

Cerebral Protection During Surgery for Acute Aortic Dissection Type A

Results of the German Registry for Acute Aortic Dissection Type A (GERAADA)

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Background—Cerebral protection during surgery for acute aortic dissection type A relies on hypothermic circulatory arrest, either alone or in conjunction with cerebral perfusion.

Methods and Results—The perioperative and intraoperative conditions of 1558 patients submitted from 44 cardiac surgery centers in German-speaking countries were analyzed. Among patients with acute aortic dissection type A, 355 (22.8%) underwent surgery with hypothermic circulatory arrest alone. In 1115 patients (71.6%), cerebral perfusion was used: Unilateral antegrade cerebral perfusion (ACP) in 628 (40.3%), bilateral ACP in 453 (29.1%), and retrograde perfusion in 34 patients (2.2%). For 88 patients with acute aortic dissection type A (5.6%), no circulatory arrest and arch intervention were reported (cardiopulmonary bypass–only group). End points of the study were 30-day mortality (15.9% overall) and mortality-corrected permanent neurological dysfunction (10.5% overall). The respective values for the cardiopulmonary bypass–only group were 11.4% and 9.1%. Hypothermic circulatory arrest alone resulted in a 30-day mortality rate of 19.4% and a mortality-corrected permanent neurological dysfunction rate of 11.5%, whereas the rates were 13.9% and 10.0%, respectively, for unilateral ACP and 15.9% and 11.0%, respectively, for bilateral ACP. In contrast with the ACP groups, there was a profound increase in mortality when systemic circulatory arrest times exceeded 30 minutes in the hypothermic circulatory arrest group ($P<0.001$). Mortality-corrected permanent neurological dysfunction correlated significantly with perfusion pressure in the ACP groups.

Conclusions—This study reflects current surgical practice for acute aortic dissection type A in Central Europe. For arrest times less than 30 minutes, hypothermic circulatory arrest and ACP lead to similar results. For longer arrest periods, ACP with sufficient pressure is advisable. Outcomes with unilateral and bilateral ACP were equivalent. (*Circulation*. 2011;124:434-443.)

Key Words: aortic dissection ■ cerebral protection ■ cerebral perfusion ■ deep hypothermic circulatory arrest ■ registries

Acute aortic dissection type A (AADA) is a life-threatening emergency associated with major morbidity and mortality. International Registry of Acute Aortic Dissection data report an in-hospital mortality rate of 26%.¹ The German Registry for Acute Aortic Dissection type A (GERAADA) was initiated to representatively survey AADA and its therapeutic reality. Forty-four cardiac surgery centers in Germany, Austria, and Switzerland have contributed data to the registry (Appendix); 1558 patients have been included so far, and an overall 30-day mortality rate of 15.9% has been revealed.² For endoluminal inspection and procedures that involve the aortic arch during AADA surgery, circulatory arrest is mandatory.

Clinical Perspective on p 443

Several cerebral protection strategies have been developed. The backbone of aortic arch surgery is hypothermic circulatory arrest (HCA). Because the brain is at highest risk during this phase, selective cerebral perfusion was introduced. We compared the cerebral protection techniques used for patients in the GERAADA registry, categorizing these methods as cardiopulmonary bypass (CPB) only, HCA, and unilateral antegrade (uACP), bilateral antegrade (bACP), or retrograde (RCP) cerebral perfusion. Primary end points of the analysis were 30-day mortality and mortality-corrected permanent neurological dysfunction (PNDmc). Secondary end points

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were perioperative complications and perioperative and postoperative times. We compared outcomes in a transverse manner between the different protection methods and longitudinally within groups according to circulatory arrest and cerebral perfusion times and temperatures.

Methods

Data Collection

GERAADA, a multicenter registry, initiated data collection in July 2006. For the present study, data collection was completed in June 2009, at which point 1558 patients were included and 44 cardiac centers had reported data on their patients. The inclusion criterion was the presence of a surgically treated AADA. Data were collected with a World Wide Web–based database. Data sets consisted of questionnaires that included more than 90 items that addressed perioperative, demographic, etiologic, and follow-up parameters.² The final clinical assessment was performed on the 30th postoperative day. Respirator times and lengths of stay in the intensive care unit and hospital were recorded beyond this time point. The centers were asked to consecutively document all AADAs treated. The data sets were checked for completeness and plausibility by an independent database-monitoring center.

Study Groups

Patients were categorized according to the cerebral protection method into one of the following groups: Surgery with CPB without circulatory arrest, with HCA alone, or with HCA in combination with uACP, bACP, or RCP. Using a drop-down menu in the questionnaire, we achieved the complete and disjunctive allocation of all patients.

End Points

Primary end points were 30-day mortality and rate of permanent neurological dysfunction (PND). The 30-day mortality included any death that occurred from the intraoperative period until the 30th postoperative day. Adopted from Ergin et al,³ PND was defined as the “presence of permanent neurological deficits that were focal (stroke) or global (parkinsonism, coma, gait disturbance) in nature and persisting at discharge from the hospital.” Patients who had relevant neurological dysfunction before surgery were excluded from this end point. To estimate the true burden of chronic neurological impairment, we corrected the PND rate for mortality (PNDmc). Patients who were neurologically impaired soon after surgery and then died were excluded from the PNDmc. PND gives the percentage of all surgically treated patients with new and persisting neurological deficits after surgery, whereas PNDmc provides the percentage of all surgically treated patients with new and persisting deficits who survived to day 30 or left the hospital with neurological dysfunction. The 30-day mortality and PNDmc end points were incorporated into a combined end point without creating redundancy problems.

Statistical Analysis

Statistics were summarized as percentages and 95% confidence intervals (CIs) for categorical variables and means with SDs for continuous variables. Patient groups were compared with the χ^2 test for categorical variables and the unpaired *t* test for continuous variables. Because several tests were performed, the probability values should be considered to be exploratory means. The descriptive statistics and tests were analyzed by referral only to cases with no missing values (complete case analysis). The influence of cerebral protection on 30-day mortality, PND, and PNDmc was analyzed with multiple stepwise logistic regressions in which the covariables age, sex, and the preoperative risk factors indicated in Table 1 were included. The results of the logistic regressions are presented as odds ratios (ORs) with confidence limits. The ORs of perfusion time and temperatures in relation to unfavorable outcome were calculated without adjustment for the other risk factors. The correlations

between variables such as perfusion time and temperature were made with the Pearson product-moment correlation.

Because this is an explorative study, the term “statistically significant” should be interpreted with care. There was no formal adjustment for the number of performed tests.

Surgical Methods

Surgical therapy for AADA optionally encompasses reconstruction of the aortic valve, root, ascending aorta, aortic arch, descending aorta, and supraaortic vessels, as well as coronary bypass grafting. These surgical interventions were not analyzed in detail in the present study because we focused on the use of cerebral protection techniques. There are many different cerebral protection strategies in use.^{4,5} We highlight the basic principles. In HCA, CPB is stopped after the patient is cooled to the target temperature. The patient's blood is drained into the venous reservoir, and the patient is put in the Trendelenburg position. The aortic arch is then opened. After reconstruction, the neo-arch is usually cannulated and perfusion restarted. uACP is performed predominantly by primary cannulation of the right axillary or subclavian artery. After systemic cooling, the arch vessels are occluded, and pump flow is reduced, which results in cerebral perfusion via the right carotid and vertebral arteries. In the case of bACP, the arch is opened after HCA is initiated, and the brachiocephalic trunk and left carotid artery are selectively intubated, usually directly from inside the aortic arch. Cerebral perfusion usually aims for a flow of 10 mL/kg body weight or a perfusion pressure of 40 to 70 mm Hg in both techniques while the lower body is in circulatory arrest. For RCP, venous drainage for CBP is installed by bicaval cannulation. During circulatory arrest, RCP is performed via the venous cannula in the superior vena cava. Cerebral perfusion techniques differ among institutions with regard to the technical details. In the present study, cerebral protection was performed according to each institution's policy.

Results

Study Population

A total of 1558 AADA patients were included in the present analysis. Of these, 209 (13.4%) had a PND and 248 (15.9%) died postoperatively within 30 days. Of those who experienced a PND, approximately one fifth, or 45 patients (21.5%), died within 30 days, which resulted in a PNDmc rate of 10.5% (164 patients). A small minority of patients (88; 5.6%) underwent ascending aortic replacement without circulatory arrest (CPB only). Various cerebral protection strategies were used during surgery on the aortic arch in the vast majority of patients (1470 [94.4%]; Figure 1). Of those, roughly one fourth underwent surgery while under HCA, whereas three fourths additionally received bACP, uACP, or RCP.

Cardiopulmonary Bypass Only: Analysis of Preoperative and Postoperative Variables

Patients in the CPB-only group did not undergo circulatory arrest and arch intervention. This cohort comprised only 5.6% of all patients. Moreover, the CPB-only group had significantly lower incidences of preoperative neurological deficit (13.6%; 95% CI 6.4% to 20.8%), peripheral malperfusion syndromes (23.9%; 95% CI 14.9% to 32.8%), and pericardial tamponade (10.2%; 95% CI 3.9% to 16.6%) than the groups with arch intervention (Table 1). In contrast, preoperative hemodynamic instability (46.6%; 95% CI 36.1% to 57.1%), intubation (11.4%; 95% CI 4.7% to 18.0%), catecholamine therapy (13.6%; 95% CI 6.4% to 20.8%), and CPR (9.1%; 95% CI 3.0% to 15.1%) were documented in a similar or only

Table 1. Preoperative, Intraoperative, and Postoperative Variables in the HCA, bACP, and uACP Groups

	HCA	bACP	uACP
No. of patients	355	453	628
Age at surgery, y mean±SD	59.77±13.67	60.41±13.81	60.93±13.11
Male sex, % (95% CI)	64.2 (59.2–69.2)	58.7 (54.2–63.3)	61.1 (57.3–65.0)
Surgery within 24 h, % (95% CI)	83.3 (79.1–87.6)	77.4 (73.3–81.5)	76.6 (72.3–80.8)
Preoperative risk factors, % (95% CI)			
Neurological deficit before surgery	21.4 (17.1–25.7)	23.4 (19.5–27.3)	17.0 (14.1–20.0)
Preoperative malperfusion syndrome	35.2 (30.2–40.2)	33.8 (29.4–38.1)	27.9 (24.4–31.4)
Hemodynamic instability	55.5 (50.3–60.7)	50.8 (46.2–55.4)	58.0 (54.1–61.8)
Catecholamine therapy	20.3 (16.1–24.5)	19.6 (16.0–23.3)	12.4 (9.8–15.0)
Pericardial effusion	26.8 (22.1–31.4)	22.7 (18.9–26.6)	34.2 (30.5–37.9)
Pericardial tamponade	20.0 (15.8–24.2)	21.6 (17.8–25.4)	17.2 (14.2–20.2)
CPR	6.2 (3.7–8.7)	6.0 (3.8–8.1)	5.4 (3.6–7.2)
Intubated	14.1 (10.5–17.7)	15.2 (11.9–18.5)	12.3 (9.7–14.8)
Aortic regurgitation ≥2nd degree	43.9 (38.8–49.1)	48.8 (44.2–53.4)	39.8 (36.0–43.6)
Postoperative outcome, % (95% CI)			
PND (overall)	14.9 (11.2–18.6)	14.1 (10.9–17.3)	12.6 (10.0–15.2)
PNDmc	11.5 (8.2–14.9)	11.0 (8.1–13.9)	10.0 (7.7–12.4)
30-Day mortality	19.4 (15.3–23.6)	15.9 (12.5–19.3)	13.9 (11.1–16.6)
Postoperative malperfusion syndrome	14.4 (10.7–18.0)	10.2 (7.4–12.9)	11.9 (9.4–14.5)
Bleeding complications	25.9 (21.4–30.5)	19.0 (15.4–22.6)	24.0 (20.7–27.4)
Revision unplanned	21.4 (17.1–25.7)	18.1 (14.6–21.7)	20.2 (17.1–23.4)
Intraoperative and postoperative times, mean±SD			
Operation time, min	326.6±142.0	345.2±111.0	318.3±101.8
HCA/CP time, min	22.7±14.3	37.6±23.6	32.2±17.9
Respirator time, h	128.5±228.0	132.4±226.0	119.5±290.8
ICU stay, d	8.7±10.8	8.9±12.5	8.4±13.9
Hospital stay, d	16.1±13.9	17.4±15.6	15.9±15.8

HCA indicates hypothermic circulatory arrest; bACP, bilateral antegrade cerebral perfusion; uACP, unilateral antegrade cerebral perfusion; CI, confidence interval; CPR, cardiopulmonary resuscitation; PND, permanent neurological dysfunction; PNDmc, mortality-corrected permanent neurological dysfunction; CP, cerebral perfusion; and ICU, intensive care unit.

marginally lower percentage of patients. All of these differences make comparisons between the CPB-only group and the other groups problematic. The 30-day mortality rate was 11.4% (95% CI 4.7% to 18.0%) in the CPB-only group, clearly lower than that of the HCA and antegrade cerebral perfusion (ACP) groups. Similarly, the frequencies of both

bleeding complications (13.6%; 95% CI 6.4% to 20.8%) and unplanned revision (5.7%; 95% CI 0.8% to 10.5%) were significantly ($P<0.05$) lower in the CPB-only group; however, PNDmc frequencies (9.1% 95% CI 3.0% to 15.1%) did not differ substantially (Table 1).

To balance the differences in the preoperative risk profiles, preoperative attributes were incorporated into a logistic model in which the HCA group's OR for 30-day mortality was 1.82 (95% CI 0.85 to 3.91) compared with the CPB-only group. The respective factors were 1.35 (95% CI 0.63 to 2.88) in the bACP and 1.29 (95% CI 0.61 to 2.73) in the uACP group. The OR for experiencing the PNDmc end point was 1.31 (95% CI 0.59 to 2.90) in the HCA group, 1.24 (95% CI 0.57 to 2.72) in the bACP group, and 1.12 (95% CI 0.52 to 2.41) in the uACP group compared with the CPB-only group.

Average operative time in the CPB-only group was 267 minutes (SD 112 minutes), which was shorter ($P<0.001$) than that of the other groups. The same was true for the durations of respirator therapy (61.35 hours, SD 136.0 hours) and intensive care unit stay (5.6 days, SD 8.7 days), both of which were approximately half as long as for patients undergoing arch intervention (both $P<0.05$).

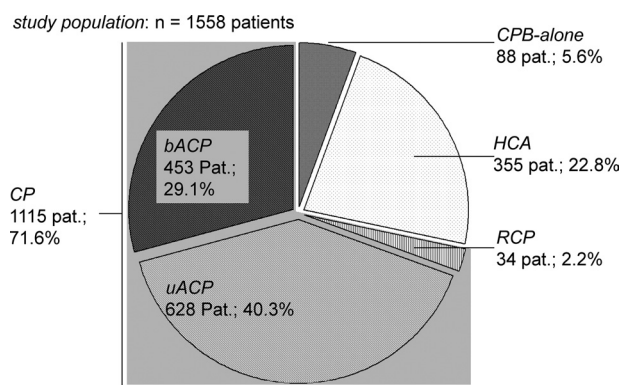


Figure 1. Frequency distribution of cerebral protection techniques. CP indicates cerebral perfusion; CPB, cardiopulmonary bypass; HCA, hypothermic circulatory arrest; bACP and uACP, bilateral and unilateral antegrade cerebral perfusion, respectively; RCP, retrograde cerebral perfusion; and pat., patients.

Hypothermic Circulatory Arrest and Antegrade Cerebral Perfusion: A Comparative Analysis of Preoperative Variables

Table 1 shows the preoperative risk profile and postoperative variables for the HCA, bACP, and uACP groups. There were no significant differences among these groups with respect to their sex and age distributions. More patients (83.3%) in the HCA group were treated within 24 hours after the onset of symptoms than in the ACP groups (77%; $P<0.05$). No significant differences were found in the preoperative risk profiles of the HCA and the bACP groups, which highlights their statistical similarity.

Similarities between the uACP and HCA groups and the uACP and bACP groups were adequate, not optimal. There were fewer cases of malperfusion syndrome and a lower rate of catecholamine therapy, but more pericardial effusion in the uACP group than in the HCA group. We observed fewer preoperative neurological deficits and malperfusion syndromes and a lower incidence of preoperative catecholamine therapy and aortic regurgitation in the uACP group than in the bACP group. Conversely, the uACP group had a higher incidence of hemodynamic instability and pericardial effusions than the bACP group (all $P<0.05$).

Only 34 individuals (2.2%) were managed with RCP, and analyses of preoperative risk factors revealed a lack of comparability with the HCA and ACP groups. The RCP patients were thus excluded from further comparative analysis.

Hypothermic Circulatory Arrest and Different Antegrade Cerebral Perfusion Strategies: Comparative Analysis of Intraoperative and Postoperative Variables

Thirty-day mortality in the HCA group (19.4%) was higher than in the bACP (15.9%) and uACP (13.9%) groups. This difference reached statistical significance ($P<0.05$) between the HCA and uACP groups, whereas the differences in mortalities between the HCA and bACP groups ($P=0.068$) and between the 2 ACP groups ($P=0.35$) did not. PNDmc varied from 10.0% in the uACP group to 11.5% in the HCA group (Table 1). Approximately 20% of patients underwent a second-look thoracotomy. Bleeding complications were documented in approximately 25% of the HCA and uACP patients and in 19% of the bACP patients ($P<0.05$).

In the multivariate analysis that balanced the various risk profiles, the OR for 30-day mortality was 0.74 (95% CI 0.50 to 1.09) in the bACP group and 0.71 (95% CI 0.49 to 1.02) in the uACP group compared with the HCA group. For the end point of PNDmc, the ORs were 0.95 (95% CI 0.61 to 1.47) and 0.85 (95% CI 0.56 to 1.30), respectively.

The total operative time was shortest in the uACP group. The effective arch intervention time differed considerably across the groups. Circulatory arrest time in the HCA group was 22.7 minutes on average, whereas mean cerebral perfusion times were 37.6 and 32.2 minutes in the ACP groups, respectively (both $P<0.001$).

In summary, there was lower mortality and a similar PNDmc rate in both ACP groups compared with the HCA group, despite the longer arch intervention time. No signifi-

cant differences appeared between the HCA and ACP groups with respect to the duration of respirator therapy, intensive care unit stay, or total hospital stay. Despite the alternating unequal distributions of preoperative risk factors, we detected no relevant differences in postoperative outcomes between the uACP and bACP groups.

Temperatures for Circulatory Arrest and Cerebral Perfusion

Complete temperature data were documented in 100% of the HCA patients and in 84.6% and 81.9% of the bACP and uACP patients, respectively. Core temperatures were measured rectally or in the urinary bladder. Very few patients (2.6%) in the HCA group were cooled below 15°C, whereas a systemic temperature between 15°C and 20°C was reached in 58.8% of patients of HCA patients. Systemic temperatures of 21°C to 25°C and 26°C to 30°C during HCA were documented in 26.9% and 6.3% of the cases, respectively (Figure 2). In all of these temperature categories, 30-day mortality ranged from 15.0% to 22.7%, and the PNDmc rate ranged from 4.5% to 15.0%, with no significant differences. Accordingly, we found no association between HCA temperature and either the 30-day mortality or PNDmc rates. As also evident from clinical practice, circulatory arrest time and lowest systemic temperature were not independent variables. We noted a clear correlation ($r=-0.44$, $P<0.001$) between higher systemic temperatures and shorter HCA times, which hampers interpretation of the temperature data. The correlation between the temperature of the cerebral perfusate and the cerebral perfusion time was not as strong in either ACP group ($r=-0.22$, $P<0.001$). Most (52%) of the bACP patients underwent surgery with cerebral perfusion temperatures between 15°C and 20°C (Figure 3). In the next-largest group, temperatures of 21°C to 25°C were applied. Perfusates colder than 15°C or warmer than 30°C were rarely used, which excluded these groups from meaningful analysis. We noted similar numbers of patients in all temperature categories in the uACP group, ranging from 74 patients in the <15°C category to 130 patients in the >30°C category (Figure 4). A trend appeared that revealed lower end points in conjunction with cerebral perfusion temperatures in the ranges of >30°C and <15°C.

Cerebral Perfusion Flow and Pressure

We collected these data from 69.8% of the patients in the bACP group and 79.1% of those in the uACP group. The average perfusion pressure in the bACP group was 64.7 mm Hg (SD 25.9 mm Hg), and the flow was 757.9 mL/min (SD 358.3 mL/min). In the uACP group, both values were slightly higher (66.4 mm Hg, SD 31.9 mm Hg and 820.2 mL/min, SD 436.5 mL/min). Pressure values of >60 mm Hg were associated with significantly better outcomes with respect to the PNDmc end point in the bACP (OR=0.4, $P=0.03$) and uACP (OR=0.4, $P=0.003$) groups. We detected a mild risk reduction in the magnitude of OR=0.6 for PNDmc with flow rates >600 mL/min in both ACP groups ($P=NS$). Pressure values >60 mm Hg and flow values >600 mL/min did not influence 30-day mortality. The present study was not designed or powered to analyze whether extremely

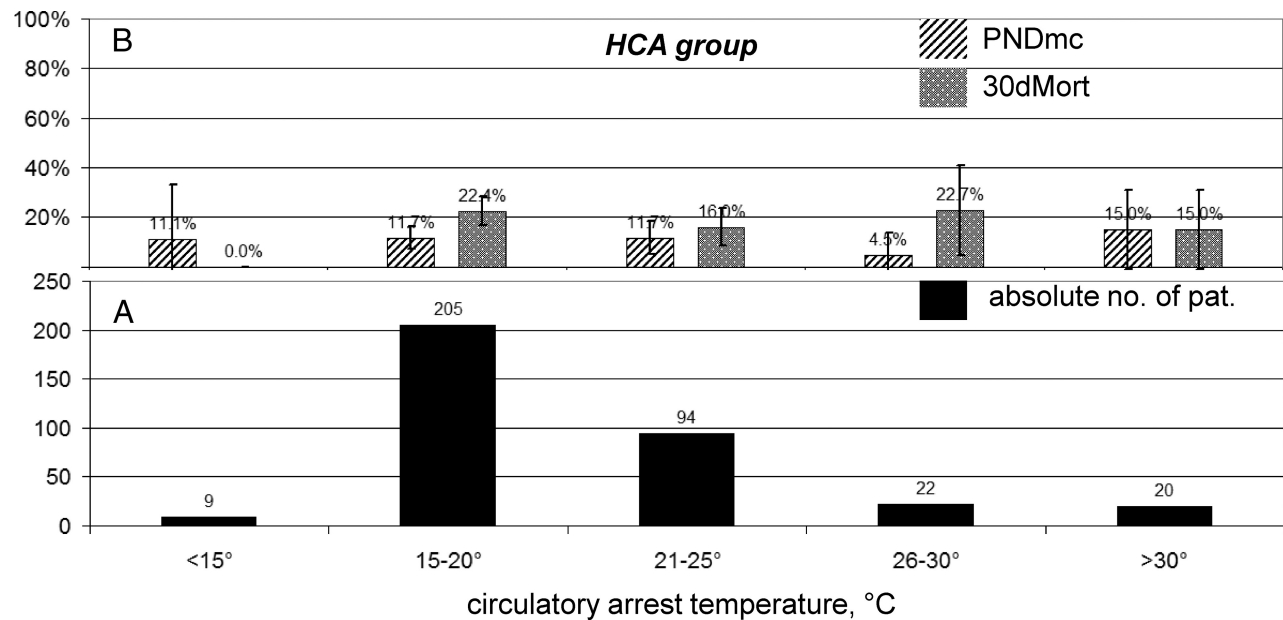


Figure 2. Hypothermic circulatory arrest (HCA) group. Absolute number of patients (**A**) and 30-day mortality (30dMort) and mortality-corrected permanent neurological dysfunction rates (PNDmc; **B**) in the various categories of circulatory arrest temperature (with 95% confidence interval). pat. indicates patients.

low flow and pressure rates would correlate with higher frequencies of unfavorable outcomes.

Duration of Circulatory Arrest and Cerebral Perfusion

Circulatory arrest times were recorded for all 355 patients in the HCA group. The duration of cerebral perfusion in the bACP and uACP groups was documented in 92.1% and 84.2% of patients, respectively. The average circulatory arrest time in the HCA group was significantly shorter ($P<0.001$) than the cerebral perfusion times in the bACP and uACP groups (Table 1).

In Figure 5, the numbers of patients in each cerebral protection group and frequencies of PNDmc and 30-day mortality are plotted against the categories of circulatory arrest and cerebral perfusion times, respectively. There were reasonable numbers of patients in the central categories (10 to 50 minutes), whereas patient numbers were critically low in the extreme categories (<10 and >50 minutes; Figure 5A), which indicates that conclusions may not be reliable for these categories.

Figure 5C illustrates 30-day mortality relative to the cerebral protective strategy and arch intervention time. With

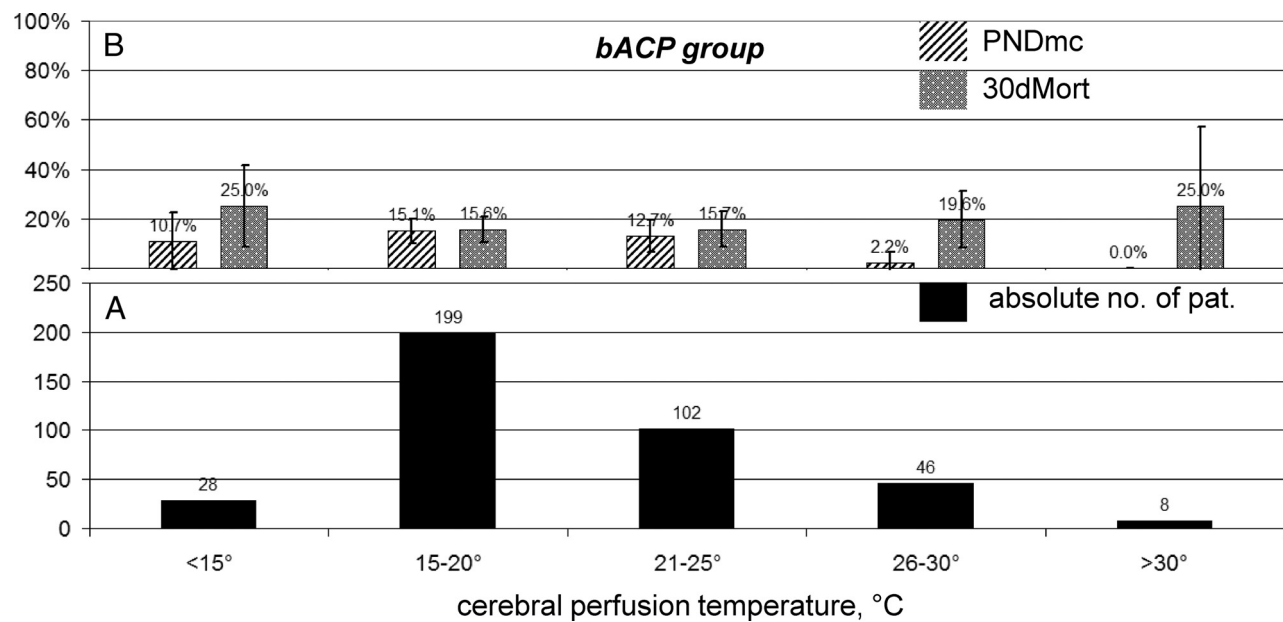


Figure 3. Bilateral antegrade cerebral perfusion (bACP) group. Absolute number of patients (**A**) and 30-day mortality (30dMort) and mortality-corrected permanent neurological dysfunction rates (PNDmc; **B**) in the various categories of cerebral perfusion temperature (with 95% confidence interval). pat. indicates patients.

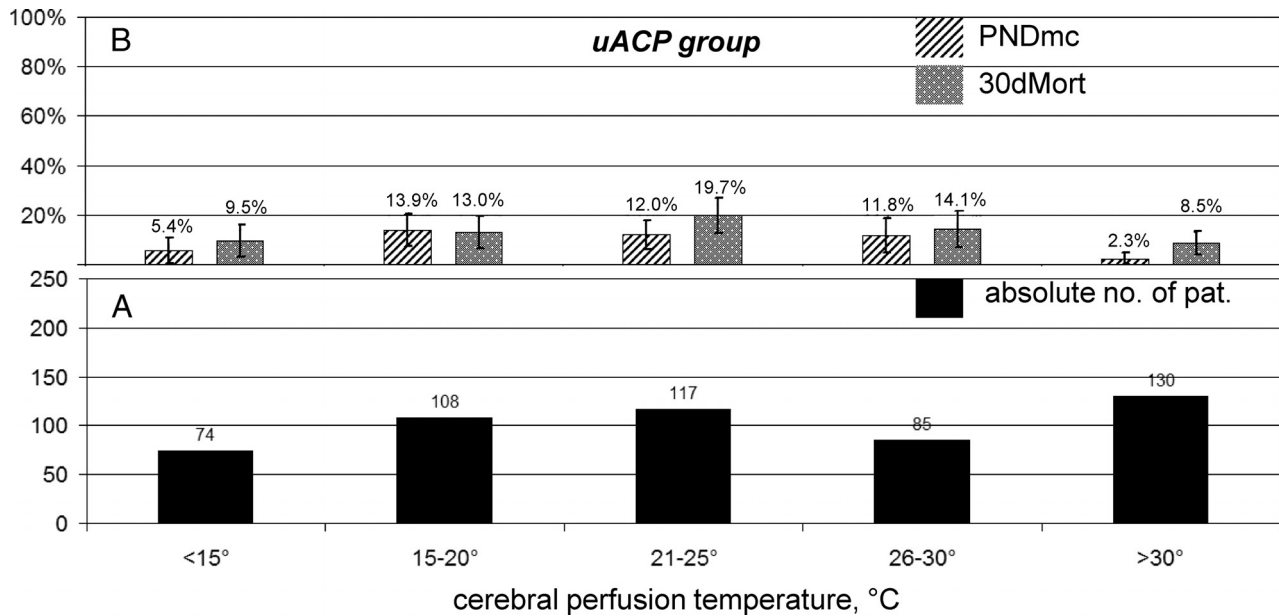


Figure 4. Unilateral antegrade cerebral perfusion (uACP) group. Absolute number of patients (**A**) and 30-day mortality (30dMort) and mortality-corrected permanent neurological dysfunction rates (PNDmc; **B**) in the various categories of cerebral perfusion temperature (with 95% confidence interval). pat. indicates patients.

circulatory arrest times <30 minutes, mortality in the HCA group was roughly 16%; however, we observed a trend toward higher mortality after 30 minutes. After 40 minutes, mortality rose to approximately 40%. Cumulative analysis revealed that surgery involving HCA times of up to 30 minutes resulted in an average mortality rate of 15.4%. When the circulatory arrest time exceeded 30 minutes, the mortality rate was 35.7%, which resulted in an OR of 3.0 ($P<0.001$). We did not detect this increase in mortality in the ACP groups until after 60 minutes of cerebral perfusion. In the bACP group, 30-day mortality for cerebral perfusion times less than 60 minutes was 13.7%, rising to 26.4% (OR 2.3, $P=0.02$) after 60 minutes. These values were similar for uACP (12.8% and 21.6%; OR 1.9, $P=0.13$). In short, cerebral perfusion times of >60 minutes doubled the mortality regardless of which perfusion technique was used.

Figure 5B shows PNDmc rates relative to the cerebral protective strategy and arch intervention time. There was no correlation between the arrest or cerebral perfusion time and the PNDmc rate. The PNDmc rate was 15.7% for HCA after 20 minutes of arrest and 23.8% after 40 minutes, which suggests an increase; however, a markedly low PNDmc rate was documented for arrests that ranged from 30 to 39 minutes, and group sizes were too small to allow reliable conclusions to be drawn in the categories >50 minutes. In the central categories between 10 and 50 minutes, PNDmc rates ranged from 5% to 13% without a time-dependent increase in the uACP and bACP groups. PNDmc rates increased slightly after 60 minutes for uACP and after 90 minutes for bACP; however, patient numbers were inadequate to generate reliable data for these categories.

Variables Influencing Hypothermic Circulatory Arrest and Antegrade Cerebral Perfusion Times

Surgery outcomes, particularly under HCA, depend on the circulatory arrest time. We analyzed the variables that con-

tributed to transgression of the critical 30-minute threshold irrespective of the cerebral protection technique used (Table 2). As expected from clinical experience, most arch inspections or partial replacements required less than 30 minutes of HCA or ACP, whereas this critical value was exceeded in the vast majority of total arch replacements. Multivariate analysis (considering the preoperative variables) revealed that compared with surgery without arch reconstructions, the OR to exceed 30 minutes was just 1.6 (95% CI 1.1 to 2.2) for partial arch replacements but 9.9 (95% CI 6.1 to 16.0) for total arch replacements and 11.3 (95% CI 5.2 to 24.8) for arch replacement with the elephant trunk technique.

Furthermore, the presence of a dissection entry in the arch and the extension of the dissection influenced the HCA and ACP times. Compared with dissections with entries just in the ascending aorta, the presence of an entry in the arch led to an OR of 1.5 (95% CI 1.0 to 2.1) to exceed the 30-minute threshold. Similarly, extension of the dissection into the arch or into the supraaortic vessels resulted in ORs of 1.7 (95% CI 1.1 to 2.6) and 2.7 (95% CI 0.6 to 12.8).

Discussion

GERAADA

There is no consensus among cardiac surgeons concerning the optimal strategy for cerebral protection in AADA surgery. The wide spectrum of AADA patients' preoperative conditions, pathological anatomies, complications, and surgical procedures, as well as the diversity of CPB strategies, hampers comparisons of postoperative outcomes and of the available literature. This problem is highlighted by the CPB-only group in the present study, which differed considerably in many of these variables from the other groups. Most studies include various arch pathologies and report experiences of individual centers or outcomes of a certain cerebral protection technique without comparison to a contemporaneous control group. In

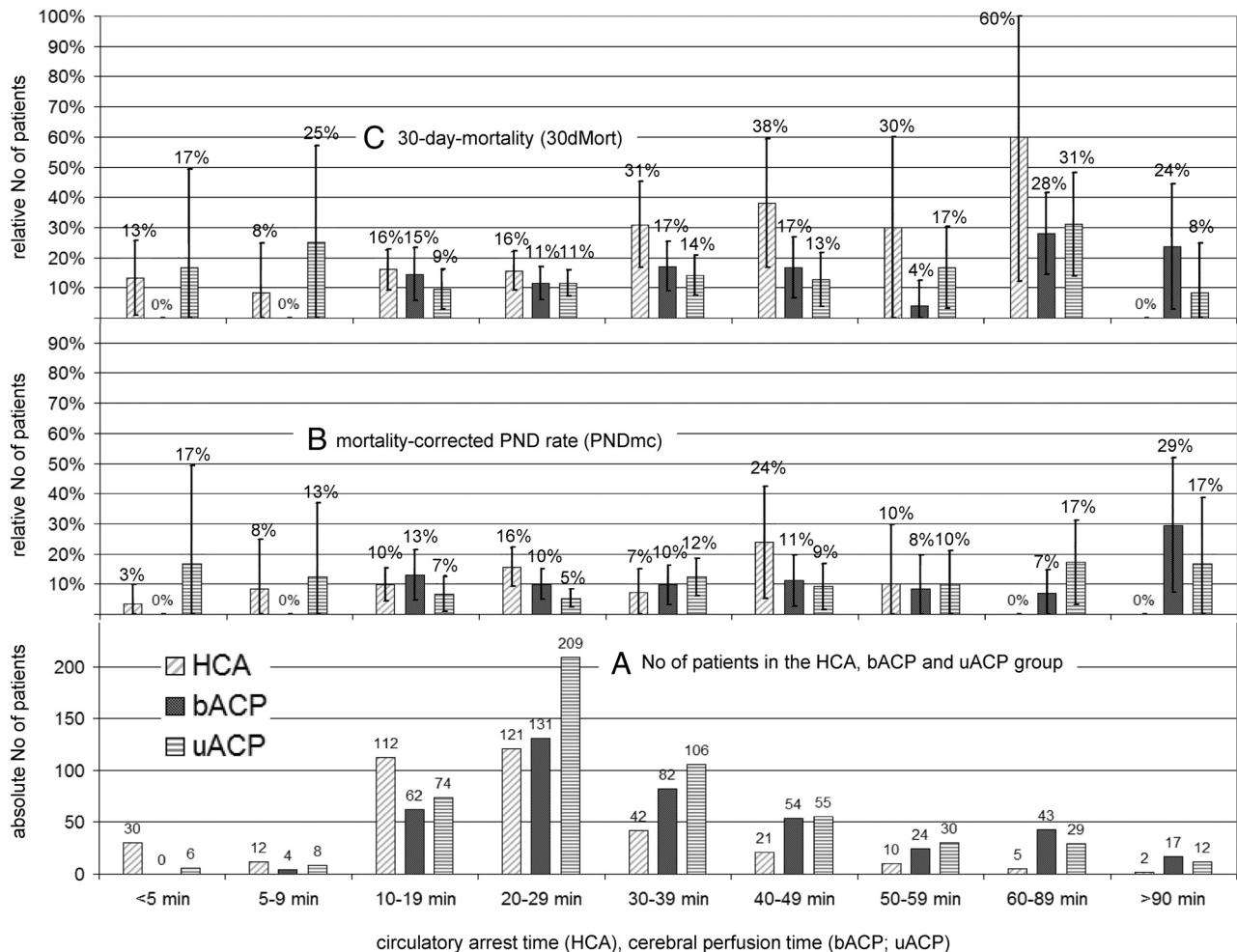


Figure 5. **A**, Hypothermic circulatory arrest group (HCA) and bilateral (bACP) and unilateral (uACP) antegrade cerebral perfusion groups. Absolute numbers of patients in the various categories of arch intervention times. **B**, Mortality-corrected permanent neurological dysfunction rates (PNDmc) relative to arch intervention times (with 95% confidence interval). **C**, 30-Day mortality (30dMort) relative to arch intervention times (with 95% confidence interval). PND indicates permanent neurological dysfunction; pat., patients.

this survey, we have provided an overview of the current daily practice of cerebral protection in AADA surgery in Central Europe. We have access to large numbers of patients, but as with most registers, sample selection bias and partial incompleteness of some items in the data sets may pose problems. Furthermore, the intraoperative and perioperative management of patients may differ substantially. These drawbacks must be balanced against ensuring sufficient statistical power when analyzing different groups.

Hypothermic Circulatory Arrest

The optimal temperature for the HCA-alone strategy is controversial. The pros and cons (ie, better organ protection versus increased risk for coagulation disorders, systemic inflammatory response syndrome, and longer pump times) must be balanced. The Griep school relies on profound hypothermia with 10°C to 15°C,³ whereas others prefer temperatures around 20°C.⁶⁻⁹ In our survey, circulatory arrest temperatures ranging between 15°C and 20°C were most common, and the next-warmest temperatures were the second-most frequent choice. The choice of temperature clearly depended on the anticipated arrest time, which effec-

tively correlated these variables and caused them to confound one another. More complex arch reconstructions require longer circulatory arrest times and carry higher endogenous mortality rates per se. Furthermore, longer arrest times may reflect technical difficulties or less experienced surgeons. It is impossible to discriminate among the procedure-, surgeon-, temperature-, and time-associated mortality rates. In the present analysis, overall 30-day mortality of AADA surgery under HCA was 19.4% compared to 15% with cerebral perfusion. This higher overall mortality was mainly due to the largely unfavorable outcomes associated with arrest times longer than 30 minutes. Below this threshold, mortality rates resembled those in the ACP groups. Svensson et al¹⁰ described the correlation between HCA time and prognosis and reported a substantial increase in neurological morbidity after 40 minutes and in mortality after 65 minutes. More recently, Kuniyara et al⁶ reported that HCA of <30 minutes at <20°C presents a rather low risk. Metabolic studies have also supported this 30-minute threshold.¹¹ In contrast to the mortality rate, which rose 3-fold after 30 minutes of HCA, we did not observe significant changes in the PNDmc rate; however, arrest times >25 minutes are known to result in

Table 2. Percentage of Patients With HCA Times or ACP Times >30 min in Relation to Pathoanatomic and Procedural Variables

	Patients With >30 min of HCA or ACP, % (95% CI)
Aortic arch procedure	
No arch replacement	22.2 (17.9–26.5)
Partial arch replacement	34.6 (30.6–38.5)
Total arch replacement	76.7 (70.1–83.3)
Elephant trunk	79.2 (67.6–90.8)
Location of dissection entry	
No entry in the arch	35.1 (32.0–38.1)
Entry in the arch	56.8 (49.7–63.8)
Extent of the dissection	
Limited to the ascending aorta	18.6 (14.8–25.6)
Involving the arch	41.5 (37.2–45.8)
Involving the supraaortic vessels	44.9 (40.2–48.6)

HCA indicates hypothermic circulatory arrest; ACP, antegrade cerebral perfusion; and CI, confidence interval.

reduced performance, at least in neuropsychological tests.¹² On the basis of these findings, cerebral perfusion is advisable, at least for interventions with expected circulatory arrest times of >30 minutes.

Cerebral Perfusion

Cerebral perfusion strategies were categorized as RCP, uACP, or bACP. In the last decade, RCP has become less popular in spite of good reported results.^{13,14} Because of our very low patient numbers, we cannot compare RCP to other forms of cerebral protection.

ACP preserves the natural flow direction, allows for higher pressure, and probably provides metabolically adequate perfusion. Perfusion pressures should usually be 40 to 70 mm Hg, and flow rates should be 10 mL · kg⁻¹ · min⁻¹ or approximately 1000 mL/min, regardless of the ACP technique used.^{7-9,15-17} In our survey, most surgeons aimed for or even exceeded these values. We detected a substantially reduced risk for PNDmc at perfusion pressures that exceeded 60 mm Hg and a mild risk reduction at flow rates that exceeded 600 mL/min. However, cerebral perfusion flows and pressures above or below these thresholds did not influence 30-day mortality. Theoretically, high cerebral perfusion pressures may carry the risk of brain edema, and ACP appears to offer some extent of cerebral protection even below the aforementioned thresholds.

The optimal cerebral perfusion temperature is also controversial. There is no published clinical evidence demonstrating the superiority of any particular temperature. Experimental studies suggest an advantage with profound hypothermia.^{15,18} Because of the lack of clinical data, cerebral perfusion temperatures vary widely across institutions, and all report favorable results. In the present study, the temperature-dependent outcome results were inconsistent, and we cannot support any particular cerebral perfusion temperature on the basis of our data.

The same holds true for the optimal temperature of the lower body for visceral protection. There is strong evidence in the literature that moderate lower-body hypothermia (>25°C) is not disadvantageous compared with lower temperatures (<25°C) and appears to be completely adequate in conjunction with ACP.^{16,19}

ACP undoubtedly extends the safe arch intervention time beyond the threshold of the safe HCA time. There are numerous reports that cerebral perfusion times ranging from 30 to 60 minutes are well tolerated.²⁰ The present data confirm this. Both uACP and bACP permitted systemic circulatory arrest times of up to 60 minutes with consistently low mortality and PNDmc rates. We detected an increase in mortality at extremely long times, but there was no significant change in the PNDmc. We cannot determine whether this resulted from inadequate cerebral protection, technical difficulties, dissection-related complications, or the increased duration of lower-body ischemia.

Differences in Cerebral Protection Strategies

AADA surgery under HCA with circulatory arrest of <30 minutes results in a 15.4% mortality rate, which resembles the outcome of surgery under ACP. However, after the 30-minute threshold was exceeded, mortality in the HCA group rose substantially, whereas it remained low in the ACP groups. There is thus no rationale for the performance of arch procedures lasting >30 minutes without implementation of cerebral perfusion.

The decision to use ACP should always take potentially harmful aspects into account. The dislodgement of debris and air during manipulation is a concern during intubation of the supraaortic vessels in bACP. This problem is avoided in uACP by cannulation of the axillary or subclavian artery.²¹ On the other hand, a right carotid artery stenosis may lead to cerebral malperfusion in uACP,²² and according to anatomic studies, 15% of patients present a circle of Willis that is incompletely closed.²³ However, in uACP via the right axillary artery, the right vertebral artery and extracranial collaterals are also perfused. Cerebral malperfusion in uACP has been rare in clinical experience, and several groups have reported impressive results.^{7,8,16} Observation of back flow from the left carotid and subclavian arteries and monitoring of transcranial oxygen saturation and left tympanic temperature may further reduce this risk.²¹ The threats of plexus injury and arterial stenosis are low.^{7,9} Disregarding cerebral perfusion, axillary artery cannulation also confers antegrade aortic perfusion from the beginning of CPB and has been shown to be superior to femoral cannulation in AADA patients.¹⁷ Which ACP strategy is the best for cerebral protection remains uncertain. Larger studies comparing uACP to bACP have generated inconsistent results,^{7,24} and we detected no relevant differences relating to outcomes. However, some surgeons find bACP technically more cumbersome because of the more complicated CPB setup and additional lines cluttering the surgical field.²¹ This is reflected by the bACP group's longer cerebral perfusion and total operation times.

Conclusions

Many factors influence the decision as to the specific procedure to use in AADA. Patient-related factors such as the extent of wall destruction, tissue quality (ie, calcification or medial necrosis), preexisting aneurysmal degeneration, and the patient's general condition play significant roles. Moreover, surgeon-related factors, ie, the specific training, individual experience, and speed, are important.

A main result of the present study is the critical threshold of 30 minutes for arch intervention time. Below this cutoff point, HCA may suffice; above it, ACP is clearly superior. We identified dissection of the aortic arch and the supraaortic branches, an entry within the arch itself, and extended arch interventions as risk factors associated with time-consuming procedures.

If a patient presents with these conditions, the likelihood is high that ACP will be necessary. The definitive extent of arch destruction may be difficult to evaluate preoperatively. In this case, we advise inspecting the aortic arch from inside the lumen during HCA under moderate hypothermia to decide which procedure is appropriate. Procedures such as plain proximal arch replacement can usually be performed within the 30-minute limit. However, if a more extensive reconstruction (in particular, total replacement of the arch and/or supraaortic branches) is being considered, ACP with sufficient perfusion pressure and flow should be initiated immediately. This appears to be simpler and faster with uACP after cannulation of the axillary artery, which resulted in equivalent outcomes compared with bACP. Because the final decision on the extent of reconstruction can often only be made intraoperatively, we believe it is essential to have ACP readily available in the operating suite for every patient undergoing surgery for AADA.

Appendix

The GERAADA Centers (ordered in descending number of recruited patients) were as follows: Universitätsklinikum Frankfurt, Abteilung für Thorax-, Herz- und Thorakale Gefäßchirurgie, Frankfurt am Main, Germany; Herzzentrum Leipzig, Klinik für Herzchirurgie, Leipzig, Germany; Universitäres Herz- und Kreislaufzentrum Freiburg-Bad Krozingen, Abteilung für Herz- und Gefäßchirurgie, Freiburg, Germany; Inselspital Bern, Universitätsklinik für Herz- und Gefäßchirurgie, Bern, Switzerland; Universitätsklinikum Heidelberg, Abteilung für Herzchirurgie, Heidelberg, Germany; Klinikum Augsburg, Klinik für Herz- und Thoraxchirurgie, Augsburg, Germany; Universitätsmedizin Mainz, Klinik für Herz-, Thorax- und Gefäßchirurgie, Mainz, Germany; Städtisches Klinikum Braunschweig, Klinik für Herz-, Thorax- und Gefäßchirurgie, Braunschweig, Germany; Universitätsklinikum Tübingen, Klinik für Thorax-, Herz- und Gefäßchirurgie, Tübingen, Germany; Klinikum Oldenburg, Klinik für Herzchirurgie, Oldenburg, Germany; Universitäres Herzzentrum Hamburg, Klinik und Poliklinik für Herz- und Gefäßchirurgie, Hamburg, Germany; Allgemeines Krankenhaus-Universitätskliniken Wien, Abteilung für Herz- und Thoraxchirurgie, Wien, Austria; Klinikum der Ludwig-Maximilians-Universität München-Großhadern, Herzchirurgische Klinik und Poliklinik, München, Germany; Westdeutsches Herzzentrum Essen, Klinik für Thorax- und kardiovaskuläre Chirurgie, Essen, Germany; Herzzentrum Dresden GmbH, Klinik für Kardiologie, Dresden, Germany; Herz- und Gefäß-Klinik Bad Neustadt, Abteilung für Kardiologie, Bad Neustadt, Germany; Universitätsklinikum Schleswig-Holstein Campus Lübeck, Klinik für Herzchirurgie, Lübeck, Germany; Kerckhoff-Klinik, Abteilung für Herz- und Thoraxchirurgie, Bad Nauheim, Germany; Universitätsklinikum des Saar-

landes Homburg, Klinik für Thorax- und Herz-Gefäßchirurgie, Homburg, Germany; Herzzentrum Duisburg, Klinik für Thorax- und Kardiovaskularchirurgie, Duisburg, Germany; Schüchtermann-Klinik Bad Rothenfelde, Abteilung für Herzchirurgie, Bad Rothenfelde, Germany; Klinikum Kassel GmbH, Klinik für Herz-, Thorax- und Gefäßchirurgie, Kassel, Germany; Universitätsklinikum Münster, Klinik und Poliklinik für Thorax-, Herz- und Gefäßchirurgie, Münster, Germany; Herz- und Diabeteszentrum Nordrhein-Westfalen, Abteilung für Thorax- und Kardiovaskularchirurgie, Bad Oeynhausen, Germany; Universitätsklinikum Aachen, Klinik für Thorax-, Herz- und Gefäßchirurgie, Aachen, Germany; Universitätsklinikum Bonn, Klinik und Poliklinik für Herzchirurgie, Bonn, Germany; Albertinen-Krankenhaus Hamburg, Abteilung für Kardiologie, Hamburg, Germany; Universitätsklinikum Würzburg, Klinik und Poliklinik für Thorax-, Herz- und Thorakale Gefäßchirurgie, Würzburg, Germany; Klinik für Herzchirurgie Karlsruhe GmbH, Karlsruhe, Germany; Klinikum Passau, Klinik für Herzchirurgie, Passau, Germany; Herzzentrum Lahr/Baden, Lahr, Germany; Bundeswehrzentral Krankenhaus Koblenz, Abteilung für Herz- und Gefäßchirurgie, Koblenz, Germany; Universitätsklinikum Rostock, Klinik und Poliklinik für Herzchirurgie, Rostock, Germany; Universitätsklinikum Schleswig-Holstein Campus Kiel, Klinik für Herz- und Gefäßchirurgie, Kiel, Germany; Robert-Bosch-Krankenhaus Stuttgart, Klinik für Herz- und Gefäßchirurgie, Stuttgart, Germany; Klinikum Fulda, Klinik für Herz- und Thoraxchirurgie, Fulda, Germany; Zentralklinik Bad Berka, Klinik für Kardiologie, Bad Berka, Germany; Klinikum Nürnberg, Klinik für Herzchirurgie, Nürnberg, Germany; MediClin Herzzentrum Coswig, Klinik für Herz- und Gefäßchirurgie, Coswig, Germany; Herz- und Gefäßzentrum Bad Bevensen, Klinik für Herz-Thorax-Chirurgie, Bad Bevensen, Germany; Martin-Luther-Universität Halle-Wittenberg, Universitätsklinik und Poliklinik für Herz- und Thoraxchirurgie, Halle, Germany; Universitätsklinikum Jena, Klinik für Herz- und Thoraxchirurgie, Jena, Germany; Sana Herzchirurgische Klinik Stuttgart, Stuttgart, Germany; Klinikum Links der Weser, Klinik für Thorax-, Herz- und Gefäßchirurgie, Bremen, Germany.

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CLINICAL PERSPECTIVE

Surgery for acute aortic dissection type A (AADA) requires cerebral protection strategies for aortic arch intervention: Hypothermic circulatory arrest (HCA) alone or with adjunct cerebral perfusion. The optimal strategy is unclear. Through the German Registry for Acute Aortic Dissection Type A (GERAADA), we surveyed the current practice and outcome of cerebral protection during AADA surgery in Central Europe. This is the largest series on this topic published so far. We compared the different cerebral protection strategies: HCA alone, unilateral antegrade cerebral perfusion, and bilateral antegrade cerebral perfusion. Furthermore, we evaluated several technical parameters, eg, perfusion pressures and temperatures within the different strategies. Study end points were mortality and neurological morbidity. The duration of arch intervention turned out to be the major factor influencing the outcome. HCA only appears to be safe for under 30 minutes, whereas antegrade cerebral perfusion doubles the safe time period. Thus, surgery with HCA appears justified only for limited arch interventions. If a more extensive arch reconstruction is required, cerebral perfusion should be initiated immediately. Unilateral and bilateral antegrade cerebral perfusion resulted in equivalent outcomes. We describe parameters that allow the time required for arch reconstruction to be estimated. Referring to our data, we discuss the different cerebral protection strategies and make detailed recommendations on the use of perfusion pressure and other items of clinical importance. This enables the readers to critically reflect and optimize their own practice.

Cerebral Protection During Surgery for Acute Aortic Dissection Type A: Results of the German Registry for Acute Aortic Dissection Type A (GERAADA)

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