Analysis of collateral blood flow to the lower body during selective cerebral perfusion: is three-vessel perfusion better than two-vessel perfusion?

Yuji Miyamoto*, Shinya Fukui, Tetsuya Kajiyama, Masatake Mitsuno, Mitsuihiro Yamamura, Hiroe Tanaka, Masaaki Ryomoto, Hiroyuki Nishi

Department of Cardiovascular Surgery, Hyogo College of Medicine, Nishinomiya, Japan

Received 28 August 2008; received in revised form 25 November 2008; accepted 2 December 2008; Available online 21 January 2009

Abstract

Objective: During selective cerebral perfusion (SCP), only the upper body is perfused. However, blood actually returns into the descending aorta through collaterals during SCP. This collateral blood flow (CBF) is thought to be important to protect the visceral organs and spinal cord from ischemia. The left subclavian artery is postulated to be important as a collateral source to the lower body. Therefore, we measured CBF and examined whether a perfusion technique (three- or two-vessel perfusion) affects CBF to the lower body during SCP. Methods: CBF was measured in 49 patients who underwent aortic arch surgery with SCP between August 2006 and July 2008. CBF, the amount of blood returning into the descending aorta during SCP, was measured under conditions of constant flow during SCP, with three-vessel cannulation that included the left subclavian artery, or with two-vessel cannulation that excluded the left subclavian artery. To prove visceral perfusion during SCP, hepatic (n = 22) and stomach (n = 5) tissue blood flows were measured using a laser-Doppler flowmeter. Results: The mean perfusion flow rate during SCP was 804 ± 91 ml/min. The mean CBF under three-vessel perfusion (53 ± 34 ml/min, 6.5 ± 3.8% of SCP) was significantly (p < 0.0001) higher compared with that under two-vessel perfusion (43 ± 29 ml/min, 5.3 ± 3.1% of SCP). There was substantial perfusion in the visceral organs during SCP as determined by laser-Doppler flowmeter. Conclusion: Visceral organs were perfused to some extent through collaterals and protected from ischemia during SCP. Left subclavian arterial perfusion enabled significant CBF to the lower body. Considering this CBF, three-vessel perfusion appears to be better than two-vessel perfusion during SCP; however, the choice of perfusion technique may not be so important under conditions of hypothermia because the difference in CBF between the two methods was small.

Keywords: Selective cerebral perfusion; Collateral blood flow; Three-vessel perfusion; Visceral perfusion; Tissue blood flow

1. Introduction

Selective cerebral perfusion (SCP) associated with deep hypothermia is a major brain protection method in aortic arch surgery and has gained popularity [1,2]. During SCP, usually only the upper body is perfused while the lower body is not. However, it is well known that blood returns into the descending aorta through collaterals during SCP. This collateral blood flow (CBF) is postulated to be important to protect visceral organs and the spinal cord from ischemia while there is no active perfusion to the lower body. However, to date, there has been no report describing the degree of CBF or its clinical consequences during SCP. Perfusion to the left subclavian artery is believed to be important to protect the brain when the circle of Willis is imperfect [3—5], and the left subclavian artery is generally postulated to represent a collateral source to the lower body; however, it is unknown whether perfusion of the left subclavian artery is important as a collateral source to the lower body. Thus, we measured the amount of CBF and examined whether the perfusion technique (three-vessel perfusion including the left subclavian artery or two-vessel perfusion excluding it) affects CBF to the lower body during SCP.
two emergent ruptured cases, 18 with acute Stanford type A dissection, five with chronic dissecting aneurysm, and three with annulo-aortic ectasia. Procedures included total arch replacement (three branches) in 22 patients, partial arch replacement (two branches) in 10, hemiarch replacement (no branch) in eight and graft replacement of ascending aorta in nine. Concomitant surgery included Bentall operation in four, CABG in three and AVR in one (Table 1). All study patients (or the patients’ families in the emergent cases) signed an informed consent form before study entry, and the study was approved by the ethics committee of the University Hospital of Hyogo College of Medicine.

2.2. Surgical technique

All operations were performed through median sternotomy with the aid of cardiopulmonary bypass (CPB). An arterial cannula was inserted into the ascending aorta and/or femoral artery. A two-staged venous cannula was used in most cases. Myocardial protection was provided with antegrade and retrograde intermittent cold blood cardioplegia. The whole body was cooled to bladder temperatures of 20 °C to protect the lower body from ischemia. Short deep hypothermic circulatory arrest was induced; then SCP was started with a 14 F cannula to the brachiocephalic artery and 10 F cannulae to the left carotid artery and left subclavian artery. Total flow of SCP was controlled at around 500 ml/m²/min (approximately 13 ml/kg/min) by a single pump to maintain radial arterial pressure of 60 mmHg. In the standard total arch replacement, a quadrifurcated collagen-impregnated woven Dacron graft was used. A vent tube to the left ventricle through the right upper pulmonary vein was always inserted. In the patients with true aneurysm, an occlusion balloon into the descending aorta was applied and thoraacoabdominal perfusion was resumed to protect visceral organs when the circulatory arrest time of the lower body extended over 40 min. This reperfusion (2 l/min regardless of the body size) was performed for 15 min with the blood at 20 °C. In the patients with dissection, this method was not performed because the occlusion balloon was ineffective.

2.3. Measurement of CBF

The amount of blood returning into the descending aorta during SCP was measured as CBF under the condition of constant flow with three-vessel perfusion that included the left subclavian artery, or with two-vessel perfusion that excluded the left subclavian artery. A suction tube was inserted into the descending aorta. The collected blood was accumulated in the cardiotomy reservoir and its volume was measured. These measurements were started 5 min after commencing SCP. The duration of measurement was 1 min. Measurements were performed twice for each type of perfusion. Three-vessel perfusion was routinely maintained after these measurements.

2.4. Measurement of tissue blood flow (liver and stomach)

To prove visceral perfusion during SCP, tissue blood flows (ml/min/100 g) of liver (n = 22) and stomach (n = 5) were measured using a laser-Doppler flowmeter (Omega Flow Company, Tokyo, Japan) [6]. A small incision was made in the upper peritoneum and a probe was applied directly to the liver and stomach. These measurements were performed before cardiopulmonary bypass, after starting CPB (cooling), during systemic circulatory arrest, during SCP (approximately 30 min after starting SCP), after re-starting CPB (re-warming) and after the termination of CPB.

2.5. Statistical analysis

Statistical analysis was performed using StatView, version 5.0 (Abacus Concepts, Berkeley, CA, USA). Quantitative variables approximating a normal distribution are presented as mean ± SD. Continuous variables were analyzed using Wilcoxon’s signed rank test and 95% confidence intervals (CI). A p value <0.05 was considered to be significant.

3. Results

Six patients were excluded from the CBF study. In five patients (three with acute dissection and two with chronic dissection) in whom the dissection extended to neck vessels and the false-lumen was patent, blood from SCP partially detours through re-entry of the neck vessels before flowing into the brain. A similar phenomenon occurred in one patient with an aberrant right subclavian artery. In these six patients, a large amount of blood returned into the descending aorta (approximately 30–50% of the total amount of SCP). This blood is thought of not as a collateral flow, but as a shunt flow through the re-entry in the neck. Therefore, data from 43 patients were analyzed for the CBF study.

3.1. Operation

The mean operative time was 7.5 ± 1.1 h (range, 5.2–9.6 h). The mean CPB time was 228 ± 46 min (range, 167–370 min). The mean cross-clamp time was 131 ± 37 min (range, 72–260 min). The mean SCP time was 108 ± 55 min (range, 19–191 min). The mean time for open distal anastomosis was 58 ± 17 min (range, 25–99 min). There were two in-hospital deaths in emergent cases. Mortality rate was 4.1% (2/49) in total. There were two neurological

Table 1

<table>
<thead>
<tr>
<th>Procedure</th>
<th>No. (total n = 49)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total arch replacement</td>
<td>22</td>
</tr>
<tr>
<td>Partial arch replacement</td>
<td>10</td>
</tr>
<tr>
<td>Hemiarch replacement</td>
<td>8</td>
</tr>
<tr>
<td>Ascending replacement</td>
<td>9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atherosclerotic aneurysm</td>
<td>23</td>
</tr>
<tr>
<td>Acute type A dissection</td>
<td>18</td>
</tr>
<tr>
<td>Chronic dissection</td>
<td>5</td>
</tr>
<tr>
<td>Annulo-aortic ectasia</td>
<td>3</td>
</tr>
</tbody>
</table>

The amount of blood returning into the descending aorta during SCP was measured as CBF under the condition of constant flow with three-vessel perfusion that included the left subclavian artery, or with two-vessel perfusion that excluded the left subclavian artery. A suction tube was inserted into the descending aorta. The collected blood was accumulated in the cardiotomy reservoir and its volume was measured. These measurements were started 5 min after commencing SCP. The duration of measurement was 1 min. Measurements were performed twice for each type of perfusion. Three-vessel perfusion was routinely maintained after these measurements.

2.4. Measurement of tissue blood flow (liver and stomach)

To prove visceral perfusion during SCP, tissue blood flows (ml/min/100 g) of liver (n = 22) and stomach (n = 5) were measured using a laser-Doppler flowmeter (Omega Flow Company, Tokyo, Japan) [6]. A small incision was made in the upper peritoneum and a probe was applied directly to the liver and stomach. These measurements were performed before cardiopulmonary bypass, after starting CPB (cooling), during systemic circulatory arrest, during SCP (approximately 30 min after starting SCP), after re-starting CPB (re-warming) and after the termination of CPB.

2.5. Statistical analysis

Statistical analysis was performed using StatView, version 5.0 (Abacus Concepts, Berkeley, CA, USA). Quantitative variables approximating a normal distribution are presented as mean ± SD. Continuous variables were analyzed using Wilcoxon’s signed rank test and 95% confidence intervals (CI). A p value <0.05 was considered to be significant.

3. Results

Six patients were excluded from the CBF study. In five patients (three with acute dissection and two with chronic dissection) in whom the dissection extended to neck vessels and the false-lumen was patent, blood from SCP partially detours through re-entry of the neck vessels before flowing into the brain. A similar phenomenon occurred in one patient with an aberrant right subclavian artery. In these six patients, a large amount of blood returned into the descending aorta (approximately 30–50% of the total amount of SCP). This blood is thought of not as a collateral flow, but as a shunt flow through the re-entry in the neck. Therefore, data from 43 patients were analyzed for the CBF study.

3.1. Operation

The mean operative time was 7.5 ± 1.1 h (range, 5.2–9.6 h). The mean CPB time was 228 ± 46 min (range, 167–370 min). The mean cross-clamp time was 131 ± 37 min (range, 72–260 min). The mean SCP time was 108 ± 55 min (range, 19–191 min). The mean time for open distal anastomosis was 58 ± 17 min (range, 25–99 min). There were two in-hospital deaths in emergent cases. Mortality rate was 4.1% (2/49) in total. There were two neurological
complications (one patient with stroke and one with transient dysfunction).

3.2. Collateral blood flow

The mean SCP flow was 804 ± 91 ml/min (range, 650–1050 ml/min). The distribution of CBF (%) under three-vessel perfusion is shown in Fig. 1. CBF (%) ranged from 2% to 18%. The majority of patients had a CBF (%) of less than 10%. Distribution had no co-relation with age or type of disease. Mean CBF under three-vessel perfusion (53 ± 34 ml/min, 6.5 ± 3.8% of SCP) was significantly (mean difference 10 ml/min [95% CI 5.1—14.1], \(p < 0.0001\)) higher compared with that under two-vessel perfusion (43 ± 29 ml/min, 5.3 ± 3.1% of SCP), as shown in Fig. 2.

3.3. Tissue blood flows (liver and stomach)

The changes in tissue blood flows in liver and stomach are shown in Fig. 3. Tissue blood flows in both liver and stomach showed similar changes. Before starting CPB, mean tissue blood flows were 15 ml/min/100 g in the liver and 17 ml/min/100 g in the stomach; these levels decreased slightly after starting CPB. During deep hypothermic circulatory arrest, the flows became almost zero. During SCP, the flows were 2.3 ± 1.2 ml/min/100 g in the liver and 4.9 ± 4.0 ml/min/100 g in the stomach. During re-warming and after CPB, the flows resumed to the pre-CPB levels.

4. Discussion

In aortic arch surgery, brain protection is a major issue. The safe time limit for deep hypothermic circulatory arrest is generally believed to be 30 min, but there is almost no time limit with the SCP technique in respect of brain protection under hypothermia. Little attention is paid to the lower body (visceral organs and spinal cord) during SCP; usually only the upper body is perfused during SCP, while the lower body is not, so there should be a time limit on SCP owing to the risk of ischemia to the lower body under normothermia. The safe time limit to prevent lower body ischemia at 20–25 °C is empirically recognized as 50–60 min [6]. Lately, systemic temperature during SCP has been elevated from 18–20 °C to 25–28 °C in some institutes [6,7]. In this situation, end-organ protection of the lower body may become a problem. If there was no perfusion at all in the lower body during SCP, we believe that the safe time limit should be less than 50–60 min, even under hypothermia. However, it is well known that blood actually returns into the descending aorta through collaterals during SCP. This collateral flow is thought to be important to protect visceral organs and the spinal cord from ischemia, when there is no active perfusion to the lower body.

![Fig. 2. Comparison of CBF between three- and two-vessel perfusions under the condition of constant SCP flow. CPB: cardiopulmonary bypass. CA: circulatory arrest.](image)

![Fig. 3. Changes in tissue blood flows in liver and stomach.](image)

![Fig. 4. Presumable mechanism of CBF (collateral blood flow).](image)
body. Because there has been no report describing the degree of CBF and its clinical consequences during SCP, we focused on CBF.

In our study, CBF ranged from 2% to 18% of SCP with a mean of 6.5%. Does this CBF really perfuse the lower body? As shown in Fig. 4, CBF may flow solely into the descending aorta through arterioles. CBF flowing into the visceral organs and spinal cord through arterioles and capillaries is real perfusion of end-organs; this CBF returns into the inferior vena cava, but its amount cannot be measured directly. We measured only the amount of CBF in the descending aorta. Therefore, to prove that real perfusion through CBF exists in the visceral organs, we measured the tissue blood flows in the liver and stomach. This tissue blood flow is a measure of the surface flow of an organ [8]. The absolute value of this measurement may not have any correlation with the total blood flow of the organ; however, it is enough to know whether perfusion exists in the organ. In our study, it was shown that visceral organs were perfused to some extent through collaterals during SCP.

The left subclavian artery is generally postulated to be a collateral source to the lower body. Perfusion via the left subclavian artery is believed to be important to protect the brain when the circle of Willis is imperfect [3–5]. In a study of healthy volunteers, it was reported that an entirely complete circle of Willis existed in only 42%, and complete posterior circulation was seen in 52% [9]. Moreover, neurological complications after occlusion of the left subclavian artery in thoracic endoluminal repair were reported [10,11]. Thus, the left subclavian artery must be important for brain circulation. However, it is unknown whether perfusion of the left subclavian artery is important as a collateral source to the lower body. Therefore, we examined whether a perfusion technique (three-vessel perfusion or two-vessel perfusion) affects CBF to the lower body during SCP. In this study, however, all patients underwent three-vessel perfusion for most of the duration of SCP and underwent two-vessel perfusion for only a very short time (two min in total). Therefore, clinical results of both perfusion techniques cannot be compared.

Because CBF under three-vessel perfusion was significantly higher compared with that under two-vessel perfusion, at a constant total flow of SCP, we think that perfusion to the left subclavian artery enables significant collateral flow to the lower body. But the difference between the two methods was 10 ml/min; 53 ml/min in three-vessel, and 43 ml/min in two-vessel. This difference was relatively small, so the clinical meaning of this value is as yet unknown. In addition, this study was performed under deep hypothermia, therefore, vasoconstriction of collaterals might have occurred; vasoconstriction of collaterals would be less under mild or normal temperatures.

5. Conclusion

There was a meaningful collateral blood flow to the lower body during SCP. Hence, we think that visceral organs are perfused to some extent through collaterals during SCP. Theoretically, three-vessel perfusion appears better than two-vessel perfusion during SCP in terms of this collateral blood flow; however, the perfusion technique may not be so important under conditions of hypothermia, because the difference in CBF between the two methods was small.

References


Appendix A. Conference discussion

Dr M. Czerny (Vienna, Austria): The authors measured collateral blood flow during selective cerebral perfusion and examined whether a perfusion technique, three- or two-vessel perfusion, affects collateral blood flow to the lower body during this period. They measured it quantitatively as well as by tissue Doppler flow.

In my impression, this study addresses a timely topic and is of clinical interest as well as a well-written manuscript was provided. I would like to ask you some short questions potentially ameliorating the understanding of your study.

The core temperature in this series was 20 degrees centigrade, which is quite low to our understanding. Why did you choose such a low core temperature in these patients in the setting of selective cerebral perfusion?

Dr Miyamoto: Do you mean why temperature was 20 degrees Celsius?

Dr Czerny: Yes. Actually, your core temperature was 20 degrees centigrade.

Dr Miyamoto: Yes.

Dr Czerny: Despite you had selective antegrade cerebral perfusion. Why did you choose such a low core temperature?

Dr Miyamoto: About the brain protection, SCP is so good that the very low temperature is not needed.

But the lower body ischemia may become a problem at moderate hypothermia. I worry about the lower body ischemia. If there is no perfusion at all in the lower body, the safe time limit to prevent lower body ischemia should be very short even under hypothermia. So this is why we lowered the temperature deeply.
**Dr Czerny:** Furthermore, do you think the effect of improved collateral blood flow is being reached by additional selective antegrade perfusion of the left subclavian artery, or could the same effect be reached by simple clamping of the vessel thereby preventing retrograde flow via the left vertebral artery into the distal arch? Do you think that just clamping the left subclavian artery has the same effect?

**Dr Miyamoto:** No. A perfusion cannula was always inserted into left subclavian artery. So there was no retrograde flow via left subclavian artery into the aorta. First, the three-vessel perfusion was started, then left subclavian artery was just clamped, but the total flow was kept constant under two-vessel perfusion.

**Dr Czerny:** And the period of circulatory arrest seems quite extensive in your series, being more than 50 min. Is this due to the extent of repair, or are there other reasons for that? Actually, what I do mean is that you had more than 50 min of arrest.

**Dr Miyamoto:** Do you ask about 50 min arrest of lower body?

**Dr Czerny:** Yes, I think in your manuscript you mentioned that you had more than 50 min of circulatory arrest, which seems quite long.

**Dr Miyamoto:** I didn’t mention the circulatory arrest time in my presentation at all. For the distal anastomosis, we used double layer technique to prevent bleeding. This is the reason for the long time. Probably the circulatory arrest time should be less than 5 min before starting the SCP. We need only a couple of minutes.

**Dr Czerny:** And finally, have you seen any differences in surrogates of intestinal ischemia like serum lactate levels or liver enzyme release between the two-vessel or three-vessel technique as finally this might provide us with insight into the clinical applications of your findings? The serum lactate levels or liver enzymes after surgery, were they different?

**Dr Miyamoto:** After surgery, there was no difference in those parameters at all between the two perfusion techniques.