Operations on the thoracic aorta and antegrade selective cerebral perfusion: our experience with 462 patients

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Aortic aneurysm; Aortic dissection; Cardiac surgery.

Background. **We retrospectively analyzed the hospital mortality and neurologic outcome after surgery on the thoracic aorta with the aid of antegrade selective cerebral perfusion to determine a predictive risk model.**

Methods. **Between October 1995 and May 2002, 462 patients (mean age 62.7 ± 11.7 years) underwent surgery on the thoracic aorta using antegrade selective cerebral perfusion. The indication for surgery was acute type A dissection in 132 patients (28.6%), degenerative aneurysm in 258 (55.8%), and post-dissection aneurysm in 72 (15.6%). One hundred and forty-one patients (30.5%) were operated on urgently; concomitant procedures were performed in 190 patients (41.1%). The mean cerebral perfusion time was 63 ± 39 min. Predictors of hospital mortality and neurologic outcome were identified by univariate and multivariate analysis of the preoperative and intraoperative variables.**

Results. **The hospital mortality rate was 10.2%. Stepwise logistic regression identified an urgency status (odds ratio-OR 5.2, p = 0.001), a history of a central neurologic event (OR 4.1, p = 0.007) and coronary artery bypass graft (OR 3.2, p = 0.039) as being independent determinants for hospital mortality. The transient neurologic dysfunction rate was 6.2%. An urgency status (OR 3.4, p = 0.003) and a history of a central neurologic event (OR 5.1, p = 0.002) were independent determinants of transient neurologic dysfunction. An urgency status (OR 6.0, p = 0.011) was the only independent determinant for permanent neurologic dysfunction (3.8%). A cerebral perfusion time > 90 min was not associated with an increased risk of hospital mortality and permanent or transient neurologic dysfunction.**

Conclusions. **Antegrade selective cerebral perfusion proved to be a safe method of brain protection allowing complex aortic repair to be performed with encouraging results in terms of hospital mortality and neurologic outcome.**

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Brain protection is a primary concern during surgery of the thoracic aorta. Available techniques of cerebral protection include deep hypothermic circulatory arrest alone or in combination with retrograde cerebral perfusion and antegrade selective cerebral perfusion (ASCP). All three methods have both advantages and disadvantages.

In our institutions, ASCP is the method of choice employed to protect the brain from ischemic injuries when aortic procedures requiring a period of circulatory arrest > 30 min are undertaken.

The aim of the present study was to evaluate the results of ASCP with moderate hypothermic circulatory arrest in patients undergoing surgery of the thoracic aorta, and to determine the independent predictive risk factors for hospital mortality and neurologic outcome.

Methods

Patients' profile. Having defined the common perioperative variables (see Appendix), a total of 462 medical records of patients who underwent thoracic aorta operations using ASCP at the St. Antonius Hospital (Nieuwegein, The Netherlands) and S. Orsola Hospital (Bologna, Italy) between October 1995 and May 2002 were retrospectively examined and included in the study.

There were 297 men (64.3%) and 165 women (35.7%) whose age ranged from 21 to 85 years (mean 62.7 ± 11.7 years). Of the entire cohort, 321 patients (69.5%) were submitted to an elective procedure whereas 141 (30.5%) underwent urgent operation. The indication for surgery was acute type A dissection in 132 patients (28.6%), chronic post-dissection aneurysm in 72 (15.6%),

and a degenerative aneurysm in 258 (55.8%). Thirty-six patients (7.8%) presented with coronary artery disease, 22 (4.8%) had a history of cerebrovascular disease, 48 (10.4%) had chronic obstructive pulmonary disease, and 14 (3.0%) had chronic renal insufficiency (creatinine > 120 μmol/l). All patients submitted to an elective procedure underwent preoperative evaluation of the cerebral circulation including Doppler ultrasound of the extracranial vessels, digital subtraction angiography of the extracranial and intracranial circulation and carotid compression testing by means of electroencephalographic monitoring to evaluate occlusion intolerance or a transcranial Doppler ultrasound study.

Operative technique. The anesthetic management and methods of brain and myocardial protection were similar in both institutions.

Induction of anesthesia was achieved with propofol 2 mg/kg, fentanyl 2 μg/kg and pancuronium 0.1 mg/kg. Propofol and fentanyl were used for the maintenance of anesthesia. For all patients, pH control was carried out using the alpha-stat method.

A median sternotomy was used in 395 (95.6%) patients and a median sternotomy plus anterolateral thoracotomy in 6 (1.4%). In the remaining 12 (3%) patients, the diseased aorta was exposed through a left posterolateral thoracotomy. After systemic heparinization, cardiopulmonary bypass was instituted using a cannula for arterial return placed in the ascending aorta or in the femoral artery and a venous single-two stage cannula placed in the right atrium or a long venous cannula introduced through the left femoral vein and placed within the right atrium. The left side of the heart was vented through the right superior pulmonary vein. Myocardial protection was achieved with cold crystalloid cardioplegia and topical pericardial cooling.

Details of our cannulation technique and method of ASCP with moderate hypothermic circulatory arrest have been previously described[1-3]. Briefly, having instituted cardiopulmonary bypass and cooled the patients' body temperature 22-26°C (nasopharyngeal temperature), the systemic circulation was arrested and the diseased aorta opened. With the patient in Trendelenburg position and under direct visual control, 15F retrograde coronary sinus perfusion cannulas (Medtronic DLP, Chase Medical Inc., Houston, TX, USA), connected to the oxygenator with a separate single-roller pump head, were inserted into the innominate and left common carotid arteries through the aortic lumen. Having accurately positioned the cannulas, the balloons at their tip were manually inflated and fixed using an encircling tape. The left subclavian artery was clamped or occluded with a Fogarty catheter (Baxter Health Care, Irvine, CA; IFM Clearwater, FL, USA) in order to avoid the steal phenomenon.

The cerebral flow was started at a rate of 10 ml/kg/min and adjusted to maintain a right radial arterial pressure between 40 and 70 mmHg. The introduction of the cerebral perfusion catheters usually required < 3 min.

During open distal anastomosis, the blood flow to the lower half of the body from the femoral artery, when cannulated, was arrested or reduced to 500 ml/min.

Tools of cerebral monitoring included: a right radial arterial pressure line in all cases, electroencephalography, determination of the regional oxygen saturation in the bilateral frontal lobes by means of near-infrared spectroscopy and, when available, transcranial Doppler measurement of the blood velocity of the middle cerebral artery to confirm the proper placement and function of both cannulas. Transesophageal echocardiography was routinely used to assess cardiac contractility, blood flow conditions, aortic pathology and the presence of intracardiac air.

The extent of the aortic replacement and the associated procedures are listed in table I.

En bloc or separated graft techniques were used to re-implant the arch vessels when a complete aortic arch replacement was performed[4,5].

Statistical analysis. Continuous variables were expressed as mean ± 1 SD and categorical variables as percentages. All preoperative and intraoperative variables were first analyzed using univariate analysis (unpaired two-tailed Student's t-test, χ^2 test or Fisher's exact test as appropriate) to determine whether any single factor influenced the in-hospital mortality and neurologic outcome. A p value < 0.05 was considered as statistically significant.

The analyses for permanent neurologic dysfunction (PND) and transient neurologic dysfunction (TND) were conducted separately. Risk factors for PND (stroke or coma) were examined in all patients who survived the operation long enough (24-36 hours) to undergo an appropriate neurologic evaluation, and risk factors for TND (postoperative confusion, agitation, delirium, prolonged obtundation or transient parkinsonism with negative brain computed tomography scanning and complete resolution before discharge) were assessed in all operative survivors without PND. Variables with a p value < 0.05 in the univariate analy-

Table I. Extent of aortic replacement and associated procedures.

Extent of replacement	
Aortic arch only	29 (6.3%)
Ascending aorta + arch	164 (36.8%)
Total thoracic aorta	19 (4.1%)
Arch + descending aorta	15 (3.2%)
Ascending aorta or hemiarch	229 (49.6%)
Associated procedures	
Aortic valve replacement	32 (6.9%)
Bentall	118 (25.5%)
Aortic root remodeling	25 (5.4%)
Homograft	2 (0.4%)
Coronary artery bypass grafting	25 (5.4%)
Elephant trunk	87 (18.8%)

sis were examined using multivariate analysis by forward stepwise logistic regression to evaluate the independent risk factors for in-hospital mortality, PND and TND. The SPSS 8.0 software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

Results

Cardiopulmonary bypass data. The mean cardiopulmonary bypass time was 201 ± 63 min (range 82-493 min), and the mean myocardial ischemic time was 124 ± 46 min (range 28-280 min). The mean ASCP time was 63 ± 39 min (range 16-248 min) (Fig. 1).

In-hospital mortality. The average in-hospital mortality was 10.2% (47/462), being 5.3 and 21.8% for elective and urgent surgery respectively (p = 0.038). Causes of death included: multiorgan failure (n = 21), septic shock (n = 5), neurologic lesions (n = 2), myocardial infarction (n = 2), low cardiac output (n = 5), bleeding (n = 4), bowel ischemia (n = 2), and rupture of a distal aneurysm (n = 6).

At univariate analysis, the following factors were found to have a significant influence on the in-hospital mortality: urgency status (p = 0.001), a history of a central neurologic event (p = 0.004), preoperative renal insufficiency (p = 0.044), and coronary artery bypass grafting (p = 0.035). Multivariate analysis revealed that an urgency status (odds ratio-OR 5.2, p = 0.001), a history of a central neurologic event (OR 4.1, p = 0.007) and coronary artery bypass grafting (OR 3.2, p = 0.039) were independent predictors of in-hospital mortality (Table II). The extent of aortic replacement and an ASCP duration > 90 min were not statistically correlated with an increased risk of in-hospital mortality.

In-hospital morbidity. PND, which was evaluated in all patients who survived the operation long enough to undergo an adequate neurologic examination, was reported in 17 of 452 patients (3.8%). At univariate analysis, an urgency status (p = 0.003) was found to be significantly correlated with the occurrence of PND. At multiple logistic regression analysis, an urgency status (OR 6.0, p = 0.011) was found to be an independent predictor of PND (Table III).

TND, which was evaluated only in patients without permanent neurologic lesions, occurred in 27 of 435 patients (6.2%). An urgency status (p = 0.002), a history of a central neurologic event (p = 0.007), coronary artery bypass grafting (p = 0.040) and aortic valve replacement (p = 0.030) were associated with a significantly increased risk of TND at univariate analysis. Stepwise logistic regression analysis indicated an ur-

Table II. Logistic regression analysis for in-hospital mortality.

Variable	OR	95% CI	p
Urgency	5.2	2.85-10.74	0.001
Previous stroke/TIA	4.1	1.37-10.45	0.007
Coronary artery bypass grafting	3.2	1.06-10.32	0.039

CI = confidence interval; OR = odds ratio; TIA = transient ischemic attack.

Table III. Logistic regression analysis for permanent and transient neurologic dysfunction.

Variable	OR	95% CI	p
Permanent neurologic dysfunction			
Urgency	6.0	1.33-9.61	0.011
Transient neurologic dysfunction			
Urgency	3.4	1.60-8.05	0.003
Previous stroke/TIA	5.1	1.77-10.37	0.002

CI = confidence interval; OR = odds ratio; TIA = transient ischemic attack.

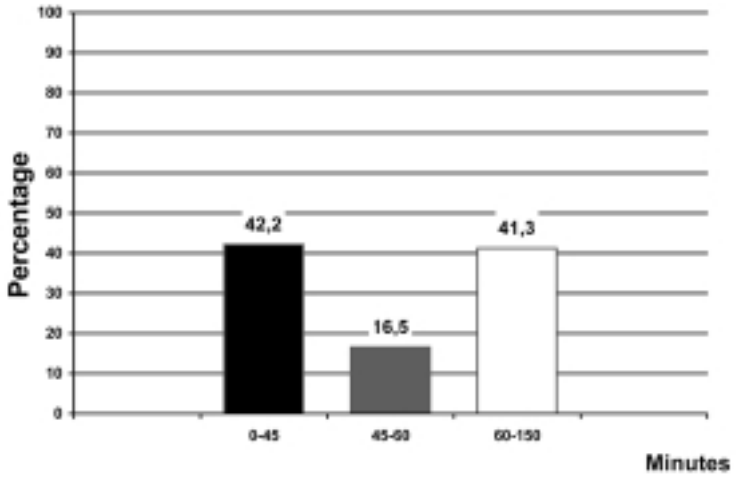

Figure 1. *Distribution of patients by antegrade selective cerebral perfusion time.*

gency status (OR 3.4, p = 0.003) and a history of a central neurologic event (OR 5.1, p = 0.002) as independent predictors of TND (Table III). An ASCP duration > 90 min was not a significant risk factor for PND or TND.

Other postoperative complications included bleeding requiring a repeat thoracotomy in 68 patients (14.7%) and a postoperative myocardial infarction (serum creatine phosphokinase level > 300 IU/l with a creatine phosphokinase-MB fraction > 3%) in 18 patients (3.9%). Pulmonary complications requiring mechanical ventilatory support > 5 days occurred in 71 patients (15.4%) and renal failure requiring temporary hemodialysis occurred in 21 patients (4.5%).

Discussion

In our Institutions, ASCP is currently being used as the method of choice for brain protection during complex aortic arch reconstruction for the following reasons:

• we demonstrated that an ASCP time > 90 min and the extent of aortic replacement are not associated with an increased risk of in-hospital mortality and of an adverse neurologic outcome[1];

• ASCP can be used with moderate (instead of deep) hypothermia. Tanaka et al.[6] have demonstrated that, at a rectal temperature of 25°C with a perfusion pressure of ≥ 40 mmHg, a cerebral flow rate equal to half the physiological value is optimal for the maintenance of aerobic cerebral metabolism. The Japanese group also demonstrated that under alpha-stat pH management, at a temperature of 20°C with a perfusion pressure of ≥ 40 mmHg, cerebral autoregulation is maintained. These findings constitute the scientific background of our clinical ASCP application which includes a flow rate of 10 ml/kg/min, a perfusion pressure between 40 and 70 mmHg, a cerebral perfusion temperature of 20°C and a nasopharyngeal temperature at circulatory arrest of 22-25°C. The moderate levels of hypothermia, in contrast to deep hypothermia, permit a shorter total perfusion time and thus a lower likelihood of microembolism, coagulopathy, hemorrhage and pulmonary and renal dysfunction[7-9]. Moreover, if it is true that cardiopulmonary bypass duration is the most important risk factor for in-hospital mortality in case of surgery of the thoracic aorta[5,10,11], an improved hospital survival may be expected if the implementation of moderate hypothermia instead of deep hypothermia may significantly shorten the cardiopulmonary bypass time[12,13];

• the entire experimental literature, comparatively investigating the effects of ASCP, deep hypothermic circulatory arrest and retrograde cerebral perfusion on brain energy metabolism, supports the idea that ASCP is superior to the other methods in maintaining an aerobic brain metabolism even after a prolonged period of circulatory arrest as demonstrated by morphologic, histopathologic and biochemical findings as well as by behavioral and clinical examinations[14-19];

• manipulation and cannulation of the arch vessels have been indicated as important drawbacks of ASCP since they a) increase the embolic risk in patients with atherosclerotic aortic arch aneurysms, b) increase the risk of damage of the arch vessels and of brain malperfusion in patients with acute aortic dissection, and c) render a complex procedure even more complex due to a reduced surgical visibility and to the necessity of preparing the arch vessels and installing the ASCP system. Certainly, the cannulation of the arch vessels represents an important phase of the procedure and great care has to be taken. However, in our experience it always required < 3 min to insert the ASCP cannulas into the arch vessels and to establish cerebral perfusion. The surgical visibility may be adequate if the ASCP catheters are placed toward the patient's head. They are not traumatic and positioned quite distally in the arch vessels where the likelihood of plaque, atheroma, clots or dissection is very low. It was always easy, during dissection repairs, to identify the true lumen of the arch vessels through the aortotomy, and our cerebral monitoring tools could always confirm the correct positioning of the catheters and the symmetric distribution of blood to the two hemispheres. In cases of severe atheroma, clots or dissection involving both the aortic arch and the proximal segment of the arch vessels, the separated graft technique may be effective in reducing the brain embolization risk and in improving the neurologic outcome of patients[20].

However, although the utilization of ASCP has been indicated as the best tool for protection of the brain from ischemic injuries, transient and permanent neurologic damage continues to occur.

The aim of the present thesis was to identify, among intraoperative and postoperative factors, those that may result in an increased in-hospital mortality and an adverse neurologic outcome. Interestingly, the extent of the aortic replacement and the duration of ASCP did not increase the risk of in-hospital mortality and of an adverse neurologic outcome. This underscores the fact that ASCP provides the unique advantage of facilitating complex and time-consuming aortic arch operations thus permitting unhurried and meticulous aortic reconstructions. During dissection repairs, this seems to be particularly important[21].

Among the analyzed variables, urgency and a history of stroke/transient ischemic attack emerged as the most important risk factors for in-hospital mortality and an adverse neurologic outcome.

The observed difference between our elective and urgent results is still important. If, on the one hand, this constitutes a good reason to accelerate the diagnostic process and to shorten the pathway to the operative theater for patients with type A acute dissection, at the same time rendering the most innovative technologies of cerebral monitoring and the best surgical techniques

and strategies of cerebral protection available, on the other hand, it allows us to consider a more aggressive surgical timing to operate, under elective circumstances, on those patients who are at high risk of rupture or dissection such as patients with Marfan syndrome, connective tissue disorders and bicuspid aortic valves.

In conclusion, ASCP has been demonstrated to be a safe and reliable method of brain protection allowing complex aortic procedures to be performed with acceptable results in terms of in-hospital mortality and of an adverse neurologic outcome. The ASCP duration does not increase the risk of in-hospital mortality and of an adverse neurologic outcome permitting unhurried and meticulous aortic reconstruction. It can be safely used with moderate hypothermia requiring a shorter duration of cardiopulmonary bypass as compared to deep hypothermic circulatory arrest with or without retrograde cerebral perfusion. A more aggressive surgical timing for patients at risk of rupture/dissection and adjunctive improvements in brain protection methods for patients with cerebrovascular disease will probably contribute to a further reduction in in-hospital mortality and in the frequency of an adverse neurologic outcome in our patients.

Appendix. Preoperative, intraoperative and postoperative variables included in the analysis.

- Age
- Gender
- Aortic pathology (chronic aneurysm; acute type A aortic dissection; post-dissection aneurysm)
- Acute type A aortic dissection
- Impending aneurysmal rupture
- Status (elective, urgency)
- Preoperative renal insufficiency (serum creatinine > 250 μmol/l)
- Preoperative chronic obstructive pulmonary disease (forced expiratory volume in 1 s 50-70%, medical therapy)
- Hypertension
- Preoperative central neurological events (stroke/transient ischemic attack)
- History of coronary artery disease (myocardial infarction, positive result to any diagnostic investigation for coronary artery disease)
- Previous cardiovascular operation through a median sternotomy
- Surgical approach (median sternotomy; median sternotomy plus left anterolateral thoracotomy)
- Extent of aortic replacement (isolated aortic arch; ascending aorta + arch; total thoracic aorta; arch + descending thoracic aorta, ascending aorta or hemiarch, others)
- Arch vessels reimplantation (en bloc technique; separated graft technique)
- Concomitant aortic valve replacement
- Concomitant Bentall procedure
- Concomitant aortic root remodeling
- Concomitant homograft
- Concomitant aortic valve commissure resuspension
- Concomitant coronary artery bypass grafting
- Concomitant mitral valve replacement or repair
- Concomitant elephant trunk
- Associated procedures (all combined)
- Cardiopulmonary bypass time (min)
- Myocardial ischemic time (min)
- Antegrade selective cerebral perfusion time (min)
- In-hospital death
- Cause of death
- Permanent neurologic damage (stroke, coma, new focal or multiple brain lesions detected by means of computed tomography scan or magnetic resonance imaging)
- Transient neurologic dysfunction (postoperative confusion, agitation, delirium, prolonged obtundation or transient parkinsonism with negative brain computed tomography scanning and complete resolution before discharge)
- Postoperative renal insufficiency requiring hemodialysis
- Postoperative respiratory insufficiency requiring mechanical ventilatory support > 5 days
- Postoperative myocardial infarction (ECG, serum creatine phosphokinase level > 300 IU/l with creatine phosphokinase-MB fraction > 3%)
- Bleeding requiring rethoracotomy

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