

# The Methodologies of Hypothermic Circulatory Arrest and of Antegrade and Retrograde Cerebral Perfusion for Aortic Arch Surgery

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In spite of recent advances in thoracic aortic surgery, postoperative neurological injury still remains the main cause of mortality and morbidity after aortic arch operation. The use of cardiopulmonary bypass (CPB) and hypothermic circulatory arrest, temporary interruption of brain circulation, transient cerebral hypoperfusion, and manipulations on the frequently atheromatic aorta all produce neurological damages. The basic established techniques and perfusion strategies during aortic arch replacement number three: hypothermic circulatory arrest (HCA), antegrade cerebral perfusion (ACP), and retrograde cerebral perfusion (RCP). During the past decade and after several experimental studies, RCP lost its previous place in the armamentarium of brain protection, giving it up to ACP as a major method of brain perfusion during HCA. HCA should be applied at a temperature of  $\approx 20^{\circ}\text{C}$  with long-lasting cooling and rewarming and should not exceed by itself the time of 20–25 min. RCP does not seem to prolong safe brain-ischemia time beyond 30 min, but it appears to enhance cerebral hypothermia by its massive concentration inside the brain vein sinuses. HCA combined with ACP, however, could prolong safe brain-ischemia time up to 80 min. Cold ACP at  $10^{\circ}\text{--}13^{\circ}\text{C}$  should be initially applied through the right subclavian or axillary artery and continued bihemispherically through the left common carotid artery at first and later the anastomosed graft, with a mean perfusion pressure of 40–70 mm Hg. The safety of temporary perfusion is being confirmed by the meticulous monitoring of brain perfusion through internal jugular bulb  $\text{O}_2$  saturation, electroencephalogram, and transcranial comparative Doppler velocity of the middle cerebral arteries. (*Ann Thorac Cardiovasc Surg* 2008; 14: 138–148)

**Key words:** aortic arch surgery, hypothermic circulatory arrest, cerebral perfusion, neurological injury, cerebral protection

## Introduction

Despite recent advances in surgical techniques and cerebral protection methodologies, brain injury in the form of temporary or permanent neurological dysfunction (TND and PND) remains the major cause of morbidity

and mortality following aortic arch surgery.<sup>1–4)</sup> Three are the basic established techniques and perfusion strategies during aortic arch replacement: hypothermic circulatory arrest (HCA), antegrade cerebral perfusion (ACP), and retrograde cerebral perfusion (RCP). Although 10 years ago the vast majority of surgeons tended to use RCP, nowadays only 15%–20% of them continue to practice this method, and only under certain circumstances.<sup>5)</sup> Many experimental and clinical studies have contributed to this swift change, which showed that RCP finally offers only a trivial amount of perfused volume in the brain capillaries, and thus its main benefit is brain hypothermia.<sup>6–8)</sup> Also during those 10 years, clinical studies have failed to show

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any benefit of RCP whatsoever in comparison to HCA regarding brain metabolic improvement and neurological or neuropsychological outcomes.<sup>9–11)</sup> However, some authors persist that this trivial brain flow of RCP (10%–20% of the perfused blood) meets the metabolic demands during deep hypothermic conditions, enhances corporeal hypothermia, and also may decrease neural intracellular acidosis.<sup>12–14)</sup> Nevertheless, regardless of any of formerly practiced cerebral protection methods, specific criteria for the sites of perfusion, volume, pressure, and temperature of perfusate have not yet been uniformly established. There is a wide variation concerning the details of these methods, and in our opinion it results to noncomparable outcomes among institutions. Operative mortality for aortic arch replacement has ranged from 6% to 23%, the incidence of PND from 2% to 16%, and the incidence of TND from 5.6% to 37.9%.<sup>1,2,12,15–23)</sup> Therefore a standard application method for all of the three protective methods is very crucial, at least for early results. Here we will try to present the most popular strategies concerning cerebral protection and their possible contributions to brain protection according to recent views.

## A. Methodology of HCA

### A1. The safest arterial cannulation

The possible sites of cannulation in aortic arch surgery are either the femoral or the axillary (subclavian) artery. The first has been used for quite a long time and is related to severe complications because of the malperfusion of cerebral or abdominal organs, especially in cases of aortic dissection.<sup>24,25)</sup> Recent comparative (but nonrandomized) studies have shown that the axillary artery's cannulation obtains improved results concerning various neurological outcomes.<sup>26–28)</sup> However, some authors still tend to use femoral cannulation and consider it as a “first choice” in terms of safety, even for patients with aortic dissection.<sup>29)</sup> The use of axillary cannulation for an application of HCA bears the advantages of avoiding peripheral arteriopathy and of being able to use the same cannula later for ACP.<sup>30–32)</sup> On the contrary, the use of suitable femoral cannulation is safe and indicated in all but acute dissection cases and in cases in which the surgeon wishes to apply a lower body, or “thoraco-abdominal” hypothermic perfusion, combined with ACP.<sup>33,34)</sup>

### A2. Final systemic temperature

The application of systemic hypothermia has two goals: first to protect all the organs by reducing metabolic rate,

and second to protect the brain and the heart from any undesirable rewarming during HCA. Although the cerebral blood flow can safely be interrupted for only 4–5 min at 37°C, at lower temperatures such time is inversely proportionally prolonged. The final temperature widely varies among different institutions, from 28( to 10(C. Since 1990, Bachet et al.<sup>18)</sup> have proposed the use of a higher temperature hypothermia of 25°–28°C to avoid the harmful results of deep hypothermia. Kazui's “school,”<sup>24)</sup> and more recently most of the European centers,<sup>20,23,30)</sup> has supported the latter by coming up with great neurological outcomes. To the contrary, however, most surgeons of the “American school” of Griep-Coselli still insist on a deep-cold hypothermia of 10°–13°C,<sup>5,6,13,35–37)</sup> which Griep introduced in 1975, and it offers excellent neurological results. Experimental studies by the use of hemodynamic cerebral parameters, indices of brain metabolism, and postoperative behavioral tests showed that brain perfusion at 10°–15°C offers significantly better protection versus that of 20°–25°C.<sup>38)</sup> Differences between these two “schools” focus mostly on the mode of cerebral perfusion (antegrade or retrograde) and on perfusate temperature. Some authors maintain a higher systemic temperature of 25°–28°C while they are perfusing the brain antegradely with perfusate at a temperature of 6°–12°C.<sup>18)</sup> Other authors have showed that with systemic hypothermia of 22° to 26°C and simultaneous application of ACP, the incidence of TND, even in emergency cases, did not exceed that of 5%.<sup>23,30)</sup> Griep suggests an application of HCA at an esophageal temperature of 10° to 13°C,<sup>35)</sup> but Safi does not unless an electroencephalogram (EEG) silence had been obtained because he considered isoelectric EEG the end point denoting maximum suppression of neurological activity as a result of hypothermia.<sup>36)</sup> Coselli applied HCA at an even lower systemic temperature of 8°–12°C in combination with RCP's perfusate of 8°–10°C, and the reported incidence of PND and TND does not exceed 3%–5%.<sup>37)</sup>

### A3. “Safe” duration of HCA

A “safe” duration of circulatory arrest depends on the final temperature of the brain and its constant restoration by avoiding any undesirable rewarming. McCullough et al.<sup>39)</sup> showed, that the predicted safe duration of HCA at 15°C is only 29 min and at 10°C about 40 min. Experimental studies showed that the cerebral tissue PO<sub>2</sub> was decreased to almost zero after 30 min of circulatory arrest, and after the onset of rewarming, a significant delay in the return of cerebral tissue PO<sub>2</sub> to baseline levels was

observed.<sup>40,41)</sup> Clinical studies have shown a persistent loss of cognitive function (lasting more than 6 weeks) and deterioration in postoperative cognitive scoring-testing in patients who underwent aortic arch surgery by using HCA for more than 25 min at 10°C.<sup>2)</sup> According to this, it is obvious that a “safe” duration of HCA at a higher systemic temperature should be much shorter. Indeed, Fleck *et al.*<sup>21)</sup> showed that the incidence of TND was 14% for HCA time of less than 30 min and about 38% for HCA time of more than 40 min. However, Kouchoukos *et al.* have claimed that HCA at a systemic temperature of 12°–18°C is probably safe for 45–60 min in most patients.<sup>42,43)</sup>

A useful method to decrease HCA-time is to use it intermittently and in combination with hypothermic cardiopulmonary bypass (CPB). It has been shown that mortality by using HCA alone at 14°–18°C is fivefold higher than that of operated patients under hypothermic CPB at 22°–26°C plus intermittent short time (<15 min) HCA.<sup>44)</sup> A clinical study showed the significantly higher “neurotoxicity” of HCA versus CPB at the same temperature (15°C) by evaluating the changes of the serum levels of S-100β.<sup>45)</sup> They observed significant higher indexes in the group of HCA, significantly correlated only with HCA time. Another alternative method to extend the “safe” time of HCA consists of applying HCA intermittently with low-flow (“trickle”) CPB along with ice packing of the head. An experimental study of a combination of head ice packing with low-flow (“trickle”) CPB to protect the brain showed (a) that HCA caused an impairment of cerebral metabolism, directly proportional to its duration; (b) a significant recovery of metabolic function (improving >50%) in the group with head ice packing; (c) a “trickle” of a CPB of only 5–10 ml/kg/min during deep hypothermia is superior to an HCA application at the same temperature; (d) in spite of cooling at 18°C for 30 min, the brain requirements for O<sub>2</sub> persist at high levels, just even before HCA begins.<sup>46)</sup>

Kouchoukos proposed at the first RCP application to construct the “graft-to-arch” anastomosis, followed by ACP application, to decrease HCA time.<sup>42)</sup> On the same basis, Rokkas and Kouchoukos introduced the “arch-first technique” by which they first do the anastomosis of a graft to the aortic arch, and just after and directly through the graft they antegrately perfuse the brain at a systematic temperature of 20°C.<sup>47)</sup>

#### A4. Methodology of cooling and rewarming

The cooling phase should be gradual, scrupulous, thorough, and long enough to obtain a homogenous alloca-

tion of blood to the various organs.<sup>6,48)</sup> A second reason for this is to prevent a gradual up drift of temperature during HCA.<sup>35)</sup> For a final bladder and esophageal temperature of 10°–13°C, cooling should last at least 30 min,<sup>35)</sup> or even more than 50 min.<sup>48)</sup> During cooling, pump flow should be restored at levels of 2.2–2.4 L/min/m<sup>2</sup> with a “temperature gradient” (blood-nasopharyngeal) not exceeding 7°C<sup>48)</sup> or 10°C.<sup>6,35)</sup> After the reinstatement of CPB, some surgeons utilize a short period of 5 min with hypothermic reperfusion at 15°C to attenuate neural injury.<sup>49)</sup> The rewarming phase should also be gradual with blood temperature not exceeding 10°C gradient<sup>6,35)</sup> so as to avoid a possibly catastrophic cerebral vasoconstriction<sup>50)</sup> or an abrupt increase of oxygen demand/supply ratio of the brain.<sup>35,48)</sup> Ehrlich *et al.* experimentally showed that direct rewarming after HCA at 20°C contributed to a significant higher intracranial pressure and a higher degree of brain edema in comparison to cold reperfusion at 15°C for 20 min, followed by rewarming.<sup>49)</sup>

The final temperature at the termination of rewarming after HCA seems to be a significant factor.<sup>48)</sup> Most authors propose a final nasopharyngeal temperature not above 36°C, and rewarming should be discontinued when the patient reaches 35°C (or when the bladder temperature is at 30° to 32°C).<sup>6)</sup> Harrington *et al.* suggested perfusing and rewarming of the patient for 10–20 min after nasopharyngeal temperature reached 36.5°C.<sup>48)</sup>

According to the appropriate levels of hematocrit during pre-, and post-HCA CPB, most authors agree that it should range from 22% to 30%, with a proportional relationship to the core temperature. During deep hypothermia, blood viscosity increases, and only if hematocrit is decreased will a sufficient flow be obtained in the brain capillaries.<sup>48)</sup>

#### A5. Topical (head) cooling

During HCA, a gradual undesirable rewarming of the brain should be prevented by the low body temperature of arrest (10°–13°C) as well as by the packing of the head in ice.<sup>6,35,50,51)</sup> An experimental study has shown that a recovery of the metabolic function is more than 50% improved in the group with their heads packed in ice in comparison to those that are not.<sup>46)</sup>

Systems of continuous cooling of the head during HCA have recently been developed. They consist of a cooling cap and an incorporated circuit of continuously circulated water at a desirable temperature.<sup>52)</sup>

#### A6. Monitoring during HCA

The usual monitoring during HCA includes temperature, EEG, somatosensory-evoked potentials (SEPs), and oxygen saturation of the jugular venous bulb (SvO<sub>2</sub>).<sup>6,35</sup> Most anesthesiologists consider SvO<sub>2</sub> the key for safe and plain monitoring of aortic arch surgery. The use of a retrograde jugular bulb cannula to monitor brain temperature and transcranial oxygen saturation through SvO<sub>2</sub> measurement also represents a very useful tool.<sup>48</sup> It should exceed the level of 95% so that maximal metabolic suppression will be confirmed, since continuous oxygen extraction is an index of significant ongoing cerebral metabolic activity.<sup>6,35,38,53–55</sup> Some surgeons consider EEG an absolutely necessary application at circulatory arrest because it actually represents neural-cell “arrest.”<sup>12,36,37</sup> Others do not believe so because in some cases of EEG silence, the SvO<sub>2</sub> of the venous bulb was observed to be low.<sup>6,38,41,53</sup> Coselli et al.<sup>56</sup> showed that none of the temperatures from a single site or from a combination of sites consistently predicted EEG silence. It occurred within a wide range: for nasopharyngeal from 10° to 24°C, for esophageal from 7.2° to 23°C, and for rectal from 12.8° to 28.6°C. According to Spielfogel et al.,<sup>6</sup> the routine use of SEPs is indicated only for a replacement of distal aortic arch as well as for a significant portion of the descending aorta, and not for the proximal aortic arch. In contrast, others consider it as a useful tool to determine the optimal level of induction of arrest.<sup>57</sup> Another indication of SEPs, in our opinion, could be the cases of aortic arch replacement just by using lower-body temperatures above of 20°–22°C, which may produce spinal cord ischemia after a long HCA time. Bachet acknowledged this potential risk if HCA-time exceeds 30 min.<sup>58</sup> Some studies used perioperative S-100β serum levels to estimate the severity of neurological injury during aortic arch replacement. They observed (a) a significantly greater increase of levels after HCA than after CPB at the same temperature;<sup>45</sup> (b) levels related to HCA time, but not to CPB-time;<sup>45</sup> (c) normal levels after 24 h following CPB, and after 48 h following HCA;<sup>45</sup> (d) in patients with persistent or high levels after HCA (>6 μg/L), a neurological injury was frequently expected;<sup>59</sup> and (e) no significant differences between groups with adjunctive methods of brain perfusion (ACP or RCP) during HCA.<sup>60,61</sup>

## B. Methodology of ACP

### B1. Temperature of perfusate

The aim of ACP during HCA concerning brain protection is to keep the brain’s metabolic waste away during

ischemia, to meet the demands of brain metabolism, and to restore brain temperature at selected levels. Most authors mention that the temperatures of perfusate in use are kept from 10° to 13°C.<sup>23,30,31,35,58,61</sup> Even Bachet et al.,<sup>18</sup> who applied HCA at 25°–28°C, perfused the brain at 6° to 12°C. Some others suggest applications of HCA and ACP, both at a temperature of 15°C.<sup>42,43,48,62</sup> In spite of this, Kazui’s “school” has recently proposed the adoption of a higher perfusion temperature, just 2°–3°C less than systemic, namely, at 20°–22°C.<sup>3,4,6,20,22,23,30,63,64</sup> Plenty of comparative experimental studies have contributed to this confusion, which showed completely different results. Strauch et al.<sup>38</sup> indicated that brain metabolism and neurological outcomes after ACP with perfusate at 10°–15°C is significantly better than that of 20°–25°C. In contrast, another comparative experimental study in the same model species showed that during 120 min of HCA at 20°C, ACP at 20°C has offered better brain protection than that at 10° or at 30°C.<sup>65</sup>

### B2. Flow and pressure of perfusate

There is an enormous differentiation among institutions concerning the pressures and flows of infusion, as well as the route of ACP application. The absence of corresponding experimental studies, differentiation in observations from monitoring, variation in routes of perfusion, and applied systemic temperatures are some of the major causes for that. For most authors, the basic criterion of sufficient perfusion flow to the brain is a restoration of mean right radial pressure (during ACP), 40–70 mm Hg,<sup>20,22,23,33,66,67</sup> or 60–70 mm Hg directly in the carotid arteries.<sup>18</sup> Kazui et al. introduced the arbitrary flow of 10 mL/kg/min as a threshold for ACP, aiming to obtain a right radial pressure above 40 mm Hg<sup>4,5,68,69</sup> by using a single pump and cannulation of all three arch branches<sup>70</sup>—a method later adopted by many centers.<sup>3,20,22,23,33,66</sup> Under these circumstances, optimal flow ranges from 600–1,000 mL/min.<sup>3,6,67</sup> Only Bachet’s<sup>18,69</sup> and Numata’s<sup>68</sup> groups applied cerebral perfusion flow in lower levels: 250–350 and 500 mL/min, respectively. Both reported “acceptable” (because of high applied temperatures) incidences of neurological complications. Numata et al.<sup>68</sup> reported an incidence of TND 5.8%, and Bachet et al.<sup>18</sup> of 9.3%, and 96.5% of their patients showed signs of normal awakening within the first 8 h after operation. It is remarkable that when ACP is hemispheric (through the right subclavian or innominate artery), flow is much lower than that of bihemispheric (plus through the left common carotid artery) perfusion.

Dossche et al.<sup>67)</sup> reported a flow of 400 mL/min in cases of innominate artery perfusion, and 800 mL/min if the left common carotid artery was additionally perfused. In case of even “peripheral” cannulation, e.g., of the brachial artery, measured flow is even lower: 500–600 or 8–10 mL/kg/min.<sup>66)</sup>

### **B3. Hemispheric or bihemispheric perfusion**

Until around 1998, ACP had been “selective,” that is, through a direct cannulation of at least 2 out of 3 arch vessels.<sup>71–75)</sup> This “bihemispheric” perfusion was considered more effective because it overcame the anomalies of Willis’s circle.<sup>58,66,69,73)</sup> In 1998, Byrne et al. proposed the “nonselective” cerebral perfusion by using the right axillary artery as a route for ACP during HCA. In their opinion, it was safe, less time-consuming, and it avoided complications as a result of maneuvers for the selective cannulation of aortic arch branches.<sup>76)</sup>

Dossche et al.<sup>67)</sup> showed in a nonrandomized study that concerning the early outcomes of hemispheric and bihemispheric ACP: (a) there were no differences regarding the neurological complications, but a significant favorable impact of the bihemispheric ACP on hospital mortality did appear; (b) in 8% of their patients, Willis’s circle was incomplete or absent, and in those patients, left-hemispheric perfusion was put at risk. They suggested an application of a deeper systemic hypothermia in cases of hemispheric ACP. However, another clinical study with selective hemispheric ACP through the right axillary artery showed a low incidence of both TND and PND (5.8 and 0.8%, respectively).<sup>68)</sup>

The most severe drawback of “hemispheric” ACP application is related to possible abnormalities of Willis’s circle; instead of a normal existence of three “communicating” arteries (1 anterior and 2 posteriors),<sup>66)</sup> one or two of them may be absent in 2% to 15% of patients with consequent ischemia in the other hemisphere during ACP.<sup>67,77,78)</sup> For that reason, “hemispheric” ACP through the right subclavian or axillary artery, should be supplemented with synchronous left common artery perfusion.<sup>67,68,77)</sup> In spite of this, “hemispheric” perfusion in a few patients through an even peripheral artery, like the right brachial artery, showed no neurological postoperative dysfunction. However, they observed a significant reduction of blood flow of the left middle cerebral artery in comparison to the right.<sup>66)</sup> Another study<sup>79)</sup> reported the same observation for the left hemispheric circulation during the right axillary artery perfusion. However, the reported incidence of PND and TND in this and other

studies<sup>80,81)</sup> were similarly low (1.3% and 4.8%, respectively).

During “hemispheric” or “bihemispheric” ACP, the left subclavian artery is to be occluded using a Fogarty catheter or a clamp to avoid steal phenomenon from this vessel.<sup>4,18,20,23,33,61,67)</sup> Others preferred to routinely supplementally perfuse this vessel as well.<sup>22,60,82)</sup> The supplemental occasional perfusion of the left subclavian artery is indicated in the following cases: (a) if the right vertebral artery is occluded or has severe atherosclerotic lesions;<sup>63)</sup> (b) if we know or suspect a lack of normal transhemispheric communication (e.g., indices from monitoring);<sup>31,63)</sup> (c) if we know that the left vertebral artery is dominant;<sup>61,63)</sup> and in our opinion, (d) if there are indications of carotid artery disease (history of TIAs, stroke, or operation).

### **B4. Monitoring of ACP**

The classical monitoring of ACP should be based on the bilateral pressure measurement of the right radial artery and also the left common carotid artery pressures, independent of “hemispheric” or “bihemispheric” perfusion. This pressure should be restored to from 40 to 60 mm Hg<sup>4,6,18,20,33,63,67)</sup> and should not exceed an upper limit of 70 mm Hg so as to avoid brain edema.<sup>6,20,23,41)</sup> According to Harrington et al.,<sup>48)</sup> in case of axillary cannulation, radial artery pressure for technical reasons does not necessarily correlate with carotid artery pressure, and a cannula pressure or a direct right carotid artery pressure is required. Some authors consider the mean pressure of a superficial temporal artery more reliable and restore it at the same previously mentioned levels.<sup>61,80)</sup>

Bilateral transcranial Doppler is another useful tool for the blood velocity measurement of the middle cerebral artery, especially in cases of “hemispheric” perfusion.<sup>23,70,66,67)</sup> A 2.5 MHz pulse ultrasonography transducer is bilaterally positioned over the temporal “sound window” for comparative continuously measurement of blood velocity of the middle cerebral artery.<sup>64)</sup>

Serial internal jugular bulb venous oxygen saturation is an essential index concerning brain metabolism. It should be restored constantly above 95%.<sup>5,6,35,65)</sup> The transcranial Doppler oximeter by means of a near-infrared spectroscopy (NIRS, Somanetics, or INVOS) is a reliable tool for an estimation of left hemispheric perfusion.<sup>5,23,35,48,65)</sup>

Two-channel serial EEG is mainly useful for an induction of HCA (with the advent of EEG-silence),<sup>12,37,56)</sup> and not for confirmation of sufficient contralateral flow

in the case of “hemispheric” perfusion. However, it is still indicated by some authors.<sup>23)</sup>

The control of acid-base derangements by using an Alpha-stat method of pH control is preferable and advantageous for adults.<sup>48,59,60)</sup> Its use allows the pH to change with a gradual reduction of temperature as the buffering capacity for H<sup>+</sup> increases, resulting in a mild alkalosis.<sup>48)</sup> In contrast, the control of acid-base balance by using the pH-stat method restores pH derangement by adding CO<sub>2</sub>, which on one hand causes beneficial cerebral vasodilation,<sup>81)</sup> but on the other, it may increase cerebral edema and cause microembolization.<sup>48)</sup>

## C. Methodology of RCP

### C1. Temperature of perfusate

Unlike the case of ACP, in which there is a wide differentiation on temperatures of perfusate, in the case of RCP, what is uniformly used is 10°–12°C.<sup>15,36,58,84)</sup> This low temperature is of very crucial importance for brain protection, especially in the case of RCP, because studies have shown that enhanced cranial hypothermia, which is obtained by RCP, is beneficial to the brain.<sup>8)</sup> This indirect blessing from enhanced cooling was attributed to a reperfusion of nonbrain capillaries and to venoarterial and venovenous shunting.<sup>6,7)</sup> However, a final temperature of brain lower than 10°C is to be avoided because it may be associated with brain damage.<sup>39)</sup>

### C2. Pressures and flows of perfusate

Like ACP, applied pressures and flows of RCP present slight variations among institutions. Ueda, who introduced the method, recommends a pressure of infusion not above 20–25 mm Hg in order to avoid brain edema.<sup>39,85)</sup> Indeed, experimental studies have shown that perfusion pressure of 20 mmHg can restore higher levels of neural ATP and lower levels of lactate and cerebral water content.<sup>86)</sup> In contrast, RCP with pressure above 25 mm Hg resulted in a high increase of the cerebrospinal fluid pressure and therefore in brain edema.<sup>87,88)</sup> Even though most authors have followed these guidelines,<sup>13,19,26,37,59,89,90)</sup> others recommend high pressures, around 25 to 35 mmHg<sup>61)</sup> or even higher, such as 40 mm Hg.<sup>39)</sup> The basic arguments of restoring higher infusion pressure (20–25 mm Hg) and flows, are the following: (a) according to cadaveric studies, 88%–100% of human beings bear valves in the internal jugular vein, at the venous angle, or at the jugular-subclavian junction.<sup>91,92)</sup> Fortunately, only in 10%–20% of these cases the valves are resistant to retrograde perfu-

sion of the brain, even at pressures of 70 mm Hg.<sup>91)</sup> It is noteworthy that retrograde flow through the superior vena cava of cadavers varied widely from 0 to 2,500 mL/min: 0 mL/min in 4 of 7 cases, 6 mL/min in 1 of 7 cases, 340 mL/min in 1 of 7 cases, and 2,500 mL/min in 1 of 7 cases.<sup>91)</sup> (b) Most (80% to 90%) of the infused through superior vena cava blood flow are finally deviated through the azygos and other collateral veins (veins of the head, neck, thoracic wall, and upper extremities) to the inferior vena cava (IVC).<sup>7,87)</sup> (c) A large amount of infused blood is entrapped in the cerebral sinus, and only a trivial amount, just 3% met the brain capillaries,<sup>88)</sup> or less than 10% or even 13% of RCP inflow returned to the aortic arch vessels.<sup>7,93)</sup> For these reasons and despite any limitations of the above experimental studies (there are many anatomical and physiological differences in cerebral circulation among humans and animals), some prefer to adjust the flow rates of infused blood to maintain desirable average superior vena cava pressure, which corresponds to median flow rates, 100–500 mL/min.<sup>6,15,21)</sup> Initially, the flow required may be of the highest levels; however, once the venous capacitance vessels have been filled, a flow of lower levels is usually sufficient to maintain infusion pressure at desirable levels and to avoid brain edema.<sup>47)</sup>

### C3. Occlusion of the azygos vein and/or of the IVC

Concerning the mode of infusion and according to all the above, during RCP a temporary snaring of superior vena cava around the catheter is indicated to partially keep out the deviation of blood into the IVC.<sup>60,85,86,94)</sup> A temporary occlusion of IVC for the same reason during RCP is contraindicated because studies have shown that this occlusion causes massive fluid sequestration, massive brain edema, and therefore major histopathological injury in the brain.<sup>95,96)</sup>

## D. Separated or en block arch anastomosis

Kazui et al.<sup>4,65,71,75)</sup> and others<sup>3,23,80)</sup> prefer the separated anastomotic technique of 3 aortic arch branches with branched graft, and they consider it advantageous for the following reasons: (a) possible atherosclerotic lesions of the region can be excluded; (b) in case of dissection, repair is constructed at the intact tissue of each branch; (c) the risk of local recurrence is minimized because the diseased aortic wall is completely resected; and (d) possible anastomotic bleeding is easily controlled. On the other hand, this time-consuming method requires about 80 ±

32 min mean ACP time,<sup>4,65</sup>) or  $127 \pm 52$  min,<sup>22</sup>) in comparison to the “en block” anastomosis method, which needs a much shorter time: less than 30 min,<sup>47</sup>)  $32 \pm 15$  min,<sup>38</sup>)  $34 \pm 13$  min,<sup>59</sup>)  $29 \pm 2$ – $36 \pm 2$ ,<sup>13,37</sup>) or (even in aortic dissection)  $41 \pm 16$  min.<sup>97</sup>)

## E. Pharmaceutical manipulations

Unfortunately, until today there has been no pharmacological medication to reliably protect the ischemic brain.<sup>48</sup>) However, Svensson et al.,<sup>60</sup>) and also Dorotta et al.,<sup>98</sup>) have reported some “possibly beneficial neuroprotective” medication by

(a) thiopental (protection of neural membrane, neurocognitive improvement) 5 mg/kg, 5 minutes before induction of arrest,<sup>48,60</sup>)

(b) lidocaine (protection of neural membrane, neurocognitive improvement) 200 mg, just before the arrest’s application,<sup>60</sup>)

(c) magnesium sulphate (protection of neural membrane), 2 g simultaneously with lidocaine infusion,<sup>60</sup>)

(d) mannitol (reducing oedema), 25 g into the prime, and 12.5 g given intravenously after the termination of circulatory arrest,<sup>48,60</sup>)

(e) aprotinin (anti-inflammatory, reducing the modulation of embolic load, reducing bleeding),  $2\text{--}4 \times 10^6$  before CPB,<sup>98</sup>)

(f) steroids membrane stabilization,<sup>98</sup>) but neurohyperglycemia and increased neural ischemia,<sup>48,60</sup>) 30 mg/kg before CPB,

(g) b-blockers (improving neurocognitive deficit),<sup>98</sup>) and

(h) acadesine (reducing stroke rate).<sup>98</sup>)

## F. Conclusions—guidelines

Aortic arch surgery has developed dramatically in the past 30 years so that currently it may be performed with acceptable mortality and morbidity rate. Experimental research has contributed to the understanding of pathophysiological mechanisms of brain ischemia and reperfusion, and advances in the technical means of monitoring have improved surgical methods for brain protection. Although there are not yet guidelines for aortic arch surgery in specific or aortic surgery in general, we still retain satisfactory knowledge on the principles of these operations. The key points of the methodology of aortic arch surgery can be summarized in the following:

(a) The establishment of right subclavian or right axil-

lary artery as a routine regarding arterial cannulation (especially in aortic dissection). It will be used later as a route for ACP.

(b) The cornerstone of aortic arch surgery is an application of HCA. It should be applied at a final temperature of  $\leq 20^\circ\text{C}$  with a long cooling time of  $\geq 30$  min (and until 50 min, depending on the final body’s temperature), and with a stable jugular bulb oxygen saturation of  $>95\%$ . The drifting of temperature should be gradual, avoiding differential temperature (esophageal-blood) gradient of  $>10^\circ\text{C}$ . Rewarming should be also gradual, lasting at least 20–30 min and with a gradient of temperature  $<10^\circ\text{C}$ .

(c) Ice packing of the head is a very important means of deep brain hypothermia restoration, to prevent its undesirable rewarming.

(d) The HCA time in sole application should not exceed 20–25 min. In every case with expected HCA time  $>25$  min, ACP or RCP supplement should be performed.

(e) The establishment of ACP as a standard method of brain perfusion during HCA. Its flow should begin at 10 mL/kg/min and adjust to obtain a perfusion pressure from 40–60 mm Hg. The route of perfusion may be through the axillary or subclavian artery alone in the case of “hemispheric” cerebral perfusion, or through the left common carotid artery in the choice of “bihemispheric” perfusion. The mode of perfusion is to be bihemispheric, according to transcranial Doppler indices in every patient.

(f) The temperature of cerebral perfusate should be restored at  $10^\circ\text{--}13^\circ\text{C}$ .

(g) The “first-arch technique” with “en block” branch anastomosis (whenever possible), followed by direct ACP through the graft, should be the method of choice for a drastic shortening of HCA-time.

(h) Continuous jugular bulb SvO<sub>2</sub>, EEG-silence, right and left radial artery pressure, and the transcranial Doppler for middle cerebral artery velocity during ACP should be used in combination for monitoring.

(i) For the supporters of RCP, the temperature of perfusate should be at  $10^\circ\text{--}12^\circ\text{C}$ , and the flow should be adjusted to achieve a superior vena cava pressure achieving 20–25 mm Hg, or a flow of 100–500 mL/min. For that adjunctive protection, keep in mind that the safe prolongation of HCA time is not more than 30 min.

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