Perfusing the microcirculation.
Did five decades of cardiopulmonary bypass teach us how to achieve optimal perfusion?
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What is optimal flow?
- Reference value
  - CI (2.0-2.4 LPM/m²)
  - 70 mL/kg
- SvO₂ > 65%

What is an optimal circulation?
- Maintain homeostasis
- O₂ delivery
- CO₂ removal
- Preserve organ function

This is particular important at a microcirculatory level
What is optimal microcirculation?

- Pressure
  - Viscosity
  - Resistance
  - CO
- DO2
  - Hematocrit / hemoglobin
  - CO
- Blood markers
  - Cr, Tr, S100β, NAG, lactate, blood gas, etc

Microcirculation

Tissue cylinder


\[ Q_b = 4 \text{mL/min/cm}^3; \quad L_c = 0.1 \text{cm}; \quad C_r = 5 \text{ µm} \]

\[ Q_b = 0.62 \text{ mL/min/cm}^3; \quad L_c = 0.1 \text{ cm}; \quad C_r = 5 \text{ µm} \]
What do we know?

Pressure - tissue perfusion
MAP <50 mmHg vs >50 mmHg

Hemodilution and functional capillary density
Is transfusion the answer?

Fig. 4. Comparison of microvascular oxygen distribution in arteries, veins, and tissue after Level 2 hemorrhage and the two experimental groups (fresh [gray] and stored [black]). Data are presented as mean ± SD. In both experimental groups, the changes were significantly different from Level 2 and from each other (* p < 0.05).
Summary

- FCD is as critical for tissue survival as Oxygen supply
- Increasing plasma viscosity restores FCD up to 75% hemodilution
- Oxygen delivery is more important than fixed pump flow and absolute Hct values
Hemolysis and the microcirculation

- Free plasma hemoglobin
- White blood cell activation
- Cell microparticles
- Platelet activation

<table>
<thead>
<tr>
<th>Free plasma Hb [mg/dL]</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
</tr>
<tr>
<td>Pre</td>
</tr>
</tbody>
</table>

Weight: 80 kg
TBV: 5.3 L
Damaged blood: 7.3 mL

Rother 2005
Hemolysis and NO

Activated plts and the microcirculation

- 3-4 w old pigs
- 10’ normothermic bypass
- 40’ cooling (Trec = 15°C)
- 60’ DHCA
- Rewarming till 37°C
Platelet activation and tissue perfusion

1. Initiation

Adapted from Rinnevaare DM et al. Antithrombotic Thromb Vasc Biol. 2009;29:e14-48, with permission from Lippeinase Williams & Wilkins (www.lww.com).
2. Amplification

“Priming” amounts of thrombin activate platelets and amplify coagulant activity on the platelet surface.

3. Propagation

TF-bearing Cell

Activated Platelet

Large amount of thrombin

Adapted from Reference [1] et al. "Activated Platelet Function." Date: [Year], doi: [DOI], with permission from [Publisher's Name].

Activation of coagulation and organ dysfunction

Thrombin activates platelets

Pre-op (grade 4) Post-op + aprotinin (grade 4)

Date: [Year]
How can we adapt flow to a patient's metabolic needs

By retrospective analysis of organ function, blood markers and morbidity

What we need is a multivariate online analysis of risk during cardiopulmonary bypass  Charles Wildevuur

Which parameters?

**CARDIAC OUTPUT**

- Changes based on metabolic needs
- Usually in the range of 2.8 to 3.0 L/min/m²
- May increase up to 15 L/min/m²
- CO with arterial oxygen content, determines the oxygen delivery (DO₂)
- Guaranty oxygen need (VO₂)
- Pulsatile flow

The role of pump flow is to guarantee an adequate O₂ supply to the organs

**CPB FLOW**

- Adjusted by the perfusionist based on temperature and blood pressure
- 2.0 to 3.0 L/min/m²
- Adequacy of the pump flow controlled with SvO₂ monitoring
- Qp with arterial oxygen content, determines the oxygen delivery (DO₂)
- Should guaranty oxygen need (VO₂)

Anesthesia and VO₂

- 37°C: 4 mL/kg/min
- 37°C + anesthesia: 2-3 mL/kg/min
- 28°C + anesthesia: 1-2 mL/kg/min

O₂ consumption decreases with approx. 7% per 1°C
Formulas

\[
\text{CaO}_2 = (\text{SaO}_2 \times \text{Hb} \times 1.34) + (\text{PaO}_2 \times 0.003)
\]

\[
\text{CvO}_2 = (\text{SvO}_2 \times \text{Hb} \times 1.34) + (\text{PvO}_2 \times 0.003)
\]

\[
\text{DO}_2 = \text{Cl} \times \text{CaO}_2 \times 10
\]

\[
\text{VO}_2 = \text{Cl} \times (\text{CaO}_2 - \text{CvO}_2) \times 10
\]

\[
\text{O}_2ER = \frac{\text{VO}_2}{\text{DO}_2}
\]

\[
\Delta\text{PCO}_2 = \text{PvCO}_2 - \text{PaCO}_2
\]
Hypothesis

- If DO$_2$ is a prime variable
- If most perfusionists work with a fixed CI

Must hemoglobin influence quality of Perfusion

Haematocrit during CPB

Lowest HCT on CPB is associated to:
- Reopening
- Bleeding
- Perioperative MI
- Cardiac arrest
- Stroke
- Coma
- Prolonged ventilation
- IABP
- Renal failure
- MOF
Conclusions

- Evidence based relationship between low Hct and outcome
- Most likely due to a low DO$_2$
- The kidney, perfused with a low O$_2$ content, is more vulnerable than other organs
Conclusions

- Scarce information on $\text{DO}_2$ during CPB
- With a constant pump flow, $\text{DO}_2$ is directly related to Hct
- Most CPB cases are performed at 32 - 34°C
- Pump flow = 2 - 3 L/min/m²
- $\Rightarrow$ Hct = cte $\Rightarrow$ $\text{DO}_2$ varies with 50%

“current guidelines for calculating pump flow during normothermic bypass may be reconciled to better match prebypass systemic oxygen delivery with oxygen delivery during CPB.”
Table 1. Postoperative Mortality, Morbidity, and Hospital Length of Stay of 2,150 Patients (University of Turku) Patients Operated According to Peak Blood Lactate Levels During Cardiopulmonary Bypass

<table>
<thead>
<tr>
<th>Lactate</th>
<th>Death within 30 days</th>
<th>Neurologic</th>
<th>Microvascular complication</th>
<th>Major complications</th>
<th>Pulmonary</th>
<th>Renal</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 4.4 mmol/L</td>
<td>3.4%</td>
<td>13.6%</td>
<td>0.0007</td>
<td>4.5%</td>
<td>12.7%</td>
<td>0.001</td>
</tr>
<tr>
<td>4.4 to 9.9 mmol/L</td>
<td>3.0%</td>
<td>13.2%</td>
<td>0.0010</td>
<td>3.9%</td>
<td>19.0%</td>
<td>0.0001</td>
</tr>
<tr>
<td>&gt; 10 mmol/L</td>
<td>2.5%</td>
<td>25.0%</td>
<td>0.0001</td>
<td>6.4%</td>
<td>7.5%</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Immediate HL Late HL No HL

Length of stay (mean ± SD)

<table>
<thead>
<tr>
<th>Immediate HL</th>
<th>Late HL</th>
<th>No HL</th>
</tr>
</thead>
<tbody>
<tr>
<td>44.0 ± 10.8</td>
<td>54.0 ± 15.4</td>
<td>34.3 ± 8.2</td>
</tr>
</tbody>
</table>

Maillet 2003

AEROBIC METABOLISM

\[ \text{C}_6\text{H}_12\text{O}_6 + 6 \text{O}_2 \rightarrow 6 \text{CO}_2 + 6 \text{H}_2\text{O} + 36 \text{ATP (RQ = 1.0)} \]

(Acetate)

\[ \text{C}_16\text{H}_{32}\text{O}_2 + 23 \text{O}_2 \rightarrow 16 \text{CO}_2 + 16 \text{H}_2\text{O} + 130 \text{ATP (RQ = 0.71)} \]

(Fatty acid)

ANAEROBIC METABOLISM

Glucose + 2 ADP \rightarrow 2 \text{H}^+ \text{lactate} + 2 \text{ATP (Lactic acid)}

\[ \text{H}^+ \text{lactate} + \text{Na}^+\text{HCO}_3^- \rightarrow \text{Na}^+ \text{lactate} + \text{H}_2\text{CO}_3 \]

\[ \text{H}_2\text{CO}_3 \rightarrow \text{H}_2\text{O} + \text{CO}_2 \]
Optimal flow and outcome

Ranucci 2005

Optimal flow and outcome

von Heymann 2006

Optimal flow and outcome

von Heymann 2006

Optimal flow and outcome

von Heymann 2006
**Optimal flow and outcome**

**Conclusions**

- A minimum DO₂ is required during CPB – f(Qb, Hb, T)
- CO₂ derived parameters are indicators of tissue perfusion
- Ratio DO₂i/VCO₂i provides online information on the quality of perfusion

**Conclusions**

- A DO₂ of 270 mL/min/m² is enough at 34°C
- SvO₂ > 75% is no guarantee
- CO₂ derived variables are better than O₂ derived variables in predicting "lactic shock"
Develop an algorithm

\[ \text{DO}_2/\text{VCO}_2 \text{ ratio } < 5 \]

- Augment pump flow
- Increase Hb content
- Decrease T, check anesthesia level

Final conclusions

- Optimal flow is difficult to access due to
  - Pathology (ischemic vs valve)
  - Endothelial dysfunction (diabetes)
  - Perfusion, anesthesia and surgical practice
    (hemodilution, volatile anaesthetics, temperature, etc)
- Today most analysis is done by postoperative retrospective analysis of morbidity and or blood markers
- Continuous online analysis of \( \text{O}_2 \) and \( \text{CO}_2 \) derived parameters allows dynamic control of blood flow based on metabolic needs