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European Journal of Cardio-thoracic Surgery 38 (2010) 46—51
EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY
www.elsevier.com/locate/ejcts

Antegrade cerebral protection in thoracic aortic surgery: lessons from the past decade☆

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Received 15 October 2009; received in revised form 2 January 2010; accepted 6 January 2010; Available online 24 February 2010

Abstract

Objective: Prolonged deep hypothermic circulatory arrest (DHCA) adversely affects outcome and quality of life in thoracic aortic surgery. Several techniques of antegrade cerebral perfusion are routinely used: bilateral selective antegrade cerebral protection (SACP) by introducing catheters in the innominate and left carotid artery, unilateral perfusion through the right axillary antegrade cerebral perfusion (RAACP) or a combination of right axillary perfusion with an additional catheter in the left carotid artery (RAACCP), resulting also in bilateral perfusion. The aim of the present study was to analyse the impact of the different approaches on the quality of life (QoL). **Methods:** The data of 292 patients who underwent surgery of the thoracic aorta using DHCA at our hospital between January 2004 and December 2007 have been analysed and a follow-up was performed focussing on QoL, assessed with the Short Form-36 Health Survey Questionnaire (SF-36). Results were analysed according to the type of cerebral perfusion and the duration of DHCA. **Results:** Patients' characteristics were similar in all groups. Of the total, 3.4% patients underwent DHCA (average 8.3 $\pm$ 6.4 min) without ACP, 45.9% underwent SACP (average DHCA of 15.6 $\pm$ 7.1 min), 40.4% had RAACP (average DHCA of 28.1 $\pm$ 11.6 min) and 9.4% bilateral perfusion (RAACCP) (average DHCA of 43.1 $\pm$ 16.7 min). The average follow-up was 23.2 $\pm$ 15.1 months. QoL was preserved in all groups. For DHCA above 40 min, bilateral ACP provides superior midterm QoL than unilateral RAACP (average SF-36 95.1 $\pm$ 44.4 vs 87.6 $\pm$ 31.3; $p = 0.072$). **Conclusions:** When midterm QoL is assessed, bilateral SACP provides the best cerebral protection for prolonged DHCA (>40 min).

Keywords: Cerebral perfusion; Aortic surgery; DHCA; Quality of life

1. Introduction

The use of hypothermic circulatory arrest (HCA) has been established as a standard step for patients who require a surgical repair of the aortic arch and for those undergoing surgery because of acute aortic dissection type A (AADA). The neurological outcome as well as the recovery of subtle neurocognitive deficits after a period of circulatory arrest is of great interest [1]. It has been shown that cerebral oxygen metabolic rate of the brain is still around 25% at 20 °C body temperature; however, at this temperature level, a circulatory arrest up to 20 min is still safe [2,3]. Antegrade cerebral perfusion (ACP) allowed to safely prolong the duration of HCA [4]. During the past years, different strategies of delivering ACP were used in our department:

1. selective antegrade cerebral perfusion (SACP) through thin perfusion catheters introduced in the innominate and left carotid artery,
2. antegrade perfusion through the cannula placed into the right axillary artery for arterial return during cardiopulmonary bypass (CPB) [5–7], allowing unilateral flow only (RAACP), and
3. combined perfusion through the right axillary cannula with an additional catheter in the left carotid artery (RAACCP).

To provide adequate perfusion to both hemispheres during ACP via the right carotid artery only (during RAACP), the circle of Willis has to be competent. Autopsy study estimates the circle of Willis to be insufficient in about 15% of patients [8,9]. The aim of this study was to assess the impact of these different strategies of ACP on outcome and midterm quality of life (QoL).

2. Patients and methods

Between January 2004 and December 2007, a total of 292 consecutive patients underwent surgery on the ascending aorta or the aortic arch requiring deep hypothermic circulatory arrest (DHCA) at our institution. All in-hospital

☆ Presented at the 23rd Annual Meeting of the European Association for Cardio-thoracic Surgery, Vienna, Austria, October 18–21, 2009.

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doi:10.1016/j.ejcts.2010.01.016

Table 1
Patient characteristics.

	Group A (without ACP)	Group B (SACP)	Group C (RAACP)	Group D (RAACCP)	*p* value
Demographics					
Patients (%)	12	133	118	29	
Age (years)	67.9 ± 75	64 ± 11	62.5 ± 10	65 ± 10	0.209
Male (%)	8 (67%)	86 (65%)	87 (74%)	23 (79%)	1.0
Preoperative data					
Type A dissection	4 (33%)	16(12%)	69 (58%)	22 (75%)	0.001
Intra-operative data					
Composite graft	6 (75%)	64 (31%)	47 (40%)	10 (34%)	0.081
Operation time (min)	258 ± 46	215 ± 58	256 ± 85	291 ± 91	<0.001
ECC time	142 ± 34	130 ± 47	150 ± 47	173 ± 64	<0.001
DHCA time	7.3 ± 2.3	15.6 ± 7.1	28 ± 11.6	43 ± 16.7	<0.001
Outcome data					
Mortality	1 (8.3%)	4 (3%)	5 (4.2%)	2 (6.8%)	0.061
CVI					
Persistent	0	8 (6%)	9 (7.6%)	4 (13.7%)	0.057
Transient	2 (16%)	11 (8.2%)	9 (7.6%)	4 (13.7%)	0.372
Length of stay (days)	13.3	10 ± 3	12 ± 5	11 ± 2	0.079

ECC: extracorporeal circulation, DHCA: deep hypothermic circulatory arrest, CVI: cerebrovascular insult.

data were assessed. Mean age was 64 ± 10.6 years, and 204 patients were male (69.8%). A total of 176 patients (60.2%) underwent surgery because of aneurysm of the ascending aorta and/or aortic arch and were operated electively. As many as 111 patients (38%) had emergency surgery because of AADA. The patient characteristics are depicted in Table 1.

A complete follow-up was performed in all patients discharged from the hospital, focussing on the QoL. QoL was assessed using the Short Form-36 Health Survey Questionnaire (SF-36). Details of this validated questionnaire have been published previously [10,11]. The SF-36 consists of 36 short questions reflecting QoL in eight different aspects: bodily pain (abbreviated BP, two items); mental health (MH, five); vitality (VT, four); social functioning (SF, two); general health (GH, five); physical functioning (PF, 10); and role functioning, both emotional (RE, three) and physical (RP, four). Role functioning reflects the impact of emotional and physical disability on work and regular activity (the individual's normal everyday role). Raw points were transformed, generating a score for each dimension ranging from 0 to 100, with 100 reflecting best functioning.

Swedish normal population (n = 8930) scores are used as a standard population for comparison (range, 85—115). Results were compared between the different types of cerebral protection during DHCA.

As the mother tongue of the majority of our patients is German, we used the German version of the SF-36. Among the cases in which the questionnaire was not answered, the majority was explained by language problems as most of the Italian- and many of the French-speaking patients were not able to answer such a questionnaire in a foreign language. However, as we have previously shown, patient characteristics are not different among the different languages [12,13]. Even with the mentioned language problems, 210 patients (72%) correctly filled out the SF-36 questionnaire.

2.1. Surgical procedures

All patients received standard general anaesthesia. All operations were performed through a median sternotomy. The following procedures were carried out: a modified Bentall was performed in 127 patients (43.5%), and supracoronary repair of the ascending aorta was carried out in 165 patients (56.5%). In all patients of this study, the distal anastomosis was performed during a period of circulatory arrest (DHCA) at the level of the proximal arch or as a total arch replacement.

During the cooling phase, the tympanic temperature was closely monitored to achieve symmetrical cooling. The patients were cooled with a maximal temperature gradient of 10 °C to a targeted tympanic temperature of 18 °C. The body core temperature was measured in the urinary bladder and goal temperature was below 24 °C. Topical cooling was applied by covering the head with an ice pack.

Brain regional oxygen saturation was measured using the INVOS® system. The goal was to keep the oxygen saturation above 60% during the circulatory arrest.

DHCA was initialised after administration of 20 mg kg^{-1} pentobarbital 2—3 min prior to the arrest. In 12 patients (4.4%), circulatory arrest was performed without cerebral perfusion.

In all forms of cerebral perfusion, the perfusate was cold (18—20 °C), oxygenated blood. SACP was used in 133 patients (45.5%): balloon-blocked perfusion catheters are placed in the innominate and in the left carotid artery after removing the aortic clamp and the aortic cannula. SACP is performed with oxygenated blood at a pressure of 50—60 mmHg, corresponding to a flow of 250—300 ml min^{-1} (150 ml min^{-1} 1 in each catheter). In 118 patients (40.4%), cannulation for arterial return during CPB was performed directly through the right axillary artery, using an 8F DLP cannula. We did not use cannulation through a side graft. During DHCA, the innominate artery and the left carotid artery are clamped or occluded with a balloon catheter. Perfusion pressure is kept between 50 and 60 mmHg at a flow of 800–1000 ml min^{-1} to compensate the loss through the right mammary artery. Finally, these two techniques were combined in 29 patients (9.9%) in whom the right axillary artery was cannulated and an additional perfusion catheter was placed into the left carotid artery for bilateral perfusion of the brain. The catheter in the left carotid artery delivered a flow of 150 ml min^{-1}, pressure 50–60 mmHg; the flow through the right axillary artery was reduced to 500 ml min^{-1}. We did not routinely clamp the left subclavian artery during circulatory arrest.

The cooling and rewarming protocol remained the same during this study. In the patients assessed during the period of this study, we did not combine cerebral perfusion with moderate hypothermia (26–28 °C). We started this strategy in 2008. The intra-operative data are summarised in Table 1.

Data are presented as mean values ± standard deviation. A Kruskal–Wallis test and a Mann–Whitney test were used for the comparison of the variables. A p value of less than 0.05 was considered significant.

3. Results

The main outcome data are summarised in Table 1. According to the type of cerebral perfusion, patients were divided into four groups: group A (12 patients, 4.4%) without cerebral perfusion, group B (133 patients, 45.5%) with SACP, group C (118 patients, 40.4%) with RAACP and group D (29 patients, 9.9%) with the combination of cerebral perfusion through the right axillary artery cannula and a catheter in the left carotid artery (RAACCP). Among these four groups, there were significantly more patients with an AADA in groups C and D, as the cannulation of the right axillary artery is our obligatory approach in patients with AADA (group A: 33%, group B: 12%, group C: 58% and group D: 75%, $p < 0.001$). The more complex surgical situation in groups C and D is also reflected in the substantial longer duration of DHCA (7 ± 2 min in group A, 15 ± 7 min in group B, 28 ± 11 min in group C and 43 ± 16 min in group D, $p < 0.001$). The difference of pathologies between the groups explains at least partially the differences between overall operation times (258 ± 65 min in group A, 217 ± 66.4 min in group B, 259 ± 80.5 min in group C and 292 ± 91.7 min in group D, $p < 0.001$.) and duration of CPB, which was also significantly different among the four groups ($p < 0.001$).

In-hospital mortality was not significantly different among the four groups: one patient died in group A (8.3%), four patients in group B (3%), five in group C (4.3%) and one died in group D (3.7%) ($p = 0.61$). The incidence of postoperative neurological deficits was higher in group C (7.6%) and group D (17%) than in group B (6%) but this did not reach statistical significance ($p = 0.057$). There was no patient with a persistent neurological deficit in group A. The incidence of transient neurological dysfunction was not significantly different among the four groups. Other complications and length of stay did not show any significant difference ($p = 0.079$).

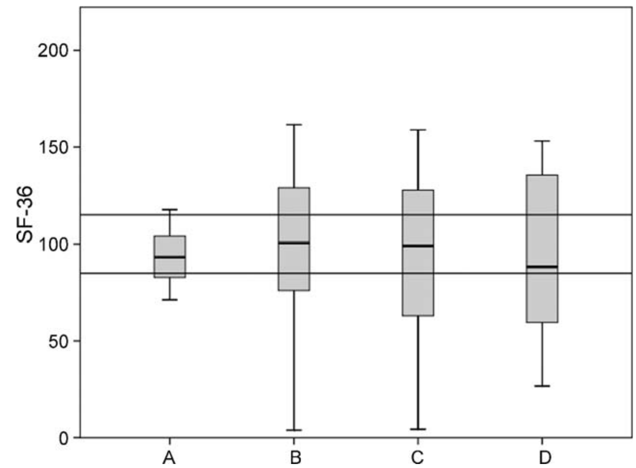

Fig. 1. Average SF-36 scores in group A: DHCA; group B: SACP; group C: RAACP; and group D: RAACCP.

QoL was assessed prospectively after a mean interval of 23.2 ± 15 months following surgery. Average QoL scores were similar in all four groups for a duration of DHCA up to 20 min and were within the reported range of an age- and sex-matched standard population (Fig. 1). In group A, there was no DHCA longer than 20 min and in group B, only four patients had DHCA above 30 min. This reflects the lesser complexity of the surgical procedures, which were performed electively in the large majority of the cases. In groups C and D, a substantial number of patients had DHCA periods of 30–39 min (27 patients in group C (22%)); four patients in group D (17%)) and above 40 min (13 patients in group C (12%); 14 patients in group D (58%)), because of the more complex pathology (greater number of AADA and complete arch repair in these groups). In these patients, QoL was better preserved when the cerebral protection was performed using bilateral perfusion (Fig. 2). In patients who required duration of DHCA over 40 min, the results of the QoL scores still remained comparable to an age- and sex-matched standard population (Fig. 2).

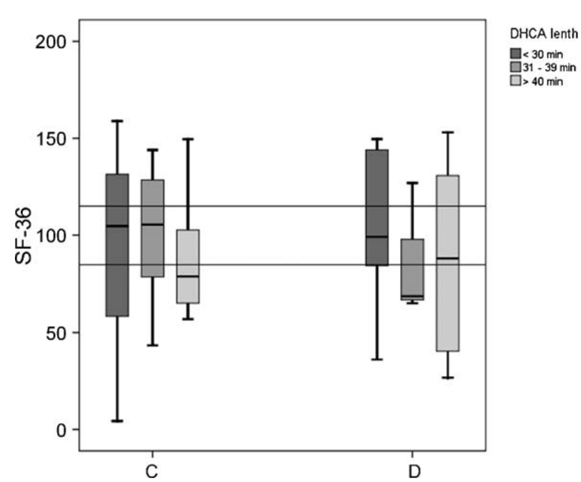

Fig. 2. Average SF-36 scores group C: unilateral compared to group D: bilateral depending on the duration of DHCA.

Subgroup analysis of the eight different aspects of QoL assessed with SF-36 revealed that limitations are mainly found in the aspects of vitality as well as in social and physical function.

4. Comment

The advantage of a HCA during surgical procedures on the ascending and aortic arch surgery is evident, as it allows to perform distal anastomosis in a well-exposed, bloodless surgical field. In AADA, this technique facilitates identification and fixation of the intimal flap using biologic glue and/or pericardial or Teflon strips. Several groups have demonstrated that systemic hypothermia around 20 °C protects the brain during a period of circulatory arrest by reducing the cerebral oxygen metabolic rate [2,3]. However, animal studies have shown that the cerebral metabolic rate at 20 °C is still active at approximately 20% of its normal level. In previous clinical studies, we were able to show that DHCA without cerebral perfusion is safe as long as the period of arrest is not longer than 20 min: in this case, patients had a preserved QoL compared with a standard population [4]. Experiencing above 20 min of DHCA without additional cerebral protection, we reported significantly reduced scores of QoL in the midterm follow-up.

The optimal method for cerebral protection during HCA is still a matter of discussion. Bachet and colleagues reported, as early as in 1999, excellent results with antegrade cold blood perfusion [14] and the Yale group published recently series of patients operated under deep hypothermia as the sole method of brain protection. They found preserved cognitive function after DHCA, but reported an increased stroke rate in patients with long duration (>40 min) of DHCA [15,16]. Regarding the results of previously published studies and based on our own experience, we are convinced that SACP allows to safely extend the period of circulatory arrest [4]. Using porcine models, several groups were able to show a reduced apoptosis rate in the hippocampus and a preserved oxygen tension in the brain during DHCA with ACP [17,18].

ACP is today a well-accepted method to improve neurological and neurocognitive outcome in patients operated under HCA. The technique of arterial return through the right axillary artery (RAACP) during CPB and use of this access for ACP has been first described by Sabik and colleagues in patients who required aortic arch repair [6]. One of the major advantages of RAACP is the fact that fewer manipulations are needed at the level of the aortic arch and the supra-aortic vessels. In one report, this was thought to be one of the explanations for the observed reduction in major neurological complications compared with SACP with balloon-blocked catheters [5]. In the present study, major neurological complications, such as persistent neurological deficits or transient neurological dysfunction (TND), show no significant difference among the four methods of cerebral protection during DHCA. Although the incidence of TND is slightly higher in groups B and D, than in group C, where there is no manipulation of the supra-aortic branches with perfusion catheters. In a previous study, we addressed the importance of TND on postoperative QoL [19]. The introduction of thin perfusion catheters under visual control onto the aortic arch or the supra-aortic vessels can be done easily and without major manipulation. With today's imaging technologies, preoperative assessment of the distal ascending aorta/aortic arch and the anatomy of the supra-aortic vessels allow proper planning of the procedure.

As with many other teams, we found axillary artery cannulation advantageous in AADA. Most often, the right axillary artery is not dissected and CPB can safely be established through this access. We found this strategy less risky than direct cannulation of the ascending aorta or the femoral artery.

This study confirms that different techniques of cerebral perfusion may be performed according to the complexity of the procedure and the expected duration of the circulatory arrest. In elective cases with expected short duration of DHCA (not longer than 15—20 min), deep hypothermia as the sole method of cerebral protection is sufficient, but SACP adds safety if the duration of circulatory arrest is prolonged because of any technical difficulty. In this case, introduction of two catheters in the supra-aortic vessels is simple. In patients with AADA and in those with more complex pathologies of the aortic arch, the duration of circulatory arrest may be expected to be longer. In AADA and in aortic re-do operations, we favour cannulation of the right axillary artery and place an additional catheter in the left carotid artery. Technically speaking, groups B and D in this series do not differ with regard to cerebral perfusion. The reported difference in their outcome is explained by the nature of the patient's presentation. In HCA times below 20 min on the average in group B, it would be very difficult to see an advantage of bilateral versus unilateral ACP. Many groups have published on QoL after surgery on the thoracic aorta with circulatory arrest. One thing, which emerged as a fact, is that the duration of circulatory arrest *per se* is the most important risk factor for an impaired QoL. The importance of the best possible brain protection is therefore best seen in patients with long arrest times — in this study, groups C and D (Fig. 2). Our data confirm the fact that the longer the duration of DHCA, the more do the patients profit from bilateral ACP.

5. Conclusions

Average QoL scores were similar in all groups with different methods of cerebral protection for a duration of DHCA up to 20 min and were within the reported range of an age- and sex-matched standard population. In patients who required a duration of DHCA over 40 min, the results of the QoL scores remained still comparable to an age- and sex-matched standard population as long as bilateral ACP was performed. When QoL is reduced, limitations are mainly found in the aspects of vitality as well as social and physical function. In conclusion, different types of cerebral perfusions protect the brain during circulatory arrest. Careful planning of surgery includes evaluation of the expected complexity at the aortic arch level and the choice of the optimal cerebral protection strategy. This tailored approach warrants adequate cerebral protection and preservation of age-matched QoL.

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Appendix A. Conference discussion

Dr Y. Okita (*Kobe, Japan*): Professor Carrel's group presented the postoperative quality of life of patients who underwent ascending aorta or arch replacement using distal opening technique with various methods of brain protection. A complete follow-up was achieved and all patients' QOL score was analysed using the SF-36 questionnaire. They concluded that bilateral antegrade cerebral perfusion provided a better QOL outcome.

I have several questions with this study. The author included the patients with acute aortic dissection as well as patients who underwent emergency surgery. Acute dissection is quite different from other conditions in terms of urgency or cerebral circulation and so on. Actually, the group who had right axillary artery cannulation had a longer pump time, deeper hypothermic circulatory arrest time, and higher morbidities because three-quarters or a half of this patient group consisted of patients who had acute type A dissection. How are the results going to be if you could exclude these acute aortic syndrome patients?

Dr Krähenbühl: It's absolutely true that there are different pathologies which mix the results a little bit. But we do think that patients with aortic dissection type A are already at a high risk for neurological damage. And in focusing on the outcome in these patients, we think that this protection strategy has been shown to be better.

Dr Okita: Number two, how many patients had ascending aorta replacement only, and how many had a total arch replacement in your study?

Dr Krähenbühl: In acute aortic dissection type A, our strategy is to do as much as is needed for survival of the patient. We do not do total arch replacement in cases of acute aortic dissection type A unless it is really necessary for the survival of the patient. So total arch replacements were not so many in these groups.

Dr Okita: So number three, about the temperature, the authors stated that the target temperature in the deep hypothermic circulatory arrest was at 18 degrees. How about the other patients, is it the same, 18 degrees?

Dr Krähenbühl: All the patients had the same cooling and rewarming protocol during this study. So what we do is we go down to about 20 degrees body temperature and then we perfuse with 18 degrees the brain. So that we did same in all groups, all patients.

Dr Okita: So next question is, the follow-up was completed in all survivors. So when was the SF-36 test done, at the discharge or in the last follow-up? The result of SF-36 has changed as time goes by. Regarding the follow-up, I found a big standard deviation and I wonder if the time duration from surgery to SF-36 varies greatly from patient to patient?

Dr Krähenbühl: No. The patients were discharged and about 1, 1-1/2 years later they receive the SF-36 score. So that was the same in all patients.

Dr Okita: So final question, the authors did not show postoperative CT or MRI images. Usually cerebral images can demonstrate the cause of neurological deficits, such as embolic stroke or watershed hypoperfusion type. Do you have any data or CT scan or MRI?

Dr Krähenbühl: I'm sorry, I didn't understand your question. You want CT scan?

Dr Okita: Yes, postoperative CT scan, MRI, of those who had cerebral insult.

Dr Krähenbühl: To see whether it was ischaemic or bleeding.

Dr Okita: Or embolic.

Dr Krähenbühl: Or embolic. Well, if a patient has neurological damage postoperatively, we perform usually a CT scan to exclude that it's haemorrhage, because this would affect what we would do later on. So we have a CT scan in all patients with neurological dysfunction. We do not regularly do a CT scan in patients only showing delirium or things that, we don't do a CT scan.

Dr A. Lomeo (*Catania, Italy*): We run a similar study and we found a bias, because your test is compared with a normal population and the people we operate on most of the time are not cerebrally normal since they are old and they have atherosclerotic disease. So don't you think that whenever possible it would be a good idea to run the test before the operation and after.

And the second question, how long after the operation did you run the test?

Dr Krähenbühl: First question, you're absolutely right, it would be a perfect, much better message if you could say, okay, the patient was like that before surgery and he was like that, absolutely. It's hard to do in cases of aortic dissection type A. But other than that, you're absolutely right.

And the mean follow-up time was about 20 months. So it was a study which we did in a 5-year period, so we sent them the questionnaire between 1 and 1-1/2 years after the surgery.

Dr C. Hagl (*Hannover, Germany*): I absolutely agree with your conclusions that bilateral perfusion is probably better than unilateral. Why are you not using it routinely? I don't understand why there were patients who were treated exclusively with hypothermic circulatory arrest, others received unilateral, and the remaining bilateral selective perfusion. What were your selection criteria?

Dr Krähenbühl: It's because it was an evolution. In elective cases we always put two catheters, because it doesn't make a difference whether you put one or two, so you do two.

And in cases of dissection, we used axillary artery. And when we started with antegrade cerebral perfusion, we did it with one catheter, and then later on started, yes, it's easy to put another one. So now we do bilateral antegrade perfusion in all our patients.