITBV or GEDV as a result of an aortic aneurysm. If there is an abdominal aortic aneurysm and you are using an axillary arterial line there is no error.

9. Does pleural fluid influence the measurement of extravascular lung water (EVLW)?

Pleural fluid is not measured as EVLW for two reasons:

1. The capillary surface that is in contact with the pleural fluid is very small in comparison to the pulmonary capillary network. Thus, the temperature loss to the pleural fluid is negligible.
2. The distance for diffusion is very large requiring a long time for equilibrium.

10. What is the clinical value of dP/dt ?

dP/dt is a direct measurement of contractility. The dP/dt is a measure of how fast the pressure is rising during systole. If you measure pressure close to the aortic valve, the rise in blood pressure during ventricular systole is proportional to the force of contraction. We measure blood pressure either in the femoral or axillary artery; thus, the increase in pressure during systole is somewhat blunted. However, the rise is still indicative of the force of ventricular contraction. You can use dP/dt to document the effects of inotropic drugs.

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Stroke Volume Variation

Vascular Access

Risk analysis of the femoral arterial access

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Comparison of arterial accesses

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Axillary artery access

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Long radial artery catheters

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Sample Case Studies

Case 1

A 63 year old male patient, came for total hip re-replacement. The patient was a heavy smoker, and 26 years previously had pulmonary embolism after a similar operation. The patient underwent uneventful anesthesia but about 4 hours into the surgical procedure he developed frank alveolar pulmonary edema and oxygen desaturation of less than 80%.

Although the last blood pressure measured in the OR was 150/100 mmHg, the patient arrived in the Post-Anesthesia Care Unit with a blood pressure (BP) of 63/40 mmHg and a heart rate of 137 bpm. He received dopamine and adrenaline and his BP increased to 96/93 mmHg. His arterial blood gases showed pH 7.23, pO₂ 75 mmHg (FiO₂ 1.0), pCO₂ 42 mmHg and hematocrit of 37%.

Differential diagnosis

Differential diagnosis included massive pulmonary embolism, acute MI (had intraoperative ST segment changes during the event), transfusion reaction, or reaction to methyl-metacrylate.

A femoral CCO catheter was inserted, following parameters were derived:

Parameter	Values	Interpretation
CI [l/min/m ²]	1.91	Low Cardiac Output
ITBVI [ml/m ²]	779	Normal (or little low) preload
EVLWI [ml/kg]	23	Excessive lung water (pulmonary edema)
SVV [%]	22	Significant volume responsiveness, probably hypovolemia

The high SVV and the surprisingly normal-to-low ITBV values in a patient who is hemodynamically unstable and in severe pulmonary edema led to a change in the management. The patient got more fluids and the vasopressors were gradually reduced. Transthoracic echo was inconclusive and a later TEE showed a hyperdynamic heart with a small LV end-diastolic area.

Application Note

The PiCCO values over the next 2 days were the following:

Parameter	Immediately after volume loading	First post-operative day	Second post-operative day
CI [l/min/m ²]	3.75	2.89	3.47
ITBVI [ml/m ²]	1444	972	1093
EVLWI [ml/kg]	15	5	4
SVV [%]	21	8.4	7.1

The patient was extubated on the second postoperative day with normal lung water although the chest roentgenogram still showed considerable edema.

Conclusion

The ITBV and the SVV were useful in making the diagnosis that preload was inadequate even though the patient was in pulmonary edema. Intravenous fluids, cessation of dopamine and adrenaline, PEEP and later diuresis were the key points in the successful management of this patient. The low EVLW value helped in the decision to extubate even before normalization of the chest x-ray. Available: Automated Anesthesia Record, X-rays.

Reference:

Prof. Azriel Perel, MD
Sheba Medical Center
Tel Aviv University
IL-52621 Tel Hashomer
Phone +972-(0)3-5302796
E-mail: perelao@shani.net

Case 2

The patient got jammed in his truck's drivers cabin after a traffic accident.

Diagnosis

Hemorrhagic shock, fracture of femur, lung contusion
The primary picture 1 seems to represent hypervolemia, however ITBVI and EVLWI disprove this assumption.

Picture 1



Parameters	Value
ITBVI [ml/m ²]	658
EVLWI [ml/kg]	7.9
CVP [mmHg]	14
FiO ₂ [%]	90

Therapy

Kinetic therapy and positive fluid balance resulted in clear improvement of the lungs (picture 2).

Picture 2



Parameters	Value
ITBVI [ml/m ²]	816
EVLWI [ml/kg]	8.1
CVP [mmHg]	13
FiO ₂ [%]	40

Reference:

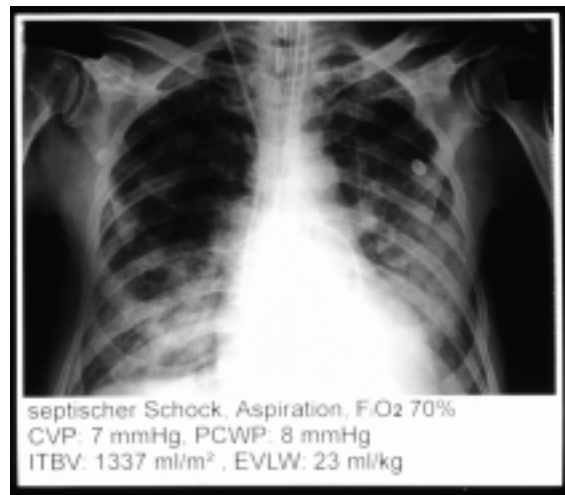
OA Dr. med. Andreas Meier-Hellmann
Klinikum der Friedrich-Schiller-Universität Jena
Klinik für Anästhesiologie und Intensivtherapie
Bachstr. 18
D-07743 Jena
Phone +49-(0)3641-933-158
E-mail: Meier-Hellmann@anae1.med.uni-jena.de

Case 3

Diagnosis

Patient with septic shock after aspiration.
Picture 1 and the filling pressures indicated more or less hypovolemia, however ITBV and EVLW clearly indicated hypervolemia and pulmonary edema.

Picture 1



Parameters	Value
ITBVI [ml/m ²]	1337
EVLWI [ml/kg]	23
PCWP [mmHg]	8
CVP [mmHg]	7
FiO ₂ [%]	70

Therapy

Negative fluid balance resulted in a clear stabilization of circulation and decreasing EVLW (picture 2).

Picture 2



Parameters	Value
ITBVI [ml/m ²]	861
EVLWI [ml/kg]	12
CVP [mmHg]	8
FiO ₂ [%]	35

Reference:

Klinikum der Friedrich-Schiller-Universität Jena

Klinik für Anästhesiologie und Intensivtherapie

Bachstr. 18

D-07743 Jena

Phone +49-(0)3641-933-158

E-mail: Meier-Hellmann@anae1.med.uni-jena.de

Case 4

Diagnosis

Patient with septic shock at peritonitis.

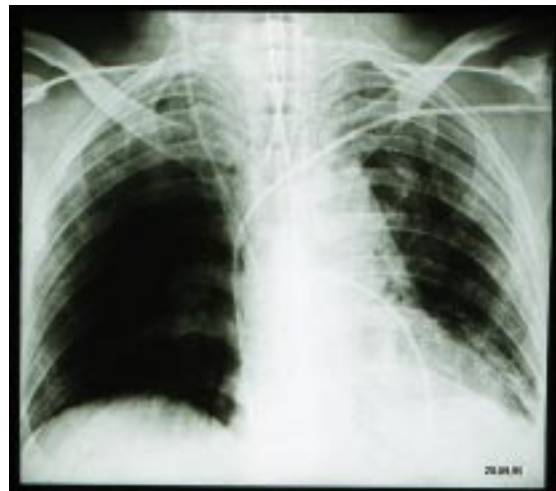
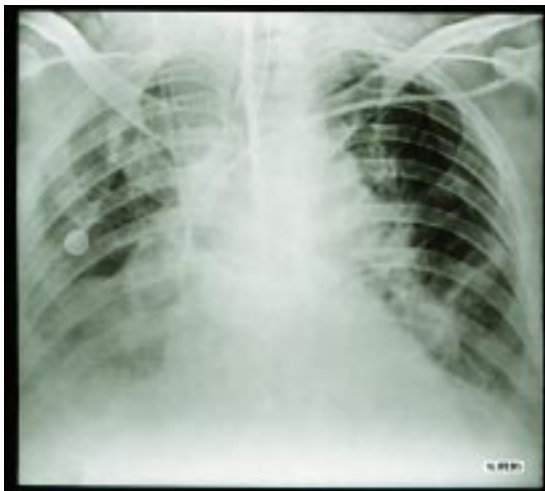
Therapy

In the early postoperative phase a positive fluid balance was aimed.

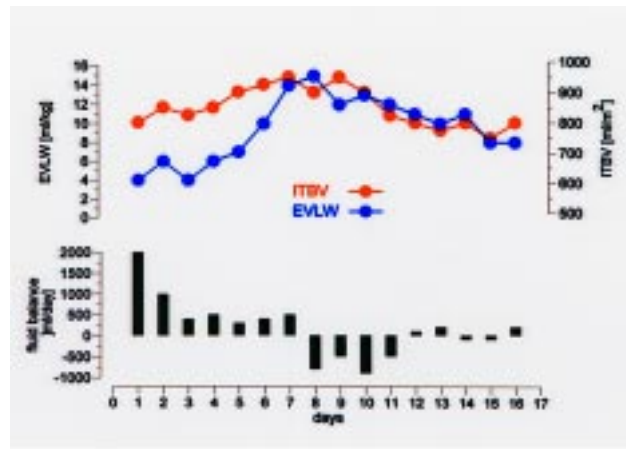
After this, a pulmonary deterioration was indicated (FiO₂ increased from 0.4 to 0.7), accompanied with an increased EVLW (picture 1).

Thereupon reserved volume therapy was performed and both, improvement of pulmonary situation and a decrease in EVLW (picture 2) was achieved.

Picture 1 Picture 2

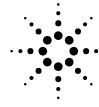


Picture 3 Trend of ITBVI, EVLWI and fluid balance over a time period of 17 days



Reference:

OA Dr. med. Andreas Meier-Hellmann
Klinikum der Friedrich-Schiller-Universität Jena
Klinik für Anästhesiologie und Intensivtherapie
Bachstr. 18
D-07743 Jena
Phone +49-(0)3641-933-158
E-mail: Meier-Hellmann@anae1.med.uni-jena.de



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1-800-291-6743

Latin America:

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5200 Blue Lagoon Drive
9th Floor
Miami, FL 33126
(305) 267-4220

Europe, Middle East and Africa

Agilent Technologies
Healthcare Solutions Group
Herrenberger Str. 110-140
71034 Boeblingen
Germany
Fax: (+49) 7031 464 1552

Asia Pacific Headquarters:

Agilent Technologies, Inc.
24F Cityplaza One
1111 King's Road
Taikoo Shing, Hong Kong
(+852) 3197 7777

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