Improvement of Quality of Life After Surgery on the Thoracic Aorta
Effect of Antegrade Cerebral Perfusion and Short Duration of Deep Hypothermic Circulatory Arrest

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Background—We have recently demonstrated that the use of deep hypothermic circulatory arrest (DHCA) during surgery for acute type A aortic dissections or thoracic aortic aneurysms adversely affect mid-term quality of life (QoL). The aim of this study is to assess the impact of DHCA duration and the potential effects of antegrade cerebral perfusion (ACP) on mid-term QoL.

Methods and Results—Between January 1994 and December 2002, 363 patients underwent surgery of the thoracic aorta with the use of DHCA at our institution. One hundred seventy-six (48.5%) presented with acute type A dissections and 187 (51.5%) presented with aortic aneurysms. ACP was used in 41 (11.3%) cases. All in-hospital data were assessed and a follow-up was performed in all survivors after 2.4±1.2 years. QoL was analyzed with the Short-Form 36 Health Survey Questionnaire (SF-36). In-hospital mortality was 8.6%. In comparison with patients having undergone DHCA <20 minutes, averaged QoL score was significantly decreased in patients with DHCA between 20 and 34 minutes (95.6±12.8 versus 81.9±15.7; P<0.01) and >35 minutes (61.8±18.3; P<0.01). Averaged QoL score was significantly better with the use of ACP, independently of the duration of DHCA.

Conclusions—DHCA duration >20 minutes, and especially >35 minutes, adversely affects mid-term QoL in patients undergoing surgery of the thoracic aorta. The use of ACP, however, improved averaged QoL score at each time period and allows DHCA to be extended up to 30 minutes, without impairment in mid-term QoL. (Circulation. 2004;110[suppl II]:II-250–II-255.)

Key Words: aortic dissection aortic aneurysm cerebral perfusion quality of life circulatory arrest

Besides considerations of technical success and general outcome, the assessment of quality of life (QoL) after major surgical interventions is of increasing interest,1,2,7 because the preservation or improvement of QoL should be the principal goal of all medical care.

Previous studies have shown that patients with acute type A aortic dissection had a postoperative QoL inferior to the QoL of patients who underwent surgery for aortic aneurysm.1 We have shown that the application of deep hypothermic circulatory arrest (DHCA) in surgery of thoracic aortic aneurysms frequently results in an impairment of QoL—as it has been observed especially in patients older than age 70 years.2 With the introduction of antegrade cerebral perfusion (ACP), the adverse neurological effects of prolonged DHCA could be markedly reduced.8,9

Still, the influence of DHCA duration on mid-term outcome with respect to mortality, morbidity, and QoL is unknown and the potential benefit of ACP on QoL, especially, remains to be elucidated. In the present study, we assessed the influence of DHCA in thoracic aortic surgery on mid-term QoL and evaluated the effects of ACP as a potential method of QoL preservation.

Methods

Between January 1994 and December 2002, 363 (61.5%) of 590 patients underwent surgery on the thoracic aorta with the use of DHCA. One hundred seventy-six (48.5%) of these patients underwent operation for acute type A dissections, and the remaining 187 (51.5%) underwent surgery for aortic aneurysms. ACP was used in 41 patients (11.3%).

The 363 patients, having undergone operation using DHCA, were divided into 3 groups, according to the duration of DHCA: (1) 196 patients (54.0%) with <20 minutes of DHCA (group 1); (2) 108 patients (29.8%) with a DHCA time of 20 to 29 minutes (group 2); and (3) 59 patients (16.3%) with a DHCA of ≥30 minutes (group 3).

All preoperative, intraoperative, and postoperative data were assessed and are displayed in Table 1. Mean follow-up was 2.4±1.2 years (range, 11 to 47 months). QoL was assessed using the Short-Form 36 Health Survey Questionnaire (SF-36).10–12 Details of this validated questionnaire have been published previously.1,2 The SF-36 consists of 36 short questions reflecting QoL in 8 different aspects: bodily pain (abbreviated BP, 2 items); mental health (MH, 5); vitality (VT, 4); social functioning (SF, 2); general health (GH, 5);
Mean operation time was 229/82 minutes in group 1, 253 minutes ± 74 minutes in group 2, and 290/82 minutes in group 3 (P<0.05). Mean duration of DHCA was 14±3 minutes, 24±3 minutes, and 38±11 minutes, with a core temperature of ±20°C (Table 1). Pentothal was administered in all patients 2 to 3 minutes before initiation of DHCA. The temperature of the perfusate for ACP was set at 8°C. ACP during DHCA with oxygenated blood was performed via catheter in the left common carotid artery and in the truncus brachiocephalicus with a pressure of 30 to 40 mm Hg, corresponding to a flow of 200 to 250 mL/min. We started to use ACP during DHCA in June 2000. Cerebral perfusion during DHCA was mainly applied in patients with an expected circulatory arrest of >20 minutes. No neuromonitoring was used during the procedure at our institution in this study collective.

Statistical Analysis
Data are presented as mean±1 SD. A Mann–Whitney U test and \( \chi^2 \) test were used for comparison between groups of continuous and nominal variables, respectively. Linear regression for the relationship between DHCA duration and averaged QoL score was analyzed. P<0.05 was considered significant.

The SF-36 questionnaire was analyzed in accordance to the SF-36 manual, replacing missing values using the described algorithm. Scores were adjusted for gender and age to be comparable with the normal population. Data were analyzed using the StatView 4.1 statistical package (Abacus Concepts).

Results

Patients Characteristics
Patients characteristics are displayed in Tables 1 and 2. Twelve patients (3.3%) had a history of preoperative neuro-
logical events. Two patients had a persistent neurological cerebrovascular insult (CVI) with neurological limitations in daily activity at admission.

Postoperative malperfusion syndrome were found in 47 patients (12.9%). Malperfusion syndrome was significantly more frequent in patients from group 2 (23.1%), in comparison to group 1 (7.1%) and group 3 (11.9%) \((P < 0.05)\).

Neurological events postoperatively were reported in 78 patients (21%). A significantly higher incidence of neurological events was found in group 3 (33.9%) in comparison to group 1 (15.3%) \((P < 0.05)\). Postoperative outcome data showed no significant differences in the incidence of neurological events if patients have been operated with or without ACP (Table 2). Patients with persistent neurological events at discharge showed a poor outcome, with a mortality rate of 60% (15 of 25 patients died during the follow-up).

SF-36

QoL scores, averaged for patients with acute type A dissections and aortic aneurysms, are summarized in Figure 1 in relation to the duration of DHCA. After 20 minutes of DHCA, averaged score of SF-36 was similar in patients with type A dissections and aortic aneurysms \((P = NS)\). The time period of <20 minutes had an average QoL score that was significantly better in patients undergoing operation for aortic aneurysms \((P < 0.05)\) (Figure 1).

In comparison to an age-matched and gender-matched standard population (results <85 reflect an impairment in QoL), averaged QoL score was significantly decreased in patients with 20 to 34 minutes of DHCA (95.6±12.8 versus 81.9±15.7; \(P < 0.05\)) and, more importantly, in those with >35 minutes (61.8±18.3; \(P < 0.05\)) (Figure 2). ACP results in a significant improvement of averaged QoL score at each time period \((P < 0.05)\) (Figure 3).

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**Table 2. Characteristics of Patients From Groups 1, 2, and 3**

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Group 1 (DHCA &lt;20 min)</th>
<th>Group 2 (DHCA 20–30 min)</th>
<th>Group 3 (DHCA &gt;30 min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>No ACP</td>
<td>ACP</td>
<td>P</td>
</tr>
<tr>
<td>Age, y</td>
<td>182</td>
<td>14</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Male</td>
<td>136</td>
<td>12</td>
<td>NS</td>
</tr>
<tr>
<td>Preoperative Data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of MI</td>
<td>14</td>
<td>1</td>
<td>NS</td>
</tr>
<tr>
<td>History of neurological event</td>
<td>6</td>
<td>1</td>
<td>NS</td>
</tr>
<tr>
<td>Outcome Data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malperfusion</td>
<td>13</td>
<td>1</td>
<td>NS</td>
</tr>
<tr>
<td>Neurological event (total)</td>
<td>28</td>
<td>2</td>
<td>NS</td>
</tr>
<tr>
<td>Transient neurological event</td>
<td>25</td>
<td>2</td>
<td>NS</td>
</tr>
<tr>
<td>Persistent neurological event</td>
<td>3</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Length of stay</td>
<td>13.4±10.4</td>
<td>14.1±8.3</td>
<td>NS</td>
</tr>
</tbody>
</table>

Comparison between patients operated without and with antegrade cerebral perfusion (ACP). MI indicates myocardial infarction; NS, not significant.

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**Figure 1.** Age-matched and gender-matched comparison for the averaged SF-36 score for patients undergoing operation for aortic aneurysms and acute type A dissection. Results are displayed in relation to the duration of DHCA.
The subgroup analyses of all the 8 aspects assessed with the SF-36 (Figures 4 through 6) revealed normal results in all aspects in comparison with an age-matched and gender-matched standard population (scores < 85 reflect a significant impairment) in patients from group 1 (Figure 4). With increasing DHCA time (groups 2 and 3), patients undergoing operation without ACP showed significantly lower results for the aspects physical functioning (PF), social functioning (SF), and vitality (VT) (P < 0.05), reflecting limitations in daily activity (Figures 5 and 6).

Discussion
The impact of the duration of DHCA and the effect of ACP on mid-term QoL in patients undergoing thoracic aortic surgery is of increasing interest. We report our results of 363 patients in whom DHCA was used (out of a collective of 590 patients who underwent surgery on the thoracic aorta). Surgical outcome is similar to that of other studies.13,14 Observed morbidities are also in the already reported range.8,9 In our collective, the use of ACP did not reduce the incidence of neurological events.8,9

The results of the present study generally confirm our previous findings showing superior QoL in patients with thoracic aortic aneurysms as compared with patients with acute type A dissections.9 However, according to the findings displayed in Figure 1, it is evident that the difference in the averaged QoL scores of these 2 diseases is mostly derived from the patients who had DHCA between 14 and 19 minutes. After 20 minutes of DHCA, the averaged score of SF-36 is not different between the 2 groups.

According to the findings illustrated in Figure 2, DHCA periods of >20 minutes and especially of >35 minutes are associated with a significant decrease in mid-term QoL.

Based on the results of several mid-term and long-term studies, the generally accepted assumption considered DHCA at ~18°C for durations of up to 40 minutes or even more as safe, regarding mortality and morbidities.9 In this study, which is the first to our knowledge to assess the influence of DHCA duration on QoL, we found that DHCA periods of >20 minutes and especially of ≥35 minutes have a significant adverse effect on mid-term QoL. Taking into account these findings and focusing on mid-term QoL,
which is apparently more sensitive to the duration of DHCA than mortality and morbidity, one may assume that DHCA of ≥35 minutes should be avoided. Griepp et al recently reported their results of a study using an animal setting and cerebral metabolism in pig brains. They found that metabolism was reduced with decreasing temperature as expected from the fact that chemical processes slow down. However, metabolism at a core temperature of 20°C was still at 20% of its normal level. These findings suggest that pig brain activity at this temperature is still high enough to cause diffuse brain damage (ie, by cell necrosis) if blood circulation is arrested.

Detailed analysis of the 8 different aspects assessed with the SF-36 revealed significant impairments of the aspects physical functioning (PF), social functioning (SF), and vitality (VT) in DHCA time >20 minutes in patients undergoing operation without ACP (groups 2 and 3) (Figures 5 and 6). These results reflect limitations in daily activity. Increasing limitations in daily activity probably can explain the deterioration in the aspects general health (GH) and bodily pain (BP) reported in group 3 (Figure 6) patients who underwent operation without ACP.

QoL mainly depends on mental and psychic brain performance and on impairments caused by pain. Because we chose the follow-up to be at a time later than 12 months postoperatively, influence of postoperative pain on QoL was minimal, as shown by rare symptoms of postoperative pain in our patients. The largest influence on QoL in this study is therefore related to the mental and psychic brain performance. We have reasons to suspect that low average scores of QoL may be the main consequence of diffuse brain damage induced by DHCA. This observation is further supported by the fact that the application of ACP resulted in a significant improvement of QoL scores for all DHCA periods (<20, 20 to 29, ≥30 minutes) (Figure 3). The correlation between QoL impairment and DHCA duration may also suggest that in humans, 18°C core temperature provides only an incomplete cerebral protection, which may result in a diffuse brain damage.

For all patients referred to in this study in whom ACP has been applied, the temperature of the perfusate for ACP was set at 8°C. We know from data published by Griepp that at this temperature, pig brain metabolic activity is reduced to 11% of its normal level. With respect to optimizing ACP temperature, several effects need to be observed. Although slower chemical processes and reduced enzyme activities with their effect on apoptosis at lower temperatures are regarded as beneficial, other effects such as possible degen-
eration of proteins, and especially chromatin condensation, need to be observed.17–19

Decreasing autoregulation with lower temperatures leads to blood flow requirements higher than suggested by the O2 consumption under these conditions (luxury perfusion4).

In this context, it also may be interesting to further investigate the potential additional benefits of applying norepinephrine to control these hemodynamic changes during ACP.

Because most human organs, apart from the brain, are less sensitive to hypoxemia, it is not necessary to lower the body temperature to the same temperature of the brain. Therefore, the technique described by Bachet et al, with a cold head (10°C to 12°C) and a warm body (22°C to 28°C), is considered, based on the findings in the present study, a good approach to improve mid-term QoL in patients undergoing surgery on the thoracic aorta. We therefore concluded that duration >20 minutes, but especially >35 minutes, of DHCA in patients undergoing surgery on the thoracic aorta results in significant mid-term QoL impairment. With the use of ACP, however, averaged QoL score was significantly better in comparison with an age-matched and gender-matched standard population at each time period and allows the extension of DHCA up to 30 minutes.

References
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