Deep hypothermic circulatory arrest and antegrade selective cerebral perfusion during ascending aorta–hemiarch replacement: A retrospective comparative study

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Objective: We sought to compare the results of ascending aorta–hemiarch replacement by using 2 different methods of cerebral protection in terms of hospital mortality, neurologic outcome, and systemic morbidity and to determine predictive risk factors associated with hospital mortality and neurologic outcome after ascending aorta–hemiarch replacement.

Methods: Between January 1995 and September 2001, 289 patients (mean age, 62.2 ± 13.2 years; urgent status, 122/289 [42.2%]) underwent ascending aorta–hemiarch replacement with the aid of antegrade selective cerebral perfusion (161 patients) or deep hypothermic circulatory arrest (128 patients).

Results: Overall hospital mortality was 11.4% (deep hypothermic circulatory arrest group, 13.3%; antegrade selective cerebral perfusion group, 9.9%; P = .375). A logistic regression analysis revealed acute type A dissection (P = .001; odds ratio, 4.3) and age of greater than 70 years (P = .019; odds ratio, 2.5) to be independent predictors of hospital mortality. The permanent neurologic dysfunction rate was 9.3% (deep hypothermic circulatory arrest group, 12.5%; antegrade selective cerebral perfusion group, 7.6%; P = .075). Logistic regression analysis revealed acute type A dissection (P = .001; odds ratio, 6.7) and history of cerebral infarction–transient ischemic attack (P = .038; odds ratio, 3.4) to be independent predictors of permanent neurologic dysfunction. The transient neurologic dysfunction rate was 8.0% (deep hypothermic circulatory arrest group, 7.1%; antegrade selective cerebral perfusion group, 8.7%; P = .530). Acute type A dissection (P = .001; odds ratio, 5.1) was indicated as an independent predictor of transient neurologic dysfunction by means of logistic regression. Renal dysfunction (postoperative creatinine level of >250 μmol/L; deep hypothermic circulatory arrest, 10 [7.8%]; antegrade selective cerebral perfusion, 6 [3.7%]; P = .030), as well as prolonged intubation time (deep hypothermic circulatory arrest, 3.8 ± 6.3 days; antegrade selective cerebral perfusion, 2.2 ± 2.5 days; P = .005) were more common in the deep hypothermic circulatory arrest group.

Conclusion: The use of antegrade selective cerebral perfusion and deep hypothermic circulatory arrest during ascending aorta–hemiarch replacement resulted in acceptable hospital mortality and neurologic outcome. Reduced postoperative intubation time and better renal function preservation were observed in the antegrade selective cerebral perfusion group.
Use of optimal methods of brain, spinal, and myocardial protection, as well as prevention and treatment of hemorrhage and coagulopathy, are primary concerns during operations of the thoracic aorta.

Current methods of brain protection include deep hypothermic circulatory arrest (DHCA), retrograde cerebral perfusion, and antegrade selective cerebral perfusion (ASCP). All 3 methods have advantages and disadvantages.

In our institute ASCP is currently the method of choice for cerebral protection, especially for patients requiring complex aortic arch repairs. When a circulatory arrest time of less than 30 minutes is anticipated, the selection of the brain protection method (between DHCA and ASCP) depends on the surgeon’s preference.

This study was undertaken to determine the predictive risk factors associated with hospital mortality and neurologic outcome in patients undergoing ascending aorta–hemiarch replacement with ASCP and DHCA. A comparison between the 2 techniques was also performed in terms of hospital mortality, neurologic outcome, and systemic morbidity.

**Patients and Methods**

Between January 1995 and September 2001, 289 patients underwent ascending aorta–hemiarch replacement at the St Antonius Hospital, Department of Cardiothoracic Surgery, Nieuwegein, The Netherlands.

Medical records were reviewed for clinical variables, including preoperative status, intraoperative data, and early postoperative complications (see Appendix). There were 189 (65.3%) men and 100 (34.7%) women, with a mean age of 62.2 ± 13.2 years (age range, 23–85 years). The indications for surgical intervention were acute type A dissection in 122 (42.2%) patients and chronic postdissection aneurysm or degenerative aneurysm in 167 (57.8%) patients.

Cerebral protection was achieved by means of DHCA in 128 patients (DHCA group, 44.3%) and ASCP and moderate hypothermia in 161 patients (ASCP group, 55.7%). The year in which the operation was performed did not influence the selection of the brain preservation technique used. Patient demographics were essentially similar in the 2 groups (Table 1).

All patients having elective surgery underwent preoperative evaluation of cerebral circulation with Doppler ultrasonography of the extracranial vessels, digital subtraction angiography of the extracranial and intracranial circulation, carotid compression tests with monitoring by means of electroencephalography to evaluate occlusion intolerance, or a transcranial Doppler ultrasonographic study when available.

**Operative Technique**

Induction of anesthesia was obtained with 2 mg/kg propofol, 2 μg/kg fentanyl, and 0.1 mg/kg pancuronium. Anesthesia was maintained with propofol and fentanyl. For all patients, pH balance control was carried out by using the alpha-stat method. No pharmacologic neuroprotective agents were administered. Aprotinin was used sporadically.

Cerebral monitoring was achieved by means of a right radial arterial pressure line, electroencephalography, regional oxygen saturation in the bilateral frontal lobes with near-infrared spectroscopy, and transcranial Doppler ultrasonographic measurement of the blood velocity of the middle cerebral arteries.

The proximal thoracic aorta was approached by means of a median sternotomy in all cases. After systemic heparinization, cardiopulmonary bypass (CPB) was instituted with a cannula for arterial return to the ascending aorta or the femoral artery and a venous single 2-stage cannula in 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, maintaining the myocardial temperature at or below 14°C.

In the DHCA group core cooling was instituted during CPB to produce profound hypothermia. During this period, usually requiring 30 to 40 minutes, the proximal repair was performed. The head was packed in ice to prevent warming of the central nervous system. When a flat-line electroencephalogram was achieved, circulation was arrested, and the distal repair was carried out. On completion of the procedure, gradual warming was carried out by means of CPB, limiting the gradient between blood and body temperature to less than 10°C, with a maximum blood temperature of 37°C. A warming blanket was also used. Central warming was usually discontinued at a rectal temperature of 35°C.

Details of our cannulation technique and method of ASCP with moderate hypothermic circulatory arrest have been previously described. Cerebral perfusion was initiated at a rate of 10 mL×min⁻¹×kg⁻¹ and adjusted to maintain a right radial arterial pressure of between 40 and 70 mm Hg.

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

The extent of the aortic replacement and the associated procedures are listed in Table 2.

**Statistical Analysis**

Continuous variables were expressed as the mean ± 1 SD and were analyzed by using the unpaired 2-tailed t test. Categoric variables were presented as percentages and were analyzed with the χ² test or Fisher exact test when appropriate. All preoperative and intraoperative variables were first analyzed by using univariate analysis to determine whether any single factor influenced hospital mortality and neurologic outcome. Variables that achieved a P value of less than .05 in the univariate analysis were examined by using multivariate analysis with forward stepwise logistic regres-
sion to evaluate independent risk factors for hospital mortality, permanent neurologic dysfunction (PND), and transient neurologic dysfunction (TND).

The analysis for PND (stroke or coma) and TND (postoperative confusion, agitation, delirium, prolonged obtundation, or transient parkinsonism with negative brain computed tomographic scanning results and complete resolution before discharge) were conducted separately. Risk factors for PND were examined in all patients who survived the operation long enough to undergo neurologic evaluation. Risk factors for TND were assessed in all operative survivors without PND. Statistical analysis was performed with SASS 10.0 statistical software (SASS Inc).

Results
Hospital Mortality
Circulatory arrest and perfusion data are summarized in Table 3.

There were 33 (11.4%) in-hospital deaths. Hospital mortality for elective surgery was 5.8%, and that for urgent surgery was 17.8% \((P = .001)\). Causes of death were multiorgan failure \((n = 14)\), PND \((n = 5)\), distal aneurysm rupture \((n = 4)\), pneumonia \((n = 4)\), hemorrhage \((n = 2)\), mediastinitis \((n = 2)\), low cardiac output \((n = 1)\), and bowel ischemia \((n = 1)\).

Univariate analysis revealed that acute type A dissection \((P = .001)\), age greater than 70 years \((P = .018)\), history of cerebral infarction–transient ischemic attack \((TIA); P = .041)\), and Bentall procedure \((P = .012)\) were significant predictors of mortality. A stepwise logistic regression analysis showed that acute type A dissection \((P = .001); odds ratio [OR], 4.3; 95% confidence interval [CI], 1.90-9.67\) and age greater than 70 years \((P = .019); OR, 2.5; 95% CI, 1.57-5.23\) were independent predictors of hospital mortality.

Hospital Morbidity
PND occurred in 27 (9.3%) patients. Univariate analysis revealed acute type A dissection \((P = .001)\) and history of cerebral infarction–TIA \((P = .018)\) to be predictors of stroke. These findings were confirmed by means of stepwise logistic regression (acute type A dissection: \(P = .001\); OR, 6.7; 95% CI, 2.44-18.41; history of cerebral infarction–TIA: \(P = .038\); OR, 3.4; 95% CI, 1.07-11.42)
TABLE 3. CPB data

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<th>Total group, n (%)</th>
<th>DHCA, n (%)</th>
<th>ASCP, n (%)</th>
<th>P value</th>
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<tr>
<td>CPB time (min)</td>
<td>198 ± 74</td>
<td>197 ± 54</td>
<td>198 ± 60</td>
<td>.982</td>
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<tr>
<td>Myocardial ischemic time (min)</td>
<td>119 ± 46</td>
<td>105 ± 41</td>
<td>129 ± 48</td>
<td>.001</td>
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<tr>
<td>Total cerebral protection time (min)</td>
<td>35 ± 21</td>
<td>29 ± 9</td>
<td>42 ± 20</td>
<td>.001</td>
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<tr>
<td>Nasopharyngeal temperature (°C)</td>
<td>16.1 ± 2.8</td>
<td>18.2 ± 2.8</td>
<td>23.2 ± 2.6</td>
<td>.001</td>
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TND occurred in 21 (8.0%) of the 262 patients who survived surgical intervention without PND. Univariate analysis indicated that acute type A dissection (P = .002) and ejection fraction of less than 50% (P = .048) were significant predictors of TND. Concomitant procedures (P = .066) and history of cerebral infarction–TIA (P = .075) were of borderline significance. Stepwise logistic regression showed acute type A dissection (P = .001; OR, 5.1; 95% CI, 1.87-14.19) to be an independent predictor of TND.

Hospital morbidity included pulmonary complications requiring mechanical ventilatory support for more than 5 days in 36 (12.5%) patients, renal failure requiring temporary hemodialysis in 5 (1.7%) patients, and postoperative myocardial infarction (serum creatine phosphokinase level of >300 IU/L with a creatine phosphokinase-MB fraction of >3%) in 18 (6.2%) patients. Mean drain blood production was 1524 ± 1090 mL (range, 180-7200 mL). Thirty-five (12.1%) patients underwent a repeat thoracotomy for bleeding. Patients received an average of 5.3 ± 4.2 units of packed red cells (range, 0-25 units). The average blood product consumption, defined as fresh frozen plasma and platelet consumption, was 5.7 ± 3.9 units per patient (range, 0-21 units). Univariate analysis revealed redo operations (P = .026) and CPB time of greater than 240 minutes (P = .012) to be risk factors for a greater consumption of packed red cells and blood products.

**DHCA Versus ASCP**

The mean CPB times were similar in the DHCA and ASCP groups (DHCA, 198 ± 54 minutes; ASCP, 198 ± 60 minutes; P = .982) as a result of prolonged myocardial ischemic protection (DHCA, 105 ± 41 minutes; ASCP, 129 ± 48 minutes; P = .001) and total cerebral protection (DHCA, 29 ± 9 minutes; ASCP, 42 ± 20 minutes; P = .001) times in the ASCP group (Table 3). In fact, more extended aortic tissue replacement and a larger number of aortic root repairs were performed in the ASCP group (Table 2).

Hospital mortality and morbidity of the 2 groups are compared in Table 4.

Hospital mortality was 13.3% (17/128) in the DHCA group and 9.9% (16/161) in the ASCP group (P = .375). PNDs were more common in the DHCA group (16 [12.5%]) than in the ASCP group (11 [7.6%]), although statistical significance was not reached (P = .075). TND occurred in 7.1% of the DHCA group and 8.7% of the ASCP group (P = .530). Univariate analysis (Table 5) revealed that a circulatory arrest time of greater than 25 minutes was associated with an increased risk of TND in the DHCA group (P = .021), whereas ASCP duration had no effect on neurologic outcome. Renal dysfunction (postoperative creatinine level of >250 µmol/L; DHCA, 10 [7.8%]; ASCP, 6 [3.7%]; P = .030) and prolonged intubation time (DHCA, 3.8 ± 6.3 days; ASCP, 2.2 ± 2.5 days; P = .005) were more common in the DHCA group. No differences were observed between the 2 groups in terms of drain blood production (P = .809) or packed red cells (P = .529) and blood products consumption (P = .347).

**Discussion**

Despite the fact that the results of the surgical intervention of the thoracic aorta have gradually improved, hospital mortality and neurologic and systemic complications still remain considerable. In our series hospital mortality was 11.4% (5.8% and 17.8% in elective and urgent procedures, respectively).

Acute type A aortic dissection and advanced age were independent predictors of hospital mortality, confirming previous reports. PND and TND rates were 9.3% and 8%, respectively. In accordance with other clinical reports, the presence of acute type A aortic dissection and a history of cerebral infarction–TIA predicted the occurrence of postoperative adverse neurologic outcome.

Washiyama and colleagues have demonstrated that a canine brain having a previous cerebral infarction is more susceptible to ischemia during aortic arch operation by using ASCP as a consequence of an accelerated anaerobic metabolism and an increased extracellular glutamate release in the brain from the previous infarction.

Kazui and colleagues recently reported a postoperative PND rate of 3.3% in a group of 220 patients undergoing aortic arch replacement with aortic branched grafts and ASCP. The presence of a previous cerebral infarction was an independent determinant of PND, with a relative risk of 21.8 on multivariate analysis.

Similarly, a history of cerebrovascular disease has been
shown to be an independent predictor of postoperative stroke in aortic arch replacement with DHCA alone.\textsuperscript{3,4}

DHCA with or without retrograde cerebral perfusion and ASCP are currently being used as methods of brain protection.

Technical simplicity and avoidance of aorta and arch vessel manipulation, as well as a bloodless operative field, make DHCA an attractive method of brain protection, especially during ascending aorta–hemiarch replacement, when a short period of circulatory arrest is anticipated. However, hypothermia-associated coagulopathy\textsuperscript{7} and pulmonary, renal, and microembolic complications\textsuperscript{8} are important disadvantages cited in the literature.

ASCP provides several advantages: the circulatory arrest time can safely be extended up to 90 minutes,\textsuperscript{1} allowing more complex aortic repair to be performed, and moderate (nasopharyngeal temperature 25°C) instead of profound hypothermia can be used with reduced coagulative and systemic complications. Criticism against ASCP includes technical complexity, reduced surgical visibility, and manipulation of the aortic arch and arch vessels, especially in cases of acute dissection or severely atherosclerotic aortic arch aneurysm.

In the current study we compared DHCA and ASCP in terms of hospital mortality and neurologic and systemic morbidity in a group of patients undergoing ascending aorta–hemiarch replacement.

In our series the patients in the ASCP group had a more extended aortic tissue replacement and a larger number of aortic root repairs. Nevertheless, hospital mortality and neurologic outcome were comparable in the 2 groups; reduced intubation time and better renal function recovery were noted in the ASCP group.

TND seems to be a manifestation of subtle but diffuse brain injury associated with long-lasting cognitive impairment undetectable by means of conventional imaging techniques and directly correlated to inadequate brain protection.\textsuperscript{9}

In our series a circulatory arrest time of greater than 25 minutes was associated with an increased risk of TND in the DHCA group.

Reich and colleagues\textsuperscript{10} have demonstrated that a DHCA time of 25 minutes or greater is associated with memory and fine motor deficits, as well as with prolonged hospital stays. McCullough and colleagues\textsuperscript{11} have recently demonstrated that the cerebral metabolic rate is still 17% of the baseline at 15°C and that the safe duration of circulatory arrest at 15°C is only 29 minutes. These findings probably indicate that circulatory arrest times of 45 to 60 minutes were too optimistically indicated as safe.\textsuperscript{4}

Surprisingly, no significant differences in terms of retorhacotomy for bleeding, drain blood loss, and blood products consumption was observed between the 2 groups. This was probably because of similar mean CPB times in the 2 groups or damage of the blood components occurring during perfusion through the small ASCP cannulas.

In conclusion, even though this study carries the risks inherent to the use of retrospective data, some important conclusions can be reached: (1) the use of DHCA and ASCP resulted in acceptable results in terms of hospital mortality and neurologic outcome during ascending aorta–hemiarch replacement; (2) only preoperative patient characteristics, such as acute type A aortic dissection, age greater than 70 years, and history of cerebral infarction–TIA, affected hospital mortality and neurologic outcome; (3) in the DHCA group a circulatory arrest time of more than 25 minutes was associated with an increased risk of TND; and (4) reduced

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<th>TABLE 4. DHCA versus ASCP</th>
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<tr>
<td>Hospital mortality</td>
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<td>PND</td>
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<td>TND</td>
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<td>Intubation time (d)</td>
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<td>Postoperative creatinine &gt;250 μmol/L</td>
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<td>Postoperative dialysis</td>
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<td>Postoperative MI</td>
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<td>Rethoracotomy for bleeding</td>
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<td>Drain blood production</td>
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<td>Packed red cells</td>
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<td>Blood products consumption</td>
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Mi, Myocardial infarction.

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<th>TABLE 5. TND patient distribution by DHCA time</th>
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<td>TND</td>
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<td>Yes</td>
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In our series a circulatory arrest time of greater than 25 minutes was associated with an increased risk of TND in the DHCA group.
postoperative intubation time and better renal function recovery were observed in the ASCP group.

References


