Conventional vs. Goal Directed Perfusion (GDP) Management: Decision Making & Challenges

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Why do we need a new measure of perfusion adequacy
How do you define adequate perfusion?

- 2.2 to 2.6 l/min/m² adjusted for temperature
- Mean arterial pressure > 50 mmHg
- SvO₂ > 65%
- PvO₂ > 40 mmHg
- Lactate < 2 mmol/l
The results of the present study indicate that even though the present flow recommendations result in acceptable mixed venous saturation, it does not protect individual vital organs from deoxygenation. One
Problems with $SvO_2$

Adequacy of Perfusion during Hypothermia: Regional Distribution of Cardiopulmonary Bypass Flow, Mixed Venous and Regional Venous Oxygen Saturation

Hypothermia and Distribution of Flow and Oxygen

Table 2  Effect of change in perfusion temperature on oxygen delivery, extraction and consumption

<table>
<thead>
<tr>
<th></th>
<th>Normothermia</th>
<th>Hypothermia</th>
<th>Rewarming</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivery (ml/min/m²)</td>
<td>388±27</td>
<td>364±32</td>
<td>401±38</td>
</tr>
<tr>
<td>Extraction (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VCS</td>
<td>20.2±4.8</td>
<td>17.7±8.2</td>
<td>27.2±9.2&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>VCI</td>
<td>22.7±7.4</td>
<td>20.4±5.0</td>
<td>39.5±6.4&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Consumption (ml/min/m²)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VCS</td>
<td>88±12</td>
<td>79±13&lt;sup&gt;c&lt;/sup&gt;</td>
<td>109±15&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>VCI</td>
<td>95±8.8</td>
<td>83±11&lt;sup&gt;c&lt;/sup&gt;</td>
<td>158±21&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> $p<0.05$ rewarming versus normothermia; <sup>b</sup> $p<0.05$ rewarming versus hypothermia; <sup>c</sup> $p<0.05$ hypothermia versus normothermia; <sup>d</sup> $p<0.05$ VCI versus VCS.

VCS = vena cava superior; VCI = vena cava inferior

Problems with SvO$_2$

- Regional deoxygenation occurs during normothermic and hypothermic perfusion.
- Mixed venous SvO$_2$ is only a partially reliable indicator of regional oxygen transport.
- The discrepancy increases with increasing hypothermia.
- There is strong evidence for on-line monitoring of regional oxygenation as a guide to management and quality assurance of perfusion.

In conclusion, we showed that the type of DO₂ optimization, specifically increases in FiO₂ versus increases in CO, could affect the capability of venous oxygen saturation to measure the adequacy of oxygen supply. Interpreting venous saturation at high arterial partial pressures of oxygen values should be performed with caution.

Figure 1 - Panel A: Effect of increasing DO₂ on the SvO₂ through changes in the inspired fraction of oxygen (FiO₂, solid line) or cardiac output (dashed line) under normal and high oxygen supply conditions sufficient to attain optimal oxygen consumption in all peripheral compartments. Panel B: Effect of increasing DO₂ on the SvO₂ through changes in the inspired fraction of oxygen (FiO₂, solid line) or cardiac output (dashed line) under low oxygen supply conditions that caused the oxygen consumption to be supply limited.
The increase in DO$_2$ by increasing the FiO$_2$ from 21 to 100% was only 11% (solid line).

The mixed SvO$_2$ increases disproportionately to increases in FiO$_2$ than increases in DO$_2$ from increasing CO.

Hgb = 14 g%
PaCO$_2$ = 40
pH = 7.4
Lactate and AKI

- Increasing lactate load leads to increased probability of AKI
- “most of the cause of hyperlactemia is due to inadequate oxygen supply can be identified after the CPB phase”
- Is there a better way to detect and prevent lactate development during CPB?
### Goal Directed Perfusion (GDP)

**Problems with lactate monitoring**

- **Important end indicator of adequacy of perfusion**
- **Affected by many factors**
  - Age, complex surgery, CPB time, diabetes, acid base level, vasoactive intervention, renal function
  - **Hyperlactemia > 4 mmol/l = 6 x mortality**
  - **Blood flow to tissue is required to see systemic lactate levels**
  - **By the time you see increasing lactate levels it may be too late for perfusion intervention**

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**Critical DO2**

<table>
<thead>
<tr>
<th>Critical DO2</th>
<th>Peak Arterial Blood Lactate (mMol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>200</td>
<td>3.0</td>
</tr>
<tr>
<td>220</td>
<td>2.5</td>
</tr>
<tr>
<td>240</td>
<td>2.0</td>
</tr>
<tr>
<td>260</td>
<td>1.5</td>
</tr>
<tr>
<td>280</td>
<td>1.0</td>
</tr>
<tr>
<td>300</td>
<td>0.5</td>
</tr>
<tr>
<td>320</td>
<td>0.0</td>
</tr>
<tr>
<td>340</td>
<td>0.0</td>
</tr>
<tr>
<td>360</td>
<td>0.0</td>
</tr>
<tr>
<td>380</td>
<td>0.0</td>
</tr>
</tbody>
</table>

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SvO2 > 70%, PvO2 > 40 mmHg
pH = 7.35 – 7.45
pCO2 = 32-42 mmHg

“the ultimate aim of perfusion is to provide satisfactory tissue gas exchange” p.258

Each organism is its own control
Patients with same BSA, but very different physical characteristics may receive the same pump flow.

They might have different oxygen delivery \( (DO^2) \) needs.

BSA indexed flow rate is independent of hemoglobin.
Why do we need Goal Directed Perfusion (GDP)?
(a new monitor of perfusion adequacy)

**Oxygen delivery nadir not hematocrit nadir**
- Acute Kidney Injury
- Sensitive and reproducible marker

**Problems with conventional measures of perfusion adequacy**
- Dysoxygenation and measures of SvO2
- Problems with lactate monitoring
- Early warning of cellular respiration mismatch

**NEED: Continuous real time information**
Complete respiratory cycle
- Oxygen delivery
- Oxygen Consumption
- Carbon Dioxide Production

---

**Aerobic Respiration:**
\[
38 \text{ ADP} + C_6H_{12}O_6 + 6\text{O}_2 \rightarrow 6\text{CO}_2 + 6\text{H}_2\text{O} + 38 \text{ATP}
\]

**Anaerobic Respiration:**
\[
2\text{CH}_3\text{COCOO}^- + 2\text{NAD}^+ + 2\text{H}_2\text{O} \rightarrow 2\text{CH}_3\text{COO}^- + 2\text{NADH} + 2\text{H}^+ + 2\text{CO}_2
\]
Anaerobic Metabolism During Cardiopulmonary Bypass: Predictive Value of Carbon Dioxide Derived Parameters

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Department of Cardiothoracic Anesthesia, Policlinico San Donato, Milan, and the Thoracic and Cardiovascular Unit, Department of Surgery and Bioengineering, University of Siena, Siena, Italy

Background. Hyperlactatemia during cardiopulmonary bypass (CPB) is a common event and is associated to a high morbidity and mortality after cardiac operations. The present study is aimed to identify the possible predictors of hyperlactatemia during CPB among a series of oxygen and carbon dioxide derived parameters measured during CPB.

Methods. This is a prospective observational study on 54 patients undergoing cardiac surgery with CPB. Hyperlactatemia was defined as an arterial lactate concentration higher than 3 mMol/L. Serial blood lactate assays have been performed during CPB, and their association to a number of oxygen and carbon dioxide derived parameters was explored.

Results. Arterial blood lactate concentration was positively correlated to the CPA duration, the carbon dioxide elimination, and the respiratory quotient, and negatively correlated to the presence of the aortic cross-clamping, the body surface area, the ratio between the oxygen delivery and the carbon dioxide production, and the arterial oxygen saturation. Predictors of hyperlactatemia during CPB are a carbon dioxide production higher than 60 mL - min⁻¹ - m², a respiratory quotient higher than 0.9, and a ratio between oxygen delivery and carbon dioxide production lower than 3.

Conclusions. Carbon dioxide derived parameters are representative of hyperlactatemia during CPB, as a result of the carbon dioxide produced under anaerobic conditions through the buffering of protons by the bicarbonate system. The carbon dioxide elimination rate measured at the exhaled site of the oxygenator may be used for an indirect assessment of the metabolic state of the patient. (Ann Thorac Surg 2006;82:2189–95) © 2006 by The Society of Thoracic Surgeons

* O2 delivery and CO2 production during cardiopulmonary bypass as determinants of acute kidney injury: time for a goal-directed perfusion management? - De Somer, 2011
** Anaerobic Metabolism during Cardiopulmonary Bypass: Predictive Value of Carbon Dioxide Derived Parameters - Ranucci, 2006
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Hyperlactatemia during cardiopulmonary bypass: determinants and impact on postoperative outcome

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Abstract

Introduction Hyperlactatemia during cardiopulmonary bypass is relatively frequent and is associated with an increased postoperative morbidity. The aim of this study was to determine which perfusion-related factors may be responsible for hyperlactatemia, with specific respect to hemodilution and oxygen delivery, and to verify the clinical impact of hyperlactatemia during cardiopulmonary bypass in terms of postoperative morbidity and mortality rate.

Methods Five hundred consecutive patients undergoing cardiac surgery with cardiopulmonary bypass were admitted to this prospective observational study. During cardiopulmonary bypass, serial arterial blood gas analyses with blood lactate and glucose determinations were obtained. Hyperlactatemia was defined as a peak arterial blood lactate concentration exceeding 3 mmol/l. Pre- and intraoperative factors were tested for independent association with the peak arterial lactate concentration and hyperlactatemia. The postoperative outcome of patients with or without hyperlactatemia was compared.

Results Factors independently associated with hyperlactatemia were the preoperative serum creatinine value, the presence of active endocarditis, the cardiopulmonary bypass duration, the lowest oxygen delivery during cardiopulmonary bypass, and the peak blood glucose level. Once corrected for other explanatory variables, hyperlactatemia during cardiopulmonary bypass remained significantly associated with an increased morbidity, related mainly to a postoperative low cardiac output syndrome, but not to mortality.

Conclusion Hyperlactatemia during cardiopulmonary bypass appears to be related mainly to a condition of insufficient oxygen delivery (type A hyperlactatemia). During cardiopulmonary bypass, a careful coupling of pump flow and arterial oxygen content therefore seems mandatory to guarantee a sufficient oxygen supply to the peripheral tissues.
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Abstract

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Conclusion Hyperlactatemia appears to be related mainly to a condition of Insufficient oxygen delivery (type A hyperlactatemia). During CPB, a careful coupling of pump flow and arterial oxygen content therefore seems mandatory to guarantee a sufficient oxygen supply to the peripheral tissues.
GDP Monitor™ in a nutshell

- Oxygen venous saturation might not be a precise enough indicator to determine the respiratory metabolism of the patient:
  - Mixed blood coming from different organs of the body could result in a masked hypoperfusion situation (e.g. kidney)

- Oxygen Delivery seems to be a more reliable indicator of good perfusion and predictor of AKI occurrence

- In the ratio with Carbon Dioxide production, DO2 also offers indications on lactate metabolism

- With a target value of DO2 and DO2/VCO2 clinicians have two important additional indicators of patient’s status

* O2 delivery and CO2 production during cardiopulmonary bypass as determinants of acute kidney injury: time for a goal-directed perfusion management? - De Somer, 2011
** Anaerobic Metabolism during Cardiopulmonary Bypass: Predictive Value of Carbon Dioxide Derived Parameters –Ranucci, 2006
<table>
<thead>
<tr>
<th>Measurement Point</th>
<th>9:42 AM</th>
<th>10:38:02 AM</th>
</tr>
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<tbody>
<tr>
<td>CO2exh</td>
<td>28 mmHg</td>
<td></td>
</tr>
<tr>
<td>Ve</td>
<td>2 l/min</td>
<td></td>
</tr>
<tr>
<td>Qb</td>
<td>4.42 l/min</td>
<td></td>
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<tr>
<td>PaO2</td>
<td>339 mmHg</td>
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</tr>
<tr>
<td>SvO2</td>
<td>90 %</td>
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</tr>
<tr>
<td>Hct_gdp</td>
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<tr>
<td>PvO2</td>
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<td></td>
</tr>
<tr>
<td>SaO2</td>
<td>98 %</td>
<td></td>
</tr>
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<td>Body Surface Area (BSA)</td>
<td>1.8 m^2</td>
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<table>
<thead>
<tr>
<th>Result</th>
<th>DO2i</th>
<th>425.72 ml/min/m^2</th>
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<tr>
<td></td>
<td>VO2i</td>
<td>32.71 ml/min/m^2</td>
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<td>VCO2i</td>
<td>35.78 ml/min/m^2</td>
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<tr>
<td></td>
<td>DO2i/VCO2i</td>
<td>11.8990</td>
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<tr>
<td></td>
<td>VCO2i/VO2i</td>
<td>1.0937</td>
</tr>
<tr>
<td></td>
<td>VO2i/DO2i</td>
<td>0.08</td>
</tr>
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</table>
How do we use Goal Directed Perfusion (GDP)

*a new measure of perfusion adequacy*

- **Oxygenation Profile**
  - Oxygen Delivery Index (DO$_2$i)
    - Manage hemoglobin flow to maintain DO$_2$i > 260 ml/min/m$^2$
  - Oxygen Consumption (VO$_2$)
    - Monitor patient response to changing metabolic expectations
      - Temperature, anesthetic changes, vasoactive agent use
  - Oxygen Consumption to Delivery Indexed Ratio (VO$_2$i/ DO$_2$i)
    - Percentage of oxygen delivered being consumed by patient

- **Carbon Dioxide Profile**
  - Carbon Dioxide Production Index (VCO$_2$i)
    - Alert when exceeds > 60 ml/min/m$^2$
    - Must be considered along with the oxygenation profile
  - Oxygen Delivery Carbon Dioxide Ratio Index (DO$_2$i/ VCO$_2$i)
    - Indicator of oxygen to CO$_2$ mismatch (anaerobic metabolism)
Decision Making on CPB: Blood Flow

Conventional CPB

- Lactate
- Cardiac Index
- SvO₂
- Temp
- MAP

GDP

- Hgb
- Oxygen Delivery
- DO₂ᵢ
- Temp?
- DO₂ᵢ/VCO₂ᵢ
- MAP
<table>
<thead>
<tr>
<th>DO2i</th>
<th>DO2i / VCO2i</th>
<th>VCO2i / VO2i</th>
<th>VO2i / DO2i</th>
<th>VO2i</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oxygen Delivery Index</strong>&lt;br&gt;Is CI adequate for current [Hgb]&lt;br&gt;Goal : DO2i &gt; 270&lt;br&gt;Modified by DO2i/VCO2i</td>
<td><strong>Oxygen Delivery to Carbon Dioxide Production Ratio</strong>&lt;br&gt;Is the DO2i adequate for the current metabolic rate&lt;br&gt;Global measure&lt;br&gt;Goal : &gt; 5</td>
<td><strong>Respiratory Quotient</strong>&lt;br&gt;Are you in an anaerobic state? Is the patient producing carbon dioxide at a faster rate than they are consuming oxygen&lt;br&gt;Distribution of blood flow&lt;br&gt;High SVR&lt;br&gt;Low Temp&lt;br&gt;Vascular Occlusion&lt;br&gt;Goal : 0.8-1.2</td>
<td><strong>Oxygen Extraction Ratio</strong>&lt;br&gt;Is the patient consuming more than 30-35% of the delivered oxygen.&lt;br&gt;May be reaching limit of current blood flow to meet metabolic demand.&lt;br&gt;Goal : &lt; 35%</td>
<td><strong>Oxygen Consumption Index</strong>&lt;br&gt;Current rate of oxygen consumption&lt;br&gt;Useful to compare to current oxygenator transfer capacity and anesthetic level.&lt;br&gt;No goal. Relative to VCO2i</td>
</tr>
</tbody>
</table>
University of Colorado Experience

Effect of GDP Learning on Outcome

- Oxygen Delivery (DO2i) not the only important parameter
  - DO2i / VCO2i
- Better circuit management
  - Patient CBV
  - Hemoglobin management
  - Interruption/restrictions to poor venous return
- Stage the learning process
  - Staff integration in to routine management process

nadir DO2i and AKI %

- Start AKI Rate = 25%
- Inspire + Primox, Focus mainly on DO2i. AKI = 8.4%
- DO2i / VCO2i AKI = 5%
What are we learning today?

- Grouped cumulative data shows equal rates of AKI among genders
- When we look at procedure or pathology based data there is a gender difference
• The minimum oxygen delivery DO2i profile required to support patients and maintain the DO2i/VCO2i ratio may be different based on:
  • Gender
  • Pathology
  • Ischemic preconditioning

• The future will develop perfusion specific management plans based on type of procedure and gender to further customize an oxygen delivery profile and reduce end organ dysfunction
Does every transfusion improve tissue respiration?

- Link transfusion decision to hard evidence of patient need and symptoms
- Document efficacy of transfusion
- Do not react on hematocrit nadir alone
  - Low pre-operative hemoglobin
  - Unable to maintain DO2i or DO2i / VCO2i with blood flow alone
  - Sustained blood loss
- Document patient symptoms of need for PRBC transfusion and document appropriate patient response.
In the setting of hemoglobin values exceeding 6 g/dL while on CPB, it is reasonable to transfuse red cells based on the patient’s clinical situation, and this should be considered as the most important component of the decision making process. Indications for transfusion of red blood cells in this setting are multifactorial and should be guided by patient-related factors (i.e., age, severity of illness, cardiac function, or risk for critical end-organ ischemia), the clinical setting (massive or active blood loss), and laboratory or clinical parameters (e.g., hematocrit, SVO2, electrocardiogram, or echocardiographic evidence of myocardial ischemia etc.). (Level of evidence C) IIa

Most CPB Patients

Table 3. American Society of Anesthesiology Guidelines for Transfusion of Packed Red Cells in Adults [682]

- Transfusion for patients on cardiopulmonary bypass with hemoglobin level ≤ 6.0 g/dL is indicated [173, 174, 683, 684].
- Hemoglobin level ≤ 7.0 g/dL in patients older than 65 years and patients with chronic cardiovascular or respiratory diseases justifies transfusion [177, 685].
- For stable patients with hemoglobin level between 7 and 10 g/dL, the benefit of transfusion is unclear [7, 174, 175].
- Transfusion is recommended for patients with acute blood loss more than 1,500 mL or > 30% of blood volume.
- Evidence of rapid blood loss without immediate control warrants blood transfusion.
Red Blood Cell Transfusion: A Clinical Practice Guideline From the AABB.

Recommendation 1: The AABB recommends adhering to a restrictive transfusion strategy (7 to 8 g/dL) in hospitalized, stable patients (Grade: strong recommendation; high-quality evidence).

Recommendation 2: The AABB suggests adhering to a restrictive strategy in hospitalized patients with preexisting cardiovascular disease and considering transfusion for patients with symptoms or a hemoglobin level of 8 g/dL or less (Grade: weak recommendation; moderate-quality evidence).

Recommendation 3: The AABB cannot recommend for or against a liberal or restrictive transfusion threshold for hospitalized, hemodynamically stable patients with the acute coronary syndrome (Grade: uncertain recommendation; very low-quality evidence).

Recommendation 4: The AABB suggests that transfusion decisions be influenced by symptoms as well as hemoglobin concentration (Grade: weak recommendation; low-quality evidence).
Guideline 10.2: Oxygen delivery and consumption calculations should be utilised to evaluate and optimize gas exchange.

Guideline 11.2: Appropriate blood flow rate should be determined by evaluation of:
- Oxygen delivery and consumption
Challenges

- New paradigm for perfusion management
  - Surgeons
  - Anesthesiologists
  - Your perfusion staff

- Patient Outcomes
  - Adjusting traditional work flow to track patients and collect data
  - Data analysis tools

- Equipment
  - Capnography
  - Accuracy of current in-line saturation/hemoglobin monitors
  - Interface

TOGETHER WE IMPROVE LIVES
Summary

- GDP connects patient unique metabolic markers to perfusion management
  - It is easy to use
  - Complete picture (delivery-utilization-end product)

- GDP is an opportunity for perfusion to significantly impact patient outcome (Reducing AKI = big $$$$$$)

- The perfusion community must:
  - Adopt measures of oxygen delivery and carbon dioxide production in descriptions of perfusion adequacy
  - Not rely on general indexed flow as adequate perfusion
  - Learn to use new tools for measuring our performance
  - Take the time to follow our patients and measure the end result of our work