Non-invasive monitoring of haemodynamic status

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Non-invasive monitoring of haemodynamic status
Haemodynamic status of a patient?

- Cardiac output
  - Stroke Volume
    - Preload + Ventricular compliance
    - Afterload
      - Systolic pressure
        » Pleural pressure
        » Outflow impedance
          - Vascular compliance
          - Vascular Resistance
            - Chamber radius = Preload
    - Contractility
  - Heart Rate
Haemodynamic status of a patient?

- Oxygen Delivery
  - Hemoglobin
  - $\text{PaO}_2$
  - $\text{SaO}_2$
- Oxygen Uptake
  - Central venous saturations
  - Mixed venous saturations
- Oxygen Extraction Ratio
- PCO2
Haemodynamic status of a patient?

• Microcirculation?
  – Oliguria
  – Mental detoriation
  – Lactic Acidosis
  – Liver failure
  – Bowel ischaemia
  – Adrenal insufficiency
  – ....
Monitoring !!!!

- Intermittent or continuous
- Manual or automatic
- Fun or boring
- Invasive or Non-invasive

- A searchlight cannot be used effectively without a fairly knowledge of the territory to be searched.

  Fergus Macartney, FRCP

- You need the right tool to do the job
- A fool with a tool is still a fool
What is invasive?

- Periferal venous line
- Arterial line
- Central Venous Line
- Pulmonary Artery Catheter
- Trans oesophageal cardiac ultrasound
Why not just use invasive? CVP and PAOP!

- Because it hurts?
- Increased patient risk of Central Line placement
- Ability to measure similar variables less invasive
- Increased cost
- Inaccurate measurements
- Incorrect interpretation and application of measured variables
- Lack of proven benefit in the overall management of patients.
- Fail to predict
  - Ventricular filling volume
  - Cardiac performance
  - Respons to volume infusion
In septic patients?

Cardiac filling pressures are not appropriate to predict hemodynamic response to volume challenge*

David Osman, MD; Christophe Ridel, MD; Patrick Ray, MD; Xavier Monnet, MD, PhD; Nadia Anguel, MD; Christian Richard, MD; Jean-Louis Teboul, MD, PhD

Objective: Values of central venous pressure of 8–12 mm Hg and of pulmonary artery occlusion pressure of 12–15 mm Hg have been proposed as volume resuscitation targets in recent international guidelines on management of severe sepsis. By analyzing a large number of volume challenges, our aim was to test the significance of the recommended target values in terms of prediction of volume responsiveness.

Design: Retrospective study.

Setting: A 24-bed medical intensive care unit.


Intervention: None.

Measurements and Main Results: A total of 150 volume challenges in 96 patients were reviewed. In 65 instances, the volume challenge resulted in an increase in cardiac index of ≥15% (responders). The pre-infusion central venous pressure was similar in responders and nonresponders (8 ± 4 vs. 9 ± 4 mm Hg). The pre-infusion pulmonary artery occlusion pressure was slightly lower in responders (10 ± 4 vs. 11 ± 4 mm Hg, p < .05). However, the significance of pulmonary artery occlusion pressure to predict fluid responsiveness was poor and similar to that of central venous pressure, as indicated by low values of areas under the receiver operating characteristic curves (0.58 and 0.63, respectively). A central venous pressure of <8 mm Hg and a pulmonary artery occlusion pressure of <12 mm Hg predicted volume responsiveness with a positive predictive value of only 47% and 54%, respectively. With the knowledge of a low stroke volume index (<30 mL·m⁻²), their positive predictive values were still unsatisfactory: 61% and 69%, respectively. When the combination of central venous pressure and pulmonary artery occlusion pressure was considered instead of either pressure alone, the degree of prediction of volume responsiveness was not improved.

Conclusion: Our study demonstrates that cardiac filling pressures are poor predictors of fluid responsiveness in septic patients. Therefore, their use as targets for volume resuscitation must be discouraged, at least after the early phase of sepsis has concluded. (Crit Care Med. 2007; 35:64–68)

Key Words: central venous pressure; pulmonary artery occlusion pressure; volume challenge; volume responsiveness; septic shock

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Figure 3. Individual values (open circles) and mean ± sd (closed circles) of pre-infusion pulmonary artery occlusion pressure (PAOP) (both expressed in millimeters of mercury) in responders (R) and nonresponders (NR).
In healthy “volunteers”

Pulmonary artery occlusion pressure and central venous pressure fail to predict ventricular filling volume, cardiac performance, or the response to volume infusion in normal subjects

Anand Kumar, MD; Ramon Anel, MD; Eugene Bunnell, MD; Kalim Habet, MD, MD; Sergio Zanotti, MD; Stephanie Marshall, RN; Alex Neumann, MS; Amjad Ali, MD; Mary Cheang, MS; Clifford Kavinsky, MD, PhD; Joseph E. Parrillo, MD

Conclusions: Normal healthy volunteers demonstrate a lack of correlation between initial central venous pressure/pulmonary artery occlusion pressure and both end-diastolic ventricular volume indexes and stroke volume index. Similar results are found with respect to changes in these variables following volume infusion. In contrast, initial end-diastolic ventricular volume indexes and changes in end-diastolic ventricular volume indexes in response to saline loading correlate strongly with initial and postsaline loading changes in cardiac performance as measured by stroke volume index. These data suggest that the lack of correlation of these variables in specific patient groups described in other studies represents a more universal phenomenon that includes normal subjects. Neither central venous pressure nor pulmonary artery occlusion pressure appears to be a useful predictor of ventricular preload with respect to optimizing cardiac performance. (Crit Care Med 2004; 32:691–699)
Pulmonary artery occlusion pressure and central venous pressure fail to predict ventricular filling volume, cardiac performance, or the response to volume infusion in normal subjects

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Figure 2. Relationship between A, initial central venous pressure (CVP) and stroke volume index (SVI); B, changes in central venous pressure and SVI in response to saline; C, initial pulmonary artery occlusion pressure (PWP) and SVI; and D, changes in PWP and SVI in response to saline in group 1 subjects. No significant relationship was found between initial values for either central venous pressure or PWP and SVI or changes in these variables following 3 L of saline infusion.
Wrong Way
What is Non-Invasive?

- Non Invasive Blood pressure Monitoring
- Pulse oxymeter
- Clinical signs of dehydration
  - Sunken eyes
  - Skin color
  - Temperature
  - Turgor
  - Heart rate
  - Fontanel
- Urine output
- Chest Examination and X-ray
What will we discuss??
Minimal Invasive?

• Volumetric approach
  – ITTV (Intra-Thoracic Thermal Volume)
  – ITBV (Intra-Thoracic Blood Volume)
  – EVLW (Extra Vascular Lung Water)
  – GEDV (Global End Diastolic Volume)

• A-line
  – SPV (Systolic pressure variation)
  – PPV (Pulse pressure variation)

• Pulse contour analysis
  – SVV (Stroke volume variation)

• PLR (Passive leg raising)

• Microcirculation

• (Oesophageal Doppler)

• (Transthoracic bioimpedance measurement)
The volumetric Approach based on transpulmonary thermal dilution

• Volume based estimation of ventricular preload (not pressure based)

• The transpulmonary thermal-dye dilution test
  – Indocyanin green dilution $\rightarrow$ ITBV
  – Thermal dilution: Mean Transit time (MTt) $\rightarrow$ ITTV

• The single transpulmonary thermodilution technique.
  – Thermal dilution: Mean Transit time (MTt) $\rightarrow$ ITTV
  – Thermal dilution: The down slope time of the transpulmonary thermal dilution curve (DStT) $\rightarrow$ PTV
What am I talking about?

- **ITTV** Intra-Thoracic Thermal Volume
- **ITBV** Intra-Thoracic Blood Volume
- **PTV** Pulmonary Thermal Volume
- **GEDV** Global End Diastolic Volume
- **EVLW** Extra Vascular Lung Water

A schematic representation of the relevant chambers and the derivation of intrathoracic blood volume and extravascular lung water.

How do ITBV and GEDV help us?

• Better correlation of ΔITBV/GEDV with ΔCO/SV/oxygen delivery than Δ CVP/PAOP BUT
• CO and GEDV/ITBV are both calculated from the same thermodilution curve, obviously they are linked.
• The whole model is based on a few principles which do not correlate with the reality
  – Pulsatile flow instead of constant flow
  – Injection time is never instant
  – Distribution is never instant and complete
• ITBV and GEDV are static (non continuous) indicators of preload
  ≠ Preload responsiveness
• Invasive!
Is there a role for EVLW?

- EVLW measurements provide an estimate of pulmonary oedema (not reliably detected clinically or by chest radiography).
  - Cut off
    - >10ml/kg ARDS
    - > 15ml/kg mortality rate 65% (double of patients <10 ml/kg)
  - If used in an algorithm it may improve outcome (1)
- Dual indicator technology is cumbersome
  - PiCCO and LiDCO?
- No Published studies have validated the accuracy of PiCCO derived EVLW measurement
- Non continuous measurement
- Invasive!

SPV, PPV and SVV and “fluid” responsiveness

- Basic principles
- Formulas SPV and PPV
- Limitations SPV, PPV and SVV
- Measurement methods SVV and CO
- Restrictions SVV and CO
- Fluid Responsiveness: Studies and reviews
- Remark
On the preload-dependent part of the Starling curve, a given increase in preload (fluid bolus, A) elicits a marked rise in stroke volume (B). On the flatter preload-independent portion of the curve, the same fluid challenge elicits a far lesser increase in stroke volume (A).

Basic principles

Fig. 5

mmHg
150

150
60

Pmax
Pmin

SPV

Relationship of systolic pressure variation to mechanical ventilation. ΔDown is measured relative to the systolic pressure at end expiration. SPV, systolic pressure variation.

Basic principles

• Cyclic changes in the loading conditions of the ventricles during Positive Pressure Ventilation
• During inspiration
  – Preload of the RV ↓
    • Decrease in venous return pressure gradient
  – Afterload of the RV ↗
    • Inspiratory increase in transpulmonary pressure
    → Decrease in RV Stroke Volume
• Decrease in the Left Ventricle filling 2 – 3 heart beats later
  → Decrease in LV Stroke volume, minimal during expiration
• The ΔSV will be higher when the ventricle operates on the steep part of the Frank-Starling Curve
Formulas: SPV, PPV

**SPV** = Systolic Pressure Variation

\[ SPV = SBP_{\text{max}} - SBP_{\text{min}} \]

**PPV** = Pulse Pressure Variation

\[ PPV = \frac{PP_{\text{max}} - PP_{\text{min}}}{(PP_{\text{max}} + PP_{\text{min}})/2} \]

**Pulse Pressure (PP)** = Systolic blood pressure – Diastolic blood pressure
Limitations of SPV, PPV and SVV

- No spontaneous breathing
- No irregular heartbeat
- Volume controlled ventilation with TV of 8-10 ml/kg ideal body weight.

- Most of the ICU-patients are **NOT** candidates
- A trick in the magicians sleeve?
Measurement: SVV and CO
Arterial Pressure Waveform Analysis APWA

• Transpulmonary Dilution methods
  – Periodic calibration with measured CO
    • Pulse contour Analysis: PiCCO (thermal bolus)
    • Pulse Power analysis: PulseCO (LiDCO) (Lithium bolus)

• Calculation of standard deviation of the arterial pressure wave over a 20 seconds period
  – Couples this data to an algorithm based on demographic data (age, sex, height and weight)
    • FloTrac / Vigileo
Limitations of APWA

- All forms of APWA still require some degree of Intravascular access.
  - PiCCO
    - Specialized femoral artery catheter
    - Central Venous Catheter
  - LiDCO
    - Standard arterial line
    - Standard peripheral venous canulae
  - FloTrac/Vigileo
    - Standard arterial line
- Transpulmonary thermodilution can be inaccurate in the presence of
  - Intracardiac shunts
  - Intrathoracic Haemorrhage
- APWA measurements are less accurate with significant variations in SVR
  - Recalibration
### Table 1. Characteristics and findings with pooled results (95% confidence interval) of studies included in meta-analysis

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>n</th>
<th>Patient</th>
<th>Dynamic Variable</th>
<th>Fluid Challenge</th>
<th>TV (mL/kg)</th>
<th>Device</th>
<th>Cardiac End Point</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tavernier (31)</td>
<td>1998</td>
<td>15</td>
<td>ICU-sepsis</td>
<td>Y</td>
<td>500 mL HES</td>
<td>8-11</td>
<td>PAC</td>
<td>SVI</td>
</tr>
<tr>
<td>Michard (32)</td>
<td>1999</td>
<td>14</td>
<td>ICU-ARDS</td>
<td>N</td>
<td>10 PEEP&lt;sup&gt;c&lt;/sup&gt;</td>
<td>7-12</td>
<td>PAC</td>
<td>CI</td>
</tr>
<tr>
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<td>ICU-sepsis</td>
<td>N</td>
<td>500 mL HES</td>
<td>8-12</td>
<td>PAC</td>
<td>CI</td>
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<tr>
<td>Berkenstadt (34)</td>
<td>2001</td>
<td>15</td>
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<td>100 mL HES&lt;sup&gt;b&lt;/sup&gt;</td>
<td>10</td>
<td>PiCCO*</td>
<td>SVI</td>
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<tr>
<td>Reuter (35)</td>
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<td>Reuter (36)</td>
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<td>N</td>
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<td>13-15</td>
<td>PiCCO</td>
<td>CI</td>
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<tr>
<td>Reuter (37)</td>
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<td>N</td>
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<td>10</td>
<td>PiCCO</td>
<td>SVI</td>
</tr>
<tr>
<td>Bendjeldj (38)</td>
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<td>16</td>
<td>Post C.Surg</td>
<td>Y</td>
<td>10 PEEP&lt;sup&gt;c&lt;/sup&gt;</td>
<td>8-10</td>
<td>PAC</td>
<td>SVI</td>
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<tr>
<td>Rex (39)</td>
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<td>14</td>
<td>Post C.Surg</td>
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<td>PAC</td>
<td>SVI</td>
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<td>Kramer (40)</td>
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<td>21</td>
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<td>PiCCO</td>
<td>SVI</td>
</tr>
<tr>
<td>Marx (41)</td>
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<td>N</td>
<td>500 mL HES</td>
<td>8-10</td>
<td>PiCCO</td>
<td>SVI</td>
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<tr>
<td>Hofer (42)</td>
<td>2005</td>
<td>35</td>
<td>Post C.Surg</td>
<td>N</td>
<td>250 mL gelatin x 2</td>
<td>1000 mL CR/500 HES</td>
<td>8-10</td>
<td>PAC</td>
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<tr>
<td>Wiesenack (45)</td>
<td>2005</td>
<td>20</td>
<td>C.Surg&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Y</td>
<td>7 mL/kg HES</td>
<td>8</td>
<td>PiCCO/PAC</td>
<td>SVI</td>
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<tr>
<td>Feissel (46)</td>
<td>2005</td>
<td>20</td>
<td>ICU-sepsis</td>
<td>N</td>
<td>8 mL/kg HES</td>
<td>8-10</td>
<td>TTE</td>
<td>CI</td>
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<tr>
<td>Solus-Biguenet (47)</td>
<td>2006</td>
<td>8</td>
<td>Hepatic surgery</td>
<td>N</td>
<td>250 mL gelatin&lt;sup&gt;b&lt;/sup&gt;</td>
<td>8-10</td>
<td>PAC</td>
<td>SVI</td>
</tr>
<tr>
<td>Charron (48)</td>
<td>2006</td>
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<td>ICU-mixed</td>
<td>Y</td>
<td>100 mL HES</td>
<td>8-10</td>
<td>TEE</td>
<td>SV</td>
</tr>
<tr>
<td>Natalini (49)</td>
<td>2006</td>
<td>22</td>
<td>ICU-mixed</td>
<td>Y</td>
<td>500 mL HES</td>
<td>8</td>
<td>PAC</td>
<td>CI</td>
</tr>
<tr>
<td>Wyffels (50)</td>
<td>2007</td>
<td>32</td>
<td>Post C.Surg</td>
<td>Y</td>
<td>500 mL HES</td>
<td>8-10</td>
<td>TEE</td>
<td>CI</td>
</tr>
<tr>
<td>Feissel (51)</td>
<td>2007</td>
<td>23</td>
<td>ICU-sepsis</td>
<td>Y</td>
<td>8 mL/kg HES</td>
<td>8-10</td>
<td>TEE</td>
<td>CI</td>
</tr>
<tr>
<td>Lee (52)</td>
<td>2007</td>
<td>20</td>
<td>Neurosurg&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Y</td>
<td>7 mL/kg HES</td>
<td>10</td>
<td>Esophageal Doppler</td>
<td>SVI</td>
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<tr>
<td>Cannesson (53)</td>
<td>2007</td>
<td>25</td>
<td>C.Surg&lt;sup&gt;a&lt;/sup&gt;</td>
<td>N</td>
<td>500 mL HES</td>
<td>8-10</td>
<td>PAC</td>
<td>CI</td>
</tr>
<tr>
<td>Cannesson (54)</td>
<td>2008</td>
<td>25</td>
<td>C.Surg&lt;sup&gt;a&lt;/sup&gt;</td>
<td>N</td>
<td>500 mL HES</td>
<td>8-10</td>
<td>PAC</td>
<td>CI</td>
</tr>
<tr>
<td>Auler (55)</td>
<td>2008</td>
<td>59</td>
<td>Post C.Surg</td>
<td>N</td>
<td>20 mL/kg LR</td>
<td>8</td>
<td>PAC</td>
<td>CO</td>
</tr>
<tr>
<td>Belloni (56)</td>
<td>2008</td>
<td>19</td>
<td>C.Surg&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Y</td>
<td>7 mL/kg HES</td>
<td>8</td>
<td>LiDCO/PAC</td>
<td>CI</td>
</tr>
<tr>
<td>Cannesson (57)</td>
<td>2008</td>
<td>25</td>
<td>C.Surg&lt;sup&gt;a&lt;/sup&gt;</td>
<td>N</td>
<td>500 mL HES</td>
<td>8-10</td>
<td>PAC</td>
<td>CI</td>
</tr>
<tr>
<td>Hofer (58)</td>
<td>2008</td>
<td>40</td>
<td>Post CABG</td>
<td>N</td>
<td>8-10</td>
<td>8-10</td>
<td>FloTrac&lt;sup&gt;a&lt;/sup&gt;/PiCCO</td>
<td>SVI</td>
</tr>
<tr>
<td>Biasis (59)</td>
<td>2008</td>
<td>35</td>
<td>Liver transplant</td>
<td>N</td>
<td>Albumin 20 mL x BMI</td>
<td>8-10</td>
<td>FloTrac/TEE</td>
<td>CO</td>
</tr>
</tbody>
</table>
Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: A systematic review of the literature*

Paul E. Marik, MD, FCCM; Rodrigo Cavallazzi, MD; Tajender Vasu, MD; Amyn Hirani, MD

Table 2. Ability of dynamic and static hemodynamic variables to predict volume responsiveness: pooled data with 95% confidence intervals

<table>
<thead>
<tr>
<th></th>
<th>Correlation (r)</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPV</td>
<td>.78 (.74-.82)</td>
<td>0.94 (0.93-0.95)</td>
</tr>
<tr>
<td>SPV</td>
<td>.72 (.65-.77)</td>
<td>0.86 (0.82-0.90)</td>
</tr>
<tr>
<td>SVV</td>
<td>.72 (.66-.78)</td>
<td>0.84 (0.78-0.88)</td>
</tr>
<tr>
<td>LVEDAI</td>
<td>—</td>
<td>0.64 (0.53-0.74)</td>
</tr>
<tr>
<td>GEDVI</td>
<td>—</td>
<td>0.56 (0.37-0.67)</td>
</tr>
<tr>
<td>CVP</td>
<td>.13 (-.01-.28)</td>
<td>0.55 (0.48-0.62)</td>
</tr>
</tbody>
</table>

PPV, pulse pressure variation; SPV, systolic pressure variation; SVV, stroke volume variation; LVEDAI, left ventricular end-diastolic area index (derived from transesophageal echocardiography); GEDVI, global end-diastolic volume index (derived from transpulmonary thermodilution); CVP, central venous pressure.

Table 3. Pooled performance estimates (with 95% confidence intervals) from the studies where the true/false positive/negative results could be calculated

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PPV (n = 14)</th>
<th>SVV (n = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROC area</td>
<td>0.94 (0.92-0.96)</td>
<td>0.84 (0.81-0.87)</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.89 (0.82-0.94)</td>
<td>0.82 (0.75-0.89)</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.88 (0.81-0.92)</td>
<td>0.86 (0.77-0.92)</td>
</tr>
<tr>
<td>Positive likelihood</td>
<td>7.26 (4.46-11.80)</td>
<td>5.77 (3.43-9.72)</td>
</tr>
<tr>
<td>Negative likelihood</td>
<td>0.12 (0.07-0.21)</td>
<td>0.21 (0.15-0.30)</td>
</tr>
<tr>
<td>Diagnostic odds ratio</td>
<td>59.86 (23.88-150.05)</td>
<td>27.34 (13.46-55.53)</td>
</tr>
</tbody>
</table>

PPV, pulse pressure variation; SVV, stroke volume variation; ROC, receiver operating characteristic.

Figure 1. Standardized receiver operating characteristic (SROC) curve with confidence and predictive ellipses for the 14 studies that allowed abstraction of the true/false positive/negative values for the ability of the pulse pressure variation to predict volume responsiveness. SENS, sensitivity; SPEC, specificity; AUC, area under the curve.
Stroke Volume and Pulse Pressure Variation for Prediction of Fluid Responsiveness in Patients Undergoing Off-Pump Coronary Artery Bypass Grafting

Christoph K. Hofer, MD; Stefan M. Müller, MD; Lukas Furrer, MD; Richard Klaghofer, PhD; Michele Genoni, MD; and Andreas Zollinger, MD
Remark

• Comparison between methods of CO monitoring is expressed in terms of bias and limits of agreement.
• Limits of agreement of +/- 30% are generally considered acceptable for a new method of CO measurement.
• The FloTrac/Vigileo system does not live up to this limits of agreement in most studies (average error of 46% in one study, Mayer et al), the adapted algorithm has been refined though.
• Biancofiore et al found a percentage error of 54% between FloTrac (latest software) and PCA derived CO measurements. The greatest degree of bias occurring under conditions of low SVR

The magicians sleeve? PLR = Passive Leg Raise?

• How to do it and how long?
  – Different studies different methods: No uniformity
  – Starting supine or semirecumbent
  – Duration 60s, 90s, 120s, 240s, 300s

• What to look at
  – CO/ABF/SV/VTIAo
    • TTE/oesophageal Doppler
    • PAC
    • SVV (PAC, PiCCO and FloTrac/Vigileo)
  – PP Variation

• What is responsive?
  – $\Delta$ SV/SVI/ABF/CO/CI > 12-15%
  – Fluid challenge: 300 - 500 ml Chrystalloids/Colloids
Table 4: Results of subgroup analysis: pooled values (95% confidence intervals) of correlation coefficient and area under the receiver operating characteristics curve (AUC) in subgroups: controlled ventilation versus spontaneous inspiratory efforts, sinus rhythm versus arrhythmias, supine versus semirecumbent starting position.

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Correlation $r$</th>
<th>$p^*$</th>
<th>AUC</th>
<th>$p^*$</th>
</tr>
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<tbody>
<tr>
<td>Ventilation</td>
<td></td>
<td></td>
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<tr>
<td>Adapted</td>
<td>0.81 (0.53–0.93)</td>
<td>0.97</td>
<td>0.94 (0.87–1.00)</td>
<td>0.74</td>
</tr>
<tr>
<td>Inspiratory efforts</td>
<td>0.81 (0.74–0.87)</td>
<td></td>
<td>0.95 (0.91–0.99)</td>
<td></td>
</tr>
<tr>
<td>Cardiac rhythm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sinus rhythm</td>
<td>0.73 (0.58–0.84)</td>
<td>0.15</td>
<td>0.96 (0.92–0.99)</td>
<td>0.94</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td>0.83 (0.75–0.89)</td>
<td></td>
<td>0.96 (0.89–1.03)</td>
<td></td>
</tr>
<tr>
<td>Starting position</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supine</td>
<td>0.78 (0.64–0.87)</td>
<td>0.39</td>
<td>0.93 (0.87–1.00)</td>
<td>0.62</td>
</tr>
<tr>
<td>Semirecumbent</td>
<td>0.83 (0.75–0.89)</td>
<td></td>
<td>0.95 (0.92–0.97)</td>
<td></td>
</tr>
</tbody>
</table>

* Test for interaction
Microcirculation?

- Characteristics of the normal microcirculation
- Microcirculation in disease states.
- Heterogeneity of microvascular perfusion?
- Techniques used to evaluate the microcirculation
- Evaluation of tissue oxygenation
Characteristics of the normal microcirculation

- Vessels < 100 microns
- Arterioles
  - Vascular tone
  - Local modulation according to O₂-demand
- Capillaries
  - Thin endothelial surface
  - O₂ and nutrient exchange and elimination of cellular waste products
  - Architecture differs among organs
- Venules
  - Merge into larger ones
  - Leukocyte adhesion, rolling and migration
  - Permeability changes
Microcirculation in disease states.

- **Sepsis**
  - Functional capillary density decreases
  - Shutdown is heterogeneous

- **Low flow conditions**
  (haemorrhage/cardiovascular shock)
  - Functional capillary density decreases
  - Shutdown is heterogenous

- **Reperfusion**
  - Heterogenous bloodflow due to inflammatory respons
Fig. 2 Venous O$_2$ saturation can be low in conditions associated with microvascular shunting. When perfusion is heterogeneous, a low venous oxygen saturation can also be encountered. If total flow to the tissue is decreased (bottom panel), venous oxygen saturation decreases but this fails to reflect an improvement in perfusion heterogeneity.
Capillary density

Figure 2. Examples of high and low capillary density. The capillary density was calculated similar to the technique of De Backer et al.1 A grid of equidistant vertical and horizontal lines was superimposed on the image. The vessel density was calculated as the number of small vessels (<20 μm) intersecting the lines of the grid divided by the total length of the lines yielding the number of small vessels per millimeter. The image in A represents a high capillary density, and the image in B represents a low capillary density.

Techniques used to evaluate the microcirculation

• Clinical evaluation
  – Mottled skin
  – Acrocyanosis
  – slow recoloration time
  – increased central to toe temp gradient

• Biomarkers
  – Lactate levels
  – Hyaluronan levels.

• Lack Specificity and Sensitivity
Devices to look at Microcirculation

• Evaluation of the microcirculation in the microvascular bed in which it is implemented.
• Does this represent all microvascular beds?
  – Mechanism implicated in microvascular disease
  – Organ microvascular architecture
  – Local factors (vasoconstriction/pressure)
• Some areas are more relevant than others (relationship with outcome)
Devices to look at Microcirculation

• Laser Doppler Flowmetry
  – Measures flow in a variable volume between 0.5 and 1 mm³ → at least 50 micro vessels.
  – Misses heterogeneity changes

• Microvideoscopic techniques
  – Experimental conditions, not in humans

• Nailfold videocapillaroscopy
  – Very sensitive to changes in temperature
  – Suitable to investigate the microvascular effects of chronic disease (diabetes, vasculitis and arteritis)
OPS and SDF

- OPS = Orthogonal polarization spectral
- SDF = Sidestream DarkField

Both are videomicroscopic imaging techniques that can be applied at the bedside.

- Used in organs with thin epithelial layers
  - Skin
  - Conjunctiva
  - Gingiva
  - Sublingual area
  - Ileostomies and colostomies
  - Rectal mucusa

- They measure
  - Vascular density
  - Heterogeneity of perfusion
Orthogonal polarization spectral (OPS) imaging technique. Polarized light is directed to the tissue. Light reflected by the superficial layers is still polarized and discarded by the orthogonal filter. Light reflected from the depth of the tissues has encountered many scattering events and has lost its polarized characteristics so is not discarded by the orthogonal filter; this light is absorbed by hemoglobin contained in red blood cells so that these will be seen as gray/black bodies on the screen.

Sidestream dark field (SDF) imaging technique. Green light is provided by the lateral sides of the device. Light reflected by superficial layers fails to reach the center of the device where the optics are located. Light reflected from the depth of the tissues reaches the center of the device; this light is absorbed by hemoglobin contained in red blood cells so that these will be seen as gray/black bodies on the screen.

Evaluation of tissue oxygenation

- Venous oxygen saturation
  - Misleading for microvascular dysfunction
- PO$_2$ electrodes
  - Sensitive to the highest PO$_2$ in the sampling volume (0.5 mm$^3$ = >100 microvessels)
- Reflectance Spectroscopy
- Near Infrared Spectroscopy
- PCO$_2$-derived measurements
  - Gastric tonometry (technical problems)
  - Sublingual capnometry (research purposes)
    - PSLCO$_2$-diff
Sublingual capnometry versus traditional markers of tissue oxygenation in critically ill patients*

Paul E. Marik, MD, FCCM; Aleksandr Bankov, MD, FRCA

**Objective:** The purpose of this study was to determine the prognostic value of sublingual Pco\textsubscript{2} (P\textsubscript{SL}co\textsubscript{2}), lactate concentration, and mixed venous oxygen saturation (S\textsubscript{MV}o\textsubscript{2}) in hemodynamically unstable intensive care patients and, additionally, to compare the temporal changes of these variables in response to treatment.

**Setting:** Medical/surgical intensive care unit.

**Subjects:** Fifty-four patients, mean age 58 ± 8 yrs.

**Interventions:** Oxyhemodynamic variables, arterial lactate concentration, and P\textsubscript{SL}co\textsubscript{2} were recorded in unselected sequential intensive care patients undergoing pulmonary artery catheterization. A data set was obtained immediately after insertion of the pulmonary artery catheter and repeated 4 and 8 hrs later.

**Measurements and Main Results:** Twenty-one patients had severe sepsis or septic shock. Twenty-seven (50%) patients died. The initial P\textsubscript{SL}co\textsubscript{2}-Paco\textsubscript{2} gradient (P\textsubscript{SL}co\textsubscript{2}-diff) and the initial P\textsubscript{SL}co\textsubscript{2} were highly predictive of outcome (\(p = .0004\) and \(p = .004\), respectively); however, there was no difference in the arterial lactate concentration and S\textsubscript{MV}o\textsubscript{2} between the survivors and non-survivors. The P\textsubscript{SL}co\textsubscript{2}-diff had the best receiver operator characteristic characteristics (area under the curve, 0.75), with a P\textsubscript{SL}co\textsubscript{2}-diff >25 mm Hg being the best discriminator of outcome. With treatment, the P\textsubscript{SL}co\textsubscript{2}-diff decreased in both survivors and non-survivors; however, the lactate and S\textsubscript{MV}o\textsubscript{2} remained relatively unchanged during the study period.

**Conclusions:** The baseline P\textsubscript{SL}co\textsubscript{2}-diff and P\textsubscript{SL}co\textsubscript{2} were better predictors of outcome than traditional markers of tissue hypoxia and were more responsive to therapeutic interventions. The P\textsubscript{SL}co\textsubscript{2}-diff and/or P\textsubscript{SL}co\textsubscript{2} may prove to be a useful marker for goal-directed therapy and for assessing the response to clinical interventions aimed at improving tissue oxygenation. (Crit Care Med 2003; 31:818–822)

**Key Words:** intensive care unit; critical care; oxygen delivery; sublingual capnometry
Lactate (mmol/L)
PSLCO$_2$-diff (mm Hg)

$\text{SmVO}_2$ (%)

Hours

- ▲ Lactate Alive
- ● Lactate Dead
- ▲ PSLCO$_2$-diff Alive
- ○ PSLCO$_2$-diff Dead
- ▽ $\text{SmVO}_2$ Alive
- ○ $\text{SmVO}_2$ Dead

* p=0.02 compared to baseline
# p=0.0004; alive vs dead
Figure 1. Receiver operating characteristic (AUC) for the sublingual CO₂-arterial gradient (PsIICO₂-diff), arterial lactate concentration, and mixed venous oxygen saturation (SmvO₂) in predicting mortality.
References


References


