The effectiveness of high-flow regional cerebral perfusion in Norwood stage I palliation

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Abstract

Objective: Regional cerebral perfusion (RCP) has been shown to provide cerebral circulatory support during Norwood procedure. In our institution, high-flow RCP (HFRCP) from the right innominate artery has been induced to keep sufficient cerebral and somatic oxygen delivery via collateral vessels. We studied the effectiveness of HFRCP to regional cerebral and somatic tissue oxygenation in Norwood stage I palliation.

Methods: Seventeen patients, who underwent the Norwood procedure, were separated into two groups: group C (n = 6) using low-flow RCP and group H (n = 11) using HFRCP (mean flow: 54 vs 92 ml kg⁻¹ min⁻¹, P < 0.0001). The mean duration of RCP was 64 ± 10 min (range, 49–86 min) under the moderate hypothermia. Chlorpromazine (3.0 mg kg⁻¹) was given to group H patients before and during RCP to increase RCP flow. The mean radial arterial pressure was kept <50 mmHg during RCP. To clarify the effectiveness of HFRCP for cerebral and somatic tissue oxygenation, cerebral regional oxygen saturation (rSO₂) and systemic venous oxygenation (SvO₂) during RCP were compared between the two groups. Changes in the lactate level before and after RCP, and changes in the blood urea nitrogen (BUN), creatinine, lactate dehydrogenase (LDH), and creatine kinase (CK) levels before and after surgery, were also compared between the groups.

Results: Mean rSO₂ was 82.9 ± 9.0% in group H and 65.9 ± 10.7% in group C (P < 0.05). Mean SvO₂ during RCP was 98.2 ± 4.3% in group H and 85.4 ± 9.7% in group C (P < 0.01). During RCP, lactate concentration significantly increased in group C compared with that in group H (P < 0.001). After surgery, the LDH and CK levels significantly increased in group C compared with that in group H (P < 0.05). Conclusions: Our study revealed that HFRCP preserved sufficient cerebral and somatic tissue oxygenation during the Norwood procedure. The reduction of vascular resistance of collateral vessels increased both cerebral and somatic blood flow, resulting in improved tissue oxygen delivery.

Keywords: Norwood procedure; Cardiopulmonary bypass; Hypoplastic left heart syndrome; Neonate

1. Introduction

In Norwood stage I palliation, the various methods of cerebral protection have been reported, including a deep hypothermic circulatory arrest (DHCA) and low-flow regional cerebral perfusion (RCP). The DHCA, which provides surgeons a bloodless and clean operative field, has been used as an adjunctive therapy with cardiopulmonary bypass (CPB). However, because of neurologic complications, RCP has been used as the most reliable cerebral protection in aortic arch reconstruction [1–3]. The maintenance of cerebral oxygen saturation during RCP has been demonstrated with near-infrared spectroscopy (NIRS) [2,4,5]. In 2001, Pigula et al. reported that regional low-flow perfusion provides somatic circulatory support during neonatal arch surgical procedures, and that support of the subdiaphragmatic viscera should improve the ability of neonates to survive the postoperative period [5]. Then, in 2004, the maintenance of cerebral and somatic oxygen saturation during RCP was demonstrated with NIRS by a Wisconsin group [6].

In our institute, since 2007, high-flow RCP (HFRCP) from the right innominate artery has been induced to maintain sufficient cerebral and somatic oxygen delivery via collateral vessels. These collateral vessels include the communicating vessels within the cerebral circulation and the collateral systems, such as internal mammary arteries, which allow the lower part of the body to be perfused through the right innominate artery. We previously reported the effectiveness of HFRCP using the NIRS devices to assess changes in oxyhemoglobin saturation in the two different regional circulations, cerebral and somatic, before, during, and immediately after aortic arch repair [7]. In the present study,
the effectiveness of HFRCP for both cerebral and somatic oxygen delivery was retrospectively reviewed in Norwood stage I palliation.

2. Materials and methods

2.1. Patients and surgical technique

Between January 2005 and December 2009, 17 patients each weighing 1.9–3.5 kg (mean 3.0 kg), who underwent Norwood stage I palliation, were retrospectively reviewed.

Institutional review board approval and clinical physiologic data were obtained for all patients. These 17 patients were divided into two groups, before 2007, group C: Six patients who underwent the Norwood procedure using the low-flow RCP <70 ml kg⁻¹ min⁻¹ and, group H: Eleven patients who underwent the Norwood procedure using the HFRCP at >80 ml kg⁻¹ min⁻¹, since 2008. In group H, the maximum RCP flow was limited < nearly 100 ml kg⁻¹ min⁻¹. The patients’ demographic data in both groups are shown in Table 1. There were no significant differences in age, body weight, or the Aristotle complex score between two groups. Among all the 17 patients, seven patients (41.2%, five in group H and two in group C) needed preoperative mechanical ventilation, and 11 patients (64.7%, eight in group H and three in group C) needed inotropic support, because of unstable hemodynamics.

RCP via the right innominate artery was selected for all 17 patients. Norwood stage I palliation was performed using techniques previously described [7,8]. A 3.5-mm polytetrafluoroethylene (PTFE) tube graft was anastomosed to the innominate artery as an arterial line. While on CPB, the patient was cooled down to 25 °C. For patients with a diminutive ascending aorta, <3 mm in diameter, the ascending aorta was transected, and a cardioplegic solution was given. After cardiac arrest, the ascending aorta was incised vertically down to the sinus level and anastomosed to the main pulmonary artery in a side-to-side fashion to maintain sufficient coronary blood flow. Under RCP, the descending aorta was clamped, and the main pulmonary artery was anastomosed directly to the aortic arch. The right ventricular pulmonary artery conduit was contracted through the right side of the neo-aorta using a 5- or 6-mm ePTFE graft. For patients with larger ascending aorta, under RCP, the ascending aorta, descending aorta, and main pulmonary artery was directly anastomosed without any patch materials after complete resection of ductal tissue [9].

2.2. CPB systems and techniques

Our CPB system was reported previously [10,11]. A high-flow (200 ml kg⁻¹ min⁻¹) moderate hypothermic (25 °C) CPB was used. Blood-gas management was performed using the pH-stat strategy. Further, the hematocrit level was kept at more than 25% during bypass, using transfusion of red blood cells. Deep hypothermic cardiac arrest was not used for any of the patients. Isosorbide dinitrate (ISDN, 2.0 μg kg⁻¹ min⁻¹) and chlorpromazine (3.0 mg kg⁻¹) were given to patients in group H before and during RCP to increase RCP flow. Crystalloid cardioplegic solution (10 ml kg⁻¹) was given every 25 min. After termination of the bypass, modified ultrafiltration (MUF) was performed with a polymethylmethacrylate (PMMA) hemofilter for all patients. MUF was started with an ultrafiltration rate of 20 ml kg⁻¹ min⁻¹ for 10 min. The heparinization was neutralized by protamine sulfate until the activated coagulation time had normalized. Solumedrol (30 mg kg⁻¹) was routinely given to all the patients before the bypass. Aprotinin was not used in this study.

2.2.1. Monitoring and data acquisition

In all patients, blood pressure was invasively monitored at two different sites, the right radial artery and the femoral artery. The central venous pressure was monitored with an inferior venous catheter from the right femoral vein. Arterial oxygen saturation was monitored continuously in the upper and lower extremities (Nellcor N200; Pleasanton, CA, USA). Systemic venous oxygenation (SvO₂) was monitored continuously during CPB from the venous drainage (Terumo CDI-500; Tokyo, Japan). NIRS probes were placed on the patient’s midline forehead after entry into the operating room. The probes were monitored by a dual-detector device (Somanetics INVOS 5100, Troy, MI, USA) and trended at 1-min intervals. CPB flows, temperatures, and pressures were recorded at 5-min intervals. Arterial and venous blood gases were obtained at clinically appropriate intervals, with tensions reported at 37 °C (Radiometer ABL, Copenhagen, Denmark). The mean radial arterial pressure was kept <50 mmHg during RCP, and chlorpromazine was given to the patients in group H before and during HFRCP to increase RCP flow. The plasma lactate level (mmol l⁻¹) was also monitored during procedure.

Manually recorded data were fed into a common statistical database. Each patient’s clinical data were divided into five major time periods: (1) surgical incision and preparation of CPB, (2) initiation of CPB and cooling, (3) initiation of myocardial ischemia and RCP, (4) declamping of the descending aorta and warming, and (5) separation from CPB and surgical closure. Within each time period for each patient, data were collapsed into five epochs of equal duration to create 25 distinct epochs for subsequent statistical analysis. The SvO₂ data were divided into three major time periods: (1) initiation of CPB and cooling, (2) initiation of myocardial ischemia and RCP, and (3) declamping of the descending aorta and warming from CPB. Data are summarized within intervals and periods, and presented as mean ± SD.

Table 1. Patients’ demographic data.

<table>
<thead>
<tr>
<th></th>
<th>Group H (n = 11)</th>
<th>Group C (n = 6)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (days)</td>
<td>11.6 ± 8.9</td>
<td>12.5 ± 15.6</td>
<td>0.51</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>2.7 ± 0.5</td>
<td>2.7 ± 0.4</td>
<td>0.96</td>
</tr>
<tr>
<td>Aristotle complex score</td>
<td>17.4 ± 2.9</td>
<td>16.9 ± 1.9</td>
<td>0.88</td>
</tr>
<tr>
<td>Perfusion time (min)</td>
<td>179 ± 40</td>
<td>184 ± 18</td>
<td>0.31</td>
</tr>
<tr>
<td>RCP time (min)</td>
<td>66 ± 9</td>
<td>60 ± 13</td>
<td>0.19</td>
</tr>
<tr>
<td>RCP flow (ml min⁻¹ kg⁻¹)</td>
<td>92 ± 9</td>
<td>54 ± 9</td>
<td>0.0009</td>
</tr>
<tr>
<td>Blood loss (ml)</td>
<td>95 ± 111</td>
<td>91 ± 104</td>
<td>0.95</td>
</tr>
<tr>
<td>Transfusion (ml)</td>
<td>233 ± 61</td>
<td>242 ± 95</td>
<td>0.80</td>
</tr>
</tbody>
</table>

RCP: regional cerebral perfusion.
2.3. Study protocol

Changes of cerebral regional oxygen saturation (rSO₂) and SvO₂ were collected from all 17 patients. The time courses of cerebral rSO₂ and SvO₂ were compared between groups H and C using an analysis of variance (ANOVA) for repeated measurement. The plasma lactate level was measured at six different points: at the beginning of surgery, the initiations of CPB and RCP, the end of RCP, the separation from CPB, and at the end of the surgery. The changes in the lactate level were compared between the groups, using a repeated-measures ANOVA. The intra-operative urine output was also compared between the groups. To clarify the effectiveness of HFRCP for cerebral and somatic tissue oxygenation, changes in the lactate level before and after RCP, and changes in the blood urea nitrogen (BUN), creatinine, lactate dehydrogenase (LDH), and creatine kinase (CK) level before, at 6 h, and 12 h after surgery, were also compared between the groups, again by an ANOVA for repeated measures. Mann–Whitney tests were used to compare the groups with values of P < 0.05 indicating statistical significance.

After surgery, echography through the anterior fontanel was performed in all patients to rule out brain edema and bleeding. A follow-up brain computed tomography (CT) scan was performed 2 months after surgery.

3. Results

Demographic data in the 17 patients are summarized in Table 1. There were no significant differences in perfusion time or RCP time between the two groups, nor were there significant differences in the blood loss and transfusion requirement between the two groups. The RCP flow rate in group H was significantly greater than that in group C (92 ± 9 vs 54 ± 9 ml kg⁻¹ min⁻¹, P < 0.0001). There was one early death in group C. A patient with hypoplastic left heart syndrome and pulmonary artery sling, who underwent the Norwood procedure and left pulmonary artery plasty, died of respiratory failure due to tracheobronchial stenosis.

There was no difference in mean radial artery pressure during RCP between the two groups. The univariate analyses showed that SvO₂ and cerebral rSO₂ during RCP in group H were significantly greater than those in group C (Table 2). The plasma lactate increase in group C was greater than that in group H. However, there was no significant difference in urine output during CPB between the groups.

The baseline cerebral rSO₂ was 56.3 ± 9.7% in group H and 51.3 ± 17.9% in group C, and during cooling, cerebral rSO₂ increased to 70.5% ± 11.4% in group H and 57.4% ± 15.1% in group C. During RCP, cerebral rSO₂ increased to 82.9 ± 9.4% in group H, significantly greater than that in group C (64.9 ± 17.2%) (P < 0.05). The cerebral rSO₂ decreased to 67.9 ± 10.6% in group H, and to 61.2 ± 15.3% in group C, during warming. After bypass, it remained almost the same as the baseline in both groups (Fig. 1).

![Cerebral rSO₂ during procedure](image1)

Fig. 1. The cerebral rSO₂ during surgery in two groups. The surgical procedure was divided into five major periods. Data are shown as mean and SD for each period. CPB: cardiopulmonary bypass; RCP: regional cerebral perfusion.

![SvO₂ during CPB](image2)

Fig. 2. The SvO₂ during surgery. The surgical procedure was divided into three major periods. Data are shown as mean and SD for each period. CPB: cardiopulmonary bypass; RCP: regional cerebral perfusion.

![Plasma lactate level during procedure](image3)

Fig. 3. The change of plasma lactate level during procedure. During RCP, lactate level significantly increased in group C, compared with that in group H (P < 0.05).

<table>
<thead>
<tr>
<th>Group H (n = 11)</th>
<th>Group C (n = 6)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rt. RAP (mmHg)</td>
<td>37 ± 9</td>
<td>43 ± 12</td>
</tr>
<tr>
<td>SvO₂ (%)</td>
<td>98 ± 1.2</td>
<td>85 ± 9.7</td>
</tr>
<tr>
<td>Cerebral rSO₂ (%)</td>
<td>83 ± 9</td>
<td>66 ± 17</td>
</tr>
<tr>
<td>Lactate increase (mmol l⁻¹)</td>
<td>0.8 ± 0.5</td>
<td>2.8 ± 0.9</td>
</tr>
<tr>
<td>Urine output after CPB (ml kg⁻¹)</td>
<td>3.0 ± 1.7</td>
<td>3.0 ± 1.8</td>
</tr>
</tbody>
</table>

SvO₂: systemic venous oxygen saturation; rSO₂: regional oxygen saturation; and CPB: cardiopulmonary bypass.
The $\text{SvO}_2$ during cooling was $95.1 \pm 5.4\%$ in group H and $91.6 \pm 5.8\%$ in group C. During RCP, $\text{SvO}_2$ increased to $98.1 \pm 2.8\%$ in group H; however, it decreased to $86.1 \pm 8.5\%$ in group C ($P < 0.05$). During warming, the $\text{SvO}_2$ decreased to $88.2 \pm 7.1\%$ in group H, and it remained almost the same as during RCP in group C (Fig. 2).

The change of plasma lactate level during the procedure in both groups is shown in Fig. 3. During RCP, the lactate level significantly increased in group C, compared with that in group H (group H: $5.2 \pm 1.8\%$ vs group C: $7.0 \pm 1.3\%$ mmol l$^{-1}$, $P < 0.05$).

The changes of BUN and creatinine after surgery were not different between two groups. The changes of LDH level after surgery in both groups are shown in Fig. 4. At 6 and 12 h after surgery, LDH level increased in group C, compared with that in group H (at 6 h after surgery, group H: $647 \pm 171$ vs group C: $934 \pm 379$ U l$^{-1}$, $P < 0.05$, at 12 h after surgery, group H: $582 \pm 118$ vs group C: $820 \pm 291$ U l$^{-1}$, $P < 0.05$, respectively).

The changes of CK level after surgery in both groups are shown in Fig. 5. At 6 and 12 h after surgery, CK level increased in group C, compared with that in group H (at 6 h after surgery, group H: $932 \pm 435$ vs group C: $1364 \pm 259$ U l$^{-1}$, $P < 0.05$, at 12 h after surgery, group H: $798 \pm 320$ vs group C: $1165 \pm 311$ U l$^{-1}$, $P < 0.05$, respectively).

After surgery, an echography through the anterior fontanel was performed in all patients. No patient had any cerebral edema or bleeding. A follow-up brain CT scan was performed in 10 patients (59%, three patients in group C and seven patients in group H), 2 months after surgery. No patients had any cerebral bleeding or infarction.

4. Discussion

There have been various techniques reported to avoid neurological complications after an aortic arch repair. As surgical outcomes and postoperative management have improved, neurologic problems including significant neurodevelopmental problems have been focused on after Norwood stage I palliation. The effectiveness of low-flow RCP has been reported by many centers [1–5]. However, adequate cerebral perfusion flow rate remains unclear. Recently, Sasaki et al. reported an animal experimental study concerning the optimal flow rate of antegrade RCP [12]. At 50 ml kg$^{-1}$ min$^{-1}$ of an antegrade cerebral perfusion rate, cerebral blood flow was equal to baseline CPB. An antegrade cerebral perfusion rate of 30 ml kg$^{-1}$ min$^{-1}$ provided only 60% of baseline cerebral blood flow, but cerebral oxygen extraction and regional oxygen saturation were equal to the baseline. Therefore, an antegrade cerebral perfusion rate that closely matches standard CPB conditions is between 30 and 50 ml kg$^{-1}$ min$^{-1}$. In the present study, the baseline CPB flow rate was 100 ml kg$^{-1}$ min$^{-1}$. This means that the optimal cerebral perfusion rate was between 30% and 50% of total bypass flow. In neonatal CPB, the high-flow strategy (range, 150–200 ml kg$^{-1}$ min$^{-1}$) has been used with mild or moderate hypothermia. At such time, the adequate cerebral flow rate is between 45 and 100 ml kg$^{-1}$ min$^{-1}$ in the clinical setting. For cerebral perfusion itself, the flow rate of 50 ml kg$^{-1}$ min$^{-1}$ may be sufficient with moderate hypothermia. Administration of vasodilator dilated collateral vessels, such as internal thoracic arteries, resulted in increased somatic blood flow with increased RCP flow up to 100 ml kg$^{-1}$ min$^{-1}$. In the high-flow CPB strategy, the cerebral perfusion flow is not excessive, if the adequate blood supply to the upper body is half that of the total body in neonates and small infants.

Since 2007, HFRCP from the right innominate artery has been induced to maintain sufficient cerebral and somatic oxygen delivery via collateral vessels. We previously reported the effectiveness of HFRCP in aortic arch repair [7]. The flow rate was regulated between 70 and 100 ml kg$^{-1}$ min$^{-1}$ to avoid brain edema or bleeding due to excessive cerebral blood flow. The RCP flow was also limited by the right radial arterial pressure, which was maintained at $<50$ mmHg. Our protocol regulated the doses of ISDN to 2.0 $\mu$g kg$^{-1}$ min$^{-1}$ and chlorpromazine to 3 mg kg$^{-1}$, given to the patients during bypass, to increase the RCP flow and provide sufficient cerebral and somatic oxygen delivery via collateral vessels. The present study demonstrated that there was no brain edema or bleeding just after surgery in any of the patients with HFRCP. To avoid brain edema or bleeding due to excessive cerebral blood flow, as much as possible, intraoperative pressure monitoring of the left superficial temporal artery or the right radial artery is recommended.

Hoffman et al. reported changes in cerebral and somatic oxygenation during Norwood stage I palliation using low-flow RCP [6]. They operated under continuous RCP with a flow rate...
of 30–70 ml kg\(^{-1}\) min\(^{-1}\), while cerebral oxygenation was maintained during RCP at prebypass levels with deep hypothermia. However, after rewarming and separation from CPB, cerebral oxygenation was lower compared with prebypass or somatic values. These results indicate that cerebrovascular resistance is increased after deep hypothermic CPB, even with continuous perfusion techniques, placing patients on cerebral circulation at risk postoperatively. Somatic oxygen saturation also decreased <50% during RCP in 75% of the patients. We used a vasodilator to reduce the cerebral and somatic vascular resistance before and during RCP, resulting in increased cerebral and somatic oxygen saturation during and after CPB.

Among 17 patients, there were seven patients with preoperative mechanical ventilation (two patients in group C and five in group H), and 10 patients with inotropic support because of unstable hemodynamics (two patients in group C and eight in group H). Seven patients (41.2%, two patients in group C and five in group H) had no preoperative urine output or during CPB. There were no differences in renal functions after surgery between the two groups. On the other hand, LDH and CK levels increased in group C, compared with those in group H, at 6 and 12 h after surgery. During RCP, the lactate level significantly increased in group C, compared with that in group H. These results indicated that the HFRCP provided sufficient cerebral and somatic tissue oxygenation during the Norwood procedure.

In 1999, Imoto et al. reported a special technique of descending aorta cannulation combined with RCP for Norwood stage I palliation [13]. They reported that the cannulation of the distal descending thoracic aorta through a median sternotomy seems a safe, easy, and effective technique for perfusion of the lower body in the Norwood procedure. In Japan, many hospitals use this technique without circulatory arrest or deep hypothermia throughout the operation. However, the CPB system is complicated, and CPB circuits and cannulae are crowded in small operative fields. In this technique, extracorporeal circulation with a single pump and double arterial lines are established. Therefore, the cerebral perfusion flow depends on both cerebral and somatic vascular resistance. The flow measurement of cerebral perfusion circuits should be performed, or both cerebral and somatic rSO\(_2\) monitoring would be needed.

### 4.1. Study limitations

The present study was a retrospective study, and the number of patients was small (n = 17). The postoperative course depended upon the preoperative condition and the procedure performed.

### 4.2. Conclusions

Our study revealed that HFRCP preserved sufficient cerebral and somatic tissue oxygenation during the Norwood procedure. The reduction of vascular resistance of collateral vessels increased both cerebral and somatic blood flow, resulting in improved tissue oxygen delivery. HFRCP is a safe and easy technique for Norwood stage I palliation.

### References


### Appendix A. Conference discussion

Dr V. Hraska (Sankt Augustin, Germany): First of all, let me acknowledge your group’s continuing effort to expand the limits of cerebral circulatory support during arch reconstruction. In fact, a similar study was already published by your team in the Annals this year with equal conclusions.

Now you present an extended cohort of patients concentrating only on the perfusion protocol used for stage I palliation. The essential question is, what flow is adequate to support the brain without developing edema or intracerebral hemorrhage? As was clearly demonstrated by this study, despite high regional cerebral blood flow and relatively high mean arterial pressure, no cerebroly related issues were reported. These are extremely valuable findings showing a higher level of safety with this protocol as one would expect.

But as always, the devil is hidden in the detail, so I would like to elaborate your perfusion protocol because that is probably something very special, particularly for me.

So the first question is simple. You said that your essential flow is 200 ml/kg/min and moderate hypothermia in general for both groups. Do you use any vasodilators for perfusion?

Dr Miyaji: Yes. We used vasodilators, just ISDN, for both group of patients, the low-flow and high-flow patients. And then for high-flow strategy patients we added chlorpromazine.

Dr Hraska: Yes, that is my second question. You used ISDN for both groups?

Dr Miyaji: Yes, we did.
Dr Hraska: The second question is about the use of vasodilators such as chlorpromazine. Chlorpromazine affects nearly all receptors, such as alpha 1, alpha 2, you name it.

Dr Miyaji: Yes.

Dr Hraska: Therefore, the biokinetics are very complex I think.

Dr Miyaji: Yes.

Dr Hraska: These are just the side effects which chlorpromazine is providing on cerebral perfusion.

Dr Miyaji: Yes.

Dr Hraska: I think it would be very interesting for everybody to know what the important side effects are, and what the biological half-life of chlorpromazine is in newborns?

Dr Miyaji: I am not sure. In Japan, we cannot easily use phenoxybenzamine which is an alpha blocker. When you only want to focus on vasodilation, we recommend the use of phenoxybenzamine. We use chlorpromazine as both sedative and vasodilator.

Dr Hraska: So what is the biological half-life in newborns?

Dr Miyaji: I am not sure.

Dr Hraska: That would be very valuable information for all who would consider using your protocol.

Dr Miyaji: I will check it in my protocol of the drug chlorpromazine. I remember its biological half-life is within 24 hours.

Dr Hraska: Recent evidence suggests that ISDN which you use induces inappropriate production of oxygen-free radicals. Can you comment on that?

Dr Miyaji: I am not sure. I do not have any comment on this.

Dr Hraska: So it does not look like it is completely safe?

Dr Miyaji: I agree with you.

Dr Hraska: Would you recommend this technique for premature newborns as well?

Dr Miyaji: No, I do not think so.

Dr Hraska: Why not?

Dr Miyaji: I did not perform stage I palliation for premature patients.

Dr C. Fraser (Houston, USA): As you know, our group has also favored a high-flow cerebral blood flow strategy for antegrade cerebral perfusion, but nonetheless, the issue remains not widely agreed on.

And although you have shown with your postoperative ultrasound and CT scan that there are no gross intracranial issues, I might submit that our MRI data and that of other groups would suggest that ultrasound and CT scan are really insensitive.

So I wonder what your thoughts are going forward, about prospectively looking at something more sensitive like perioperative MRI, EEG, and even neurodevelopmental outcome so you can really tease this issue apart.

Dr Miyaji: Yes, I totally agree with you. But we did not perform MRI in the current study. After surgery, almost all the patients’ chests are left open, and so it is not so easy to take an MRI just after surgery. So I think maybe a follow-up MRI scan should be performed for these patients.

Dr Fraser: And also before surgery?

Dr Miyaji: I think so, yes.

Dr J. Tweddell (Milwaukee, USA): A quick question I had. The pH strategy for perfusion, maybe I did not quite get that correct.

Dr Miyaji: Yes, that is correct.

Dr Tweddell: pH strategy?

Dr Miyaji: Yes.

Dr Tweddell: The cerebral saturations during the control group was 66%?

Dr Miyaji: Yes.

Dr Tweddell: But there was really no difference as far as you could determine from a neurological outcome standpoint?

Dr Miyaji: Yes. But actually we did not check neurological outcome in a follow-up study.

Dr Tweddell: But maybe 66% is good enough?

Dr Miyaji: I am not sure. At your presentation the day before yesterday, you recommended the cerebral saturation should be more than 80%, right? So according to your presentation, we should keep more than 80% on moderate hypothermia.

Dr Tweddell: 80% was somewhat speculative based on the hypothermic conditions and the goal to maintain a safety buffer to prevent cerebral ischemia, you have real data.

Dr Miyaji: No, I do not have real data.