Cerebral Blood Flow Velocity and Arteriovenous Oxygen Content Difference during the Rewarming Period of Cardiopulmonary Bypass

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Abstract
To examine the effect of changes in temperature on the cerebral circulation during the rewarming period of cardiopulmonary bypass (CPB), we measured blood flow velocity in the middle cerebral artery by transcranial Doppler ultrasound (TCD) and the arteriovenous oxygen content difference (a-vDO2) by intermittent sampling from the jugular venous bulb during cardiac surgery in 11 patients (mean age ± SD: 55.4 ± 10.0 years). The mean blood flow velocity was 43.5 ± 16.9 cm/s in the pre-rewarming period and 50.9 ± 19.5 cm/s during rewarming, thereby indicating a significant increase during rewarming (P < 0.05). In addition, a-vDO2 was 1.74 ± 1.00 vol.% in the pre-rewarming period and 3.09 ± 1.24 vol.% during rewarming, showing a significant increase during rewarming (P < 0.01). This widening of a-vDO2 suggests that oxygen demand was excessive relative to oxygen supply despite the increase in cerebral blood flow. We concluded that rewarming alters the cerebral circulation rapidly and may increase the risk of unbalanced cerebral oxygenation. Rapid evaluation of the cerebral circulation may be necessary during specific periods of CPB such as rewarming.

Key words: cardiac, cerebral blood flow, Doppler ultrasound, hypothermia

Introduction
Neurological complication remains one of the most serious adverse events following open heart surgery. Although the cerebral circulation during cardiopulmonary bypass (CPB) has been studied extensively in the past decade, the relationship of alterations in cerebral blood flow (CBF) and the cerebral metabolic rate for oxygen (CMRO2) during CPB to the occurrence of neurological injury is still incompletely understood. During specific periods of CPB such as rewarming, CBF and CMRO2 change rapidly, making continuous and rapid evaluation of the cerebral circulation necessary.

Transcranial Doppler ultrasound (TCD) is a noninvasive method for continuous and rapid evaluation of cerebral circulation. In this study, we measured the blood flow velocity in the middle cerebral artery (MCA) by TCD and determined the arteriovenous oxygen content difference (a-vDO2) by intermittent sampling from the jugular venous bulb to evaluate cerebral circulation during nonpulsatile mild hypothermic CPB.

Materials and Methods
After obtaining informed consent, 11 patients undergoing elective cardiac surgery were investigated. There were 9 men and 2 women ranging in age from 30 to 64 years (mean ± SD: 55.4 ± 10.0 years). Eight patients underwent coronary bypass, two underwent mitral valve replacement, and one underwent closure of ventricular septal defect. None of the patients had any history or clinical evidence of cerebrovascular disease.

All patients were premedicated with scopolamine, famotidine, and morphine. Anesthesia was induced and maintained...
with nitrous oxide, fentanyl, and pancuronium bromide. During surgery except for CPB, nitroglycerin (0.1–0.5 µg/kg/min) and prostaglandin E1 (0.02–0.1 µg/kg/min) were infused continuously. When the mean arterial pressure fell below 60 mmHg, either dopamine or norepinephrine was infused. CPB was performed in the nonpulsatile mode with a roller pump and a membrane oxygenator. The regimen for extracorporeal perfusion was standardized as follows: generalized mild hypothermia (26 to 27°C), an average flow rate of 2.0–2.5 L/min/m², and a mean blood pressure (MBP) of 50–60 mmHg. Carbon dioxide was not added during CPB according to the alpha-stat strategy for acid-base regulation during hypothermia. The rectal temperature was monitored intraoperatively. The arterial blood pressure was recorded through a radial artery catheter and a Swan-Ganz catheter was inserted for monitoring cardiac function. In addition, a venous catheter was inserted into the left internal jugular vein and was advanced to the level of the external auditory canal so that its tip was in the bulb. Cerebral venous blood was sampled from this catheter.

The blood flow velocity in the left MCA was recorded continuously throughout surgery using a transcranial Doppler device (EME, TC2-64, range-gated, emission frequency = 2 MHz). The method employed has already been described in detail2-5). The Doppler probe was usually positioned on the relatively thin temporal bone above the zygomatic arch just anterior to the ear and fixed with a bandage. With this location, blood flow in the MCA was directed towards the probe and the signal was visualized from gate positions 40 to 50 mm. (Fig. 1)

The following five periods examined: (1) pre-CPB, (2) hypothermic CPB, (3) pre-rewarming, (4) during rewarming, and (5) post-CPB. The following variables were recorded: mean blood flow velocity in the left MCA (MV), MBP, hematocrit, and arterial blood gases and internal jugular venous blood gases (ABL30, Radiometer, Denmark). The hemoglobin, oxygen content, and arteriovenous oxygen content difference (a-vDO₂) were calculated using the following formulae.

Hemoglobin (mmol/L) = (Hematocrit (%) × 1/100 - 0.0083) / 0.04856)

Oxygen content (vol.%) = 1.39 × Hemoglobin (mg/dl) × Oxygen saturation (%) × 1/100 + 0.003 × Oxygen partial pressure (mmHg)

a-vDO₂ (vol.%) = Arterial oxygen content - Jugular venous oxygen content

Data analysis was performed with a computerized statistical analysis package (Stat Flex, View Flex Inc., Tokyo). The normality of the distribution of data in each state was analyzed. If normality was not recognized during any two states, analysis was done by the Wilcoxon test. If a normal distribution was recognized for two states, analysis was done by Student’s paired t-test. All data are expressed as the mean ± SD. A P<0.05 was considered to be statistically significant.

Results

Anesthesia and surgery was uneventful in all patients.

**Table 1** Data obtained during cardiopulmonary bypass (CPB)

<table>
<thead>
<tr>
<th></th>
<th>pre-CPB</th>
<th>Hypothermic CPB</th>
<th>pre-rewarming</th>
<th>During rewarming</th>
<th>post-CPB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean blood flow velocity (cm/sec)</td>
<td>44.8±9.1</td>
<td>42.6±12.4</td>
<td>43.5±16.9</td>
<td>50.9±19.5*</td>
<td>62.4±22.6</td>
</tr>
<tr>
<td>a-v DO₂ (vol.%)</td>
<td>4.67±1.85</td>
<td>1.65±0.70**</td>
<td>1.74±1.00</td>
<td>3.09±1.24**</td>
<td>2.98±0.86</td>
</tr>
<tr>
<td>Mean blood pressure (mmHg)</td>
<td>77.5±11.2</td>
<td>51.9±5.71</td>
<td>54.5±5.5</td>
<td>53.6±10.0</td>
<td>61.5±9.6</td>
</tr>
<tr>
<td>Rectal temperature (°C)</td>
<td>34.6±0.9</td>
<td>26.5±1.0**</td>
<td>26.9±0.8</td>
<td>30.3±0.4**</td>
<td>35.6±0.9</td>
</tr>
<tr>
<td>PaCO₂a (mmHg)</td>
<td>39.3±3.0</td>
<td>38.7±6.2</td>
<td>38.2±6.9</td>
<td>38.6±3.9</td>
<td>40.4±4.2</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>32.8±2.6</td>
<td>20.0±2.9**</td>
<td>19.3±2.9</td>
<td>20.7±3.7</td>
<td>23.1±4.5</td>
</tr>
</tbody>
</table>

a-vDO₂: arteriovenous oxygen content difference.
PaCO₂a: non-temperature corrected PaCO₂ (measured at 37°C)

*P<0.05, **P<0.01 versus pre-CPB.

Anesthesia and surgery was uneventful in all patients.
There were no significant differences of PaCO2 and pump flow during CPB. The data obtained during CPB are presented in Table 1. At the introduction of hypothermic CPB, there was a significant decrease in a-vD02 (Fig. 2, P<0.01). There was no significant difference in MV between pre-CPB and hypothermic CPB, but MV showed a tendency to decrease compared with the pre-CPB value (Fig. 3). Hematocrit and MBP were decreased significantly at this point of CPB (Table 1, P<0.05).

MV increased significantly with increasing temperature during rewarming (Fig. 3, P<0.05). MV was 43.5±16.9 cm/sec in the pre-rewarming period and rose to 50.9±19.5 cm/sec during rewarming. There were no significant changes in hematocrit, MBP, and PaCO2 during rewarming (Table 1). In contrast, a-vD02 was 1.74±1.00 vol.% in the pre-rewarming period and 3.09±1.24 vol.% during rewarming, showing a significant increase (Fig. 2, P<0.01).

**Discussion**

In this study, TCD was utilized to assess cerebral blood flow during mild hypothermic CPB. TCD does not measure cerebral blood flow quantitatively, but the dynamics of blood flow are reliably reflected by changes in flow velocity assuming that the cross-sectional area of the MCA is unchanged. This is a reasonable assumption, since the MCA diameter does not vary in response to changes in temperature, PaCO2, MAP, or pump flow rate. Bishop et al. found a strong correlation between changes in the MCA flow velocity and xenon washout measurements of cerebral blood flow. In addition, Lindegaard et al. observed a very close correlation between changes in MCA flow velocity and electromagnetically measured flow in the ipsilateral internal carotid artery. Furthermore, Van der Linden et al. compared MCA blood flow velocity (measured by TCD) and venous blood flow in the ipsilateral jugular vein (measured by thermodilution method) during nonpulsatile hypothermic CPB, and found a reasonably good correlation between the two measurements. Thus TCD appears to be able to estimate cerebral perfusion during mild hypothermic CPB.

We found that there was significant decrease of a-vD02 during hypothermic CPB as compared with pre-CPB and that MV tended to decrease. Murkin et al. measured CBF by the xenon clearance method during mild hypothermic CPB with alpha-stat blood gas management, and found a significant decrease of CBF and CMRO2 compared with pre-CPB. The temperature is an important determinant of cerebral circulation during CPB. Hypothermia reduced CBF linearly and CMRO2 exponentially, so the CBF/CMRO2 ratio increases with decreasing temperature. This results in luxury perfusion of the brain. The decrease of a-vD02 in this study suggested that cerebral blood flow was relatively excess of the metabolic demand during CPB.

During the rewarming period, CMRO2 increases with increasing temperature. The flow/metabolic coupling of CBF is preserved during mild hypothermic CPB with alphastat blood gas management, and CBF increase with increasing CMRO2 during rewarming. In this study, the mean blood flow velocity was increased significantly with increasing temperature during rewarming and a-vD02 also increased significantly during rewarming. The value of a-vD02 reflects the balance between cerebral oxygen supply and demand, so this widening of a-vD02 might suggest that oxygen demand was relatively in excess of supply despite the increase in CBF and...
that oxygen extraction was consequently increased. Nakajima et al.\textsuperscript{11} monitored jugular venous oxyhemoglobin saturation (S\textsubscript{jO2}) using an oximetry catheter and observed a significant reduction during the rewarming period. As a result, they suggested that oxygen demand was increased more than oxygen supply during rewarming. Croughwell et al.\textsuperscript{12} have also reported the jugular venous desaturation (S\textsubscript{jO2}<50%) as detected by intermittent jugular bulb sampling during rewarming. An imbalance of cerebral oxygenation during rewarming from CPB may increase the risk of brain injury. Although jugular venous desaturation (S\textsubscript{jO2}<50%) was recently identified in 25% of patients during normothermia following hypothermic CPB, it was not associated with impaired postoperative performance of neuropsychologic tests\textsuperscript{12,13}. However, in patients with altered autoregulation (chronic hypertension, insulin-dependent diabetes, etc.) or severe cerebrovascular disease the mechanisms compensating for decreased cerebral oxygen delivery may be impaired and the risk of brain damage might increase. Therefore, rapid evaluation of the cerebral circulation using TCD, a-vDO\textsubscript{2} or S\textsubscript{jO2} should be necessary during specific periods of CPB such as rewarming.

Many physiologic variables influence CBF during CPB, including temperature, PaCO\textsubscript{2}, blood viscosity, intracranial pressure, and central venous pressure. Accordingly, continuous monitoring of CBF might be necessary to prevent neurological complications. TCD offers a noninvasive, continuous, and rapid evaluation of cerebral circulation and has also been utilized to detect microemboli\textsuperscript{14}. Accordingly, TCD is useful for monitoring CBF during cardiovascular surgery.

**References**


