

## REVIEW

# Non-invasive cardiac output monitoring techniques in the ICU

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**Keywords** - cardiac output measurement, intensive care unit, critically ill, non-invasive, monitoring.

## Abstract

Cardiac output (CO) measurement is an essential part of haemodynamic management in critically ill patients, especially in the intensive care unit (ICU). Since 1970 the 'clinical reference standard' for CO monitoring is the use of a pulmonary artery catheter (PAC) for thermodilution ( $TD_{PAC}$ ). Because of concerns about the safety and overall benefit of the PAC, less invasive and non-invasive techniques have emerged to measure CO in the ICU and these techniques are developing quickly. The aim of this review is to give an overview of the currently available non-invasive techniques for continuous CO monitoring such as oesophageal Doppler, partial carbon dioxide rebreathing, bioimpedance, bioreactance and volume clamping. Furthermore, we evaluate their accuracy in the setting of the ICU by comparing them with the 'gold standard'  $TD_{PAC}$ . Although the non-invasive techniques show reasonably good results in elective postoperative ICU patients, the non-invasive techniques are not able to replace  $TD_{PAC}$  for accurate CO measurements in non-elective ICU patients. Overall the non-invasive techniques seem to perform better as a trend-monitoring device as opposed to measuring absolute CO.

## Introduction

Cardiac output (CO) measurement is an essential part of haemodynamic management in critically ill patients, especially in the intensive care unit (ICU). Continuous CO measurements are preferred over intermittent measurements, and can be used as a diagnostic tool and to guide fluid therapy and the administration of inotropes and vasopressors.<sup>[1]</sup> For decades the clinical reference standard for CO monitoring is the use of a pulmonary artery catheter (PAC) for thermodilution ( $TD_{PAC}$ ). Since the publication of several observational studies showing an increased mortality, the PAC has become the subject of debate.<sup>(2-5)</sup> Later published randomised controlled trials refuted

the suggestion that the use of PAC is related to increased mortality, but they also did not show an overall benefit for the use of PAC in critically ill patients.<sup>[6-8]</sup>

Less invasive techniques using transpulmonary thermodilution still require intra-arterial (PiCCO, LiDCO, Vigileo) and central venous (PiCCO, LiDCO) access, with the risk of complications such as catheter-related infections, haemorrhage, pneumothorax, and inadvertent punctures of a major artery.<sup>[9]</sup> As not all ICU patients require an arterial and/or central venous line, the need for a reliable, non-invasive but also readily available, robust and continuous CO monitoring technique for the ICU is growing. The aim of this review is to give an overview of the currently available non-invasive techniques and to evaluate their accuracy in the setting of the ICU by comparing them with the 'gold standard' PAC.

## Methods

This is a narrative review on non-invasive CO monitoring in the ICU. Studies were identified by searching Medline (PubMed) and reference lists were checked for relevant studies up to 1 March 2017. Studies comparing continuous non-invasive CO techniques with  $TD_{PAC}$  in the setting of the ICU were included. Techniques requiring an arterial or venous catheter were considered invasive and were therefore excluded. Because echocardiography is not suitable for continuous CO monitoring, echocardiography was not included in this review. Our search resulted in five non-invasive continuous CO monitoring techniques which are described below.

## Accuracy

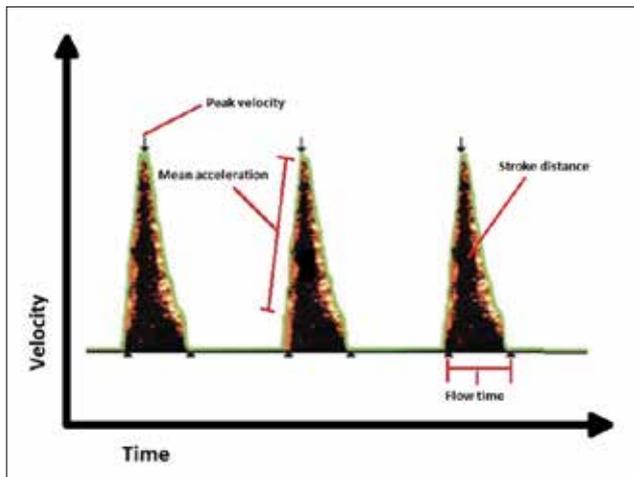
The studies included in this review use the Pearson's correlation coefficient ( $r$ ) and Bland-Altman analysis. CO-monitoring techniques are considered to be clinically interchangeable if  $r$  is larger than 0.77.<sup>[10]</sup> Bland-Altman descriptive analysis provides

the bias (mean difference between two paired measurements), precision (95% confidence interval of bias), limits of agreement (bias  $\pm$  1.96 standard deviations), and percentage error (limits of agreement expressed as a proportion of the mean CO).<sup>[11]</sup> The widely accepted cut-off value of percentage of error is 30%, as described by Critchley and Critchley.<sup>[12]</sup>

### Non-invasive continuous cardiac output monitoring techniques: Oesophageal Doppler

#### Description of the technique

This technique was first described in 1971.<sup>[13]</sup> A flexible probe with a Doppler transducer at the tip of the probe is inserted orally or nasally into the oesophagus and the transducer is positioned facing the descending aorta. CardioQ (Deltex Medical Ltd., Chichester, UK) is the clinically available oesophageal Doppler monitor (ODM). The CardioQ monitor displays a waveform (figure 1); the area under the waveform, generated by the descending aortic blood flow, is defined as stroke distance.<sup>[14]</sup> The stroke volume is calculated from the measured stroke distance and the nomogram, which is a calibrated constant that estimates the diameter of the aorta and is based on the patient's age, weight and height.<sup>[15-16]</sup> Since the probe is placed in the descending aorta, the Doppler approach cannot directly measure CO and relies on the assumption of a fixed relation where 30% of CO is diverted proximally to the descending aorta.<sup>[14]</sup>



**Figure 1.** CardioQ waveform and parameters

Velocity is shown on the Y-axis and time along the x-axis. The waveform (triangle) displays: Peak velocity, stroke distance, mean acceleration, and flow time measurements. Stroke distance is the area of the triangular waveform and is related to stroke volume. Peak velocity and mean acceleration are markers of contractility.

(Adapted from:

<http://www.deltexmedical.com/downloads/clinicaleducationguides>)

#### Clinical considerations

**Advantages:** The ODM probe can be placed in the oesophagus within a few minutes. It is easy to use; however, training is

recommended. One study suggested that practising 12 times results in reliable CO measurements.<sup>[17]</sup>

**Limitations:** Oesophageal Doppler measurement assumes a fixed relationship of blood flow between the descending aorta and proximally from the descending aorta.<sup>[15]</sup> This relationship is based on healthy individuals; however, this may be altered in ICU patients. The nomogram that the CardioQ uses is based on and valid for a large cohort of patients, but may not be adequate in an individual patient.<sup>[15,16]</sup> Moreover, the CardioQ may not be reliable in situations such as severe aortic stenosis, because of turbulent blood flow.<sup>[16]</sup> The technique is operator dependent; incorrect placement of the probe can alter the CO measurement. The risks and complications associated with ODM probe placement seem to be low, because of the small size of the probe (diameter of  $\pm$ 5 mm).<sup>[16,18]</sup> Oesophageal Doppler is contraindicated in patients with oesophageal disease and severe bleeding disorders. Although it is suggested that the probes can be used in conscious patients, in clinical practice the use is in general limited to unconscious patients. Although the ODM is capable of continuous CO monitoring the probe needs to be checked regularly because of possible probe movement. Movement of the probe results in loss of signal, which is reflected in an unsharp triangular waveform and a decrease in volume of the distinctive Doppler sound (figure 1).<sup>[16,17]</sup>

#### Accuracy

In 2004, a review<sup>[15]</sup> determined the validity of the ODM by including all studies between 1989 and 2003 comparing the ODM with pulmonary artery thermodilution (TD<sub>PAC</sub>). They found 11 validation papers reporting 21 studies; these studies involved 314 patients and 2400 paired measurements all performed in haemodynamically stable patients. The ODM seemed to perform better as a trend monitoring device (5 studies, clinical agreement 86%) than for absolute cardiac output estimation (16 studies, clinical agreement 52%). The pooled median bias from the 16 studies that reported on absolute cardiac output was 0.19 l/min (range -0.69 to 2.00 l/min). Precision overlapped zero (no bias) in 9 out of 16 studies while the other 7 suggested a minimal systemic underestimation of absolute cardiac output by ODM. Because of limited accuracy, resulting from assumption of a fixed relationship of blood flow, signal detection problems, and the use of normograms, the ODM is probably less suitable for absolute CO measurement in the ICU.<sup>[15,16]</sup> Although, based on the ability of the ODM to track changes in CO, studies have demonstrated improved patient outcome and reduced length of hospital stay when using the ODM to guide fluid therapy.<sup>[19,21]</sup>

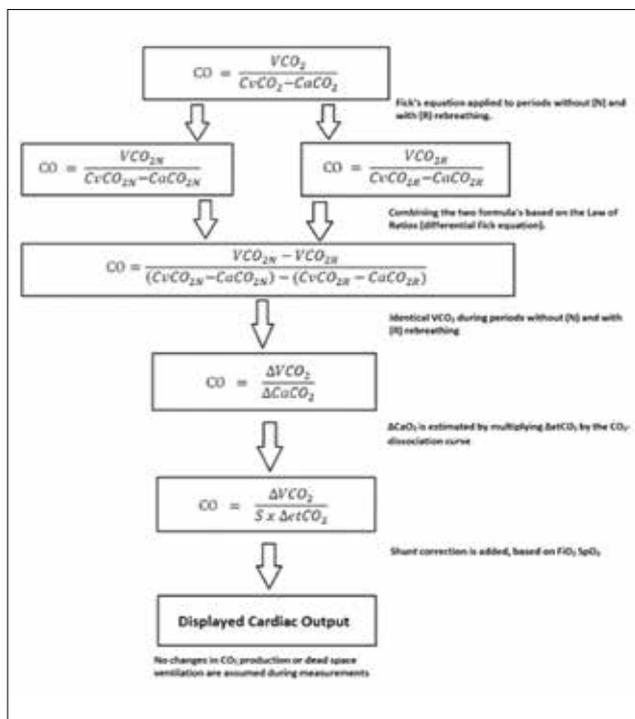
### Partial carbon dioxide (CO<sub>2</sub>) rebreathing

#### Description of the technique

The partial CO<sub>2</sub> rebreathing method uses Fick's principle applied to CO<sub>2</sub> elimination (figure 2). By alternating between

rebreathing and non-rebreathing periods, mixed venous CO<sub>2</sub> content (CvO<sub>2</sub>) can be omitted from the equation and consequently there is no need for central venous access, making it a non-invasive method.

The most widely used non-invasive cardiac output monitor that relies on this modified version of the Fick equation for CO<sub>2</sub> is the NICO (non-invasive cardiac output) monitor (Novamatrix Medical Systems Inc. Wallingford, CT, USA).<sup>[22]</sup> The computer cycles every three minutes from the non-rebreathing mode to a 50-second period of rebreathing by adding an additional dead space with a disposable rebreathing loop.<sup>[23]</sup> Moreover, the NICO monitor measures the carbon dioxide production (VCO<sub>2</sub>) with an integrated CO<sub>2</sub>/flow sensor, by calculating the difference between expired and inspired CO<sub>2</sub> concentration. The calculation of CO by the NICO monitor only reflects part of the pulmonary capillary blood flow that participates in the gas exchange.<sup>(23,24)</sup> Therefore, the NICO system includes a correction for the amount of shunted blood, based on inspired oxygen concentration (FiO<sub>2</sub>) and oxygen saturation determined by pulse oximetry (SpO<sub>2</sub>), and an adaption of Nunn's iso-shunt plots.<sup>(25)</sup>



**Figure 2.** Cardiac output measurement using the partial CO<sub>2</sub> rebreathing technique, using the differential Fick's equation

VCO<sub>2</sub> = carbon dioxide production; CaCO<sub>2</sub> = arterial CO<sub>2</sub> content; CO = cardiac output; CvCO<sub>2</sub> = mixed venous CO<sub>2</sub> content; etCO<sub>2</sub> = end-tidal CO<sub>2</sub> concentration; FiO<sub>2</sub> = fraction of inspired oxygen; N = normal ventilation; R = rebreathing; S = slope of CO<sub>2</sub> dissociation curve; SpO<sub>2</sub> = oxygen saturation obtained by pulse oximetry. (Adapted from Hofer CK, Ganter MT, Zollinger A. What technique should I use to measure cardiac output? *Curr Opin Crit Care* 2007;13(3):308-17)

### Clinical considerations

**Advantages:** The NICO system is easy to use without any previous experience and can be employed in conscious as well as unconscious patients.<sup>[22,24,26,27]</sup>

**Limitations:** This technique is restricted to the mechanically ventilated patient. The partial CO<sub>2</sub> rebreathing technique involves 50 seconds of dead space ventilation in the rebreathing period, which causes a transient rise in arterial CO<sub>2</sub> tension (PaCO<sub>2</sub>), up to 4 mmHg or 10% of the initial value.<sup>[26,28]</sup> This may make the partial CO<sub>2</sub> rebreathing technique unsuitable for patients with severe hypercapnia, raised intracranial pressure or pulmonary hypertension.<sup>[26-28]</sup> Because of the non-rebreathing and rebreathing cycle, the partial rebreathing technique has a relatively long response time, making the NICO system a less suitable monitor for continuous cardiac output monitoring as compared with the other non-invasive CO monitors described in this review.<sup>[29]</sup>

### Accuracy

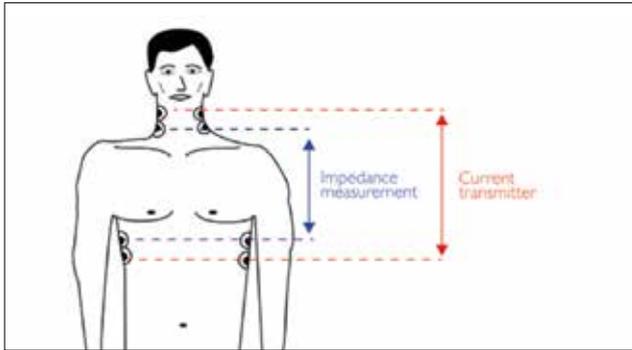
A systematic review from Peyton and Chong, published in 2010, compared the NICO system with TD<sub>PAC</sub> in a wide range of patient groups (n=435), and found a pooled weighted bias of -0.05 (±0.17) l/min, precision of 1.12 l/min and a percentage error of 44.5 (±6.0)%.<sup>[30]</sup>

Moreover, studies with conflicting results have been published, comparing the partial CO<sub>2</sub> rebreathing technique with TDPAC in a wide range of patient groups<sup>[22,26-28,31,32]</sup> reporting reasonably good results in haemodynamically stable patients on controlled mechanical ventilation, without pulmonary disease. The latest NICO monitor (NICO<sub>2</sub>) is fairly accurate in spontaneous breathing ventilation modes (with reported bias of 0.52 l/min and precision of 1.02 l/min), although only when tidal volume variations are below 10%, making it less accurate in non-sedated patients.<sup>[22,32]</sup> As, in recent years, more focus is on reducing sedation in mechanically ventilated ICU patients the partial CO<sub>2</sub> rebreathing method is not a suitable CO monitor to use in the ICU.

### Bioimpedance

#### Description of the technique

Bioimpedance cardiography is based on the theory that with every heart beat the electrical resistance (impedance) of the thorax changes, because of a shift in intrathoracic blood volume (figure 3). Impedance cardiography relies on measured changes in signal amplitude of a transmitted electrical current via four electrodes placed on the neck and thorax.<sup>[33]</sup> In order to translate this into a stroke volume, different equations are used (i.e. Kubicek,<sup>[34]</sup> Sramek,<sup>[35]</sup> and Sramek-Bernstein<sup>[36]</sup> equation). These equations differ from each other in the method used for estimation of the thorax volume. The left ventricular ejection time is deducted from the electrocardiogram (ECG).



**Figure 3.** Bioimpedance and its connection to the body surface

An alternating current is passed through the chest, where the change in impedance is related to stroke volume.

#### Clinical considerations

**Advantages:** Bioimpedance can be applied quickly and is easy to use, although familiarity with the technique is required for interpreting the reliability of the morphology of the impedance waveform, as is the case with thermodilution derived waveforms. This technique can be used in conscious as well as unconscious patients.<sup>[33,37-40]</sup>

**Limitations:** Operator error can occur with the incorrect placement of the sensors<sup>[29,40,41]</sup> and insufficient knowledge of the impedance waveform.<sup>[39,40]</sup> To avoid cannulation sites or wounds, commonly seen in patients in the ICU, the position of the electrodes sometimes needs adjustment.<sup>[42]</sup>

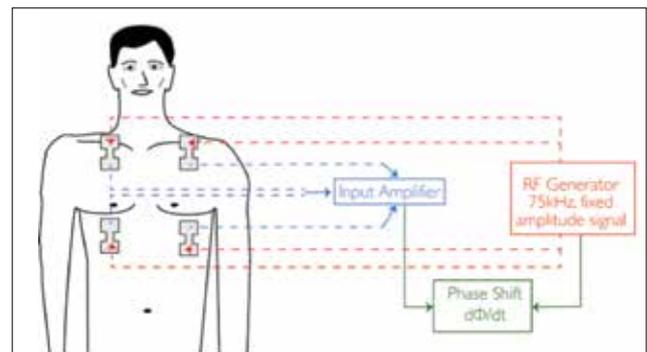
#### Accuracy

Different bioimpedance equations are used to calculate stroke volume. Van de Water et al.<sup>[33]</sup> showed that the equations differ in accuracy. In a meta-analysis of Raaijmakers et al.,<sup>[43]</sup> published in 1999, thoracic bioimpedance was compared with other techniques of CO monitoring in a wide variety of patient groups. They found a pooled correlation coefficient ( $r$ ) between bioimpedance cardiography and repeated TDPAC of 0.59 and 0.67 in cardiac patients and critically ill patients, respectively.<sup>[43]</sup> Moreover, bioimpedance is sensitive to ambient electrical noise and patient movement.<sup>[29,38]</sup> Pulmonary oedema, pleural effusion, hyperventilation, high levels of PEEP, chest tubes and variations in patient body size and skin humidity can interfere with the electrical conductivity and therefore make CO measurements inaccurate.<sup>[29,38,44-46]</sup> Moreover, because the left ventricular ejection time is determined using the interval between QRS complexes on the ECG, arrhythmias can interfere with CO measurement.<sup>[45]</sup> Overall, bioimpedance seems an unreliable method for absolute CO measurement in the ICU. However, bioimpedance has better intra-patient repeatability in post-cardiac surgery patients compared with TDPAC, possibly making it a more suitable monitor for trend analysis.<sup>[33]</sup>

## Bioreactance

### Description of technique

Bioreactance CO measurement is based on analysis of relative phase shifts of a high-frequency current, applied across the thorax.<sup>[46]</sup> These relative phase shifts are related to changes in intrathoracic blood volume, so that the peak rate of change in the relative phase shift is related to the peak aortic flow during a heartbeat.<sup>[46]</sup> The NICOM system (Cheetah Medical Inc., Boston, Massachusetts, USA), currently the only commercially available system based on bioreactance, detects this relative phase shift by detecting a high frequency current that is applied and recorded from the left and right side of the thorax, by four dual electrodes placed at the corners of the thorax (figure 4).<sup>[46]</sup> Because bioreactance is not based on changes in amplitude-like bioimpedance, it is less limited by factors such as body size, pleural and pulmonary fluid and patient movement.<sup>[46,47]</sup> Just like bioimpedance, bioreactance uses ECG signals to determine left ventricular ejection time.<sup>[46]</sup>



**Figure 4.** The NICOM system and its connection to the body surface

RF = radio frequency. The relative phase shift is determined and is used together with the rate of phase in calculations of stroke volume. (Adapted from Keren H, Burkhoff D, Squara P. Evaluation of a non-invasive continuous cardiac output monitoring system based on thoracic bioreactance. *Am J Physiol Heart Circ Physiol.*2007;293(1):H583-9)

#### Clinical considerations

**Advantages:** The NICOM monitor is easy to use and interpret and can be used in conscious as well as unconscious patients.<sup>[49]</sup> Bioreactance technology yields a signal-to-noise ratio (i.e. level of a desired signal to level of background noise) that is around 100 times superior to bioimpedance and therefore makes it, in theory, a more eligible CO monitor in the ICU.<sup>[48]</sup>

**Limitations:** Theoretically, as is the case with bioimpedance, bioreactance will overestimate the CO in patients with aortic insufficiency.<sup>[47]</sup> Moreover, measurements can be altered by nurses' interventions, movements of the patient or loss of patch adhesive which occur over time.<sup>[48]</sup>

#### Accuracy

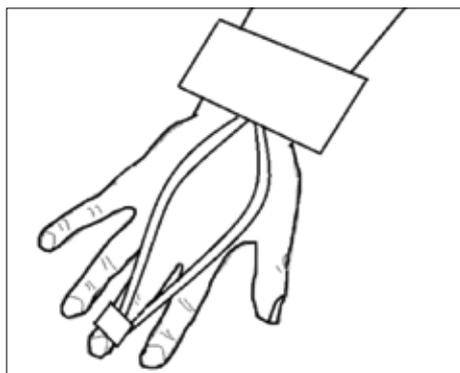
Validation studies have shown good agreement between bioreactance and  $TD_{PAC}$  in measuring CO, in postoperative cardiac

surgery patients, in awake surgical and non-surgical ICU patients and patients with pulmonary hypertension.<sup>[46-48,50]</sup> In the study by Raval et al. the NICOM monitor was also directly compared with bioimpedance (BioZ ICG Monitor, Cardiodynamics, San Diego) in awake cardiac care unit patients and it was found that bioimpedance generally underestimated CO, and also showed a higher degree of variability. Moreover, bioreactance seemed to track CO changes better than bioimpedance and can therefore be seen as a more suitable monitor for CO trend analysis.<sup>[47]</sup> Although all the aforementioned studies show promising results, it should be noted that three of the four studies received a research grant of the NICOM manufacturing company and/or the research group included consultants of Cheetah Medical Inc.<sup>[46,48,50]</sup> As bioreactance shows similarities with the bioimpedance technique we should bear in mind that future studies might show data containing more negative results. Therefore, more studies need to be conducted by independent research groups to prove whether the NICOM system is indeed an accurate CO monitor for the ICU.

### Volume clamping

#### Description of the technique

ClearSight (BMEYE, Amsterdam, the Netherlands), which was introduced in 2007 and used to be known as Nexfin, is the most studied device (figure 4).<sup>[10]</sup> The device works by combining continuous finger blood pressure measurement via the volume clamp method, brachial pressure reconstruction and the pulse contour method.<sup>[10,51-53]</sup> Continuous finger blood pressure measurement is established by wrapping the cuff around the middle phalanx of a finger. The finger cuff inflates and deflates to keep the diameter of the artery constant using photo-plethysmographic technology. The brachial pressure waveform is modified from the finger pressure waveform by an algorithm. Finally, the pulse contour method (CO-TREK) is used to estimate CO from the arterial waveform.<sup>[10,51-53]</sup>



**Figure 5.** Volume clamping technique

Volume clamping technology for measuring cardiac output is based on combining the volume clamp method and pulse contour method. Volume clamp method uses an inflatable finger cuff around the phalanx of a finger to measure finger blood pressure continuously.

#### Clinical considerations

**Advantages:** The volume clamp method is easy to use compared with the other techniques described in this review and can be used in conscious as well as unconscious patients.<sup>[10,54-56]</sup>

**Limitations:** The system is not suitable in patients with severe peripheral vasoconstriction, very oedematous fingers, a regurgitant aortic valve and in patients with an aneurysm in the proximal aorta. When used for continuous CO monitoring, the finger cuff is restricted to a maximum of 8 hours per finger. When using the newest system with two finger cuffs, continuous use is restricted to a maximum of 72 hours.<sup>[10,52]</sup>

#### Accuracy

Individual studies have contradicting outcomes.<sup>[52,56,57]</sup> In 2015 a review was written on the accuracy of non-invasive cardiac output measurements with the volume clamping method<sup>[10]</sup> including 10 studies comparing ClearSight with  $TD_{PAC}$ , PICCO measurements or - in one study - transoesophageal echocardiography measurements. Most of the studies presented in this review reported a moderate-to-good correlation between the finger cuff absolute measurements and the 'gold standard' (weighted average  $r=0.71$ ); however, almost all of these studies reported a high percentage error (weighted average 44%). ClearSight seems to perform better in patients with a higher CO, which can be explained mathematically (a larger denominator). Eight studies described the accuracy of ClearSight to track changes in CO over time; in general ClearSight changed in the same direction as the gold standard (concordance between 84 and 100%); however when looking not only at the direction but also at the amplitude of CO changes, the results are conflicting (concordance between 94% and 100% but correlation coefficients between 0.39 and 0.94). Therefore, ClearSight might perform better as a trend monitor.<sup>[55]</sup> Since the fixed algorithm incorporated to calculate CO depends on assumptions, the reliability of ClearSight might alter in different patient groups or clinical scenarios.<sup>[10]</sup>

### Conclusion

This review gives an overview of the currently available non-invasive continuous cardiac output techniques in ICU. Whereas the volume clamp method, bioimpedance and bioreactance are feasible to use in sedated as well as conscious patients, the partial carbon dioxide rebreathing technique is limited to ventilated patients with stable tidal volumes and the ODM might be uncomfortable when used in conscious patients. The finger cuff is easiest to use. All techniques perform better as CO trend monitor as opposed to providing absolute CO values. For accuracy a distinction should be made between ICU populations; in elective postoperative ICU patients, with stable tidal volumes and without pulmonary disease, the techniques have shown reasonably good results. In non-elective ICU

patients, however, the non-invasive techniques are not able to replace TDPAC, mostly because of underlying diseases which can interfere with the accuracy. To conclude, the described non-invasive techniques in this review are less effective in measuring absolute CO compared with  $TD_{PAC}$ , however can be used as CO trend monitors in elective postoperative ICU patients.

## Disclosures

Denise P. Veelo and Bart F. Geerts have received travel and research grants from Edwards Lifesciences.

The other authors declare that they have no conflict of interest.

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**NVC**

# Basiscursus echografie

dinsdag 12 juni 2018 - woensdag 13 juni 2018  
maandag 10 september 2018 - dinsdag 11 september 2018

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