Minimally Invasive Cardiac Output Monitoring Systems: 
An Overview of the Major Calibrated and Un-calibrated Techniques

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Learning objectives
1. At the conclusion of this lecture, the participant will be able to describe the technical principles of the four major groups of calibrated and un-calibrated minimally invasive cardiac output monitoring devices: 1) Pulse wave analysis 2) Transesophageal Doppler 3) Bioimpedance / Bioreactance 4) Applied Fick’s principle.
2. In addition, the participant will be able to apply an integrated approach for the use of these different devices in cardiac surgery patients taking into considerations their a) invasiveness, b) typical limitations, and c) specific additional hemodynamic information.

Introduction
- Cardiac output (CO) monitoring is typically performed to ensure tissue oxygenation in the critically ill patient.
- Until recently the pulmonary artery catheter (PAC) was widely used for this task. However, this standard practice has been challenged based on conflicting study results regarding patient outcome.
- Today a variety of minimally invasive hemodynamic monitoring techniques are available decreasing the widespread PAC use (1,2).
- Some minimally invasive techniques track stroke volume (SV) continuously and provide dynamic indices of fluid responsiveness; others allow the assessment of volumetric preload variables, and some the continuous measurement of central venous saturation via the use of proprietary catheters (3).
- All these hemodynamic variables in combination with CO may allow an improved hemodynamic assessment.
- It is important to realize that there is no “best” monitoring technique and the inherent limitations of each minimally invasive technique have to be considered when they are used in daily practice.
- Moreover, it has to be emphasized that no monitoring technique can positively influence patient outcome per se unless its use is coupled with an adequate treatment protocol (4).

A) Overview of minimally invasive hemodynamic monitoring techniques
Minimally invasive CO monitoring devices use one of four main principles to measure CO (Table 1):
1. Pulse wave analysis: Calibrated and un-calibrated systems
2. Pulsed Doppler technology
3. Bioimpedance / Bioreactance
4. Applied Fick’s principle
<table>
<thead>
<tr>
<th>Groups</th>
<th>Examples</th>
<th>Features</th>
<th>Invasiveness</th>
<th>Continuous CO</th>
<th>Additional variables</th>
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<td>Static   Dynamic</td>
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<td><strong>Pulse wave analysis</strong></td>
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<td>Calibrated</td>
<td>PICCOplus™</td>
<td>Thermistor-tipped arterial catheter</td>
<td>■</td>
<td>Beat-by-beat</td>
<td>CVP       GEDV EVLW</td>
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<td></td>
<td>LiDCOplus™</td>
<td>Lithium dilution set</td>
<td>□</td>
<td>Beat-by-beat</td>
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<td></td>
<td>EV1000™/ VolumeView™*</td>
<td>Thermistor-tipped arterial catheter</td>
<td>■</td>
<td>NA</td>
<td>CVP       GEDV EVLW</td>
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<tr>
<td>Un-calibrated</td>
<td>FloTrac/Vigileo™</td>
<td>Regular arterial line, specific arterial</td>
<td></td>
<td>Update every 20’</td>
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<td></td>
<td>LiDCOrapid™</td>
<td>Regular arterial line</td>
<td>■</td>
<td>Beat-by-beat</td>
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<tr>
<td></td>
<td>PulsioFlex™*</td>
<td>Regular arterial line, specific sensor</td>
<td></td>
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<td>Non-invasive</td>
<td>Nexfin™ HD</td>
<td>Specific pressure sensors</td>
<td>□</td>
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<td><strong>Doppler</strong></td>
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<td>TE</td>
<td>CardioQ™</td>
<td>Esophageal flow probe</td>
<td>■</td>
<td>Limitation: Probe positioning</td>
<td>-</td>
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<tr>
<td>TT</td>
<td>USCOM™</td>
<td>Flow probe</td>
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<td>Intermittent</td>
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<tr>
<td><strong>Biolimpedance/Bioreactance</strong></td>
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<td>Endotracheal</td>
<td>ECOM™</td>
<td>Specific endotracheal tube</td>
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<td>Thoracic / Whole body</td>
<td>BioZ®</td>
<td>Specific electrodes</td>
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<td>Continuous</td>
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<td>NICOM™</td>
<td>Specific electrodes</td>
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<td><strong>Applied Fick principle</strong></td>
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<td>Partial CO₂ rebreathing</td>
<td>NiCO™</td>
<td>Re-breathing loop</td>
<td>■</td>
<td>Update every 3’</td>
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</table>

Legend: CO = cardiac output, CVP = central venous pressure, EVLW = extra-vascular lung water, GEDV = global end-diastolic volume, NA = technical specifications not yet available, PPV = Pulse pressure variation, SvO₂ = central venous oxygen saturation, SVV = Stroke volume variation, TE = trans-esophageal, TT = transthoracic, *not yet available.
1. Pulse wave analysis

- Pulse wave analysis is based on the principle that SV can be derived from continuous pressure waveform measurement via an arterial line. The characteristics of the arterial pressure waveform are determined by the interaction between SV and vascular compliance, aortic impedance as well as peripheral arterial resistance (3).

- For adequate CO measurement different aspects and limitations have to be considered:
  1. Optimal arterial waveform signal is a prerequisite, i.e. damping or increased tubing resonance has to be eliminated or at least reduced.
  2. Severe arrhythmias and the use of an intra-aortic balloon pump preclude adequate performance of this technique device.
  3. Periods of hemodynamic instability, i.e. rapid changes of vascular resistance may limit reliable CO assessment. This can be especially a problem for un-calibrated devices. By contrast calibrated devices require frequent recalibration for accurate CO estimation under these conditions.

Different calibrated and un-calibrated devices are currently available. The most widely used ones are briefly described in the following section.

**PiCCO**\textsubscript{plus}™ system

- The PiCCO system (Pulsion Medical Systems, Munich, Germany) requires a dedicated thermistor-tipped catheter that is typically placed in the femoral artery, in order to assess SV on a beat-to-beat basis.

- CO system calibration is performed using intermittent transpulmonary thermodilution via a central venous line. The calibration process enables also for the adjustment of the individual aortic impedance. It has to be repeated every 8 h in hemodynamically stable patients. During situations of hemodynamic instability calibration needs to be done more frequently (5).

- A variety of studies have successfully validated the PiCCO\textsubscript{plus} system in different patient populations (6,7).

- The launch of an un-calibrated device from Pulsion Medical Systems, the PulsioFlex™ system, can be expected in 2011. The system uses a specific arterial pressure sensor, which can be connected to a regular invasive arterial pressure monitoring set.

**LiDCO**\textsubscript{TM} plus and **LiDCO**\textsubscript{TM} rapid system

- The LiDCO\textsubscript{TM} plus and LiDCO\textsubscript{TM} rapid systems (LiDCO Ltd, London, UK) use the same pulse pressure algorithm (PulseCO\textsuperscript{TM}) and track SV continuously.

- The algorithm is based on the assumption that net power change in the vascular system is the difference of the amount of blood entering the system (i.e. SV) minus the amount of blood flowing peripherally and that there is a linear relationship between netpower and netflow.

- The LiDCO\textsubscript{TM} plus requires calibration by the transpulmonary lithium indicator dilution technique, which can be performed via a peripheral venous line. By contrast, the LiDCO\textsubscript{TM} rapid does not require calibration since CO estimation relies on hemodynamic nomograms only.

- Clinical studies showed that reliable estimation of CO using PulseCO is possible as long as no major hemodynamic changes occur (8,9).
- The reliability of the lithium calibration can be negatively affected by high peak doses of muscle relaxants, which may cross-react with the lithium sensor.

- The primary indication for the un-calibrated LiDCO™ rapid is its perioperative use for stroke volume optimization. Therefore, the LiDCOrapid trend analysis is more important than absolute CO values.

**FloTrac™/Vigileo™ system**

- The FloTrac™/Vigileo™ system (Edwards LifeSciences, Irvine, CA USA) requires a proprietary transducer, the FloTrac™, which is attached to a standard non-proprietary radial or femoral arterial catheter and is connected to the Vigileo™ monitor.

- The FloTrac™/Vigileo™ system does not require calibration. In order to assess CO, the standard deviation of pulse pressure sampled during a time window of 20 seconds is correlated with ‘normal’ SV based on patient’s demographic data (age, gender, height, and weight) and a built-in database containing information regarding CO assessed by PAC in a variety of clinical scenarios. Impedance is also derived from these data whereas vascular compliance and resistance are determined using arterial waveform analysis.

- After conflicting results of initial validation studies the CO algorithm has been several times modified in the last 5 years. This resulted in an improved performance primarily in the perioperative setting (10,11). Further software modifications addressed the issue of limited accuracy during hyperdynamic situations and preliminary data showed improved CO measurements under these specific conditions (12). Accuracy of the device during rapid hemodynamic changes still remains a concern.

- A new CO monitoring device based on pulse pressure analysis that is calibrated by transpulmonary thermodilution - the EV 1000™ / VolumeView™ system from Edwards Lifesciences - is currently being tested in clinical studies and will be released in 2011.

**Nexfin™**

- The Nexfin™ HD (BMEYE B.V, Amsterdam, Netherlands) is a completely non-invasive pulse pressure analysis device, which monitors pulse pressure using photoelectric plethysmography in combination with a volume-clamp technique, i.e. an inflatable finger cuff system.

- CO is derived using the Modelflow method, i.e. a simulation of a three-element Windkessel model.

- There are so far only limited published data available (13).

**2. Doppler CO monitoring devices**

- CO can be assessed using the Doppler technique via esophageal or trans-thoracic route.

- Esophageal Doppler devices measure blood flow in the descending aorta and derive CO by multiplying the cross-sectional area of the aorta by blood flow velocity. The aortic diameter is obtained from nomograms or by direct measurement using M-mode echocardiography (14).
Esophageal Doppler - Several esophageal Doppler probes are available commercially; ODM II™ (Abbott, Maidenhead, UK), CardioQ™ (Deltex Medical Ltd, Chichester, Sussex, UK), and HemoSonic100™ (Arrow, Reading, PA, USA). The latter device is a combination of a Doppler and an M-mode probe whose production has been ceased recently. - There are several limitations for the use of esophageal Doppler devices: 1. Doppler devices assess blood flow in the descending aorta and assume a fixed partition between flow to the cephalic vessels and to the descending aorta. This may be a valid assumption in healthy volunteers, however the relationship may change in patients with co-morbidities and under conditions of hemodynamic instability. 2. Doppler probes are smaller than the conventional trans-esophageal echocardiography probes and position may change unintentionally, thus, limiting continuous monitoring. 3. Adequate Doppler Probe position is crucial for an accurate measurement of aortic blood flow. The device is operator-dependent and studies have shown that roughly 12 insertions are required to obtain accurate measurements with an intra- and inter-observer variability of 8-12% (15,16). 4. Aortic cross-sectional area is not constant but rather dynamic in any individual patient. Therefore the use of nomograms may result in less accurate CO assessment.

Transthoracic Doppler - As an alternative to the esophageal approach, the transthoracic may be used to assess CO. However, no continuous measurement is possible. - The USCOM™ device (USCOM, Sidney, Australia) targets the pulmonary and aortic valves accessed via the parasternal and suprasternal windows in order to assess CO completely non-invasively. - Validation studies have demonstrated conflicting results, which could be explained primarily by the inherent problem of signal detection variability (17,18).

4. Bioimpedance and Bioreactance - Electrical bioimpedance uses electric current stimulation for the identification of thoracic or body impedance variations that are induced by cyclic changes in blood flow caused by the heart beating. - CO is continuously estimated, using skin electrodes or electrodes mounted on an endotracheal tube, by analyzing the occurring signal variation based on different mathematical models. - Different clinical validation studies continue to show conflicting results despite the fact, that the mathematical algorithms have been repeatedly modified (19,20).

Bioreactance - Bioreactance® (Cheetah Medical Inc. Portland, OR, USA), a modification of the thoracic bioimpedance has been recently introduced. - The bioreactance technique analyzes the frequency spectra variations of the delivered oscillating current. By contrast bioimpedance is based on the analysis of transthoracic voltage amplitude changes in response to high frequency current. - Bioreactance is supposed to result in a higher signal-to-noise ratio and thus in an improved performance of the device.
- First validation studies for this technique reveal promising results (21,22).

4. Applied Fick’s principle: Partial CO₂ re-breathing

- The NICO™ system (Novametrix Medical Systems, Wallingford, USA) applies the Fick’s principle to carbon dioxide (CO₂) for CO measurement in intubated, sedated, and mechanically ventilated patients using a disposable re-breathing loop that is attached to the ventilator circuit.

- The NICO™ system consists of the proprietary re-breathing loop, a mainstream infrared sensor to measure CO₂, a disposable airflow sensor, and a pulse oximeter.

- CO₂ production is calculated as the product of CO₂ concentration and airflow during a breathing cycle, whereas arterial CO₂ content is derived from end-tidal CO₂ and its dissociation curve. Every 3 min, a partial re-breathing state is generated using the attached re-breathing loop resulting in an increased end-tidal CO₂ and reduced CO₂ elimination. Assuming that CO does not change significantly between normal and re-breathing states, the difference between normal and re-breathing ratios are used to calculate CO (14).

- There are some limitations to partial CO₂ re-breathing:
  1. It can reliably perform CO measurement only in intubated and mechanically ventilated patients with fixed ventilator settings.
  2. Patients with gas exchange abnormalities need to be excluded from monitoring.

- Validation studies showed that variations in ventilator settings, mechanically-assisted spontaneous breathing, the presence of increased pulmonary shunt fraction, and hemodynamic instability are associated with decreased accuracy of CO assessment (23,24).

B) Additional hemodynamic variables

Apart from SV and CO hemodynamic monitoring devices provide various additional hemodynamic variables (Table 1):

1. Static preload variables
2. Functional hemodynamic variables
3. Continuous central venous oxygen saturation (ScvO₂) using dedicated catheters.

1. Static preload variables

   Pressure preload variables

   - CO monitoring devices require often a central venous line for calibration of the system. Thus, central venous pressure (CVP) measurement is easily available in many cases.

   - CVP is traditionally used as an estimate of cardiac preload. However, it has to be emphasized, that true preload is defined as end-diastolic myocardial fiber tension, which cannot be measured at the bedside.

   - Several factors affect CVP including impaired right ventricular function, severe pulmonary or valvular heart disease as well as positive pressure ventilation or increased intra-abdominal pressure.

   - Fluid therapy is often guided by CVP readings. However, several studies have shown a lacking correlation between CVP and echocardiographic preload...
estimates (25,26). Moreover, CVP cannot be used to assess preload responsiveness (27).

- Therefore, the utility of CVP is limited (28) and changes in trend over time and cyclic changes induced by mechanical ventilation are more important than absolute numbers.

**Volumetric preload variables**

- The so-called volumetric preload variables are considered to be superior indicators of preload as compared to CVP or pulmonary capillary wedge pressure.
- Global end-diastolic volume (GEDV) and extravascular lung water (EVLW) are static volumetric parameters, which are determined by transpulmonary thermodilution. This technique is required for the calibration of the PiCCO plus device and the up-coming EV1000/VolumeView device.
- The thermal indicator passes from the site of injection in the central vein to the thermal indicator detection site through different central compartments. Based on different indicator passage times and the thermodilution curve GEDV and EVLW can be calculated.
- Different studies have revealed better correlations between GEDV and SV than between the latter and static pressure preload (25). GEDV may be used to better guide perioperative fluid therapy than pressure preload parameters (29). EVLW on the other hand may be used to differentiate between cardiac vs. non-cardiac pulmonary edema, and has been identified as an independent predictor of survival in critically ill patients (30).

2. **Functional hemodynamic variables**

- Pulse pressure analysis devices provide an automated quantification of stroke volume variation (SVV) and some also pulse pressure variation (PPV).
- These functional variables rely on cyclic changes in intrathoracic pressure during positive pressure ventilation which induce changes in stroke volume and pulse pressure as a result of a reduction in preload (31).
- The different functional hemodynamic variables have been shown in various studies to be able to predict fluid responsiveness whereas static preload variables have failed to do so (32).
- Different cardiovascular and ventilatory limitations such as arrhythmia, right heart failure, spontaneous breathing activity, or low tidal volume (< 8 ml/kg body weight) affect the reliability of these variables.
- Alternatively, “passive leg raising” may be used to assess fluid responsiveness (33).

3. **Central venous oxygen saturation (ScvO₂)**

- ScvO₂ can be used as global marker of the balance between systemic oxygen supply and demand (34).
- Compared to mixed venous oxygen saturation (SvO₂) that requires the placement of a pulmonary artery catheter ScvO₂ can be easily measured by blood gas analysis using a sample drawn from a central venous catheter.
- In addition to intermittent measurements, both ScvO₂ and SvO₂ can be assessed continuously using proprietary central venous and pulmonary artery catheters, respectively. These central venous catheters are available for the Vigileo™ and the PiCCO™ systems.
- ScvO₂ has been used in studies as a resuscitation endpoint in patients with severe sepsis and septic shock.
- Absolute ScvO₂ and SvO₂ values may differ considerably in different clinical situations but a strong correlation of their trends over time has been demonstrated (35).

C) Integrative concept
- No single device can comply with all clinical requirements considering the technical features and limitations of the different monitoring techniques (36).
- Thus, different devices need to be used in an integrative concept along a typical clinical patient pathway (Figure 1) based on the invasiveness of the devices and the additional hemodynamic variables (Table 1).
- Bioreactance has the potential to be used primarily on the ward or in the emergency department and its use may be expanded in the future in the perioperative and ICU setting.
- Partial CO₂-rebreathing requires an intubated and mechanically ventilated patient for CO estimation. Thus, this technique can be primarily used during an operation.
- Un-calibrated pulse pressure analysis devices are eventually the first choice for the daily routine in a perioperative setting because they provide functional hemodynamic variables and allow a comprehensive hemodynamic management.
- Calibrated systems, by contrast, may be required when postoperative complications or hemodynamic instability occur and increased accuracy of the device or volumetric variables are needed.
- PAC insertion is mandatory for patient specific therapy when limited accuracy of minimally invasive monitoring devices is suspected and when pulmonary artery pressure monitoring or right heart failure treatment is required.
Figure 1: Integrative hemodynamic concept

- Thoracic & whole body bioimpedance / bioreactance
- Transthoracic Doppler
- Applied Fick principle
- Transesophageal Doppler
- un-calibrated pulse wave analysis
- calibrated pulse wave analysis
- PAC

Invasiveness

Additional HD variables

Ward
ED
OR
ICU
Summary

- Today, different techniques provide continuous CO measurement on a minimally invasive basis.
- Different factors influence the choice of a minimally invasive technique and clinicians need to understand the underlying principles and the inherent limitations.
- Based on these principles and limitations several minimally invasive techniques may be used in an integrative approach.
- In combination with ScvO$_2$ measurement, volumetric preload assessment and functional variables provided by these techniques may obviate the need for a PAC.

References


