Antegrade selective cerebral perfusion in thoracic aorta surgery: safety of moderate hypothermia

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Abstract

Objective: Although antegrade selective cerebral perfusion (ASCP) has been demonstrated to be the best method of protection of brain ischemia during aortic arch surgery, there is no consensus regarding optimal temperature during ASCP. The study analyzed the outcomes of aortic surgery using ASCP at different degree of systemic hypothermia. Methods: Between November 1996 and November 2005, 305 patients underwent thoracic aorta surgery using ASCP. Patients were divided into two groups according to the lowest systemic temperature: moderate systemic hypothermia (≥25 °C) was used in 189 patients (group A), and a deeper hypothermia (<25 °C) in 116 patients (group B). One hundred and five patients suffered from acute type A aortic dissection. Results: The extension of aortic replacement was significantly larger in group A, while the average ASCP time was not different between groups (63 ± 37.7 min group A, 58.6 ± 35.6 min group B; p = 0.314). The 30-day mortality rate was 12.7% in group A and 13.8% in group B (p = 0.862). Permanent neurologic deficits occurred in eight patients (2.6%) without significant differences between groups (3.1% group A vs 1.7% group B; p = 0.715). Twenty-five patients (8.2%) suffered from temporary neurologic dysfunction (7.9% group A vs 8.6% group B; p = 0.833). Conclusions: In our experience, ASCP was a safe technique for thoracic aorta surgery allowing complex aortic repairs to be performed with good results in terms of hospital mortality and neurologic outcomes. The fact that there was no difference between the two groups suggests that moderate systemic hypothermia (26 °C) appears to be a safe and sufficient tool for brain protection. Moreover, the well known hypothermia-related side effects may be avoided.

Keywords: Hypothermia; Aortic aneurysm; Aortic arch repair; Cerebral protection

1. Introduction

Antegrade selective cerebral perfusion (ASCP), as demonstrated by various authors [1—4], is the best method of brain protection during aortic arch surgery. Different strategies are currently in use depending on each individual surgeon’s experience. ASCP can be used in deep hypothermia, as suggested by Griepp [4], or with moderate hypothermia as advocated by others [5—7]. Moreover, the cerebral perfusion can be performed with cold blood, the so-called ‘cerebroplegia’ of Bachet et al. [6], or with tepid blood [5]. However, the ideal degrees of systemic hypothermia and the optimal flow rate of cerebral perfusion are not yet definitively established.

In this study we analyzed our overall experience with the ASCP at different systemic temperatures in order to determine if the degree of hypothermia has an effect on the clinical and neurological outcomes.

2. Materials and methods

2.1. Patients population and data

Between November 1996 and November 2005, 305 consecutive patients at S. Orsola-Malpighi Hospital, Cardiac Surgery Department, underwent hemiarch and total aortic arch replacement for chronic aortic aneurysm and acute and chronic aortic dissection using antegrade selective cerebral perfusion with hypothermic circulatory arrest (HCA) as method of cerebral protection. The data were acquired prospectively as part of the patients’ pathway and were based upon the Italian Society of Cardiac Surgery’s dataset with some customised additions.
According to the degree of systemic hypothermia during HCA, the 305 patients were divided into two groups. The first group (group A) with a nasopharyngeal temperature of 25°C or higher consisted of 189 (62%) patients, with 129 (68.3%) males. The mean age was 62.5 ± 12.3 years. The second one (group B; nasopharyngeal temperature lower than 25°C) consisted of 116 (38%) patients with a mean age of 62.7 ± 12.7 years and 75 (64.7%) were males.

Preoperative characteristics of the patients in both groups are summarized in Table 1. Main surgical indications were chronic aneurysm and acute type A dissection in both groups (Table 1).

### 2.2. Operative technique

Operations were performed through a median sternotomy in 298 patients (97.7%) associated with left anterior thoracotomy in 7 (2.3%) when the distal descending aorta was involved.

Our method of antegrade selective cerebral protection and the technique of aortic replacement has previously been described [8,9] and can be summarized as follows. After systemic heparinization, a cardiopulmonary bypass (CPB) was instituted with an arterial cannula introduced into the femoral artery, ascending aorta or right axillary artery and with a venous single two-stage cannula introduced into the right atrium or, in few cases (reoperations and emergent cases), into femoral vein. In eight (2.6%) patients a bicaval cannulation was used. Myocardial protection was achieved with cold crystalloid cardioplegia. Cerebral monitoring was achieved by means of a right radial artery pressure line and jugular bulb venous oxygen saturation. The transcranial Doppler scan and/or near infrared spectroscopy were rarely used.

One-hundred and sixteen (38%) patients were cooled to a nasopharyngeal temperature lower than 25°C (group B) before the interruption of the systemic circulation. Since 1997, we started to apply circulatory arrest at a nasopharyngeal temperature of 25°C or higher and, with this degree of hypothermia, 189 (62%) patients (group A) were treated.

Arterial blood pH was managed according to the alpha-stat method.

After the arrest, the aorta was opened with the patient in the Trendelenburg position, then special catheters for ASCP connected to the oxygenator with a separate single roller pump head, were inserted into the brachiocephalic trunk and left common carotid arteries with the left subclavian artery clamped in order to avoid the steal phenomenon.

ASCP management was performed according to Kazui et al. protocol [5]. Cerebral perfusion was initiated at a flow rate of 10 ml/kg min and adjusted to maintain the right radial arterial pressure between 40 and 70 mmHg. The temperature of the cerebral perfusate was 1–2°C less than the core temperature (24–25°C).

In the case of right axillary artery cannulation, which was introduced in our practice in 2004 and used in 40 patients (13.11%), only the left common carotid artery was cannulated, and cerebral perfusion was obtained using the systemic pump at a flow rate of 8–10 ml/kg min and the roller pump at a flow rate of 5 ml/kg min. The innominate artery and the left subclavian artery were occluded at the time of ASCP.

Open distal aortic anastomosis was performed with systemic blood flow maintained at 0.5–1 l/min if the femoral artery was cannulated.

In the case of hemiarch replacement, an open distal anastomosis was first performed, then the ASCP was stopped, the cannulae for cerebral perfusion removed from supraaortic vessels and the systemic circulation restored and patient rewarming initiated.

In the case of total arch replacement, we performed the open distal anastomosis and then the left subclavian artery was reimplemented. After that, the proximal anastomosis was performed and the coronary blood flow restored. Once the proximal anastomosis was carried out, patient rewarming was initiated. The left carotid and the brachiocephalic trunk were then reimplemented.

In group A, 110 (58.2%) patients underwent ascending aorta and total arch replacement, while in 42 (22.2%) patients only ascending aorta and/or hemiarch were replaced.

In group B, 42.2% of the patients underwent ascending aorta and aortic arch replacement, while 33.6% of the patients underwent ascending aorta and hemiarch replacement (Table 2).

Concomitant procedures included modified Bentall in 71 (37.6%) patients in group A and in 28 (24.1%) patients in group B, Elephant trunk in 21 (11.1%) and in 10 (8.6%), respectively. The other associated procedures are shown in Table 2.

### 3. Results

The mean nasopharyngeal temperature of the group A (≥25°C) was 25.8 ± 0.8°C, compared to 21.9 ± 1.9°C of the group B (<25°C), with p value < 0.001. The mean duration of ASCP was 63 ± 37.7 min in the group A and 58.6 ± 35.6 in the group B (p = 0.314) without significant difference between the two groups. The CPB time amounted to 193.6 ± 59.4 min in the group A and 189 ± 65.9 min in the group B (p = 0.526). The myocardial ischemic time was 131.1 ± 45 min and
mortality was higher in group B than that in group A (20.8% vs
13.8%, respectively). Considering only urgent/emergent patients, the
overall in-hospital mortality was 13.1% (40 patients), which was higher in patients who underwent urgent-emergent surgery (19/109 patients (17.4%) in comparison with those who underwent elective surgery (21/196 patients (10.7%). The difference was statistically significant (p = 0.066).

In the group A (patients with preoperative chronic renal failure, 8 patients in group A (4.3%) and 7 patients in group B (6.5%) had postoperative renal failure needing hemodialysis without significant difference between the two groups (p = 0.408). Myocardial infarction occurred in seven patients (3.7%) in the group A and in two (1.7%) in the group B. Postoperative bleeding requiring surgical revision occurred in 16 patients (8.5%) and in 11 patients (9.5%) in the group B and in the group A, respectively.

Table 3

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group A (n = 189)</th>
<th>Group B (n = 116)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extent of aortic replacement (%)</td>
<td>Ascending + aortic arch</td>
<td>110 (58.2)</td>
<td>49 (42.2)</td>
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<tr>
<td>Ascending aorta/hemiarch</td>
<td>42 (22.2)</td>
<td>39 (33.6)</td>
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<td>Aortic arch</td>
<td>22 (11.6)</td>
<td>13 (11.2)</td>
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<td>Complete thoracic aorta</td>
<td>8 (4.2)</td>
<td>7 (6)</td>
<td>0.587</td>
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<td>Aortic arch + descending aorta</td>
<td>7 (3.7)</td>
<td>5 (4.3)</td>
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<tr>
<td>Other</td>
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Table 4

<table>
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<tr>
<th>Variables</th>
<th>Group A (n = 189)</th>
<th>Group B (n = 116)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital mortality (%)</td>
<td>Overall patients</td>
<td>24 (12.7)</td>
<td>16 (13.8)</td>
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<tr>
<td>Urgent/emergent surgery</td>
<td>9/61 (14.8)</td>
<td>10/48 (20.8)</td>
<td>0.656</td>
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<tr>
<td>Permanent neurologic deficit</td>
<td>6 (3.1)</td>
<td>2 (1.7)</td>
<td>0.715</td>
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<tr>
<td>Transient neurologic deficit</td>
<td>15 (7.9)</td>
<td>10 (8.6)</td>
<td>0.833</td>
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<tr>
<td>Pulmonary complications</td>
<td>28 (14.8)</td>
<td>15 (12.9)</td>
<td>0.736</td>
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<tr>
<td>Renal failure (dialysis)</td>
<td>9 (4.8)</td>
<td>9 (7.8)</td>
<td>0.203</td>
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<tr>
<td>Myocardial infarction</td>
<td>7 (3.7)</td>
<td>2 (1.7)</td>
<td>0.491</td>
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<tr>
<td>Bleeding (rethoracotomy)</td>
<td>16 (8.5)</td>
<td>11 (9.5)</td>
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Table 5

<table>
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<th>Variables</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>p</th>
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<tr>
<td>In-hospital mortality</td>
<td>Chronic aortic dissection</td>
<td>3.88</td>
<td>1.01–14.77</td>
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<td>CPB time</td>
<td>1.01/min</td>
<td>1.00–1.01</td>
<td>0.002</td>
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<tr>
<td>Permanent neurologic deficit</td>
<td>CPB time</td>
<td>1.01/min</td>
<td>1.00–1.02</td>
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<tr>
<td>Transient neurologic deficit</td>
<td>Age</td>
<td>1.12/year</td>
<td>1.07–1.24</td>
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<td>Female gender</td>
<td>3.4</td>
<td>1.11–10.64</td>
<td>0.032</td>
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<tr>
<td>Acute dissection</td>
<td>4.8</td>
<td>1.82–12.84</td>
<td>0.001</td>
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<tr>
<td>AVR</td>
<td>3.4</td>
<td>1.32–8.88</td>
<td>0.011</td>
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AVR: aortic valve replacement; CPB: cardiopulmonary bypass time.

14.8%) even if the difference did not reach statistical significance (p = 0.656) (Table 4).

In the logistic regression analysis, two factors were found to be independently related to overall in-hospital mortality: chronic aortic dissection (O.R. = 3.88; p = 0.046) and cardiopulmonary bypass time (O.R. = 1.01/min; p = 0.002) (Table 5).

The overall incidence of permanent neurologic deficit (stroke or coma) was 2.6% (eight patients). In the group A and in the group B, it was 3.1% (six patients) and 1.7% (two patients), respectively. Transient neurologic deficit occurred in 25 patients (8.2%): 15 patients (7.9%) in group A and 10 (8.6%) in group B. In both groups there was no statistically significant difference in permanent and in transient neurologic deficit (Table 4).

Multivariate analysis revealed cardiopulmonary bypass time (O.R. = 1.01; p = 0.006) to be the only independent risk factor of permanent neurologic deficit (Table 5).

Logistic regression indicated age of the patients (O.R. = 1.12/year; p < 0.001), the female gender (O.R. = 3.4; p = 0.032), acute dissection (O.R. = 4.8; p = 0.001) and aortic valve replacement (O.R. = 3.4; p = 0.011) as independent predictors of transient neurologic deficit (Table 5).

The duration of ASCP and the temperature of cooling were not found to be associated with in-hospital mortality, transient and permanent neurologic deficits.

In the group A 28 patients (14.8%) had pulmonary complications, in the group B 15 patients (12.9%). Nine patients in both groups (4.9% and 7.8%, respectively) needed postoperative hemodialysis for renal failure. Excluding the 13 patients with preoperative chronic renal failure, 8 patients in group A (4.3%) and 7 patients in group B (6.5%) had postoperative renal failure needing hemodialysis without significant difference between the two groups (p = 0.408).

4. Discussion

Although antegrade selective cerebral perfusion has been demonstrated as being the best method of cerebral...
The inadequate brain protection results from an imbalance between supply of cerebral blood flow and cerebral oxygen consumption. The cerebral oxygen consumption decreases by 50–60% of baseline value at a core temperature of 25–28 °C and further cooling does not provide the same decrease in brain oxygen consumption. However, the regional cerebral blood flow with antegrade perfusion decreases more rapidly at less than 28 °C to 62% of base line at 28 °C and to 36% at 18 °C [12]. Thus deep hypothermia may not be necessary during ASCP and cerebral oxygen demands should be met at moderate hypothermia. Furthermore, there is increasing evidence that deep hypothermia is associated with direct negative effects on cerebral neuronal integrity [13,14].

In the present study the body temperature as well as the duration of cerebral perfusion were not associated with an increased risk of permanent and transient neurologic deficits. The incidence of permanent neurologic deficit was 2.6%, perfectly comparable with recent reports, without significant differences between the two groups (3.1% group A vs 1.7% group B; p = 0.715). The only independent risk factor we found was CPB time (odds ratio, 1.01/min; p = 0.006). Transient neurologic dysfunction occurred in 25 patients (8.2%) and its rate was similar between the groups. Age was one of the independent risk factors for transient neurologic deficit and we can speculate that, in elderly patients, the brain is more susceptible to the injury which can result from the activation of the inflammatory process occurring during extracorporeal circulation (SIRS) [15,16]. The effect of temperature group was not significant by logistic regression analysis.

Overall in-hospital mortality was equivalent in both groups: 12.7% in group A and 13.8% in group B (p = 0.862). Compared with our previous experience [8,9], we have observed a worsening of the hospital survival, probably due to the fact that, considering the good results obtained with this technique, we have extended the surgical indications to extremely serious cases which would not have previously been operated on.

Our results are analogous to those obtained from similar studies. Cook and associates [17] demonstrated a comparable incidence of neurologic injury in groups of patients undergoing HCA and ASCP at moderate hypothermia (≥ 22 °C) and deep hypothermia (≤ 22 °C). Besides, lower rates of major neurologic injury and delirium were observed in the group of moderate hypothermia.

Zierer et al. [18] compared three groups of patients who underwent repair of acute Type A aortic dissection with different methods of brain protection: ASCP with moderate systemic hypothermia (30 °C), ASCP with deep hypothermia (20–24 °C), and retrograde cerebral perfusion associated with deep hypothermia (20–24 °C). They showed the lowest incidence of transient neurologic deficit (11.1%) and permanent neurologic deficit (5.5%) in the group of 30 °C ASCP even if the difference between the other groups did not reach any statistical significance.

The same group [19] confirmed the good clinical results with mild hypothermia (30–32 °C) and ASCP also in the treatment of chronic aneurysm of the aortic arch.

However, recent experimental studies in pigs demonstrated a better cerebral protection using a deeper systemic hypothermia and a lower temperature of ASCP.

Strauch et al. [20], from Mount Sinai Hospital, described a profound metabolic suppression lasting several hours after SCP, thus permitting a faster neurologic recovery in the animal groups who underwent a systemic hypothermia of 20 °C and SCP at 10 °C and 15 °C compared to animal groups in which a SCP at 20 °C and 25 °C was used.

In another study, Khaladj et al. [21] compared four groups of pigs cooled to 20 °C of body temperature, the first without, and the other three with either 10 °C, 20 °C and 30 °C of ASCP and they found that 20 °C cerebral perfusion provide a better cerebral protection over the 90 min period of ASCP. The significant difference between core and brain temperatures, in 10 °C and 30 °C groups, may have affected the results through the loss of vascular resistance and the endothelium injury leading to capillary leakage.

There are some limitations to our study that need to be considered. Firstly this is an observational study and by its retrospective nature, it is only capable of showing association between variables and outcomes, and is unable to demonstrate cause and effect. A further and important limitation in the study is the fact that the degree of hypothermia was not prospectively defined, but it was settled case by case during the operation by the single surgeon. The two groups were not perfectly comparable: the group B patients had a higher prevalence of preoperative renal insufficiency (7.8% vs 2.1%; p = 0.009) and coronary artery disease (22.4% vs 13.8%; p = 0.066), while the patients in group A underwent more frequently ascending aorta and aortic arch replacement (58.2% vs 42.2%; p = 0.009) and Bentall procedure (37.6% vs 24.1%; p = 0.017). The cross-clamp time was longer in group A then in group B confirming the fact that, in group A, the operations were more complex and time consuming. The CPB time was similar in both groups because the cooling and the rewarming of the group B patients required a longer duration of systemic perfusion.

In 2004 we started using, as arterial inflow, the right axillary artery and, since then, it is our preferred site of arterial cannulation. The antegrade perfusion through the axillary artery can avoid the disadvantages arising from retrograde perfusion through the femoral artery, such as the risk of brain embolization by thrombotic or atherosclerotic debris in atherosclerotic aneurysm, and the organ malperfusion in aortic dissection. Furthermore the manipulation of the supra-aortic vessels is reduced requiring only the cannulation of the left common carotid artery.

We were not able to demonstrate a reduction on the incidence of the well-known hypothermia-related side effects, such as post-operative bleeding, post-operative pulmonary insufficiency, etc., in the ≥25 °C group patients. This may probably be due to the fact that group A patients underwent more complex and time consuming operations that are associated with a higher incidence of post-operative complications.

In conclusion, antegrade selective cerebral perfusion is a safe technique for thoracic aorta surgery allowing complex protection in thoracic aorta surgery, the ideal temperature and the optimal flow rate of cerebral perfusion are not yet definitively established.
aortic repairs to be performed with good results in terms of hospital mortality and neurologic outcomes. Moderate systemic hypothermia at a nasopharyngeal temperature of 26°C appears to be a safe and sufficient tool for brain protection and the well known hypothermia-related side effects may be avoided. However, further randomized prospective studies are necessary to define the ideal systemic temperature and the optimal flow rate.

References


Appendix A. Conference discussion

Dr D.C. Miller (Stanford, California, USA): Three quick questions for clarification.

Where were you measuring systemic temperature-bladder, nasopharyngeal, or rectal?

Dr Pacini: We measure the nasopharyngeal temperature.

Dr Miller: Number two, you say greater than 25 degrees. How much greater? Was it closer to 25 or to 30 degrees? Asking this question another way, in the group that was greater than 25 degrees what was the median or the average systemic temperature? Were you doing these at 30 or 32 degrees?

Dr Pacini: I didn’t understand.

Dr Miller: In the warm group, what was the average temperature?

Dr Pacini: The average nasopharyngeal temperature was, as you can see here in the slide, 25.8°C.

Dr Miller: Okay. So it’s actually a pretty low temperature.

And that’s an important point. I don’t worry so much about the brain when protecting it using SACP, but I do worry about the liver, kidneys, and spinal cord when there is no flow to the lower body for upwards of an hour, as you were here. But, paradoxically, your incidence of renal failure was a little higher in the colder group.

What temperature was your SACP perfusate?

Dr Pacini: One or two degrees less than the nasopharyngeal temperature at the time of the arrest that is around 26°C. So most of the time we perfuse the brain up to 24–25°C.

Dr M. Moldovan (Bucharest, Romania): Do you measure the pressure in the cerebral circulation during this perfusion? That’s the first question.

The second one is, if I understand well, you have different flows on the right and on the left carotid artery, and this is surprising.

And the last question is, if you reawarm the head separately, because it makes a difference.

Dr Pacini: Regarding the different flows of cerebral perfusion, when we use the classic Kazui technique, we cannulate both the innominate artery and the carotid artery, and we perfuse the brain with a flow rate of 10 ml/kg min. When we use the auxiliary artery as arterial inflow, the brain is perfused with two different pump. The right hemisphere is perfuse through the auxiliary line at a flow rate of 8–10 ml/kg min, while, with a separate pump, the left side is perfuse through the left common carotid artery at a flow rate of 5 ml/kg min. We perfuse the right side at a higher flow; this is because now we stop the pump at 26°C and we want to have more flow to the brain during the systemic arrest.

Dr Y. Okita (Kobe, Japan): We have been raising the temperature as well. But we always cannulate the three, left subclavian artery, because we were worried about spinal cord complications. So I would like to ask you what is the rate of spinal cord complication?

Dr Pacini: In our series, we have not seen any case of spinal cord injury such as paraplegia or paraparesis.