# Antegrade selective cerebral perfusion and moderate hypothermia in aortic arch surgery: clinical outcomes in elderly patients[†]

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## Abstract

**OBJECTIVES**: To evaluate the outcome in elderly patients (≥75 years) undergoing elective aortic arch surgery with the aid of selective antegrade cerebral perfusion (SACP) and moderate hypothermic circulatory arrest (HCA).

**METHODS**: A series of 95 patients ≥75 years (median age 77 years, median EuroSCORE 28) undergoing elective aortic arch surgery with SACP and moderate HCA were analysed with regard to clinical outcome. Risk factors for serious adverse events (mortality, neurological injury) were determined.

**RESULTS**: Sixty-three patients (66%) underwent ascending aorta and hemiarch replacement, whereas 32 patients (34%) underwent ascending aorta and total arch replacement. Isolated arch replacement was rare. Additionally, 27% of patients underwent aortic valve replacement and 26% underwent root replacement. In-hospital mortality was 7%. Permanent neurological deficits occurred in 5%, transient neurological deficits occurred in 2%. Median SACP time was 24 min. Univariate analysis revealed femoral cannulation site (OR: 3.4; CI: 1.25–9.22, $P = 0.016$) as well as HCA ≥40 min (OR: 4.21; CI: 1.83–12.58, $P = 0.001$) as predictors of serious adverse events (mortality, neurological injury).

**CONCLUSIONS**: Summarizing, elective aortic arch surgery in elderly patients using SACP and moderate HCA provides excellent results regarding mortality and postoperative neurological outcome. Prolonged HCA time and femoral cannulation were the only predictors of serious adverse events (mortality, neurological injury).

**Keywords:** Aortic arch surgery • Elderly • Hypothermic circulatory arrest • Selective antegrade cerebral perfusion

## INTRODUCTION

Antegrade selective cerebral perfusion (ASCP) represents the most accepted method of brain protection during aortic arch surgery so far and its broad application has enabled a considerable improvement of clinical outcome [1–4]. Hypothermic circulatory arrest (HCA) has been used traditionally in various forms and extents for organ protection in aortic arch surgery [5–7]. Results in elderly patients undergoing surgery for acute and chronic aortic arch pathology are diverging and few reports focus on clinical outcome in elderly patients undergoing elective surgery [8–10]. Consequently, there are still some concerns about referring these patients for extensive aortic arch surgery.

The aim of this study was to evaluate the outcome in elderly patients (≥75 years) undergoing elective aortic arch surgery with the aid of selective antegrade cerebral perfusion (SACP) and moderate HCA.

## METHODS

### Patients

A series of 95 patients ≥75 years (median age 77 years, range 75–83 years) undergoing elective aortic arch surgery with SACP and moderate HCA was operated in two different institutions (S.Orsola-Malpighi Hospital, Bologna, Italy and University Hospital, Berne, Switzerland) between 2005 and 2011 and was analysed with regard to clinical outcome. The median EuroSCORE was 28. All patients had the underlying diagnosis of ascending aortic and/or arch aneurysm. Patient demographics are shown in Table 1. There has been no common protocol regarding conduction of extracorporeal circulation. Near infrared

**Table 1:** Descriptive characteristics of the cohort

|  | *n* overall = 95 |
| --- | --- |
| Demographics |  |
| Age, median (IQR) | 77 (76–78) |
| Female, *n* (%) | 45 (47) |
| Chronic health conditions and risk factors |  |
| Hypertension, *n* (%) | 82 (86) |
| Chronic obstructive pulmonary disease, *n* (%) | 9 (10) |
| Diabetes mellitus, *n* (%) | 8 (8) |
| Serum creatinine >200 mmol/l, *n* (%) | 3 (3) |
| Coronary artery disease, *n* (%) | 36 (38) |
| Extracardiac arteriopathy, *n* (%) | 14 (15) |
| Preoperative assessment |  |
| Impaired left ventricular dysfunction, *n* (%) | 4 (4) |
| Recent myocardial infarction, *n* (%) | 2 (2) |
| Redo surgery, *n* (%) | 13 (14) |
| Additive EUROSCORE, median (IQR) | 10 (9–12) |

Unless otherwise indicated, data are number (%). IQR: inter-quartile range; classification of chronic health conditions and risk factors according to EuroSCORE criteria.

**Table 2:** Description of the surgical strategy

|  | *n* overall = 95 |
| --- | --- |
| General |  |
| Composite graft placement, *n* (%) | 25 (26) |
| Elephant trunk repair, *n* (%) | 4 (4) |
| Frozen elephant trunk procedure, *n* (%) | 3 (3) |
| Hemiarch replacement, *n* (%) | 63 (66) |
| Aortic valve replacement, *n* (%) | 26 (27) |
| Cannulation site |  |
| Subclavian artery, *n* (%) | 29 (30) |
| Femoral artery, *n* (%) | 22 (23) |
| Brachiocephalic trunk, *n* (%) | 2 (2) |
| Ascending aorta, *n* (%) | 42 (45) |
| Additional procedures |  |
| Coronary revascularization, *n* (%) | 26 (27) |
| Mitral valve repair/replacement, *n* (%) | 8 (8) |
| Perfusion time |  |
| ECC in minutes, median (IQR) | 146 (112–182) |
| Aortic cross clamp in minutes, median (IQR) | 103 (75–124) |
| HCA in minutes, median (IQR) | 24 (16–60) |

Unless otherwise indicated, data are number (%). IQR: inter-quartile range; classification of chronic health conditions and risk factors according to EuroSCORE criteria.

spectroscopy (NIRS) for cerebral monitoring was used routinely in both centres. In order to specify the individual differences in both centres, the conduction protocols of extracorporeal circulation and SACP are described in detail for each centre below.

## Conduction of extracorporeal circulation and selective antegrade cerebral perfusion—Berne

Arterial inflow was by subclavian artery cannulation, direct aortic cannulation or by the femoral artery. Standard venous drainage was by a single two-stage cannula introduced into the right atrium. Patients were cooled to bilateral 20°C tympanic temperature and 25°C core temperature. Vasodilators, such as nitroprusside, were used to achieve homogeneous cooling by reducing peripheral vascular resistance. During rewarming, targets were bilateral 36°C tympanic temperature and 35°C core temperature. For cerebral perfusion, a blood temperature of 20°C was chosen According to the individual cannulation site for bilateral SACP— right subclavian artery or brachiocephalic trunk—flows between 500 and 750 ml/min were targeted according to the anticipated resistance of the cannulas. Most important, resistance of 50 mmHg at the level of the individual cannula was not exceeded so as not to expose the brain to episodes of excessive pressure.

## Conduction of extracorporeal circulation and selective antegrade cerebral perfusion—Bologna

Arterial inflow was by right axillary artery or innominate artery, ascending aorta or femoral artery and venous drainage was by a single two-stage cannula via the right atrium or, in few cases, into the femoral vein. If the axillary artery was chosen, a side graft to the native vessel was used in each patient. Pressure monitoring was achieved by means of the right radial artery pressure line. SACP management was performed according to Dr Kazui's protocol [2]. 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 or innominate artery cannulation, 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 SACP.

## Definition of clinical parameters

Clinical parameters and risk factors were defined according to EuroSCORE guidelines [11]. Mortality was defined as in-hospital death. Permanent neurological injury was defined as any newly developed sensorimotor deficit persisting at the time of discharge combined with a morphological correlate in cranial computed tomography or magnetic resonance imaging. Transient neurological injury was defined as functional deficit without any morphological correlate having resolved at discharge.

## Chronic health conditions and risk factors

Thirty-eight per cent of patients had coronary artery disease defined as any lesion of ≥50% in coronary angiography. Fourteen per cent of patients already had previous cardiac surgery and 9% of patients had COPD as defined by EuroSCORE guidelines (Table 1).

## Concomittant surgical procedures

Additionally to arch aortic surgery, 26% of patients underwent aortic root replacement with a biological composite graft, 27% underwent aortic valve replacement and 27% of patients underwent additional coronary artery bypass grafting (CABG).

Conventional elephant trunk procedures (4%) or frozen elephant trunk procedures (3%) were rare (Table 2).

## Cannulation sites for arterial return and HCA times

The ascending aorta was selected for arterial return in 45% of patients, the subclavian artery in 30% and the femoral artery in 23%. In the remaining 2%, the brachiocephalic trunk was chosen (Table 2). ECC times, aortic cross clamp times and HCA times are also depicted in Table 2.

## Statistical methods

Continuous data are presented as the median and inter-quartile range (range from the 25 to the 75th percentile). Discrete data are given as counts and percentages. Comparisons of continuous data were performed by Mann–Whitney $U$ tests, and groups of categorical data were compared by Fisher's exact test. Univariate regression analysis was performed to assess potential risk factors for the occurrence of the composite endpoint, serious adverse event (SAE), which was defined either by in-hospital mortality, transient and permanent neurological injury.

Results of the logistic regression model are given as the odds ratio (OR) and the 95% confidence interval (CI). A two-sided $P$-value <0.05 was considered statistically significant. All calculations were performed with SPSS 19.0 software for MacOSX.

## RESULTS

### Clinical outcome

In-hospital mortality was 7% (seven patients). Permanent neurological injury occurred in five patients (5%) and temporary neurological injury was observed in two (2%). Reasons for death were multiorgan failure as well as sequelae of already sustained neurological injury.

## Patients sustaining serious adverse events (SAE) versus none

Patients sustaining SAE were more likely to have elevated serum creatinine levels (22 versus 1%, $P = 0.001$). These patients were also more likely to have extracardiac arteriopathy (44 versus 12%, $P = 0.008$). Additive EuroSCORE levels were higher (12 versus 10, $P = 0.09$) as was the incidence of femoral artery cannulation (56 versus 20%, $P = 0.01$). Perfusion parameters such as ECC time (200 vs. 143 min, $P = 0.008$), aortic cross clamp time (130 vs. 98 min, $P = 0.02$) and HCA time (50 vs. 22 min, $P = 0.02$) also showed significant differences (Table 3).

## Univariate regression analysis

Univariate analysis revealed femoral cannulation site (OR: 3.4, CI: 1.25–9.22, $P = 0.016$) as well as HCA ≥40 min (OR: 4.21, CI: 1.83–12.58, $P = 0.001$) as predictors of SAEs (mortality, neurological injury) (Table 4).

**Table 3:** Distribution of patients by different chronic health conditions and in-hospital risk assessment stratified to in-hospital outcome

|  | SAE ($n = 9$) versus | no-SAE ($n = 86$) | $P$-value |
|---|---|---|---|
| Demographics |  |  |  |
|   Age, median (IQR) | 77 (76–79) | 77 (76–78) | 0.83 |
|   Female sex, $n$ (%) | 3 (33) | 42 (49) | 0.37 |
| Chronic health conditions and risk factors |  |  |  |
|   Hypertension, $n$ (%) | 7 (78) | 75 (87) | 0.43 |
|   Chronic obstructive pulmonary disease, $n$ (%) | 1 (11) | 8 (9) | 0.86 |
|   Diabetes mellitus, $n$ (%) | 0 (0) | 8 (9) | 0.34 |
|   Serum creatinine >200 mmol/l, $n$ (%) | 2 (22) | 1 (1) | 0.001 |
|   Coronary artery disease, $n$ (%) | 4 (44) | 32 (37) | 0.67 |
|   Extracardiac arteriopathy, $n$ (%) | 4 (44) | 10 (12) | 0.008 |
| Preoperative assessment |  |  |  |
|   Impaired left ventricular dysfunction, $n$ (%) | 0 (0) | 4 (5) | 0.51 |
|   Recent myocardial infarction, $n$ (%) | 0 (0) | 2 (2) | 0.64 |
|   Redo surgery, $n$ (%) | 2 (22) | 11 (13) | 0.43 |
|   Additive EUROSCORE, median (IQR) | 12 (10–14) | 10 (9–11) | 0.09 |
| Surgical management |  |  |  |
|   Femoral cannulation site, $n$ (%) | 5 (56) | 17 (20) | 0.01 |
|   Elephant trunk procedure, $n$ (%) | 1 (11) | 3 (4) | 0.28 |
|   Frozen elephant trunk procedure, $n$ (%) | 1 (11) | 2 (2) | 0.15 |
|   Additional procedures, $n$ (%) | 2 (22) | 32 (37) | 0.56 |
|   ECC time in minutes, median (IQR) | 200 (148–258) | 143 (110–177) | 0.008 |
|   Aortic cross clamp time in minutes, median (IQR) | 130 (100–163) | 98 (72–123) | 0.02 |
|   HCA in minutes, median (IQR) | 50 (34–89) | 22 (16–56) | 0.02 |

Unless otherwise indicated, data are number (%). IQR: inter-quartile range; ECC: extracorporal circulation; HCA: hypothermic circulatory arrest; SAE: serious adverse event composite endpoint, including death, temporary and permanent neurological deficit; classification of chronic health conditions and risk factors according to EuroSCORE criteria.

**Table 4:** Predictors of serious adverse outcome—univariate regression analysis

| Risk factor | OR | 95% CI | $P$-value |
|---|---|---|---|
| Femoral cannulation site | 3.40 | 1.25–9.22 | 0.016 |
| HCA ≥40 min | 4.21 | 1.83–12.58 | 0.001 |

## DISCUSSION

Clinical outcome in this series was favourable with regard to mortality and permanent neurological injury. Recent reports suggest continuous improvement in outcome in the general

patient population undergoing surgery for acute and chronic aortic arch pathologies [12]. However, the percentage of elderly patients in most reports is low and mixed with acute thoracic aortic events [13]. As such, this report is the first one selectively focusing on clinical outcomes in elderly patients undergoing elective surgery for aortic arch pathology with a similar perfusional concept.

It was interesting to observe, that the percentage of patients with concomitant coronary artery disease requiring simultaneous treatment was higher than in most series dealing with dilatative thoracic aortic pathology. This may well be due to the fact that some degree of obliterative arteriopathy in elderly patients is commonly seen. Fourteen per cent of patients already had undergone at least one previous open heart procedure. This fact alone combined with the results obtained underlines that redo surgery with a procedure at the level of the aortic arch is not *per se* prohibitive in these patients.

The number of concomittant surgical procedures besides ascending and arch replacement was high. Besides CABG, aortic valve replacement and also aortic root replacement were frequently performed. As the underlying diagnosis of anuloaortic ectasia is rare in elderly patients, many of them have the underlying pathology of a bicuspid aortic valve with additional ascending aortic pathology. A common indication for redo surgery after supracoronary aortic repair is dissection or dilation especially in the non-coronary sinus [14].

Cannulation seems by far more decisive regarding outcome also in the elective setting than perhaps expected. It is known that femoral cannulation has the most important impact on physiology by flow reversal and by potential embolization of atherosclerotic debris in the thoracoabdominal aorta despite the fact that some authors report favourable results at least in younger patient cohorts [15]. Cannulation sites for arterial return establishing antegrade flow patterns are more physiologic, easen SACP and do not carry the risk of cerebral embolization [16]. It remains to the preference of the individually treating physician if direct cannulation of the cranial ascending aorta or the right subclavian artery is preferred. If the choice is on the ascending aorta, care must be taken that the corresponding cerebral perfusion canulla is not inserted unintentionally too deeply in the right subclavian artery thereby compromising antegrade cerebral perfusion. This problem will not occur if the right subclavian artery is selected for arterial return. In any case, bihemispheric near infrared spectroscopy is recommended irrespective of the chosen method to reconfirm efficacy of SACP and in order to react if uni- or bihemispherical changes in saturation occur [17].

In order to gain better insights into the reasons for SAEs in this series, we stratified patients into two groups—with and without SAEs being defined as a composite endpoint of mortality as well as transient and permanent neurological injury. Patients with SAEs were more likely to have renal failure and extracardiac arteriopathy before surgery. As renal insufficiency seems to carry a greater inherent risk than diabetes mellitus and is on its way to become the most limiting factor for immediate and long-term outcome, these findings are clear [18]. The same is true for extracardiac arteriopathy as the presence of obliterative components of atherosclerosis is a surrogate for a more severe stage of the underlying disease and thereby for the risk of neurological injury and finally death. As an expected consequence, EuroSCORE levels in patients with SAEs were also higher than in patients without SAE.

In this study, total arch replacement was not associated with longer HCA times as antegrade systemic perfusion is re-established immediately after accomplishment of the descending aortic anastomosis which does not take longer than a hemiarch anastomosis. The only difference is that during replantation of the arch vessels antegrade cerebral perfusion is being done selectively via catheters. Manipulation is more extensive and thereby any risk of dislodging debris is more likely, but HCA *per se* is not affected.

In univariate regression analysis, a femoral cannulation site for arterial return and also HCA times ≥40 min were predictors of SAEs (mortality, neurological injury). The beneficial effect of subclavian artery cannulation has been described previously and seems to be the most important progress in aortic arch surgery during the last decade [12]. A linear correlation between HCA times and outcome is well known [19]. However, the time needed to accomplish repair is not a surrogate of the capability of the operating surgeon but of the extent of the underlying disease. Consequently, especially in an elderly patient population it remains a condition of experience and anticipation to make the decision between a fully anatomic repair and a limited arch repair by not fully restoring regular aortic dimensions but being extensive enough to prevent rupture.

## Limitations and strengths of the study

The main limitation of this study is its retrospective nature and the fact that no physiologic surrogates such as the frailty index could be applied in this retrospective setting. Even though this is a large cohort of elderly patients undergoing aortic arch surgery, the sample size is modest when it comes to random variability. Residual confounding by patient-management at the operating theatre and intensive care unit may be present. It is impossible to control such confounders in observational, multi-centre studies. Fortunately, serious complications are rare, thus identification of independent risk factors and therefore the justification of this concept to grant elderly patients access to this treatment has to be evaluated by future research. Nevertheless, the present study might have the potential to encourage physicians to consider treatment in a patient population, which was deemed not suitable in the majority of cases to date.

Summarizing, elective aortic arch surgery in elderly patients using SACP and moderate HCA provides excellent results regarding mortality and postoperative neurological outcome. Prolonged HCA time and femoral cannulation were the only predictors of SAEs (mortality, neurological injury).

**Conflict of interest**: none declared.

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## APPENDIX. CONFERENCE AND DISCUSSION

*Dr M. Ehrlich (Vienna, Austria)*: You and your co-authors report on a subject of great interest, the outcome of ACP and moderate hypothermic circulatory arrest in elderly patients, a population that is getting more and more challenging for us surgeons.

In your series of 95 patients, the ascending aorta was selected for arterial return in 45% of patients, the subclavian artery in only 30% and the femoral artery in 23%. Femoral cannulation site turned out to be a predictor of serious adverse events in univariate analysis, which brings me to my first question. Why was not the subclavian artery used as the arterial access site in most of these cases which would make the implementation of ACP also much easier? Secondly, did you use some kind of cerebral monitoring in this series? And last, but not least, multivariate analysis revealed HCA times greater than 40 minutes as the only independent predictor of SAE. Do you think that in these elderly patients, when longer HCA times are anticipated, one should cool to lower temperatures?

*Dr Pacini*: Regarding the first question about femoral cannulation, as I said before, in order to obtain antegrade perfusion and avoid retrograde perfusion, we try to cannulate as much as we can, the axillary artery, the ascending aorta, the aortic arch and the innominate artery. However, this is a retrospective study and the cannulation site depended on the preference of the surgeon who did the operation.

Regarding the brain monitoring, I think that both centres involved in the study use NIRS as the only method of monitoring cerebral perfusion. Of course, we also have the right and the left radial artery blood pressure, but sometimes if you cannulate the axillary artery directly, you lose the right blood pressure, so the only monitoring on that occasion is NIRS.

And the third question was? Sorry.

*Dr Ehrlich*: If you're expecting a patient to have a total arch repair, would you -

*Dr Pacini*: Regarding the extension, yes. I don't know about Berne, but in Bologna we don't care about the extension of the aortic arch replacement. Of course, patients older than 75 years who have to undergo open arch surgery are selected without associated high risk factors such as chronic renal failure or severe chronic pulmonary disease. We limited the hybrid technique, like debranching and endografting, just to patients with very severe associated disease.

*Dr M. Czerny (Berne, Switzerland)*: I just want to speak for the Berne side. Actually, I think it's a trade-off between total anatomic correction and correction implementing the most dilated parts and leaving the other parts that aren't at risk. I think this is the strategy and the trade-off we follow in these cases.

*Dr S. Takamoto (Tokyo, Japan)*: The temporary neurological dysfunction is only 2% of the whole in these older patients. Even off-pump bypass causes probably 10–20% temporary neurological dysfunction, someone gets disorientation after the surgery. Why is it so low in your study?

*Dr Pacini*: We don't know; it was strange also for us to find a very low incidence of transient neurological dysfunction.

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