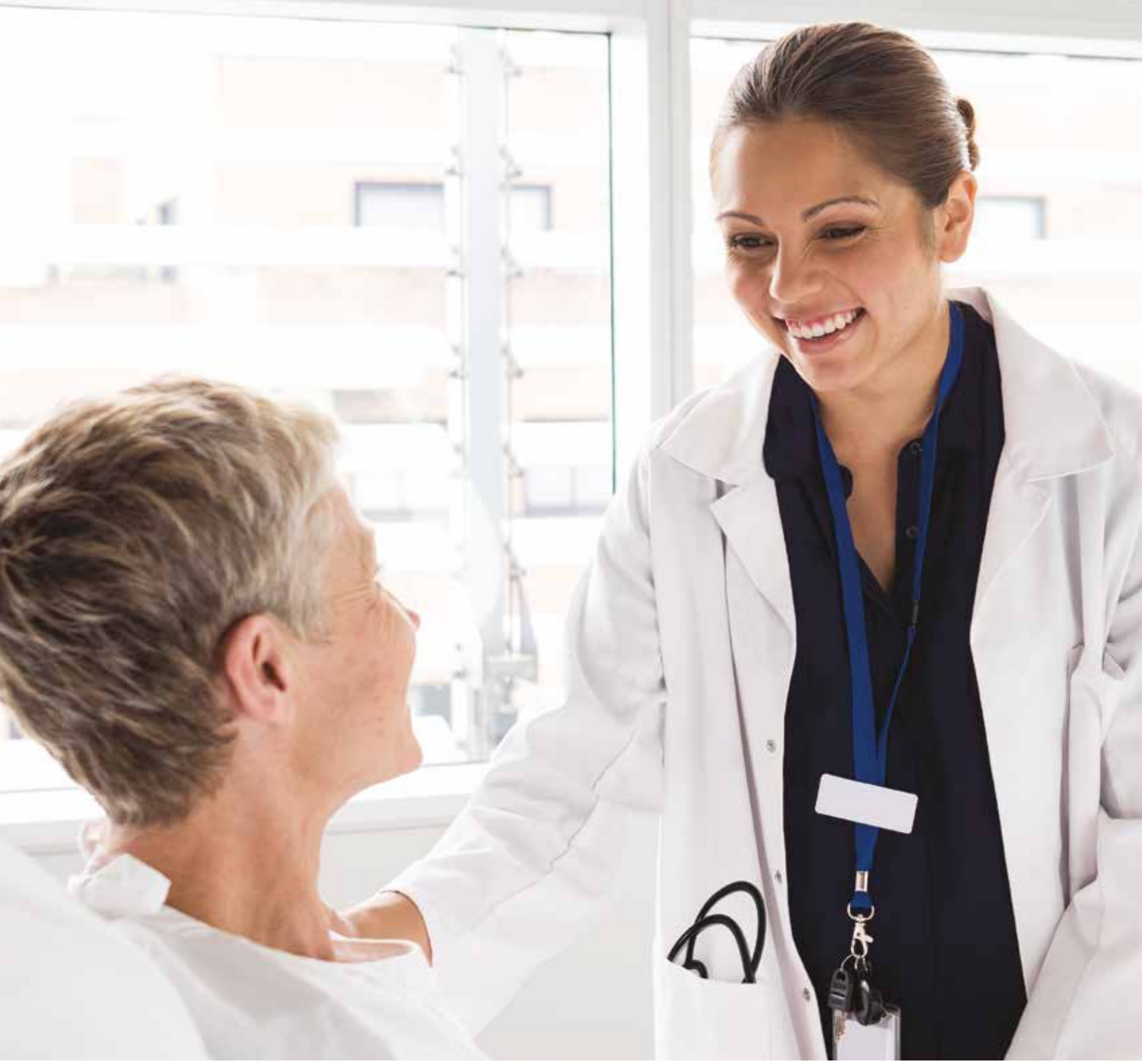


# PiCCO technology

## Hemodynamic monitoring at the highest level

GETINGE

# Simplify hemodynamics

## Understand complex conditions with PiCCO

The life of your critically ill patient depends on making the right therapeutic decision. To achieve this, you need trusted information you can rely on – such as a broad set of reliable hemodynamic parameters so you can determine the best individual treatment for that patient.

PiCCO technology was introduced in 1997 by Pulsion Medical Systems, which has more than 20 years of experience in hemodynamic monitoring. Since then, the PiCCO technology has been continuously enhanced.

Today, PiCCO technology is the established standard for advanced hemodynamic monitoring and is available with the PulsioFlex Monitoring System and integrated into monitors of the world market leaders in patient monitoring including Philips and GE.

Over the last 15 years, nearly 1,000 publications worldwide have confirmed the accuracy and clinical benefit of the PiCCO technology.

PiCCO technology is used more than 140,000 times per year in more than 60 countries.

since
1997

publications
1,000

annual PiCCO applications
140,000

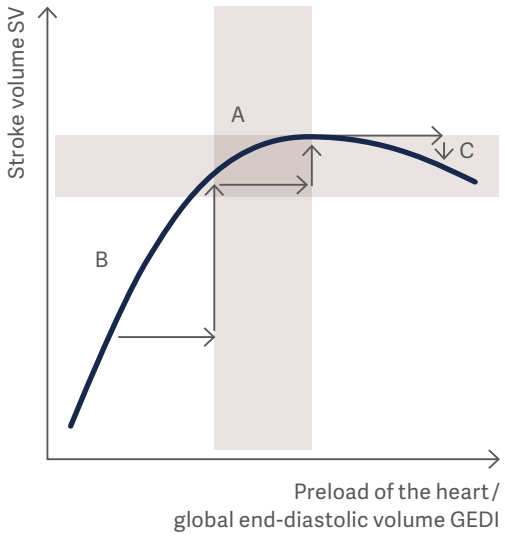
# Basics of hemodynamic monitoring

## Monitoring cardiocirculatory function is necessary for all intensive care patients.

Monitoring with standard parameters, such as ECG non-invasive blood pressure and pulse oximetry, provides insufficient information to determine an adequate treatment. Only advanced hemodynamic monitoring with minimally-invasive measurement of cardiac output and its determinants (preload, afterload, contractility) as well as the quantification of pulmonary edema can ensure the appropriate treatment.

## Frank-Starling mechanism

The Frank-Starling law states that the greater the volume of blood entering the ventricle during diastole (end-diastolic volume), the greater the volume of blood ejected during systolic contraction (stroke volume) and vice versa. This is an adaptive mechanism to compensate for slight changes in ventricular filling.



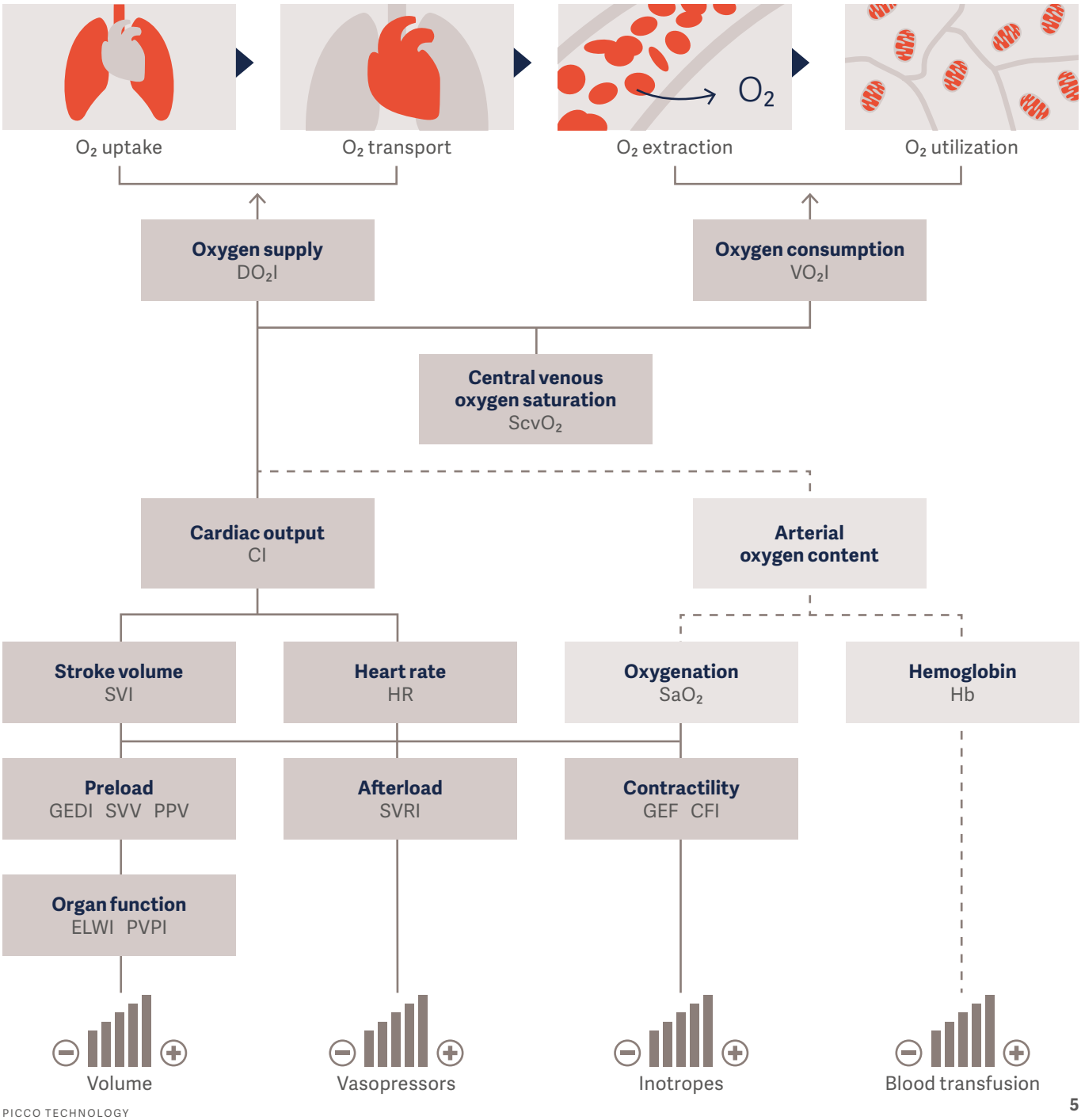

Schematic Frank-Starling curve for verification of the preload status
A = Optimal preload, B = Volume reponsive, C = Volume overload

## The power of the heart muscle depends on its initial load before the start of contraction.

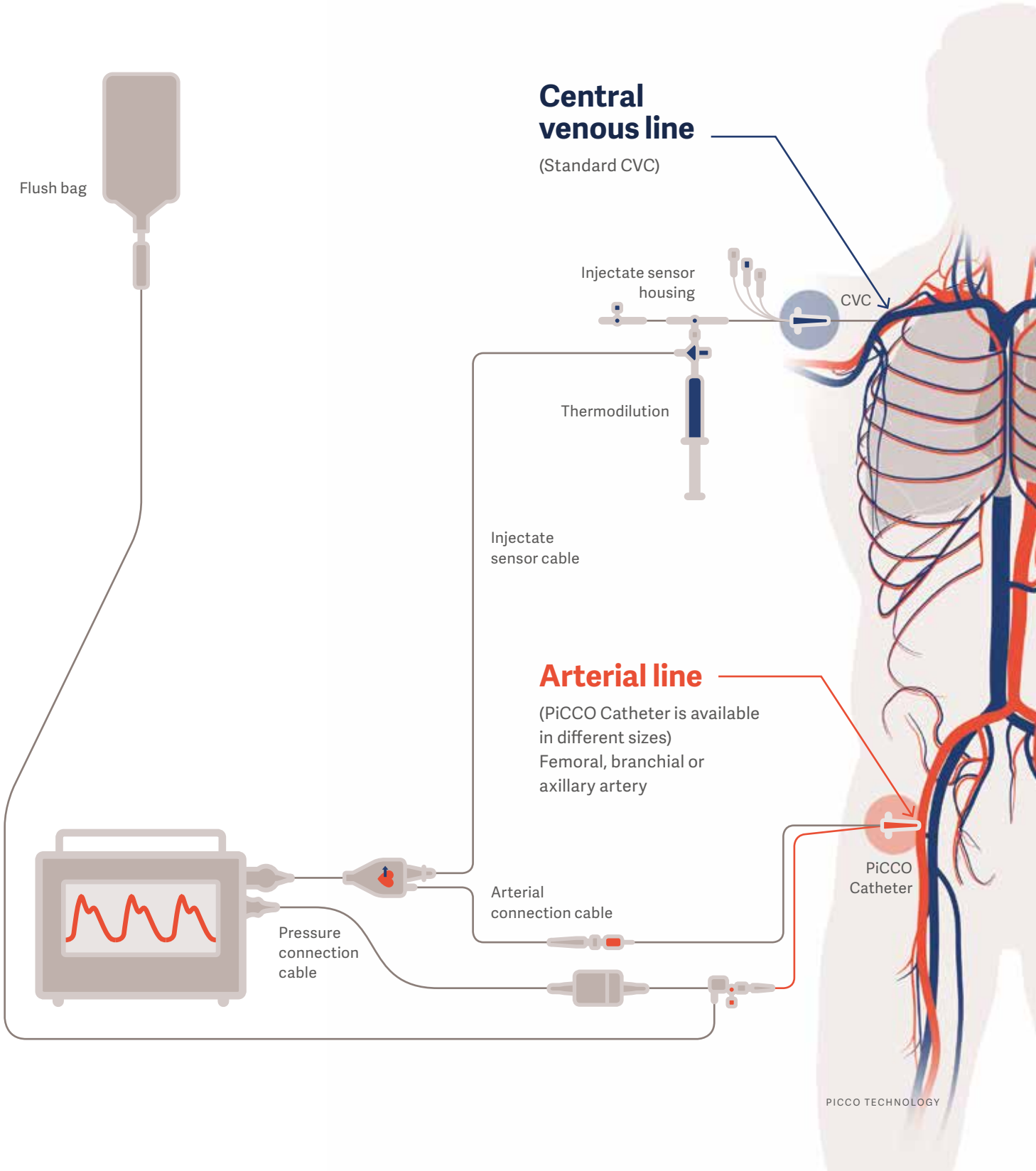
However, it can also be used to increase stroke volume by volume administration for therapeutic reasons. The force that any single cardiac muscle fiber generates is proportional to the initial sarcomere length (known as preload), and the stretch on the individual fibers is related to the end-diastolic volume of the ventricles.

An increase in preload will, to a certain extent, lead to an increase in stroke volume (SV), based on optimal myocardial muscle fiber pre-stretching. Up to a certain limit, the more the sarcomeres of the muscle cells are stretched, the greater the contraction. On the other hand, contractility may decrease in conditions of volume overload.

# Hemodynamic parameters



# How PiCCO technology works



# Two components of PiCCO technology

PiCCO technology is based on two physical principles: transpulmonary thermodilution and pulse contour analysis. Both allow the calculation of hemodynamic parameters and have been clinically tested and established for more than 20 years.[1, 2]

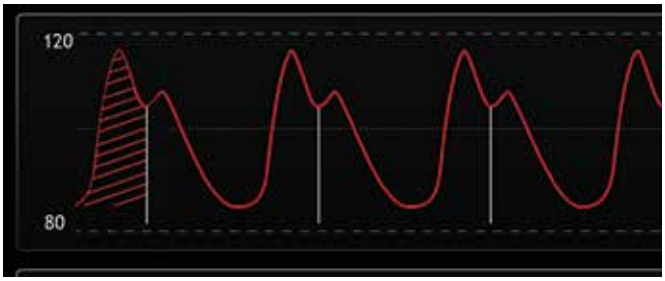
## Arterial pulse contour analysis

The pulse contour analysis provides continuous information while transpulmonary thermodilution provides static measurements. Transpulmonary thermodilution is used to calibrate the continuous pulse contour parameters.

## Transpulmonary thermodilution

For the transpulmonary thermodilution measurement, a defined bolus (for example 15 ml cold normal saline) is injected via a central venous catheter.

The cold bolus passes through the right heart, lungs and left heart and is detected by the PiCCO Catheter, which is commonly placed in the femoral artery. This procedure should be repeated approximately three times in under 10 minutes to ensure an accurate average is used to calibrate the device and to calculate the thermodilution parameters. These thermodilution parameters should be checked whenever there is a significant change in the patient's condition or therapy. It is recommended that the system be calibrated at least 3 times per day.




Arterial pulse contour analysis

The shaded area below the systolic part of the pressure curve is proportional to the stroke volume.


Transpulmonary thermodilution

# Pulse contour analysis

## The theoretical basis of pulse contour analysis was published for the first time in 1899.[3]

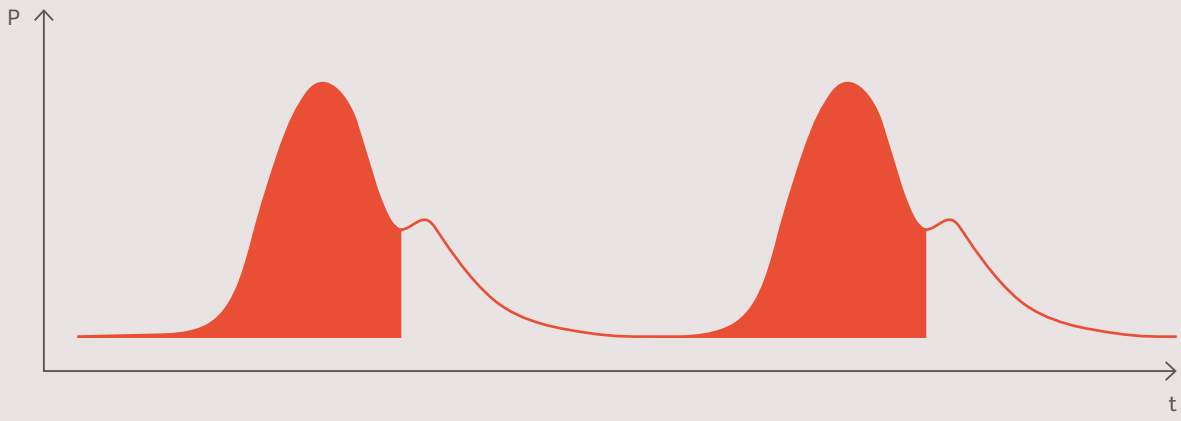
The basic idea was to use the analysis of the continuous arterial pressure signal to obtain more information than just the systolic, diastolic and mean value.

From a physiological point of view, the arterial pressure curve provides information about when the aortic valves opens (moment of the increase of the systolic pressure) and closes (incision in the pressure curve, the dicrotic notch). The time in between represents the duration of the systole and the area under the systolic part of the pressure curve directly reflects the stroke volume (SV), the amount of blood in milliliters that is ejected by the left ventricle with every single heartbeat.

However, the shape of the arterial pressure curve and thus the area under the curve is not only influenced by the stroke volume, but also by the individual compliance of the vascular system.

This is especially true in intensive care patients where a potentially rapid change in the vascular compliance occurs due to the disease process or certain medications. An individual calibration factor is determined with the initial calibration and needs to be updated regularly.[1, 4] With PiCCO technology, this calculation factor is derived from the transpulmonary thermodilution measurement.

Analysis of the arterial pressure curve for the area under the systole




With the sophisticated algorithm, the stroke volume is calculated continuously and, by multiplying the stroke volume with the heart rate, a continuous cardiac output is derived, the pulse contour cardiac output (PCCO).[5]

Patient-specific calibration factor (determined with thermodilution)

Area under the pressure curve

Shape of pressure curve

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

Heart rate

Compliance

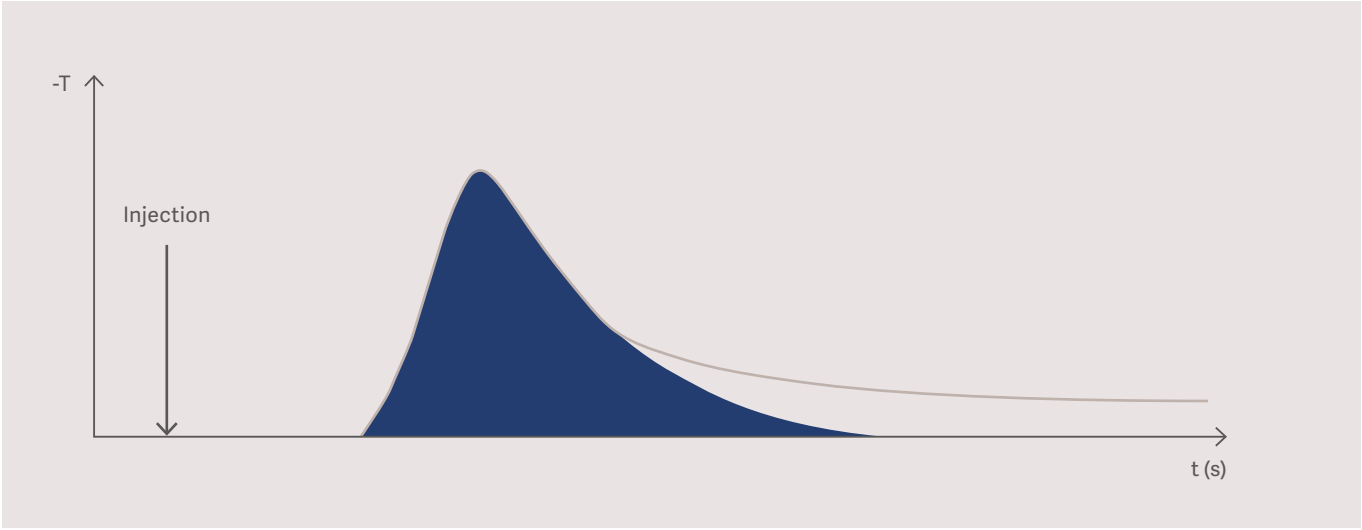
Basic formula to calculate pulse contour cardiac output (PCCO)

The PiCCO pulse contour algorithm is extensively validated and has proved to be very reliable in daily clinical routine:

## Overview of comparative studies on cardiac output measurement using PiCCO pulse contour and pulmonary arterial thermodilution [5–13]

| Reference | Accuracy (l/min) | Standard deviation (l/min) | Regression coefficient |
|---|---|---|---|
| Felbinger TW et al., J Clin Anesth 2005 | 0.220 | 0.26 | 0.92 |
| Della Rocca G et al., Can J Anesth 2003 | 0.080 | 0.72 | – |
| Mielck F et al., JCVA 2003 | -0.400 | 1.30 | – |
| Felbinger TW et al., J Clin Anesth 2002 | -0.140 | 0.33 | 0.93 |
| Della Rocca G et al., BJA 2002 | 0.040 | – | 0.86 |
| Rauch H et al., Acta Anaesth Scand 2002 | 0.140 | 1.16 | – |
| Godje O et al., Med Sci Monit 2001 | -0.020 | 1.20 | 0.88 |
| Zollner C et al., JCVA 2000 | 0.310 | 1.25 | 0.88 |
| Buhre W et al., JCVA 1999 | 0.003 | 0.63 | 0.93 |

# Transpulmonary thermodilution




The CO is calculated from the area under the thermodilution curve

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

Blood temperature

Injectate temperature

Injecate volume

Correction constant*

Area under the thermodilution curve

* comprises specific weight and specific heat of blood and injectate fluid

The cardiac output (CO) is determined from the trans-pulmonary thermodilution.

The thermodilution curves are analyzed and the CO is determined by using a modified Stewart-Hamilton algorithm.[14, 15] This method of calculating the cardiac output is also used in a similar way by the right heart (pulmonary artery) catheter.

## Overview of comparative studies on cardiac output measurement using PiCCO pulse contour and pulmonary arterial thermodilution [5–13]

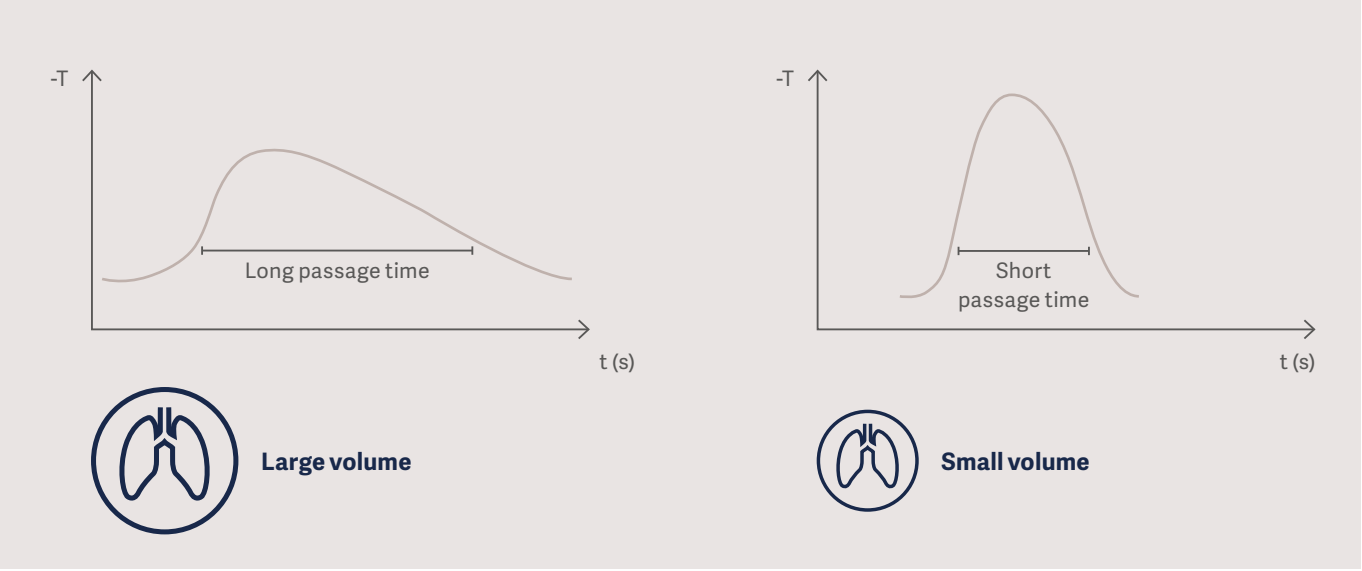
The PiCCO pulse contour algorithm is extensively validated and has proved to be very reliable in daily clinical routine.

| Author | Patient group | Age | N | n | r | Accuracy (%) | Variation (%) | |
|---|---|---|---|---|---|---|---|---|
| Della Rocca et al., 2002 | Liver transplant | 24–66 | 62 | 186 | 0.93 | +1.90 | 11.0 | |
| Friesecke et al., 2009 | Severe heart failure | 29 | 325 | | ni | 10.30 | 27.3 | (PE*) |
| Goedje et al., 1999 | Cardiac surgery | 41–81 | 24 | 216 | 0.93 | -4.90 | 11.0 | |
| Holm et al., 2001 | Burns | 19–78 | 23 | 109 | 0.97 | -8.00 | 7.3 | |
| Kuntscher, 2002 | Burns | 21–61 | 14 | 113 | 0.81 | ni | ni | |
| Mc Luckie et al., 1996 | Pediatrics | 1–8 | 10 | 60 | ni | +4.30 | 4.8 | |
| Segal et al., 2002 | Intensive care | 27–29 | 20 | 190 | 0.91 | -4.10 | 10.0 | |
| von Spiegel et al., 1996 | Cardiology | 0.5–25 | 21 | 48 | 0.97 | -4.70 | 12.0 | |
| Wiesenack et al., 2001 | Cardiac surgery | 43–73 | 18 | 36 | 0.96 | +7.40 | 7.6 | |
| Zöllner et al., 1999 | ARDS | 19–25 | 18 | 160 | 0.91 | -0.33 | 12.0 | |

N = number of patients; n = number of measurements; r = regression coefficient; ni = not indicated
* PE= percentage error according to Critchley

An advantage of transpulmonary thermodilution is that it is independent from breathing or ventilatory cycles. Additionally, because the indicator passes through the heart and lungs, intravascular and extravascular volumes can be determined inside the chest area, in particular, the preload volume and lung water.

# Physiological principles



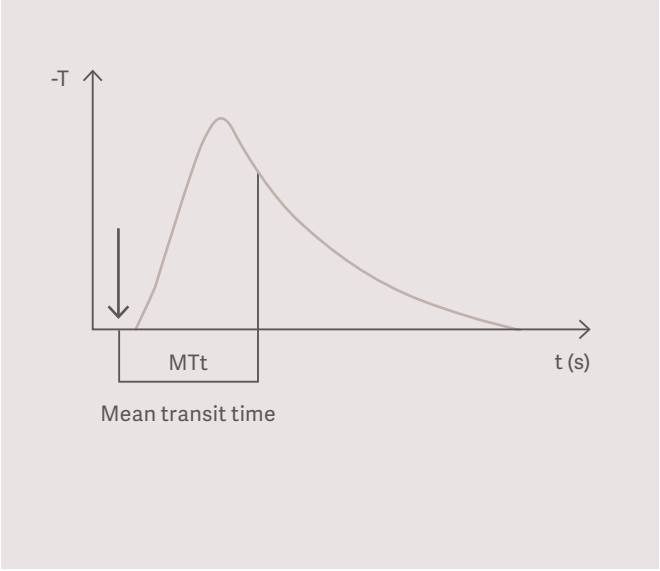

Large volume of intravascular and extravascular volumes

Small volume of intravascular and extravascular volumes

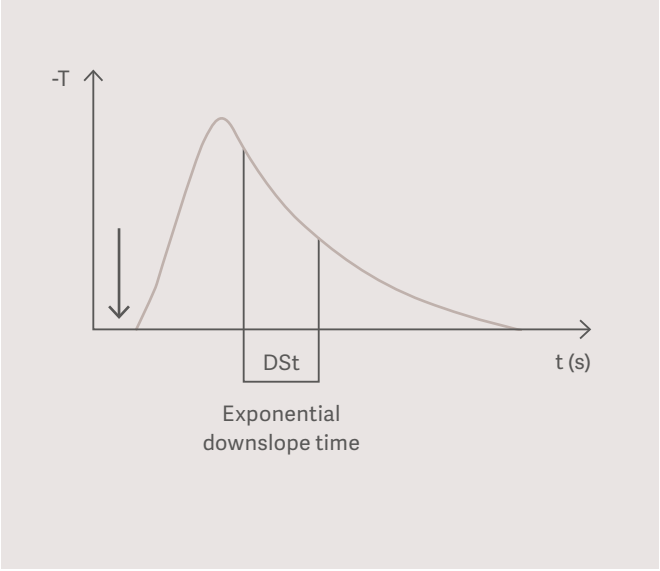
## Assessment of volumes from transpulmonary thermodilution

The shape of the transpulmonary thermodilution curve is strongly influenced by the amount of intravascular and extravascular volume between the injection point (central venous) and detection point (central arterial). This means that the larger the volume amount in the chest, the longer the passage time of the indicator and vice versa. Determination of specific transit times of the thermal indicator thus enables quantification of specific volumes in the chest.

This analysis and calculation is based on a publication by Newman et al.[17] and has also been described by other authors.[18–24]




Determination of mean transit time




Determination of exponential downslope time

## Mean transit time (MTt)

Mean transit time represents the time when half of the indicator passes the detection point (central artery). It is determined from the bisector of the area under the curve.

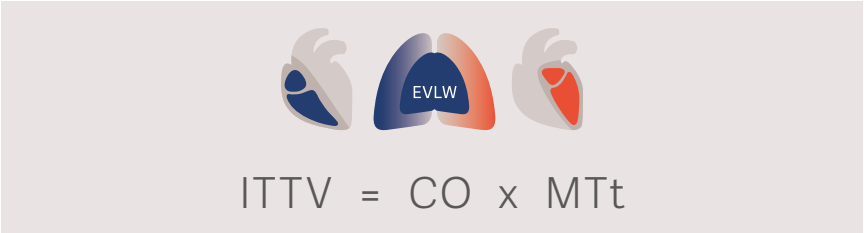
## Exponential downslope time (DSt)

The exponential downslope time represents the wash-out function of the indicator. It is calculated from the downslope part of the thermodilution curve.

Both mean transit time and exponential downslope time serve as the basis for calculation of the following volumes.

## Intrathoracic thermal volume

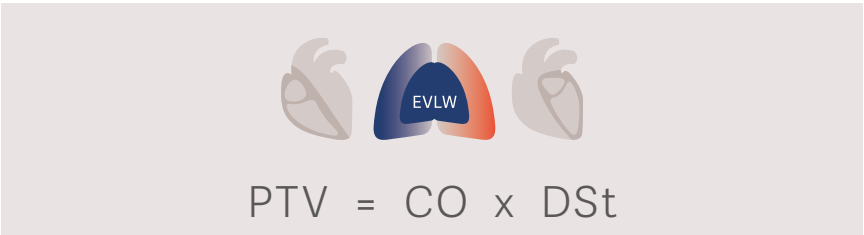
The multiplication of the mean transit time (MTt) with cardiac output (CO) represents the intrathoracic thermal volume (ITTV).




Scheme and calculation of the intrathoracic thermal volume (ITTV)

## Pulmonary thermal volume

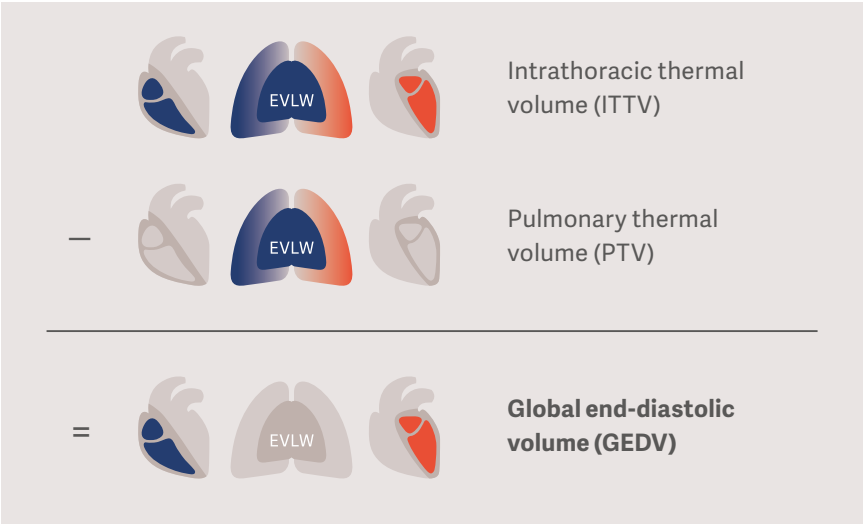
The exponential downslope time always characterizes the volume of the largest mixing chamber in a row of mixing chambers. In the cardiopulmonary systems this is the lung. Thus the multiplication of the exponential downslope time (DSt) with the cardiac output (CO) represents the pulmonary thermal volume (PTV).




Scheme and calculation of the pulmonary thermal volume (PTV)

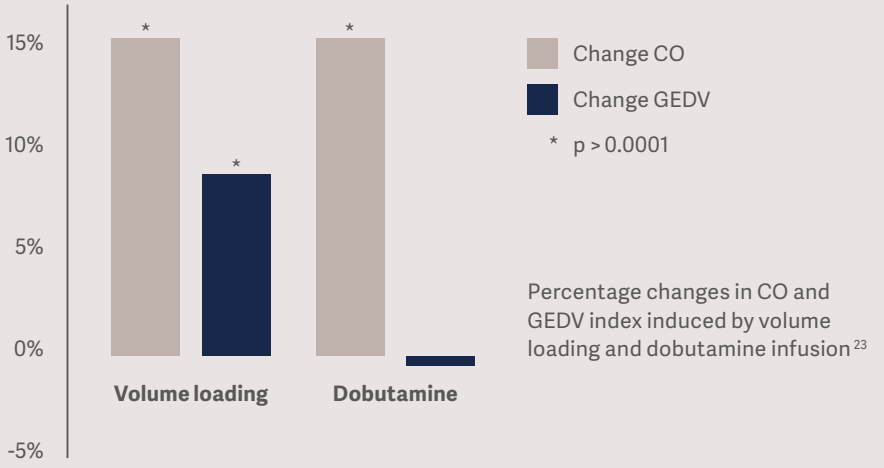
## Quantification of the preload volume

By simply subtracting the pulmonary thermal volume from the intrathoracic thermal volume, the global end-diastolic volume (GEDV) is derived. GEDV indicates the level of preload volume.




Calculation of global end-diastolic volume (GEDV)

As both cardiac output and the transit times are derived from the same thermodilution signal, this raises the question of mathematical coupling. This topic has been investigated several times,[23] clearly showing that CO increases without any corresponding increase in GEDV.

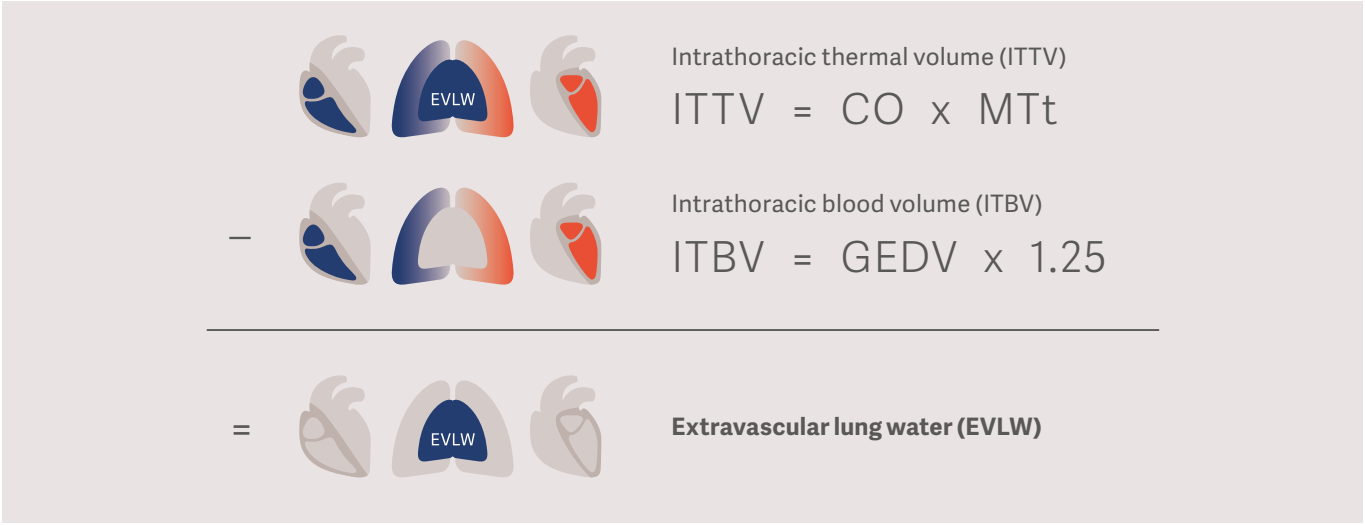



Percentage changes in CO and GEDV index induced by volume loading and dobutamine infusion[23]

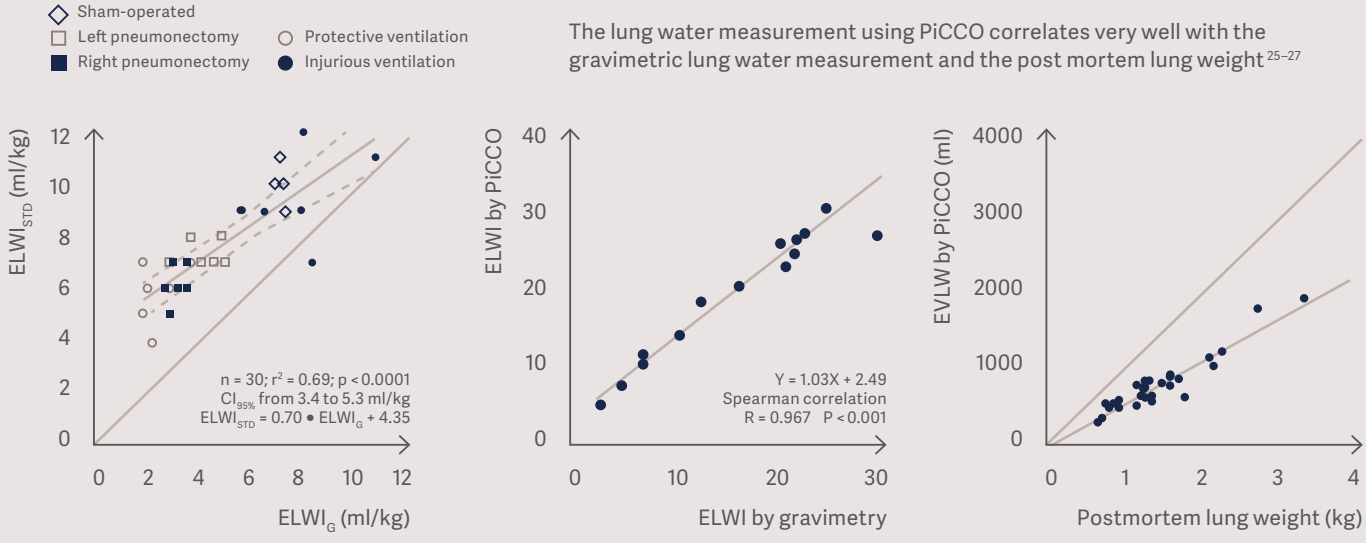
## Quantification of pulmonary edema

Using further calculations, PiCCO technology also provides quantification of the amount of pulmonary edema, expressed as extravascular lung water (EVLW). The only additional information required for this calculation is the amount of intravascular volume (ITBV). In a clinical study using double-indicator dilution technology to measure ITBV and EVLW,[24] intrathoracic blood volume was found to be consistently 25% higher than the global end-diastolic volume. Thus, the intrathoracic blood volume can simply be calculated by multiplying the global end-diastolic volume with the factor 1.25. The calculated intrathoracic blood volume (ITBV) is then subtracted from the intrathoracic thermal volume (ITTV) to derive the extravascular lung water (EVLW).

Several validation studies comparing gravimetry and lung weight show that both this method and the introduction of the fixed factor for calculation of extravascular lung water are highly accurate.[25–27]




Calculation of extravascular lung water (EVLW)



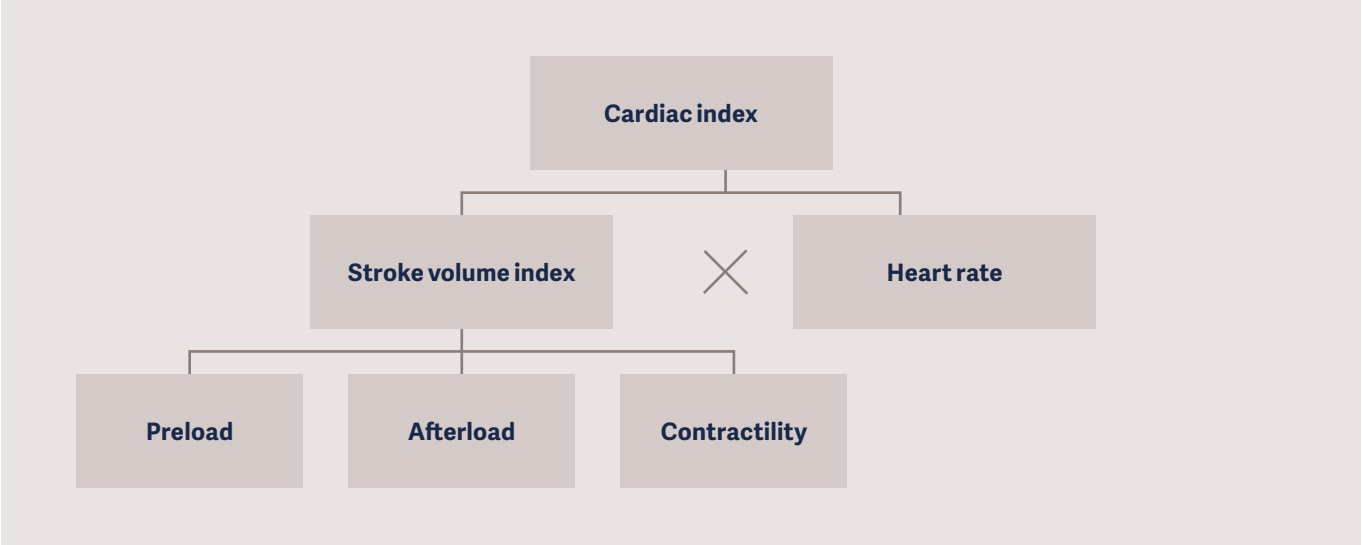
# PiCCO parameters

## Cardiac index (CI), stroke volume index (SVI)

Cardiac index is the amount of blood pumped by the heart per minute indexed to the body surface area (BSA); the cardiac index represents the global blood flow. PiCCO technology provides this information intermittently (transpulmonary thermodilution) and continuously (pulse contour analysis).

A decrease in cardiac index is a clear alarm signal and should be addressed with appropriate measures. However, the cardiac index alone is not sufficient to make a therapeutic decision, as it is influenced by several factors. Importantly, it is the product of stroke volume and heart rate. Stroke volume is dependent on preload, afterload and contractility.

Thus, in addition to the cardiac index, further information on its determinants is required for appropriate treatment.




Cardiac index and its determinants

OK

$CI_{PC}$
3–5 l/min/m²

SVI
40–60 ml/m²

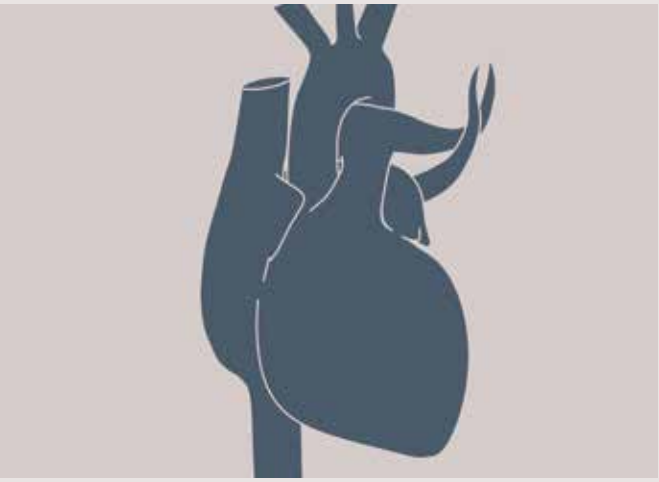
# Preload

**Global end-diastolic volume index (GEDI)**

he preload, together with afterload and contractility, is one of the determinants of stroke volume and therefore cardiac output. It is best described as the initial stretching of a single muscle cell of the heart prior to contraction, meaning at the end of diastole. As this cannot be measured in vivo, other measurements must be substituted as estimates. In the clinical setting, preload is referred to as the end-diastolic pressure or, more precisely, end-diastolic volume. A higher end-diastolic volume implies higher preload.

A higher venous pressure (CVP) and/or a higher pulmonary capillary wedge pressure (PCWP) is often regarded as an indicator of higher preload (CVP for the right heart, PCWP for the left heart). However, many studies have shown that CVP and PCWP are not reliable indicators for this purpose, mainly due to the limitation that pressure cannot directly be transferred into volume. Therefore, any volumetric parameter assessing the filling of the ventricle at the end of diastole reflects more precisely the actual preload.

In the clinical setting, preload is referred to as the end-diastolic pressure or, more precisely, end-diastolic volume.

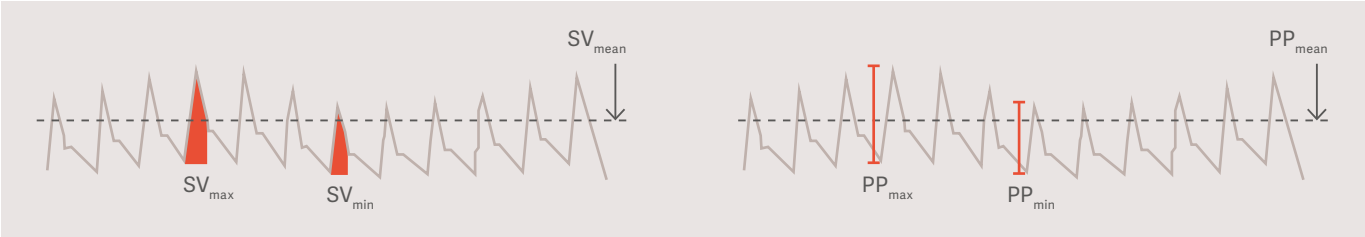


OK

GEDI

680–800 ml/m$^2$

# Volume responsiveness




Stroke volume variation (SVV)

Pulse pressure variation (PPV)

## Stroke volume variation (SVV) and pulse pressure variation (PPV)

The stroke volume variation (SVV) or pulse pressure variation (PPV) provide information as to whether an increase in preload will also lead to an increase in stoke volume as long as the patient is continuously ventilated and has a stable heart rhythm

Mechanical ventilation induces cyclic changes in vena cava blood flow, pulmonary artery blood flow and aortic blood flow. At the bedside, changes in the aortic blood flow are reflected by swings in the blood pressure curve (and thus variations in stroke volume and blood pressure). The magnitude of these variations is highly dependent on the volume responsiveness of the patient. With controlled ventilation, the rise in intrathoracic pressure during early inspiration leads to a squeezing of the pulmonary blood into the left ventricle. This process in turn increases the left ventricular preload. With a volume responsive patient, this results in an increased stroke volume or pulse pressure.

An increase in intrathoracic pressure also results in reduced right ventricular filling. With a volume responsive right heart, this will reduce the volume ejected. Thus, during late inspiration a couple of heartbeats later, the left ventricular preload will decrease as will the stroke volume or pulse pressure. The variations in stroke volume and pulse pressure can be analyzed over a 30 second time frame by the following formula:

$$SVV = \frac{(SV_{max} - SV_{min})}{SV_{mean}}$$

$$PPV = \frac{(PP_{max} - PP_{min})}{PP_{mean}}$$

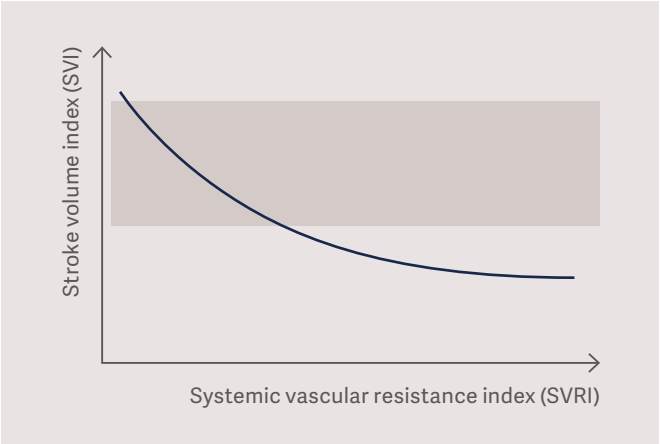
The higher the variation the more likely the patient is to be volume responsive. For proper use of the parameters, the following preconditions must be fulfilled:

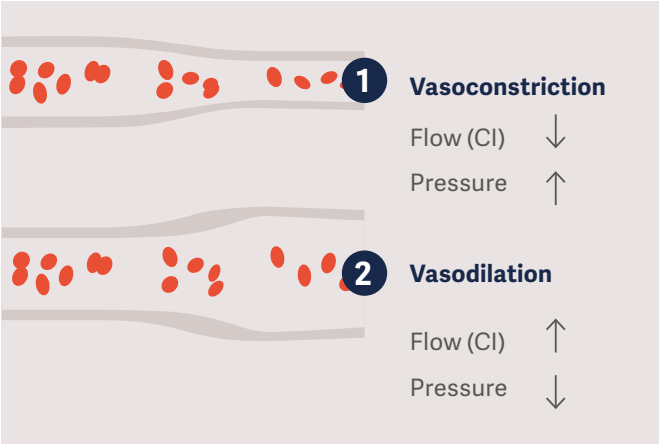
- Fully controlled mechanical ventilation with a tidal volume ≥ 8 ml/kg PBW (predicted body weight)
- Sinus rhythm
- Pressure curves free of artifacts


**SVV/PPV**

< 10%

# Afterload




## Systemic vascular resistance index (SVRI)

The afterload is another determinant of stroke volume / cardiac output. The physiological meaning of SVRI is the tension or pressure that builds up in the wall of the left ventricle during ejection. Following Laplace's law, the tension on the muscle fibers in the heart wall is the product of the pressure within the ventricle and the ventricle radius, divided by the ventricle wall thickness.

In the clinical setting things are often simplified and the afterload is seen as the resistance the heart has to pump against; the systemic vascular resistance index (SVRI) is the parameter that represents this.

- If the afterload (SVRI) is increased, the heart must pump with more power to eject the same amount of blood.
- The higher the afterload, the less the cardiac output.
- The lower the afterload, the higher the cardiac output.

If the afterload exceeds the performance of the myocardium, the heart may decompensate.

$$SVRI = \left[ \frac{(MAP - CVP)}{CI} \right] \times 80$$

OK

**SVRI**

1700–2400 dyn*s*cm$^5$*m$^2$

# Contractility

## Contractility is another factor that influences cardiac output.

Contractility of the myocardium represents the ability of the heart to contract independent of the influence from preload or afterload. Substances that cause an increase in intracellular calcium ions lead to an increase in contractility. Different concentrations of calcium ions in the cell lead to a different degree of binding between the actin (thin) and myosin (thick) filaments of the heart muscle. Direct determination of cardiac contractility is not possible in the clinical setting. Therefore, surrogate parameters are used to evaluate or estimate the contractility.

### Global ejection fraction (GEF)

Ejection fraction represents the percentage of volume in a heart chamber that is ejected with a single contraction. The measurement of the global ejection fraction offers a complete picture of the overall cardiac contractility.

$$GEF = \frac{4 \times SV}{GEDV}$$

### Cardiac function index (CFI)

The cardiac function index can be used to estimate cardiac contractility. It represents the relation of the flow (cardiac output) and the preload volume (GEDV). Thus, cardiac function index is a preload related cardiac performance parameter.

$$CFI = \frac{CI_{TD} \times 1000}{GEDV}$$

### Cardiac power index (CPI)

CPI represents the power of left ventricular cardiac output in watts. It is the product of pressure (MAP) and flow (CO). In clinical studies it has been found to be the strongest independent predictor of hospital mortality in cardiogenic shock patients.[28, 29]

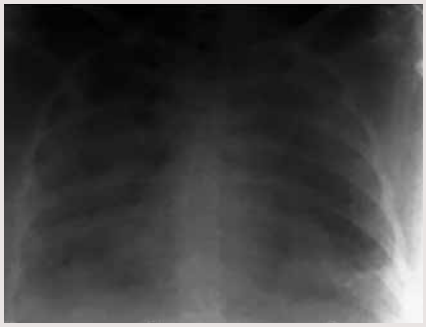
$$CPI = CI_{PC} \times MAP \times 0.0022$$

OK

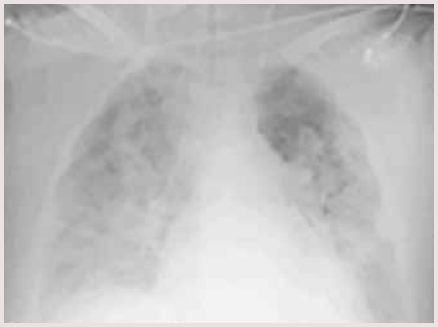
| GEF | CFI | CPI |
|---|---|---|
| 25–35% | 4.5–6.5 1/min | 0.5–0.7 W/m² |

# Assessment of pulmonary edema using PiCCO technology

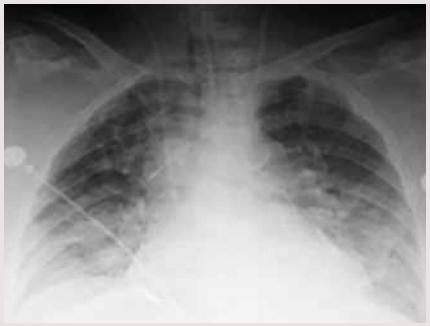
Examples of chest x-rays that do not reflect the level of pulmonary edema



**ELWI = 21 ml/kg**
Severe pulmonary edema



**ELWI = 11 ml/kg**
Moderate pulmonary edema



**ELWI = 5 ml/kg**
No pulmonary edema

## Extravascular lung water index (ELWI)

A pulmonary edema is characterized by an accumulation of fluid in the interstitium of the lung tissue and/or the alveoli. This leads to impaired gas exchange and may even cause pulmonary failure. The amount of pulmonary edema can easily be quantified at the bedside by measuring the extravascular lung water index (ELWI). The usual clinical signs of pulmonary edema (white-out on the chest x-ray, low oxygenation index, decreased lung compliance) are non-specific and reliable only later when the pulmonary edema may already be advanced. In routine clinical practice, the interpretation of a chest x-ray is most often used to estimate the amount of pulmonary edema in patients at risk. However, this approach is often inaccurate because a chest x-ray provides only a black and white density image of all components in the chest, including gas volume, blood volume, pleural effusion, bones, muscles, lung tissue, fat, and skin edema in addition to pulmonary edema.

Extravascular lung water is indexed to the body weight in kg, written as the extravascular lung water index (ELWI). By indexing to the patient's predicted body weight (PBW), underestimation of lung water, particularly in obese patients, is avoided.


**ELWI**
3–7 ml/kg

## Pulmonary vascular permeability index (PVPI)

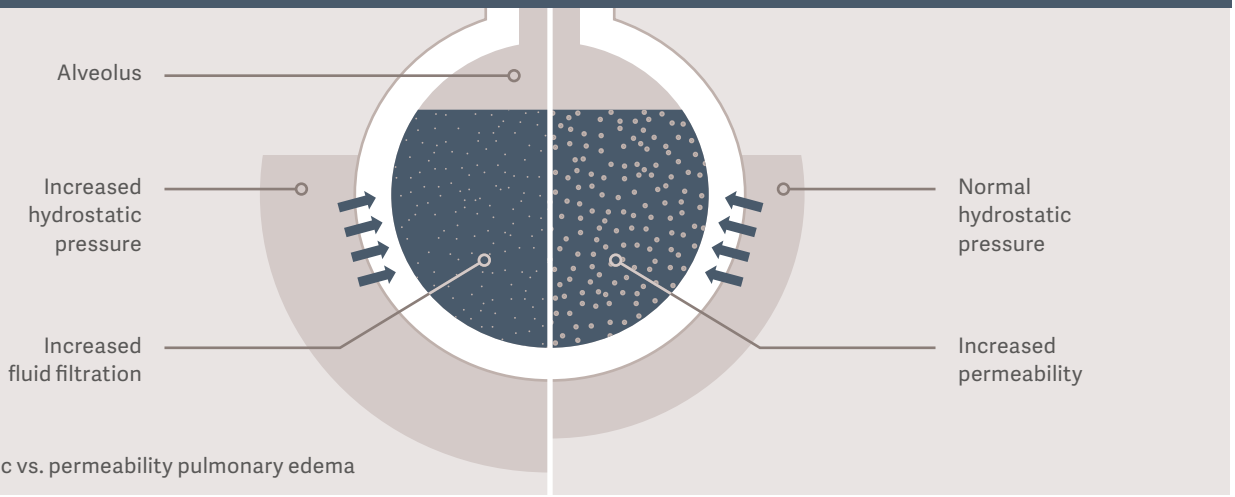
When pulmonary edema is present (measured using extravascular lung water), it is important to determine the cause so it can be treated appropriately. There are two main types of pulmonary edema:

### Cardiogenic pulmonary edema

Caused by intravascular fluid overload, hydrostatic pressure increases. This causes fluids to leak into the extravascular space.

### Permeability pulmonary edema

Vascular permeability is increased by an inflammatory reaction caused, for example, by sepsis. This leads to the increased transfer of fluids, electrolytes and proteins from the intravascular to the extravascular space, even with a normal to low intravascular fluid status and hydrostatic pressure.




Cardiogenic vs. permeability pulmonary edema

A differential diagnosis of pulmonary edema is important because the therapeutic approach is different. In cardiogenic pulmonary edema, a negative fluid balance is sought, while in permeability pulmonary edema treating the cause of inflammation is the priority. The pulmonary vascular permeability index (PVPI) enables this differential diagnosis.

This parameter is calculated from the relation between extravascular lung water (EVLW) and pulmonary blood volume (PBV). A PVPI value in the range of 1 to 3 points to a cardiogenic pulmonary edema, while a PVPI value greater than 3 suggests a permeability pulmonary edema.

OK

**PVPI**

1.0–3.0 cardiogenic edema / >3.0 permeability edema

# Applications and benefits

## PiCCO applications

PiCCO technology is indicated in patients who present with unstable hemodynamics and unclear volume status as well as in therapeutic conflicts. Those situations are usually present in:

- Septic shock
- Cardiogenic shock
- Traumatic shock
- ARDS
- Severe burn injuries
- Pancreatitis
- High-risk surgical procedures

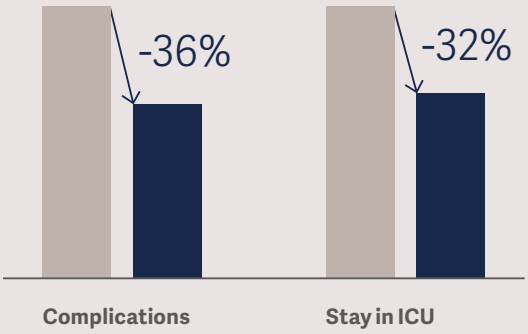
## Medical benefits

Monitoring does not lower patient mortality or morbidity, but provides valuable information that should be used to set up a treatment plan and thus apply goal-directed therapy to the patient as early as possible. The success of early goal directed therapy (EGDT) is documented in studies that have shown the following advantages:

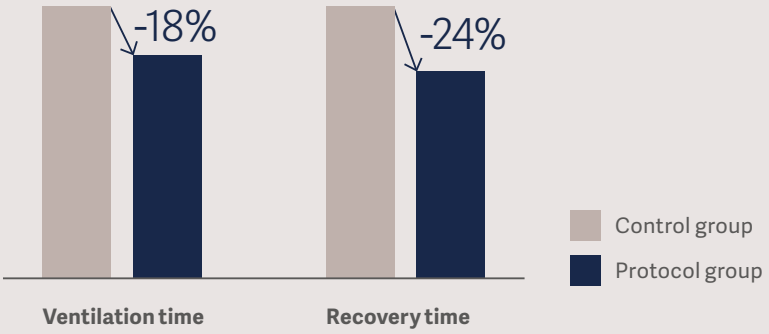
- Reduction in ventilation time
- Reduction of ICU stay
- Reduction in complications
- Reduction in recovery time

Based on validated information, goal directed therapy helps improve outcomes.

Preload – GEDV (Göpfert et al. 2013 [30])




Preload – GEDV (Göpfert et al. 2007 [31])



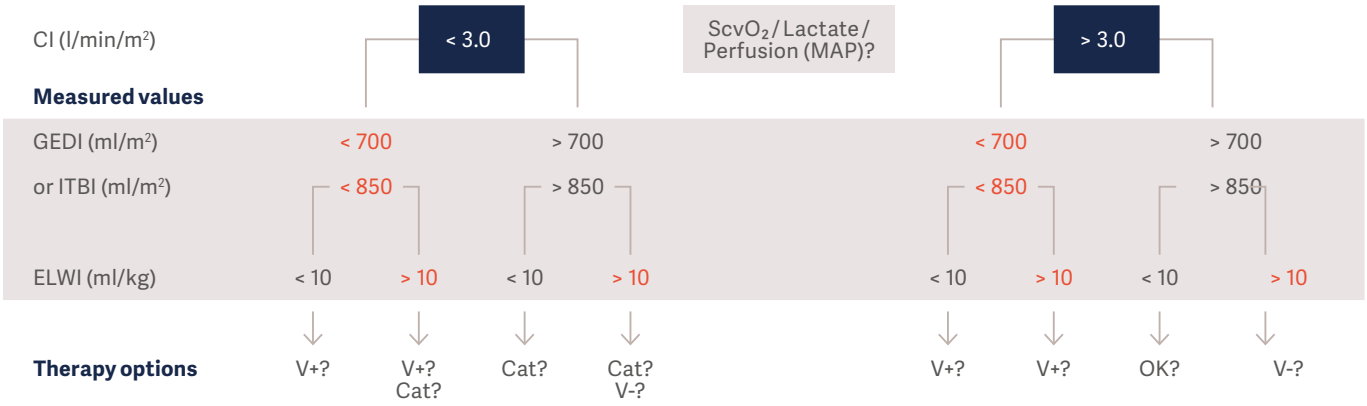
# Overview of technologies and further parameters

PiCCO technology is used with the PulsioFlex monitor. The following is a listing of the available parameters.

| Method | | PiCCO |
|---|---|---|
| **Pulse contour analysis (continuous)** | **Flow** | $CI_{PC}$, SVI |
| | **Contractility** | CPI |
| | **Afterload** | SVRI |
| | **Volume responsiveness** | SVV, PPV |
| **Thermodilution (intermittent)** | **Flow** | $CI_{TD}$ |
| | **Preload** | GEDI, ITBI |
| | **Contractility** | CFI, GEF |
| | **Organ function** | ELWI, PVPI |

## Hemodynamic decision model

This decision model is for guidance only and should not replace the individual therapeutic decisions of the treating physician.




**Targeted values**

| | |
|---|---|
| GEDI (ml/m²) (if ELWI > 10 →700–800) | > 700 |
| GEF (%) | > 25 |
| CFI (1/min) | > 5 |
| ELWI (ml/kg) (slow response) | ≤ 10 |

Volume responsiveness?
(Passive leg raising / endexpiratory occlusion test / volume challenge / SVV / PPV?)

Contractility problem?
(GEF / CFI / echo?)

V+ = volume loading, V- = volume withdrawal , Cat = catecholamine / cardiovascular agents
Please reevaluate your clinical decisions and the set target parameters.

# OEM partner modules

## Patient-centered flexibility

The versatile PiCCO technology has been developed to match and adapt to different clinical settings.

Getinge has partnered with patient monitoring market leader companies GE and Philips to offer a PiCCO module that can be seamlessly integrated into the patient monitor. Patient monitors with PiCCO modules help reduce the footprint of adding additional equipment and maintain the already familiar user interface.

All OEM partner modules are fully compatible with the original PiCCO disposable products.

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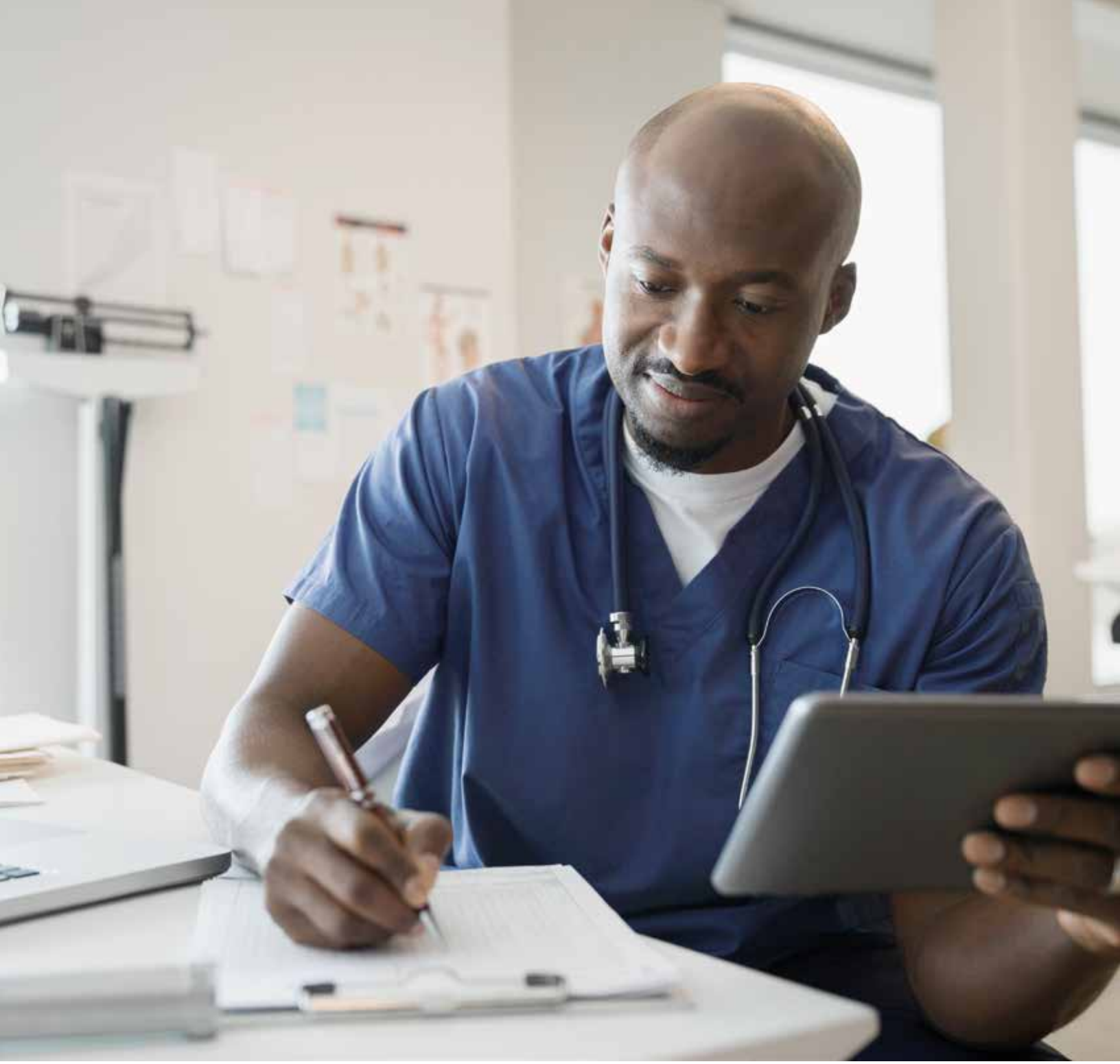

# Hand in hand for patient care

Getinge is built on a genuine compassion for people's health, safety and well-being. Founded in 1904 with roots dating back to 1838, Getinge has grown organically and through acquisitions to become a global market leader.

Our portfolio offers solutions and support throughout the clinical pathway, and features well-known and dependable product brands, such as Maquet.

Ours is a legacy of trust and an ongoing commitment to advancing medical technology. We maintain close clinical partnerships to address real-world clinical needs, helping you protect patients, proactively avoid complications, and prevent common causes of escalating healthcare costs.

As one of the world's largest medical technology companies, Getinge has the knowledge, resources and experience to help you focus on what's most important: your patients.

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