Surgery for acute type A aortic dissection: the effect of antegrade selective cerebral perfusion on the early outcome of elderly patients

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Aortic dissection; Cerebral protection; Neurologic injury.

Background. **The aim of this study was to evaluate early results and to determine predictive risk factors associated with an adverse outcome in elderly patients after acute type A aortic dissection repair using antegrade selective cerebral perfusion (ASCP). Adverse outcome was defined as the occurrence of death or permanent neurologic dysfunction.**

Methods. **From October 1995 to March 2002, 178 patients (group A < 75 years, n = 156, 87.6%; group B > 75 years, n = 22, 12.4%) underwent surgery for acute type A aortic dissection using ASCP and moderate hypothermia. An ascending aorta/hemiarch replacement was performed in 128/178 (71.9%) patients (group A 71.2%, group B 77.3%, p = NS), an ascending aorta and arch replacement in 50/178 (28.1%) patients (group A 28.8%, group B 22.7%, p = NS). Associated procedures were performed in 55/178 (20.9%) patients (group A 31.4%, group B 27.3%, p = NS), the arch vessels were reimplanted using the separated graft technique in 32/50 (64.0%) patients (group A 62.2%, group B 80.0%, p = NS). The mean ASCP time was 59 ± 27 min.**

Results. **The overall adverse outcome rate was 20.8% (group A 21.2%, group B 18.2%, p = NS). The transient neurologic dysfunction rate was 9.5% (group A 9.5%, group B 5.6%, p = NS). A logistic regression analysis revealed cardiopulmonary bypass time (p = 0.045, odds ratio 1.03/min) to be the only independent predictor of adverse outcome in group A.**

Conclusions. **During type A aortic dissection repair the implementation of ASCP resulted in an acceptable hospital mortality and neurologic outcome. If ASCP is used, the risk of hospital mortality and postoperative morbidity is similar in patients younger and older than 75 years. Duration of cardiopulmonary bypass still remains an important risk factor for hospital mortality and neurologic outcome in elderly patients.**

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Introduction

Although surgical outcomes have substantially improved after acute type A aortic dissection repair, hospital mortality and neurologic and systemic morbidity continue to be considerable[1-4].

Advanced age has been indicated as an important risk factor for hospital mortality and adverse neurologic outcome[5,6]. Thus, in elderly patients with acute type A aortic dissection, the indication for surgery as well as the extension of the aortic replacement still remain controversial, a more conservative approach being suggested by some authors[7].

Antegrade selective cerebral perfusion (ASCP) has proved to be the best method of brain protection during surgery of the thoracic aorta being capable of providing important advantages. They include: 1) the duration of ASCP time and the extent of aortic replacement are not associated with an increased risk of hospital mortality and adverse neurologic outcome[8,9], 2) ASCP is associated with lower rates of postoperative transient neurologic dysfunction (TND) as compared to deep hypothermia and circulatory arrest with or without retrograde cerebral perfusion[10], moderate (instead of profound) hypothermia may be used resulting in shorter periods of extracorporeal circulation and fewer coagulative and systemic complications[11].

Our results with ASCP during type A dissection repair have been previously reported[12,13]. The aim of the present comparative study was both to evaluate early results in elderly patients receiving ASCP as a method for brain protection during acute type A aortic dissection repair and to determine the predictive risk factors associated with an adverse outcome (hospital death or permanent neurologic dysfunction-PND) in this high-risk group of patients.

Methods

Patients. From October 1995 to March 2002, 178 patients underwent surgical repair of acute type A aortic dissection with the aid of ASCP and moderate hypothermia at the St. Antonius Hospital (Nieuwegein, The Netherlands), S. Orsola University Hospital (Bologna, Italy), G.M. Lancisi Hospital (Ancona, Italy), and Hamamatsu University Hospital (Hamamatsu, Japan) (Table I). Medical records were reviewed for clinical variables including preoperative status, intraoperative data and early postoperative complications. Patients referred for chronic dissections were excluded from the study.

One hundred and six men (59.6%) and 72 women (40.4%) with a mean age of 61.7 ± 11.8 years (range 27 to 82 years) were enrolled in the study. All patients had precordial, back or abdominal pain at the onset of symptoms. Hemodynamic instability (systolic arterial pressure < 100 mmHg) (17.4%), acute aortic valve insufficiency (15.7%), new neurologic events (stroke/transient ischemic attack) at the onset of the dissection (6.7%), and arterial hypertension (38.8%) were common preoperative findings. Patients > 75 years (group B) had more pericardial effusion, hemodynamic instability and cardiopulmonary resuscitation before surgery compared to patients < 75 years (group A) (Table II).

Preliminary diagnosis at the referring institutions was usually made by means of echocardiography, computed tomographic scan or, occasionally, by angiography. Patients referred from other institutions were immediately transferred to the operating room where transesophageal echocardiography was performed under anesthesia for final diagnostic confirmation.

The dissection always involved the ascending aorta. The tear site was located at the ascending aorta in 122 patients (68.5%), at the transverse arch in 45 (25.3%), and at the proximal descending thoracic aorta in 7 (3.9%). In the remaining 4 patients (2.2%), an entry tear was not found.

Table I. Study centers.

Study centers	Study period	No. cases
St. Antonius Hospital (Nieuwegein, The Netherlands)	1995-2002	89
S. Orsola University Hospital (Bologna, Italy)	1996-2002	43
G.M. Lancisi Hospital (Ancona, Italy)	1999-2002	26
University of Hamamatsu (Hamamatsu, Japan)	1997-2002	20

Operative technique. A median sternotomy was used in all 178 cases. After systemic heparinization, the femoral artery with the best pulsation (or the right axillary) and the right atrium were cannulated for cardiopulmonary bypass (CPB) institution. The left ventricle was vented through the right superior pulmonary vein. Myocardial protection was obtained by means of antegrade or retrograde infusion of cold crystalloid or blood cardioplegia.

Details of our cannulation technique and method of ASCP with moderate hypothermic circulatory arrest have been previously described[14-16]. Briefly, after CPB was instituted and the patients were cooled to 22-26°C of nasopharyngeal temperature, systemic circulation was arrested and the aorta opened. With the patient in the Trendelenburg position, special catheters for ASCP (Fuji System Corporation, Tokyo, Japan)[17] or two 15F retrograde coronary sinus perfusion cannulas (Med-

Table II. Patients' characteristics.

	All patients	Group A	Group B	p
No. patients	178	156 (87.6%)	22 (12.4%)	–
Age (years)	61.7 ± 11.8	59.5 ± 10.9	77.7 ± 2.4	0.000
Hypertension	69 (38.8%)	60 (38.5%)	9 (40.9%)	NS
Chronic obstructive pulmonary disease	11 (6.2%)	9 (5.8%)	2 (9.1%)	NS
Marfan syndrome	4 (2.2%)	4 (2.6%)	–	NS
Redo operation	5 (2.8%)	5 (3.2%)	–	NS
New neurologic events	12 (6.7%)	12 (7.7%)	–	NS
Old cerebral infarction	2 (1.1%)	2 (1.3%)	–	NS
Renal insufficiency (creatinine > 2 mg/dl)	6 (3.4%)	5 (3.2%)	1 (4.5%)	NS
Visceral ischemia	1 (0.6%)	1 (0.6)	–	NS
Myocardial ischemia	3 (1.7%)	3 (1.9%)	–	NS
Pericardial effusion	50 (28.1%)	38 (24.4%)	12 (54.5%)	0.005
Hemodynamic instability	31 (17.4%)	23 (14.7%)	8 (36.4%)	0.030
Cardiopulmonary resuscitation	7 (3.6%)	4 (2.6%)	3 (13.6%)	0.042
Lower extremity ischemia	9 (5.1%)	7 (4.5%)	2 (9.1%)	NS
Acute aortic valve insufficiency	28 (15.7%)	24 (15.4%)	4 (18.2%)	NS

tronic DLP, Chase Medical Inc., Houston, TX, USA) were inserted into the innominate and left common carotid arteries through the aortic lumen. The left subclavian artery was clamped or occluded with a Fogarty catheter (Baxter Health Care, Irvine, CA, USA; IFM, Clearwater, FL, USA) in order to avoid the steal phenomenon.

The cerebral perfusion was started at a rate of 10 ml/min/kg and adjusted to maintain a right radial arterial pressure between 40 and 70 mmHg. During open distal anastomosis[18,19] blood perfusion to the lower half of the body from the femoral artery was discontinued.

The intimal tear was always resected if located in the ascending aorta or in the transverse arch; the false lumen was occluded with a monofilament suture using one or two Teflon (CR Bard, Tempe, AZ, USA) felts. Gelatine-resorcinol-formaldehyde glue (GRF-glue, Fii, Saint-Just-Malmont, France) or fibrinous glue (Tissuecol, Immuno AG, Vienna, Austria) was used to reinforce the proximal and distal anastomotic sites depending on the surgeons' preference.

After the open distal anastomosis was performed, the proximal graft was cross-clamped and the extracorporeal circulation reinstituted in antegrade manner through a side branch of the prosthesis. Rewarming was started.

In all patients, a careful exploration of the aortic arch was performed. The extent of the aortic replacement, determined by the intimal tear localization and not influenced by the patients' age, and the associated procedures are summarized in table III.

Both the "en bloc repair" and the "separated graft technique"[19] were used to reimplant the arch vessels to the aortic arch when that had to be totally replaced.

At the St. Antonius Hospital (Nieuwegein, The Netherlands), S. Orsola University Hospital (Bologna, Italy), and G.M. Lancisi Hospital (Ancona, Italy) the separated graft technique was used in all patients with massive involvement of the aortic arch and/or arch vessels by the dissection. At the Hamamatsu University Hospital (Hamamatsu, Japan), the arch vessels were reimplanted to the aortic arch using a four-branched graft in all patients requiring a complete aortic arch replacement.

Our cerebral monitoring platform included: right and left radial arterial pressure lines, electroencephalography, regional oxygen saturation in the bilateral frontal lobes by means of a near-infrared spectroscopy, and transcranial Doppler when available to confirm absence of brain malperfusion at the CPB institution and proper placement and function of cerebral perfusion cannulas. Transesophageal echocardiography was routinely used during intervention.

Statistical analysis. Continuous variables were expressed as the 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 when appropriate) to determine whether any single factor influenced the adverse outcome defined as the postoperative occurrence of hospital death or PND. A p value < 0.05 was considered as statistically significant. Variables that achieved $p < 0.2$ at the univariate analysis were examined using multivariate analysis by forward stepwise logistic regression to evaluate independent risk factors for adverse outcome.

Neurologic dysfunction was assessed by surgeons, anesthesiologists and neurologists when indicated. PND defined as stroke or coma, was assessed in all patients who survived the operation long enough to undergo neurologic evaluation. TND (postoperative confusion, agitation, delirium, prolonged obtundation, or transient parkinsonism with negative brain computed tomographic scanning and complete resolution before discharge) was assessed in all operative survivors without PND.

Statistical analysis was performed using the SPSS 11.0 statistical software (SPSS Inc., Chicago, IL, USA).

Table III. Operative techniques.

	All patients	Group A	Group B	p
No. patients	178	156 (87.6%)	22 (12.4%)	–
Extent of replacement				NS
Ascending aorta/hemiarch	128 (71.9%)	111 (71.2%)	17 (77.3%)	
Ascending aorta + arch	50 (28.1%)	45 (28.9%)	5 (22.7%)	
Arch vessel reimplantation				NS
En bloc	18 (36%)	17 (37.8%)	1 (20%)	
Separated graft technique	32 (64%)	28 (62.2%)	4 (80%)	
Associated procedures	55 (20.9%)	49 (31.4%)	6 (27.3%)	NS
Aortic valve replacement	7 (3.9%)	6 (3.8%)	1 (4.5%)	NS
Aortic valve resuspension	43 (24.2%)	39 (25.0)	4 (18.2%)	NS
Aortic valve reimplantation	6 (3.4%)	6 (3.8%)	-	NS
Bentall	21 (11.8%)	20 (12.8%)	1 (4.8%)	NS
Coronary artery bypass grafting	4 (2.2%)	3 (1.9%)	1 (4.5%)	NS
Elephant trunk	15 (8.4%)	13 (8.3%)	2 (9.1%)	NS

Results

As depicted in table IV, the mean CPB, myocardial ischemic, and ASCP times as well as the lowest nasopharyngeal and rectal temperatures were similar in group A (age < 75 years) and group B (age > 75 years).

An adverse outcome occurred in 37 of 178 patients overall (20.8%). Hospital death occurred in 30 of 178 patients (16.9%) and PND occurred in 12 of 168 patients who could undergo neurologic evaluation (7.1%). TND occurred in 14 of 155 patients (9.0%) of operative survivors without PND. Causes of death were: multiorgan failure (n = 13), bleeding (n = 6), cardiac failure (n = 3), neurologic damage (n = 3), residual false lumen rupture in the ward (n = 4), and visceral ischemia (n = 1).

Adverse outcome, hospital mortality and morbidity of the two groups are compared in table V. Adverse outcome was 21.2% (33 out of 178) in group A and 18.2% (4 out of 22) in group B (p = NS). Hospital mortality was 17.3% (27 out of 178) in group A and 13.6% (3 out of 22) in group B (p = NS).

In group B, 1 patient (81 years old) died from irreversible neurologic damage after receiving a hemiarch replacement for a type A dissection complicated preoperatively by leg ischemia, hemodynamic instability requiring cardiopulmonary resuscitation. Two patients died from bleeding. Of them, one (76 years old) died in the operative room from bleeding after receiving an ascending aorta and aortic arch replacement for a dissection complicated by renal ischemia and hemodynamic instability requiring cardiopulmonary resuscitation. The second one (77 years old) died from bleeding after receiving a supracoronary ascending aorta, hemiarch replacement and aortic valve replacement. The procedure was complicated by the dissection of the right coronary artery during weaning off the extracorporeal circulation which required a second run on CPB and vein grafting of the right coronary artery.

PND occurred in 6.8% of group A and in 10.0% of group B (p = NS). TND occurred in 9.5% of group A and in 5.6% of group B (p = NS).

No differences were observed in terms of systemic morbidity, intensive care unit and hospital stays between the two groups.

In group B univariate assessment revealed cardiopulmonary resuscitation (p = 0.043), CPB time (p = 0.020) and ASCP time (p = 0.033) to be associated with an adverse outcome. CPB time (p = 0.041, odds ratio 1.03/min) was indicated as the only predictive risk factor for adverse outcome on logistic regression analysis (Table VI).

Discussion

As a result of increased life expectancy a growing number of patients are referred for aortic operations.

Despite important advances in pre- and intraoperative management as well as in postoperative care, mortality and morbidity remain considerably high after acute type A dissection repair[1-6]. Furthermore, advanced age is considered as a strong risk factor for hospital mortality, hospital morbidity and prolonged inten-

Table IV. Perfusion data.

	All patients	Group A	Group B	p
CPB time (min)	198 ± 68	202 ± 70	178 ± 58	NS
Myocardial ischemic time (min)	117 ± 48	118 ± 49	111 ± 36	NS
ASCP time (min)	59 ± 27	60 ± 29	52 ± 20	0.026
Nasopharyngeal temperature (°C)	23 ± 2	23 ± 3	22 ± 2	NS
Rectal temperature (°C)	25 ± 3	25 ± 3	24 ± 3	NS

ASCP = antegrade selective cerebral perfusion; CPB = cardiopulmonary bypass.

Table V. Adverse outcome and morbidity.

	All patients	Group A	Group B	p
Adverse outcome	42 (23.6%)	37 (23.7%)	5 (22.7%)	NS
Hospital mortality	30 (16.9%)	27 (17.3%)	3 (13.6%)	NS
Permanent neurologic dysfunction	12 (7.1%)	10 (6.8%)	2 (10.0%)	NS
Transient neurologic dysfunction	14 (9.0%)	13 (9.5%)	1 (5.6%)	NS
Postoperative dialysis	16 (9.4%)	15 (9.9%)	1 (5.0%)	NS
Intubation time > 3 days	46 (26.9%)	42 (27.8%)	4 (20.0%)	NS
Postoperative myocardial infarction	8 (4.7%)	7 (4.6%)	1 (4.0%)	NS
Rethoracotomy	22 (13.3%)	19 (12.9%)	3 (15.8%)	NS
Intensive care unit stay (days)	7.4 ± 8.0	7.5 ± 8.3	7.0 ± 5.6	NS
Hospital stay (days)	23.6 ± 22.3	23.6 ± 23.4	19.1 ± 13.7	NS

Table VI. Univariate and multivariate analysis for adverse outcome in group B.

Variable	Adverse outcome	Univariate	Multivariate	OR	95% CI
CPR		0.043			
Yes	2/3 (66.7%)				
No	2/19 (10.5%)				
CPB time (min)	162 ± 35 vs 247 ± 94	0.020	0.041	1.03/min	0.99-2.30
ASCP time (min)	49 ± 14 vs 68 ± 34	0.033			

ASCP = antegrade selective cerebral perfusion; CI = confidence interval; CPB = cardiopulmonary bypass; CPR = cardiopulmonary resuscitation; OR = odds ratio.

sive care unit stay and controversial results after acute type A dissections in elderly patients have been reported[7,20,21].

In this study, we retrospectively compared early results in two groups of patients (younger and older than 75 years) after type A dissection repair. The two groups had similar preoperative characteristics except for a higher rate of tamponade, hemodynamic instability and cardiopulmonary resuscitation in the elderly group.

The operative management was similar in both groups: the aortic arch was always explored under a period of moderately hypothermic circulatory arrest with ASCP and the aortic arch was partially or totally replaced if the entry tear was found at that site. In fact no differences in terms of extent of the aortic replacement and arch vessel reimplantation technique were observed.

ASCP with moderate hypothermia, as described by Kazui et al.[16], was employed in all patients with the same protocol including ASCP flow of 10 ml/kg/min, right radial arterial pressure between 40 and 70 mmHg, nasopharyngeal temperature between 22-25°, and complete neuromonitoring platform. Probably due to a more fragile aortic tissue, in elderly patients the distal aortic reconstruction required a slightly longer period of cerebral perfusion. CPB and myocardial ischemic times were similar in both groups.

It has been suggested that advanced age and prolonged duration of deep hypothermic circulatory arrest are important risk factors for mortality and adverse neurologic outcome in patients undergoing surgery for acute type A aortic dissection[22-24]. In our experience, the overall hospital mortality, PND and TND rates were 17.3, 6.8, and 9.5%, respectively. Despite a higher preoperative predicted risk in elderly patients, due to a higher incidence of tamponade, hemodynamic instability and cardiopulmonary resuscitation, hospital mortality and adverse neurologic outcome were similar in younger and elderly patients.

This probably underscores the neuroprotective effectiveness of ASCP which is believed to be superior to other methods of brain protection for the following reasons:

- it continuously supplies oxygenated blood to the brain supporting an aerobic metabolism even after prolonged periods of circulatory arrest;
- we have previously demonstrated that using ASCP the extent of aortic replacement and a cerebral perfusion time up to 90 min are not associated with an increased risk of hospital mortality and adverse neurologic outcome[8]. From our results, it seems possible to state that this finding can be confirmed also for elderly patients. In fact, though a more conservative approach was not used in patients with advanced age, as documented by extended aortic arch replacement rates and duration of ASCP, results were acceptable and similar to those obtained with younger patients. Moreover, a less extended aortic tissue replacement might result in an increased risk of death for rupture of residual false lumen due to a more fragile dissected aortic wall in elderly patients as suggested by Kawahito et al.[20];
- we have previously demonstrated that moderate (instead of deep hypothermia) can be used with reduced duration of CPB, and lower pulmonary, renal and coagulative morbidity[11]. Indeed, in this series, elderly patients, obviously exposed to a higher probability of postoperative complications, favorably compared with younger patients in terms of systemic morbidity, the incidence of pulmonary, renal, cardiac and bleeding complications being similar in the two groups.

We know that this study carries the risks inherent to the use of retrospective multicenter data, and the elderly group constitutes only 12.4% of all patients. However, for the statistical analysis, we combined permanent neurologic injury and death as adverse outcome to increase our sensitivity to identify, among preoperative and intraoperative factors, those that may result in adverse outcome.

In our series of elderly patients, CPB time resulted to be the only predictive risk factor for an adverse outcome. This probably suggests that, especially in elderly patients, the utilization of deep hypothermia and circulatory arrest with or without retrograde cerebral perfusion during complex aortic procedures might result in a worse outcome as a result of prolonged intervals of extracorporeal circulation required to cool down and rewarm the patient.

In conclusion, during type A dissection repair the implementation of ASCP resulted in an acceptable hospital mortality and neurologic outcome. If ASCP is used, the risk of hospital mortality and postoperative morbidity is similar in patients younger and older than

75 years. Duration of CPB still remains an important risk factor for hospital mortality and neurologic outcome in elderly patients.

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