Cardiopulmonary bypass in small baby

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Histories in CPB

In 1950 Bigelow:
the first application of hypothermia in cardiac surgery

In 1952 Lewis & Taufic:
the first application of hypothermia and inflow occlusion for repair of ASD in humans

In 1953 Gibbon:
establish the feasibility of artificially supported circulation during temporary occlusion of the pulmonary artery
successfully used extracorporeal circulation in a young woman
Histories in CPB

In 1954  Lillehei et al :
  technique of controlled cross-circulation
In 1954  Cooley :
  the application of heat exchangers
In 1960s :
  emphasized the use of bubble oxygenators
In 1970s :
  switching to membrane oxygenators

Next advances
  miniaturization of elements of the CPB circuits
  modulation of the systemic inflammatory response and injury from CPB
CPB for infants vs adults

- Immature organ systems
- Smaller circulation blood volumes
- Higher oxygen consumption rate
- Reactive pulmonary vascular bed
- Presence of intracardiac and extracardiac shunting
- Impaired temperature control
- Poor tolerance to microemboli
Immature organ systems

Liver:
  decreased clotting factors

Lung:
  fragile, potential for pulmonary edema & pulmonary hypertension

Kidney:
  sodium reabsorption & excretion, concentration & diluting mechanism are limited

Immune system:
  complement generation is low
  neonatal mononuclear cells are dysfunctional
Brain in neonates & infants

Low cerebral oxygen consumption rate:
- low cerebral blood flow
- low energy requirements (small number of active synapses)
- high activity of glycolytic enzyme

Cerebral response to hypoxia:
- circulatory adaptation
- rapid induction of electrical silence
- blood glucose tend to rise (by catecholamine release)
- in adult: intracellular acidosis ↑, neural injury ↑
- in neonate: neuroprotective (mechanism is unclear)
Smaller circulating blood volume

Circuit capacity cannot be reduced proportionate to patient size

Significant hemodilution

→ ↓ clotting factors, plasma proteins → dilutional coagulopathy
→ ↓ colloid osmotic pressure → interstitial edema
→ electrolyte imbalance
→ ↑ release of stress hormones
→ activation of complement, WBC, platelets

In neonate: as much as 200~300% of patient's blood volume
In adults: about 25~33% of patient's blood volume
Higher oxygen consumption rate

Higher flow rates per BSA to meet metabolic demands (maintained both cooling & rewarming phase of CPB)

- < 3 kg: 150 ~ 200 ml/kg/min
- 3 ~ 10kg: 125 ~ 175 ml/kg/min
- 10 ~ 15kg: 120 ~ 150 ml/kg/min
- 15 ~ 30kg: 100 ~ 120 ml/kg/min
- 30 ~ 50kg: 75 ~ 100 ml/kg/min
- > 50kg: 50 ~ 75 ml/kg/min

Switch from a relatively anaerobic metabolism in a immature heart to more aerobic metabolism.
Difference between adult and immature myocardium

- Denser structure with a higher water & protein content per gram
- Less compliant, less preload reserve, narrower range of function closer to the peak of the Frank-Starling curve
- Lower rate of maximum tension development
- Reduced inotropic reserve
- Operate under maximal adrenergic stimulation
Difference between adult and immature myocardium

- Abundant endogenous glycogen store
  : more depend on glucose metabolism from glycogenolysis

- Lower sarcoplasmic reticular calcium adenosine triphosphatase activity with less calcium sequestration
  : calcium-channel blockade → depress neonatal myocardial function more than adult heart

- Improved high-energy phosphate homeostasis
  : due to a relative deficiency of 5’ nucleotidase
<table>
<thead>
<tr>
<th></th>
<th>Pediatric</th>
<th>Adult</th>
<th>Potential Impact on Ischemia Tolerance in the Pediatric Heart</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preferred substrate for adenosine triphosphate production</td>
<td>Glucose</td>
<td>Fatty acids</td>
<td>Increase</td>
</tr>
<tr>
<td>Glycogen content</td>
<td>High</td>
<td>Low</td>
<td>Increase</td>
</tr>
<tr>
<td>Insulin sensitivity</td>
<td>Impaired</td>
<td>Normal</td>
<td>?</td>
</tr>
<tr>
<td>Calcium handling (intracellular)</td>
<td>Impaired</td>
<td>Normal</td>
<td>?</td>
</tr>
<tr>
<td>Calcium sensitivity</td>
<td>Increased</td>
<td>Normal</td>
<td>Decrease?</td>
</tr>
<tr>
<td>Antioxidant defense</td>
<td>Low</td>
<td>High</td>
<td>Decrease</td>
</tr>
<tr>
<td>5' nucleotidase</td>
<td>Low</td>
<td>High</td>
<td>Increase</td>
</tr>
<tr>
<td>Catecholamine sensitivity</td>
<td>Low</td>
<td>Normal</td>
<td>?</td>
</tr>
<tr>
<td>Ischemic preconditioning</td>
<td>Absent</td>
<td>Present</td>
<td>?</td>
</tr>
</tbody>
</table>

? = potential effect unknown.
Ischemic tolerance of the immature heart

- Immature heart has a greater tolerance to hypoxia and ischemia than the adult:
  - greater glycogen stores
  - improved anaerobic metabolism
  - better maintenance of ischemic calcium exchange
  - higher levels of adenosine triphosphate
  - increased amino acid substrate utilization
Tolerance of the immature heart to hypoxia or ischemia

- Better tolerable
  - increased glycolytic capacity
  - better preservation intracellular, high-energy phosphates
  - increased ability to utilize amino acid as substrate during hypothermic ischemia

- Lower tolerable
  - greater intracellular accumulation of lactic acid as a result of anaerobic metabolism
  - myocardial ischemic times (>85min) were associated with a significant mortality risk in infants, despite the use of cardioplegia
Ischemic tolerance of the immature heart

- Although laboratory models suggest an improved tolerance to ischemia, most research has been conducted in the normal heart.
- Adverse preoperative conditions such as acidosis, cyanosis, and hypertrophy may seriously compromise myocardial protection in the immature heart.
Special situations affecting myocardial protection in neonates with CHD

- Severe hypoxia
- Chronic cyanosis
- Children with decreased pulmonary blood flow have increased bronchial collateral flow to the left heart that can markedly compromise intraoperative myocardial protection
  - noncoronary collateral flow
    - wash out cardioplegia, rewarms the heart, causes resumption of contractile activity
Principle of myocardial protection

- Reduction of metabolic activity by hypothermia
- Arrest of contractile apparatus and electrical activity of the myocyte by administering cardioplegic solution
- Others
  - buffering the cardioplegic solution,
  - increasing osmolarity,
  - decreasing calcium content,
  - adding substrate to enhance recovery,
  - incorporate leukocyte filters in the CPB circuit
Causes of post-op Low CO

- Residual volume or pressure load – most important
- Ventricular distention
- Retraction / stretch injury to the myocardium
- Coronary artery injury
- Ventriculotomy
- Edema – inappropriate degree of hemodilution of red cells or colloid oncotic pressure
- Reperfusion condition, e.g. pressure, calcium, oxygen, additives such as adenosine and free radical scavengers
- Other perfusion factors, e.g. pH strategy
Strategies of CO$_2$ management:

Alpha stat $vs$ pH stat

**Alpha stat**: maintains pH 7.40 (temperature uncorrected)

- intracellular pH, enzymatic activity and perfusion-pressure autoregulation is preserved
- maintains cellular enzyme function
Strategies of CO₂ management: Alpha stat vs pH stat

**pH stat**: lowers intracellular pH (temperature corrected)
- suppressing cellular function
- → increase cerebral tissue oxygenation
- oxygen dissociation curve is displaced to the Rt.
- → liberating more oxygen to the tissues
- cerebral vasodilation, increase cerebral blood flow
- → decrease local edema,
- improve cerebral cooling
## Table 1: Blood gases, hematocrit, mean arterial pressure, and pump flow

<table>
<thead>
<tr>
<th>Variable Group</th>
<th>37 °C CPB</th>
<th>31 °C CPB</th>
<th>25 °C CPB</th>
<th>19 °C CPB</th>
<th>15 °C CPB</th>
</tr>
</thead>
<tbody>
<tr>
<td>PH Alpha-stat</td>
<td>7.42±0.01</td>
<td>7.35±0.01</td>
<td>7.33±0.02</td>
<td>7.41±0.01</td>
<td>7.45±0.01</td>
</tr>
<tr>
<td>PH-stat</td>
<td>7.39±0.02</td>
<td>7.31±0.02</td>
<td>7.28±0.02</td>
<td>7.26±0.03*</td>
<td>7.13±0.04*</td>
</tr>
<tr>
<td>$P_{O_2}$ (mmHg) Alpha-stat</td>
<td>42.3±1.68</td>
<td>47.2±1.35</td>
<td>45.8±1.49</td>
<td>38.5±1.78</td>
<td>34.0±1.45</td>
</tr>
<tr>
<td>$P_{O_2}$ (mmHg) PH-stat</td>
<td>46.3±2.15</td>
<td>49.9±2.29</td>
<td>46.6±2.28</td>
<td>63.1±5.20*</td>
<td>84.1±8.21*</td>
</tr>
<tr>
<td>Hematocrit (%) Alpha-stat</td>
<td>39.6±24</td>
<td>41.1±26</td>
<td>41.6±25</td>
<td>421±27</td>
<td>428±30</td>
</tr>
<tr>
<td>Hematocrit (%) PH-stat</td>
<td>39.4±22</td>
<td>40.8±24</td>
<td>41.1±25</td>
<td>419±26</td>
<td>422±28</td>
</tr>
<tr>
<td>Mean BP (mmHg) Alpha-stat</td>
<td>63.6±2.14</td>
<td>58.7±2.11</td>
<td>59.1±1.86</td>
<td>61.2±1.78</td>
<td>64.5±1.82</td>
</tr>
<tr>
<td>Mean BP (mmHg) PH-stat</td>
<td>62.6±2.50</td>
<td>60.0±1.39</td>
<td>58.1±0.68</td>
<td>60.6±1.03</td>
<td>60.2±1.17</td>
</tr>
<tr>
<td>Pump flow [ml/(kg-min)] Alpha-stat</td>
<td>68.9±3.07</td>
<td>68.1±2.97</td>
<td>69.3±2.63</td>
<td>68.1±2.79</td>
<td>67.3±2.68</td>
</tr>
<tr>
<td>Pump flow [ml/(kg-min)] PH-stat</td>
<td>70.2±3.45</td>
<td>69.3±3.26</td>
<td>70.8±3.47</td>
<td>68.9±3.12</td>
<td>67.8±2.98</td>
</tr>
</tbody>
</table>

Values are mean±SEM. *P<0.05 vs alpha-stat, CPB=cardiopulmonary bypass, Alpha-stat=alpha-stat group, pH-stat=pH-stat group.
Alpha stat vs pH stat

Fig. 1 Change in brain tissue blood flow determined by laser flowmetry during hypothermia in both the alpha-stat and pH-stat. Levels obtained during initial cardiopulmonary bypass (CPB) at 37 °C were used as baseline. *P<0.05 vs alpha-stat; †P<0.05 vs baseline within the group.

Fig. 2 Changes in brain tissue oxyhemoglobin (a) and deoxyhemoglobin (b), as well as brain tissue oxygen saturation (c) determined by NIR spectroscopy during deep hypothermic CPB in both the alpha-stat and pH-stat. In (a) and (b), the levels obtained during initial CPB at 37 °C were used as baselines. The plus and double plus sign indicate P<0.05 vs levels obtained at 37 °C CPB within the group. *P<0.05 vs pH-stat.
Hypothermia

- Reducing Oxygen requirements
  - flow rates can be reduced
- Reducing the temperature difference between the heart and body
  - enhances the safe duration of cardiac ischemia.
- Adds safety to the perfusion, since more time is available for repairs if perfusion must be interrupted because of accidents in the surgical field or failure of the perfusion apparatus.
RELATIONSHIP BETWEEN BODY TEMPERATURE AND OXYGEN CONSUMPTION
(MEAN VALUE FOR 10 DOGS)

<table>
<thead>
<tr>
<th>Temp</th>
<th>Oxygen consumption</th>
<th>Safe period for total circulatory occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>37°C</td>
<td>100%</td>
<td>4-5 min</td>
</tr>
<tr>
<td>29°C</td>
<td>50%</td>
<td>8-10 min</td>
</tr>
<tr>
<td>22°C</td>
<td>25%</td>
<td>16-20 min</td>
</tr>
<tr>
<td>16°C</td>
<td>12%</td>
<td>32-40 min</td>
</tr>
<tr>
<td>10°C</td>
<td>6%</td>
<td>64-80 min</td>
</tr>
<tr>
<td>6°C</td>
<td>3%</td>
<td>128-160 min</td>
</tr>
</tbody>
</table>

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Neurologic injury

- 10-25% of incidence
- preexisting risk (associated structural anomalies with the brain)
  - esp. in Down syndrome, CATCH 22
- injury induced by CPB
  - microembolic event, esp. air embolism
  - low cerebral flow
The systemic inflammatory response

**Stimuli**
- Blood contact with CPB surfaces
- Abnormal shear stress
- Surgical trauma
- Endotoxemia
- Ischemia

**Effects**
- Leukocyte extravasation
- Lipid peroxidation
- Edema
- Cell death

**Mediators**
- Contact system
- Complement system
- Cytokines
- Oxygen free radicals

**Organ damages**
- Myocardial dysfunction
- Respiratory failure
- Renal, neurologic and liver dysfunction
- Neurologic dysfunction
- Bleeding disorders
Basic consideration of CPB

- Circulation
- Oxygenation & CO\textsubscript{2} removal
- Temperature regulation
- Surgical exposure
- Provide the surgeon with a quiet, bloodless field for the procedure

- Adequate flow
- Adequate drainage
- Perfusion and drainage of all organs
- Unobstructed field
The pediatric CPB circuits

- Cannulation
- Perfusion pump
- Oxygenators
- Prime
- Initiation of cardiopulmonary bypass
- Delivery system of cardioplegic solution
- Weaning from cardiopulmonary bypass
- Ultrafiltration
- Anticoagulation
Current strategies for optimizing use of CPB in neonates & infants

1. Prebypass
2. Bypass
   - CPB circuit
   - hemostasis & anticoagulation
   - deep hypothermic circulatory arrest
   - ultrafiltration
   - anticoagulation
3. Postbypass
One of potential complications as a result of exposure to CPB is a systemic inflammatory response (leukocytes are partly response)

→ capillary leakage, soft tissue edema, end-organ dysfunction

=> 1. using leukocyte filter

2. high dose steroid before CPB
Prebypass

High dose steroid before CPB:

(IV methylprednisolone at 10mg/kg 8hr & 2hr before CPB)

decrease in post-CPB fluid gain

less postoperative edema

improvement in pulmonary compliance

& pulmonary vascular resistance
Bypass

1. **Steroid** is added to circuit prime

2. **Aprotinin**: protease inhibitor
   
   reduce the inflammatory response
   
   (by inhibit kallikrein and contact activation)

   reduce the postoperative bleeding

   (240 mg/m² bolus infusion at beginning and same dose in circuit prime,
   continuous infusion of 56 mg/m²/h throughout the procedure)
# Aprotinin

## Table 2: Perioperative Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Aprotinin group (n=40)</th>
<th>Control group (n=40)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cross-clamp time (min)</td>
<td>53.0±4.6</td>
<td>52.7±6.9</td>
<td>NS</td>
</tr>
<tr>
<td>CPB time (min)</td>
<td>72.2±13.8</td>
<td>75.0±7.3</td>
<td>NS</td>
</tr>
<tr>
<td>Time to extubation (min)</td>
<td>285.0±17.4</td>
<td>285.5±27.9</td>
<td>NS</td>
</tr>
<tr>
<td>No. of grafts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anesthesia time (min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postoperative bleeding</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length of ICU stay (d)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length of hospital stay (d)</td>
<td></td>
<td></td>
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</tbody>
</table>

## Table 3: CK-MB Levels

<table>
<thead>
<tr>
<th>CK-MB (IU/L)</th>
<th>Aprotinin group (n=40)</th>
<th>Control group (n=40)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK0</td>
<td>20.4±5.5</td>
<td>20.3±4.3</td>
<td>NS</td>
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<tr>
<td>CK1</td>
<td>47.8±5.5</td>
<td>52.3±7.2</td>
<td>&lt;0.01</td>
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<tr>
<td>CK2</td>
<td>42.0±12.3</td>
<td>46.9±8.5</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>CK3</td>
<td>41.5±13.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CK4</td>
<td>32.6±10.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CK, creatine kinase; CK0, before surgery; CK2, at postoperative 6th h; CK3, at postoperative 24th h.

## Table 4: Cardiac Troponin I Levels

<table>
<thead>
<tr>
<th>Troponin I (ng/mL)</th>
<th>Aprotinin group (n=40)</th>
<th>Control group (n=40)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TN0</td>
<td>0.08±0.02</td>
<td>0.07±0.02</td>
<td>NS</td>
</tr>
<tr>
<td>TN1</td>
<td>2.49±0.42</td>
<td>2.59±0.28</td>
<td>NS</td>
</tr>
<tr>
<td>TN2</td>
<td>2.87±0.47</td>
<td>3.11±0.46</td>
<td>&lt;0.05</td>
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<tr>
<td>TN3</td>
<td>2.10±0.51</td>
<td>2.39±0.53</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>TN4</td>
<td>1.38±0.39</td>
<td>1.60±0.36</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>TN5</td>
<td>0.68±0.20</td>
<td>0.78±0.26</td>
<td>NS</td>
</tr>
</tbody>
</table>

TN0, before surgery; TN1, immediately after surgery; TN2, at postoperative 6th h; TN3, at postoperative 12th h; TN4, at postoperative 24th h; TN5, on postoperative 5th day.
# Aprotinin

## Table 5  CI, S\textsubscript{v}O\textsubscript{2} and LDH Measurements

<table>
<thead>
<tr>
<th></th>
<th>Aprotinin group (n=40)</th>
<th>Control group (n=40)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>S\textsubscript{v}O\textsubscript{2}0</td>
<td>48.82±3.20</td>
<td>49.77±3.58</td>
<td>NS</td>
</tr>
<tr>
<td>S\textsubscript{v}O\textsubscript{2}1</td>
<td>48.32±2.53</td>
<td>48.02±2.86</td>
<td>NS</td>
</tr>
<tr>
<td>S\textsubscript{v}O\textsubscript{2}2</td>
<td>54.42±4.55</td>
<td>51.75±4.75</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>S\textsubscript{v}O\textsubscript{2}3</td>
<td>56.27±5.63</td>
<td>52.65±6.09</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>S\textsubscript{v}O\textsubscript{2}4</td>
<td>57.92±5.04</td>
<td>55.60±5.04</td>
<td>NS</td>
</tr>
<tr>
<td>CI0</td>
<td>2.70±0.29</td>
<td>2.74±0.30</td>
<td>NS</td>
</tr>
<tr>
<td>CI1</td>
<td>2.64±0.23</td>
<td>2.58±0.26</td>
<td>NS</td>
</tr>
<tr>
<td>CI2</td>
<td>2.73±0.28</td>
<td>2.60±0.26</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>CI3</td>
<td>2.82±0.29</td>
<td>2.69±0.25</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>CI4</td>
<td>2.83±0.30</td>
<td>2.78±0.29</td>
<td>NS</td>
</tr>
<tr>
<td>LDH0</td>
<td>214.05±13.58</td>
<td>211.22±18.95</td>
<td>NS</td>
</tr>
<tr>
<td>LDH1</td>
<td>221.87±18.71</td>
<td>235.12±26.84</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>LDH2</td>
<td>298.97±27.70</td>
<td>313.80±36.99</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

CI, cardiac index (L/min); S\textsubscript{v}O\textsubscript{2}, mixed venous oxygen saturation (%); LDH, lactate dehydrogenase (IU/ml); S\textsubscript{v}O\textsubscript{2}0, S\textsubscript{v}O\textsubscript{2} levels before surgery; S\textsubscript{v}O\textsubscript{2}1, S\textsubscript{v}O\textsubscript{2} levels immediately after surgery; S\textsubscript{v}O\textsubscript{2}2, S\textsubscript{v}O\textsubscript{2} levels at postoperative 6\textsuperscript{th}h; S\textsubscript{v}O\textsubscript{2}3, S\textsubscript{v}O\textsubscript{2} levels at postoperative 12\textsuperscript{th}h; S\textsubscript{v}O\textsubscript{2}4, S\textsubscript{v}O\textsubscript{2} levels at postoperative 24\textsuperscript{th}h; CI0, CI levels before surgery; CI1, CI levels immediately after surgery; CI2, CI levels at postoperative 6\textsuperscript{th}h; CI3, CI levels at postoperative 12\textsuperscript{th}h; CI4, CI levels at postoperative 24\textsuperscript{th}h; LDH0, LDH levels before surgery; LDH1, LDH levels immediately after surgery; LDH2, LDH levels at postoperative 1\textsuperscript{st} day.
Bypass

3. CPB circuitry

- Miniaturization of the CPB
- Using biocompatible-coated circuits (heparin-coated circuit) :
  reduce the direct contact of blood cell with foreign materials
- Using vacuum-assisted venous drainage (VAVD)
Heparin-coated circuit
Bypass

4. Deep hypothermic circulatory arrest and low flow CPB

- continuous hypothermic low flow CPB:
  - more soft tissue edema
  - diminished pulmonary function
  - substantial cerebral edema
  - damage to neural golgi apparatus

There is some acute neurologic metabolic injury after prolonged exposure to continuous hypothermic low flow CPB that is not apparent if brain is exposed to short duration of DHCA
Bypass

4. Deep hypothermic circulatory arrest and low flow CPB

**Modified DHCA:**

1) prebypass with steroid & aprotinin
2) hyperoxygenation before the initiation of DHCA
3) adequate cooling duration (≥20 min)
4) maintenance of higher Hct during the cooling phase
5) using pH stat during cooling phase
6) limiting duration of DHCA
   (by intermittent cerebral perfusion for 1-2 min at 15-20 min interval)
7) use of MUF
8) attention to postoperative cerebral energetics
   - much cerebral injury can occur
Bypass

5. **Ultrafiltration**
   reduce postoperative edema, reduce postoperative blood loss, decrease time to extubation, remove a tissue necrosis factors

- **Conventional ultrafiltration (CUF):**
  during CPB (rewarming phase)
  isovolemic exchange of fluid
  removal of fluid & activated inflammatory mediators
5. Ultrafiltration
   - Modified ultrafiltration (MUF):
     more effective in hemoconcentration & improving ventricular functional recovery after the completion of CPB remove the patient 500 to 700ml of fluid
### Table 4. Studies comparing MUF and conventional CUF in children undergoing cardiac surgery

<table>
<thead>
<tr>
<th>First author</th>
<th>Group</th>
<th>Age* (mo)</th>
<th>n</th>
<th>Ultrafiltrate (mL/h)</th>
<th>Hct (%)</th>
<th>Clinical outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wang</td>
<td>MUF</td>
<td>62</td>
<td>24</td>
<td>—</td>
<td>18</td>
<td>No difference in inotropic use, diuresis, duration of ventilation, ICU stay</td>
</tr>
<tr>
<td></td>
<td>CUF</td>
<td>44</td>
<td>26</td>
<td>—</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Thompson</td>
<td>MUF</td>
<td>13</td>
<td>43</td>
<td>95</td>
<td>28-30</td>
<td>No difference in blood product transfusions, hemodynamics, left ventricle shortening, duration of ventilation, ICU stay</td>
</tr>
<tr>
<td></td>
<td>CUF</td>
<td>9</td>
<td>67</td>
<td>68</td>
<td>28-30</td>
<td></td>
</tr>
<tr>
<td>Maluf</td>
<td>MUF + CUF</td>
<td>9</td>
<td>20</td>
<td>39</td>
<td>25</td>
<td>No difference in inotropic use, transfusions, duration of ventilation, ICU stay, hospital stay</td>
</tr>
<tr>
<td></td>
<td>CUF</td>
<td>15</td>
<td>21</td>
<td>20</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Sever</td>
<td>MUF + CUF</td>
<td>9</td>
<td>13</td>
<td>—</td>
<td>&gt;20</td>
<td>MUF + CUF: better hemodynamics, less bleeding and transfusions, shorter duration of ventilation, shorter ICU stay</td>
</tr>
<tr>
<td></td>
<td>CUF</td>
<td>13</td>
<td>14</td>
<td>—</td>
<td>&gt;20</td>
<td></td>
</tr>
<tr>
<td>Banito</td>
<td>MUF + DCUF</td>
<td>17</td>
<td>50</td>
<td>153</td>
<td>14-18</td>
<td>MUF + DCUF: high-risk patients had less transfusions, better oxygenation, shorter duration of ventilation, shorter ICU stay</td>
</tr>
<tr>
<td></td>
<td>CUF</td>
<td>30</td>
<td>50</td>
<td>29</td>
<td>14-18</td>
<td></td>
</tr>
<tr>
<td>Joumois</td>
<td>MUF + DCUF</td>
<td>13</td>
<td>10</td>
<td>&gt;200</td>
<td>—</td>
<td>MUF + DCUF: less blood loss, better alveolar-arterial oxygen gradient, shorter duration of ventilation</td>
</tr>
<tr>
<td></td>
<td>MUF</td>
<td>6</td>
<td>10</td>
<td>30</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Hiranasso</td>
<td>MUF + DCUF</td>
<td>67</td>
<td>11</td>
<td>188</td>
<td>18-28</td>
<td>MUF + DCUF: lower pulmonary vascular resistance (Fontan procedure)</td>
</tr>
<tr>
<td></td>
<td>CUF</td>
<td>74</td>
<td>11</td>
<td>25</td>
<td>18-28</td>
<td></td>
</tr>
</tbody>
</table>

MUF, modified ultrafiltration; CUF, conventional ultrafiltration; ICU, intensive care unit; DCUF, diatonic ultrafiltration. *Mean or median age of patients. †Target hematocrit during cardiopulmonary bypass. ‡Value not published. §High risk factors were neonatal age, pulmonary hypertension, and CPB duration longer than 120 minutes.
Table 1. Changes in Fibrinogen Concentration, Plasma Protein Concentration, Hematocrit, and Platelet Count During Modified Ultrafiltration After Cardiopulmonary Bypass in 20 Infants

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before CPB</th>
<th>Before MUF</th>
<th>After MUF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrinogen (mg/dL)</td>
<td>220 ± 70</td>
<td>65 ± 29</td>
<td>101 ± 45</td>
</tr>
<tr>
<td>Proteins (g/dL)</td>
<td>7.0 ± 0.7</td>
<td>2.7 ± 0.3</td>
<td>4.0 ± 0.7</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>35 ± 7</td>
<td>10 ± 1</td>
<td>9 ± 1</td>
</tr>
<tr>
<td>Platelets (1,000/µL)</td>
<td>362 ± 91</td>
<td>111 ± 1</td>
<td></td>
</tr>
</tbody>
</table>

* Data are expressed as mean ± standard deviation less than the value before CPB (p < 0.001).  
  a Significantly different from the value before MUF (p < 0.001).

CPB = cardiopulmonary bypass; MUF = modified ultrafiltration.

Table 2. Red Blood Cell Transfusion

<table>
<thead>
<tr>
<th>Transfusion</th>
<th>No UF</th>
<th>MUF</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean RBC volume transfused during CPB (mL)</td>
<td>173 ± 10.41</td>
<td>157 ± 10.52</td>
<td>0.26</td>
</tr>
<tr>
<td>Mean RBC volume transfused after CPB (mL)</td>
<td>147 ± 13.43</td>
<td>109 ± 9.17</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Mean total RBC volume transfused (mL)</td>
<td>318 ± 36.78</td>
<td>267 ± 11.89</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

* Data are presented as mean ± SEM.  
  a Student’s t test.

CPB = cardiopulmonary bypass; MUF = modified ultrafiltration; RBC = red blood cells; UF = ultrafiltration.

Table 4. Hemoglobin and Hematocrit Values During and After the Operation

<table>
<thead>
<tr>
<th>Measurement</th>
<th>No UF</th>
<th>MUF</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean hemoglobin during CPB (mmol/L)</td>
<td>5.2 ± 0.89</td>
<td>4.9 ± 0.86</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Mean hemoglobin after CPB (mmol/L)</td>
<td>5.2 ± 0.89</td>
<td>6.7 ± 0.70</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean hematocrit after CPB/MUF (%)</td>
<td>25 ± 5</td>
<td>33 ± 5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean hemoglobin 4 h after arrival at ICU (mmol/L)</td>
<td>6.8 ± 0.12</td>
<td>6.6 ± 0.99</td>
<td>0.24</td>
</tr>
<tr>
<td>Mean hematocrit 4 h after arrival at ICU (%)</td>
<td>33 ± 6</td>
<td>32 ± 5</td>
<td>0.20</td>
</tr>
</tbody>
</table>

* Data are presented as mean ± SEM.  
  a Student’s t test.  
  In the group with no ultrafiltration, values were measured after discontinuation of CPB; in the group with MUF, values were measured after MUF.

CPB = cardiopulmonary bypass; ICU = intensive care unit; MUF = modified ultrafiltration; UF = ultrafiltration.

Fig 3. (A) Red blood cell volume transfused during cardiopulmonary bypass. (B) Red blood cell volume transfused after cardiopulmonary bypass. (C) Total transfused red blood cell volume. (MUF = modified ultrafiltration; UF = ultrafiltration.)
6. Anticoagulation

The amount of heparin to be delivered based on the patient's weight (Dosage: adult 2 mg/kg, child 3 mg/kg) do not based on the patient's blood volume ←effects of hypothermia, hemodilution, pre-existing heparin therapy children require high doses of heparin to maintain ACT of 350-450 sec

> 200 sec: insertion cannula
> 400 sec: CPB start
> 480 sec: during CPB
> 750 sec: aprotinin is added
6. **Anticoagulation**

after injection of initial heparin: ACT check q 30min

- < 400 sec: 1mg/kg heparin
- 400-480 sec: 0.5mg/kg heparin

after CPB stop

Protamine dosage: 1.0 -1.5 mg for 100 unit (or mg) of heparin

- > 480 sec: protamine 130% of initial doses of heparin
- 130-150 sec: 1/10 of initial doses of protamine
- 120-200 sec: 1/5 of initial doses of protamine
Postbypass

Once separated from CPB, the patient may continue to capillary leakage and accumulate excessive soft tissue fluid for 24 to 36 hr

• Leaving a foramen defect open
• Use of inotropic agents
• Leaving the sternum open
• Placement of peritoneal dialysis catheters
• Short period of ECMO
Thank you for your attention!