Fluid balance and cerebral metabolism during CPB - Do perfusion pressure and flow rate matter?

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Content

- The experimental model
- Effects of interventions:
  - Fluid extravasation rate
  - Cerebral metabolism
- Clinical relevance

Our dear friend – the pig
**Basic structure of all experiments**

- 20-30 min of surgical preparation
- 60 min stabilization
- 60 min CPB at 38 °C
- 90 min CPB at 28 °C

**Fluid supplementation**

- Acetated Ringer’s solution at 5 ml/kg/h
- Oxygenator
- Venous reservoir 300 ml

**Plasma volume**

- Baseline values were determined by the “Carbon-monoxide method” (indicator dilution technique)
- Subsequently new values were calculated every 30 min based on
  - measured loss of blood
  - new hematocrit values
**Fluid shifts**

Net fluid balance:
- Fluid additions – Loss of urin and plasma

Fluid extravasation rate:
- Net fluid balance – ∆ Plasma volume

**Intracerebral microdialysis**

- Micro-infusion pump
- Semi-permeable membrane
- Collecting vial

**Post mortem examinations**

- Total tissue water content
  - samples from the myocardium, lungs, kidneys, liver, pancreas, GI-tract, skin, muscle and brain
- Electron microscopy
  - samples from 4 cortical regions and thalamus
  - determining the fraction of altered mitochondria
Paper 1

Does the level of mean arterial pressures during CPB affect fluid shifts?

Study design

- The low pressure (LP) group:
  - 8 young pigs on CPB
  - Infusion of phentolamine to MAP 40-45 mmHg

- The high pressure (HP) group:
  - 8 young pigs on CPB
  - Infusion of norepinephrine to MAP 60-80 mmHg

Net fluid balance
Conclusion

Fluid extravasation rate was similar in young pigs on CPB whether MAP was reduced to 40–45 mmHg or elevated to 60 – 80 mmHg by use of alpha-adrenergic agents.

Paper 2

Does the level of perfusion flow rate during CPB affect fluid shifts?

Study design

The high flow (HF) group
- 8 young pigs on CPB
- CPB perfusion flow rate of 110 ml/kg/min

The low flow (LF) group
- 8 young pigs on CPB
- CPB perfusion flow rate of 80 ml/kg/min

The choice of CPB perfusion rate

Cardiac index in anaesthetized adults
- 2,4 litre·min⁻¹·m²

Cardiac index in anaesthetized pigs
- 2 times the human reference values

HF-group: 15 % above "normal"
LF-group: 15 % below "normal"
Conclusion

In this animal model elevation of CPB flow rate was associated with a more positive intraoperative fluid balance and a trend to increased fluid extravasation rate.


Why should we care about positive fluid balance?

Fluid overload and outcome

- Morbidity
  - Pulmonary dysfunction
  - Myocardial dysfunction
  - Other organ dysfunction
- Blood transfusions
- Hospital length of stay

Toraman et al. Perfusion 2004; 19: 85-91
Will MAP ≤ 40 mmHg during CPB be inadequate in terms of supplying enough oxygen and energy to the brain?
**Cellular energy production**

1. **Blood-brain barrier**
2. **Glucose** → **Pyruvate** → **Lactate**
3. **NAD** → **NADH** → **O2**
4. **Oxidative phosphorylation**
5. **+36 ATP**

**Cerebral glycerol**

- **Energy failure** → **Activation of phospholipases** → **Membrane phospholipids** → **Free fatty acids + Glycerol**
- **Ca2+ influx** → **Glutamine receptors activation** → **Reactive oxygen species**

**Experimental design**

- **Low pressure (LP) group:**
  - 8 pigs with MAP of 40-45 mmHg by infusion of phentolamine
- **High pressure (HP) group:**
  - 8 pigs with MAP of 60-80 mmHg by infusion of norepinephrine
- **Primary endpoints:**
  - cerebral metabolic and ultra-structural markers
  - mitochondrial integrity (electron microscopy)

**Fraction of altered mitochondria**

<table>
<thead>
<tr>
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<th>HP-group</th>
<th>LP-group</th>
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<tbody>
<tr>
<td>Cortex</td>
<td>8.3%</td>
<td>31.2% ***</td>
</tr>
<tr>
<td>Thalamus</td>
<td>0.6%</td>
<td>6.7% ***</td>
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1) Having 2 of the 3 criteria: clearing, swelling, cristalysis

***: P<0.001 compared with the HP-group

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**Conclusion**

In this model, a mean arterial pressure of 40 – 45 mmHg during cardiopulmonary bypass seems to be associated with cerebral ischemia and neuronal injury.


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**Summary**

- Mean arterial pressure of 40–45 mmHg and 60-80 mmHg were associated with the same level of fluid extravasation rate during CPB.

- Increasing perfusion flow rate lead to more positive fluid balance during CPB.

- Mean arterial pressure of 40 mmHg lead to biochemical and structural cerebral changes indicating lack of oxygen and glucose during CPB.
Thank you for your attention