Selective antegrade cerebral perfusion and mild (28°C-30°C) systemic hypothermic circulatory arrest for aortic arch replacement: Results from 1002 patients

Andreas Zierer, MD,^a Ali El-Sayed Ahmad, MD,^a Nestoras Papadopoulos, MD,^a Anton Moritz, MD,^a Anno Diegeler, MD,^b and Paul P. Urbanski, MD^b

Objectives: The use of selective antegrade cerebral perfusion (ACP) makes deep hypothermia nonessential for aortic arch replacement. Consequently, a growing tendency to increase the body temperature during circulatory arrest with ACP has recently been reported from various institutions. However, very little is known about the clinical effect of different modes of ACP (unilateral vs bilateral) on neurologic morbidity. Also, the safe limits of this approach for spinal cord and visceral organ protection are yet to be defined.

Methods: Between January 2000 and January 2011, 1002 consecutive patients underwent aortic arch repair during ACP (unilateral, 673; bilateral, 329) with mild systemic hypothermia (30°C ± 2°C; range, 26°-34°C) at 2 centers in Germany. The mean patient age was 62 ± 14 years, 663 patients (66%) were men, and 347 patients (35%) had acute type A dissection. Hemiarach replacement was performed in 684 patients (68%), and 318 (32%) underwent total arch replacement.

Results: The cardiopulmonary bypass time accounted for 158 ± 56 minutes and the myocardial ischemic time, 101 ± 41 minutes. Isolated ACP was performed for 36 ± 19 minutes (range, 9-135). We observed new postoperative permanent neurologic deficits in 28 patients (3%; stroke in 25 and paraplegia in 3) and transient neurologic deficits in 42 patients (4%). All 3 cases of paraplegia occurred in patients with acute type A dissection and a broad range of ACP times (24, 41, and 127 minutes). A trend was seen toward a reduced permanent neurologic deficit rate after unilateral ACP ($P = .06$), but no difference was seen in the occurrence of transient neurologic deficits ($P = .6$). Overall, the early mortality rate was 5% ($n = 52$). Temporary dialysis was necessary primarily after surgery in 38 patients (4%). When corrected for the unequal distribution of type A dissection, neurologic morbidity, early mortality, and the need for temporary dialysis were independent of the duration of ACP and were not affected by unilateral versus bilateral ACP.

Conclusions: Current data suggest that ACP and mild systemic hypothermic circulatory arrest can be safely applied to complex aortic arch surgery even in a subgroup of patients with up to 90 minutes of ACP. Unilateral ACP offers at least equal brain and visceral organ protection as bilateral ACP and might be advantageous in that it reduces the incidence of embolism arising from surgical manipulation on the arch vessels. (*J Thorac Cardiovasc Surg* 2012;144:1042-50)

Antegrade cerebral perfusion (ACP) has become the method of choice for cerebral protection during aortic arch surgery in many centers.¹⁻⁴ However, the technical details of ACP remain controversial, including the choice

of cannulation site, uni- versus bilateral ACP, perfusion pressure during ACP, and temperature management. In particular, the ideal temperature of both the perfusate for ACP itself and the core temperature during selective ACP with systemic circulatory arrest remain a concern. With the clinical introduction of ACP, deep hypothermia became nonessential for neuroprotection, which led to a growing interest in increasing the body temperature during circulatory arrest to avoid coagulopathy or organ dysfunction after the extended period of cardiopulmonary bypass (CPB) needed for deep hypothermia. Although previous reports from the 2 contributing institutions have demonstrated safe and reproducible results using selective ACP with mild-to-moderate systemic hypothermia during aortic arch surgery, only a few data are available on the efficiency of using this approach in patients with prolonged ACP times or in the setting of acute aortic dissection.⁵⁻⁸ The present study was conducted to overcome this lack of

From the Division of Thoracic and Cardiovascular Surgery,^a Johann Wolfgang Goethe University Frankfurt am Main, Frankfurt am Main, Germany; and Cardiovascular Clinic Bad Neustadt,^b Bad Neustadt, Germany.

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Address for reprints: Andreas Zierer, MD, Division of Thoracic and Cardiovascular Surgery, Johann Wolfgang Goethe University Frankfurt am Main, Theodor Stern Kai 7, Frankfurt am Main 60590 Germany (E-mail: andreaszierer@gmx.at).

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Abbreviations and Acronyms
ACP = antegrade cerebral perfusion
ARF = acute renal failure
CA = circulatory arrest
CI = confidence interval
CPB = cardiopulmonary bypass
OR = odds ratio
PND = permanent neurologic deficit
TND = temporary neurologic dysfunction

information to gain better insight into the advantages and potential limitations of this approach, particularly in the case of prolonged selective ACP times. For this purpose, we combined the experience of 2 referral centers for aortic disease in Germany that both started early to use selective ACP and mild (28°C-30°C) systemic hypothermic circulatory arrest for aortic arch surgery.

MATERIALS AND METHODS

Between January 2000 and January 2011, 1002 consecutive patients underwent aortic arch repair during ACP with mild systemic hypothermia (30° ± 2°C; range, 26°C-34°C) at the Division of Thoracic and Cardiovascular Surgery, Johann Wolfgang Goethe University Frankfurt am Main and the Cardiovascular Clinic Bad Neustadt (Germany). The mean age was 62 ± 14 years, 663 patients (66%) were men, and 347 patients (35%) had acute type A dissection, and most patients had degenerative aneurysm (n = 618 [62%]). Other pathologic features, such as porcelain aorta, false aneurysm, or infection, were the cause of surgery in the remaining 37 patients. Detailed preoperative patient characteristics are listed in Table 1. The study was approved by the 2 institutional review boards, and individual patient consent for the study was waived.

Surgical Protocol Applied in Frankfurt

The standardized surgical and perfusion and temperature management protocols for aortic arch surgery used has been previously described in detail.⁷⁻⁹ In brief, the left radial artery and 1 of the femoral arteries was cannulated for continuous blood pressure monitoring. A transesophageal echocardiographic probe was placed and used for confirmation of the diagnosis and assessment of aortic valve function. Temperature probes

were placed for esophagopharyngeal and rectal or bladder temperature monitoring. Although we used a rectal temperature probe from until 2007, we replaced it by a bladder temperature probe in the latter one half of the series. The patient was positioned on the operating table in the supine position. The right axillary artery was directly cannulated (18F-22F flexible arterial cannula; Edwards Lifesciences, Irvine, Calif) followed by cannulation of the right atrium in a standard fashion. The acid-base balance was maintained using the alpha-stat method. CPB was started, and cooling was limited to 28°C-32°C rectal temperature, depending on the expected time of arch repair according to the findings on the preoperative computed tomography scan. The innominate and left carotid artery were snared with silicone elastomer loops and occluded at the initiation of selective ACP. After opening the aortic arch, the left subclavian artery was blocked by insertion of a Fogarty catheter (Edwards Lifesciences) to obtain a bloodless operative field. At that point, the elastomer loop snared around the left common carotid artery was temporarily loosened, and an arterial line was placed inside the vessel for additional perfusion of the left hemisphere (Figure 1). This arterial line was simply connected as a side branch to the arterial CPB cannula. This bilateral ACP was the method of choice between 2005 and 2010. Before 2005 and after 2010, the trend was toward unilateral ACP to avoid the potential risk of creating cerebral emboli while manipulating on the arch during insertion of the second arterial inflow cannula. Selective ACP was conducted with a perfusate temperature of 30°C in a pressure-controlled manner. The perfusion pressure was controlled on the pump unit and kept at 75 to 85 mm Hg, allowing for a mean flow of 1.6 ± 0.2 L/min. At that point, the arch resection or repair was performed.

In patients with type A dissection, the inner and outer layers of the arch wall were dried carefully and glued with a 2-component glue (Colle Chirurgicale, Cardial, Saint-Etienne, France). The distal repair was then completed in a standard fashion using a collagen-coated, woven polyester vascular graft (InterVascular, La Ciotat Cedex, France). Our routine approach was to reimplant the arch vessels en bloc. All suture lines were reinforced with Teflon felt. After completion of the arch repair, the elastomer loops around the innominate and left common carotid artery were released, the Fogarty catheter was withdrawn from the left subclavian artery, and the arch vessels were carefully de-aired, followed by reconstitution of full body perfusion by way of the right axillary artery. Neurovascular monitoring consisted of cerebral saturation assessment using near-infrared

FIGURE 1. Open distal aortic arch repair during bilateral antegrade cerebral perfusion and mild systemic hypothermic circulatory arrest. After opening the aortic arch, the left subclavian artery was blocked by insertion of a Fogarty catheter to obtain a bloodless operative field. At that point, the elastomer loop snared around the left common carotid artery was temporarily loosened and an arterial line placed inside the vessel for additional perfusion of the left hemisphere.

TABLE 1. Patient demographics

Characteristic	Value
Patients	1002
Age (y)	62 ± 14
Men	663 (66%)
Acute type A dissection	347 (35%)
Degenerative aneurysm	618 (62%)
Other pathologic features	37 (3%)
Marfan syndrome	35 (3%)
Coronary artery disease	176 (18%)
Aortic valve stenosis	43 (4%)
Aortic valve regurgitation >2°	206 (21%)
Preoperative neurologic dysfunction	42 (4%)
Previous cardiac surgery	99 (10%)

Data presented as mean ± standard deviation or n (%).

spectroscopy, which was introduced in our routine in the latter half of the series. A total of 477 patients were operated on in Frankfurt.

Surgical Protocol Applied in Bad Neustadt

At the Cardiovascular Clinic Bad Neustadt, the arterial return for CPB was achieved by isolated cannulation of the right or left common carotid artery in the vast majority of patients. Alternative cannulation of the innominate artery or simultaneous carotid and femoral cannulation with a Y-shaped line was considered in selected patients with extended aortic surgery or those with acute aortic dissection with malperfusion.⁵ This technique of double cannulation was also used occasionally in prolonged arch repair to limit an extended period of circulatory arrest (CA) by re-establishing lower body perfusion after completing the distal anastomosis (Figure 2). The decision to choose the particular cannulation technique was made preoperatively according to the findings from computed tomography, which was performed in all patients.

The cannulation technique has been previously described.^{5,6} In brief, the right or left common carotid artery was routinely prepared through a separate approach in the neck along the medial margin of the sternocleidomastoid muscle. In all patients, after heparinization, the exposed segment of the artery was crossclamped and an 8- or 10-mm vascular sealed polyester graft anastomosed to the artery. If additional cannulation of the femoral artery was considered necessary, it was done simultaneously in the usual manner, and both arterial lines were connected with a Y-shaped tube for arterial in-flow from 1 pump (Figure 2). After connecting the arterial line and cannulating the right atrium, CPB was started. In all patients, systemic CA during selective ACP was used for arch repair. Systematic cooling was performed using the alpha-stat method for acid-base management. The neurovascular monitoring varied during the study period and currently consists of pressure measurement in both radial arteries and cerebral saturation assessment using near-infrared spectroscopy.¹⁰ The deepest temperature was determined by the surgeon in accordance with the expected period of CA, with a target rectal temperature adapted to the

approximate scope of CA: about 32° to 34°C for 15 minutes, 30° to 32°C for 30 minutes, and 28° to 30°C for 45 minutes or longer. However, cerebral perfusion was always performed at an arterial blood temperature of 28°C. The arch arteries were crossclamped at the beginning of CA. Unilateral cerebral perfusion at a constant blood temperature of 28°C was set by simply reducing the arterial flow to a mean flow of 1.2 L/min when the left common carotid artery was used for perfusion and, considering the flow to the right arm, to a mean flow of 1.7 L/min when the innominate artery or the right common carotid artery was used.

During cerebral perfusion, the Y-shaped line can be used to perfuse the other brain hemisphere for bilateral cerebral perfusion, if deemed necessary. During rewarming, the Y-shaped arterial line was used to switch the arterial perfusion from the cannulated artery to the aortic graft and, as mentioned, can be used to limit the duration of CA by re-establishing body perfusion in complex procedures. Isolated anastomosing of supra-aortic arteries with respective graft branches is the preferred technique for arch repair, for which vascular prostheses with 4 side branches (InterGard Aortic Arch; InterVascular, La Ciotat, France) are used. In acute dissection, curative replacement of the entire dissected aortic wall was attempted whenever possible, and the use of glue was avoided.¹¹ In Bad Neustadt, during rewarming, the Y-shaped arterial line was used to switch the arterial perfusion from the cannulated artery to the aortic graft. A total of 525 patients were operated on in Cardiovascular Clinic Bad Neustadt during the study period.

Rewarming Protocol

In both institutions, during rewarming, the temperature gradient between the oxygenated blood (arterial line) and the patient's core temperature was set at a maximum of 10°C, with a peak temperature of blood leaving the oxygenator of 38.5°C. Thus, we were able to rewarm the patients 1°C every 5 to 7 minutes. Important details of perfusion management for the entire cohort are summarized in Table 2.

Statistical Analysis

All perioperative data were collected prospectively. The study endpoints were the operative outcomes, including neurologic morbidity, visceral organ failure, and early mortality. The following definitions were used in the present study. Temporary neurologic dysfunction (TND) was defined as the presence of reversible postoperative motor deficit, confusion, agitation, or transient delirium. The computed tomography findings were required to be

FIGURE 2. Schematic illustration of complete aortic arch replacement demonstrating method for limiting duration of circulatory arrest and unilateral cerebral perfusion. After completing the distal anastomosis (1) and crossclamping (CC) the aortic arch graft and its side branches, the graft was cannulated through the fourth side branch and perfusion of lower body was re-established. Cerebral perfusion was re-established step-by-step after completing each additional anastomosis (2-4), starting with the left carotid artery (LCA), followed by the left subclavian artery (LSA) and innominate artery (IA). Next, the arterial line branch to the carotid artery was crossclamped and arterial return performed through the aortic arch graft exclusively. Surgery was completed by proximal aortic and cardiac repair and re-establishment of myocardial perfusion (5). For additional details, see the text.

TABLE 2. Details of antegrade cerebral perfusion

Variable	Value
Unilateral ACP (n)	673 (67%)
Right common carotid artery	340
Right axillary artery	151
Left common carotid artery	144
Innominate artery	38
Bilateral ACP (n)	329 (33%)
Right axillary/left common carotid artery	324
Innominate/left common carotid artery	5
ACP flow (L/min)	1.6 ± 0.4
Perfusion pressure during ACP (mm Hg)*	86 ± 14
ACP perfusate temperature (°C)	29 ± 1
Isolated ACP time (min)	36 ± 19
<30 min (n = 643)	23 ± 5
30-59 min (n = 294)	48 ± 8
Rewarming (n)	
Through right axillary artery	477
Through Y-shaped arterial line and aortic graft	525

Data presented as n (%) or mean ± standard deviation. ACP, Antegrade cerebral perfusion. *As measured on arterial return cannula of cardiopulmonary bypass circuit.

normal, with resolution of all symptoms before discharge. Permanent neurologic deficit (PND) was defined as the presence of either new focal (stroke) or global (coma) permanent neurologic dysfunction. Early mortality was defined as death during the initial hospitalization or within 30 days postoperatively for discharged patients. Continuous data are reported as the mean $\pm$ standard deviation. Fisher's exact test was used to compare differences for categorical variables between the different indications for surgery (acute type A dissection vs other indications), different ACP times (<30, 30-59, and 60-90 minutes), and unilateral versus bilateral ACP. Odds ratios (ORs) are reported with 95% confidence intervals (CIs). Multivariate analysis (stepwise backward regression) was used to determine the preoperative and intraoperative risk factors that were significant independent predictors of adverse neurologic outcomes, increased early mortality, and an increased incidence of renal failure. A total of 22 variables were analyzed: age, year of operation, gender, hypertension, coronary artery disease, pulmonary disease, previous stroke, peripheral vascular disease, smoking history, Marfan syndrome, previous cardiac surgery, cardiogenic shock, aortic insufficiency, presence of acute type A dissection, ACP cannulation site, unilateral versus bilateral ACP, different ACP times (<30, 30-59, vs 60-90 minutes), lowest core temperature, aortic valve preservation versus replacement, hemiarch versus total arch replacement, concomitant coronary artery bypass grafting, and acute renal failure (ARF). All statistical analyses were performed with StatView, version 5.0, for Windows software (SAS Institute, Inc, Cary, NC).

For the purposes of this report, acute postoperative renal failure was defined as a threefold increase in serum creatinine from baseline or a urine output of less than 0.3 mL/kg/h for more than 24 hours. Acute postoperative hepatic failure was defined by a rapid decline in hepatic function characterized by jaundice, coagulopathy (international normalized ratio > 1.5), a substantial increase in transaminases, and hepatic encephalopathy in patients with no evidence of previous liver disease.

RESULTS

Operative Outcomes

Total replacement of the aortic arch was performed in 318 patients (32%) and hemiarch replacement in 684 (68%). The mean CPB time was 158 $\pm$ 56 minutes, and myocardial ischemic time accounted for 101 $\pm$ 41 minutes. The isolated ACP time was 36 $\pm$ 19 minutes. The mean lowest core temperature was 30° $\pm$ 2°C. Additional details of the surgical procedures performed are listed in Table 3. Re-exploration for bleeding had to be performed in 59 patients (6%; Table 4). No local or vascular complications occurred in relationship to the artery cannulated; however, in 5 patients

TABLE 3. Operative data and surgical procedures

Variable	Value
CPB time (min)	158 $\pm$ 56
Crossclamp time (min)	101 $\pm$ 41
Isolated ACP time (min)	36 $\pm$ 19
Lowest core temperature (°C)	30 $\pm$ 2
Hemiarch replacement	684 (68%)
Total arch replacement	318 (32%)
Aortic valve repair	305 (30%)
Aortic valve conduit	199 (20%)
Aortic valve replacement	106 (11%)
Coronary artery bypass grafting	163 (16%)
Other concomitant procedures	45 (4%)

Data presented as mean $\pm$ standard deviation or n (%). CPB, Cardiopulmonary bypass; ACP, antegrade cerebral perfusion.

TABLE 4. Operative outcomes

Outcome	Value
Intensive care unit stay (d)	2 $\pm$ 16
Prolonged ventilation (>7 d)	51 (5%)
Re-exploration for bleeding	59 (6%)
Acute renal failure requiring hemofiltration	38 (4%)
Temporary neurologic deficit	42 (4%)
Permanent neurologic deficit	28 (3%)
Stroke/coma	25 (2.5%)
Paraplegia	3 (0.3%)
Early mortality	52 (5%)

Data presented as mean $\pm$ standard deviation or n (%).

with axillary cannulation, local neurologic dysfunction was noted. With regard to direct cannulation of the right axillary artery, no case of malperfusion or compartment syndrome of the arm developed, no were cases of cerebral hyperperfusion observed in patients with carotid cannulation.

Mortality

The early mortality rate was 5% (52 patients). Of these 52 patients, 8 had been admitted to the operating room in unstable hemodynamic condition and cardiopulmonary resuscitation. All 8 patients were diagnosed with acute type A aortic dissection. The causes of early mortality are listed in Table 5. Multivariate regression analysis identified the presence of acute type A dissection (OR, 3.3; 95% CI, 1.7-6.4) and concomitant coronary artery bypass grafting (OR, 2.5; 95% CI, 1.5-4.3) as independent predictors of early mortality.

Type A dissection. The subanalysis by surgical indication revealed that early mortality (8%, 29/347) was greater among the patients who presented with acute type A aortic dissection compared with the remaining patients (4%, 23/655; $P = .001$; Figure 3).

Duration of ACP. Early mortality increased stepwise from patients with ACP times of less than 30 minutes (3%, 21/643) to patients with ACP times of 30 to 59 minutes (8%, 23/294) to patients with ACP times of 60 to 90 minutes (11%, 7/62; $P \geq .005$). In an additional analysis, the 3 ACP groups were corrected for the unequal distribution of

TABLE 5. Causes of early mortality (n = 52 [5%])

Cause of early mortality	Patients (n)
Multiorgan failure	17
Respiratory failure	10
Preoperative CPR with coma	8
Low output syndrome	7
Gastrointestinal bleeding	4
Stroke	4
Aneurysm rupture	2

CPR, Cardiopulmonary resuscitation.

FIGURE 3. Early mortality was defined as death during initial hospitalization or within 30 days postoperatively for discharged patients. The early mortality rate was 5% (52/1002 patients). Early mortality (8%; 29/347) was greater for patients who presented with acute type A aortic dissection than for the remaining patients (4%; 23/655; $P = .001$). Early mortality increased stepwise from patients with antegrade cerebral perfusion (ACP) times less than 30 minutes (3%, 21/643) to patients with ACP times of 30 to 59 minutes (8%, 23/297) to patients with ACP times of 60 to 90 minutes (11%; 7/62; $P \geq .005$). On additional analysis, the 3 ACP groups were corrected for the unequal distribution of patients diagnosed with acute type A dissection: 21% (133/643) in less than 30-minute group versus 56% (165/297) in 30- to 60-minute group versus 79% (49/62) in the 60- to 90-minute group. When excluding all patients with type A dissection, no difference was seen in early mortality among the 3 groups of ACP duration (3% [17/510], 4% [5/129], 0% [0/13]; $P \geq .6$). PTS, Patients; DISS, dissection.

patients diagnosed with acute type A dissection: 20% (131/643) in the less than 30-minute group versus 56% (165/294) in the 30- to 60-minute group versus 79% (49/62) in the 60- to 90-minute group. When excluding all patients with type A dissection, no difference was found in early mortality among the 3 groups of ACP duration (3% [17/512], 4% [5/129], and 0% [0/13]; $P \geq .6$).

Unilateral versus bilateral ACP. No difference was found in early mortality between patients with unilateral ACP (5%, 37/673) and those with bilateral ACP (5%, 15/329; $P = .64$).

Neurologic Complications

New postoperative neurologic complications such as PND occurred in 28 patients (3%), and TND was detected in 42 patients (4%). Of the 28 patients with PND, 25 experienced a stroke or coma and 3 (0.3%) developed paraplegia. All 3 cases of paraplegia occurred in patients with acute type A dissection and a broad range of ACP times (24, 41, and 127 minutes). Most of the TNDs in the present series were temporary delirium ($n = 37$), and 5 patients experienced a transient motor deficit. Of the cases of transient motor deficit, 2 were isolated to

the right arm as a result of intraoperative constriction of the brachial plexus in 1 patient and iatrogenic nerve lesion of the pectoralis nerve in 1 patient. Multivariate regression analysis identified a history of stroke (OR, 2.9; 95% CI, 1.6-5.3) as the only independent predictor of postoperative PND.

Type A dissection. The PND and TND rate in the subset of patients diagnosed with acute type A dissection was 4% (14/347) and 5% (19/347), respectively, comparable to the 2% PND (14/655) and 4% TND (23/655) rate among the remaining patients ($P \geq .1$).

Duration of ACP. In the 643 patients with an ACP time of less than 30 minutes, the PND (3%, 17/643) and TND (4%, 25/643) rates were well comparable to the PND (3%, 8/297) and TND (5%, 14/297) rates of the 297 patients with ACP times of 30 to 59 minutes and the PND (5%, 3/62) and TND (5%, 3/62) rates of the 62 patients with ACP times of 60 to 90 minutes ($P \geq .4$ between groups).

Unilateral versus bilateral ACP. A trend was seen toward a reduced PND rate (2%, 14/673) after unilateral ACP compared with that (4%, 14/329) after bilateral ACP ($P = .06$). No difference was seen in the occurrence of TND (4%, 30/673; vs 4%, 12/329) with either perfusion strategy ($P = .6$).

Visceral Organ Complications

Renal failure requiring venovenous hemofiltration occurred in 38 patients (4%). Three patients with acute type A dissection and ACP times of 37, 51, and 112 minutes developed early postoperative hepatic failure. Multivariate regression analysis identified advanced age (OR, 1.7; 95% CI, 1.1-2.5) and presence of acute type A dissection (OR, 2.7; 95% CI, 1.4-5) as independent predictors of postoperative renal failure.

Type A dissection. Patients with acute type A dissection had a greater incidence of renal failure (6%, 20/347) than the remaining patients (3%, 18/655; $P = .02$).

Duration of ACP. The incidence of ARF increased from 2% in patients with an ACP time of less than 30 minutes (15/643) to 6% in patients with an ACP time of 30 to 59 minutes (18/297) and 8% in patients with an ACP time of 60 to 90 minutes (5/62; $P \geq .006$). In an additional analysis, the 3 ACP groups were corrected for the unequal distribution of patients diagnosed with acute type A dissection. When excluding all patients with type A dissection, no difference was found regarding the incidence of ARF among the 3 ACP duration groups (3% [13/510], 4% [4/132], 8% [1/13]; $P \geq .3$).

Unilateral versus bilateral ACP. No difference was seen with regard to postoperative renal failure between the patients who received unilateral ACP (4%, 28/673) and those who received bilateral ACP (3%, 10/329; $P = .48$).

DISCUSSION

The classic treatment of aortic arch pathologic today is performed during open distal anastomosis.¹² Thus, physiologic blood flow to the brain and visceral organs is disrupted for the time of completion of aortic arch repair. Different strategies to protect the brain, spinal cord, and visceral organs during arch repair have been advocated. Deep hypothermia, as introduced by Griepp and colleagues,¹³ improves the ischemic brain tolerance considerably and has therefore enabled the development of modern aortic arch surgery as we know it today. It is still a widely used method of cerebral protection and offers good results when the duration of deep hypothermic circulatory arrest is limited 30 minutes; however, the risk of stroke increases significantly after 40 minutes.¹⁴ The duration of CPB needed for cooling and rewarming, coagulopathy, and organ dysfunction have been identified as additional limitations. In an attempt to extend the safe limits of arch repair by avoiding deep hypothermia, several techniques of ACP have been proposed. Bachet and colleagues¹ and Kazui and colleagues² can certainly be considered as the pioneers of the modern era of ACP. Despite an increasing acceptance of ACP at many centers worldwide, technical details of ACP are still being discussed and the safe limits of this approach are yet to be defined. This is particularly true if mild to moderate core

temperatures ($\sim 30^\circ\text{C}$) are chosen during selective ACP, such as the 2 contributing centers from the present study have been practicing for years.

In the present combined experience, the operative mortality rate for patients undergoing aortic arch replacement was 5%. This is fairly low compared with the reported 13% (range, 6%-23%) averaged from 5 classic series of aortic arch repair^{1,15-18} and comparable to the 3% in-hospital mortality rate from recent data published on selected patients with limited aortic arch reconstructive times (<45 minutes).¹⁹ Similar to a previous study published by Moon and Sundt,²⁰ multivariate regression analysis identified the presence of acute dissection as an independent predictor of operative mortality, and the early mortality rate was significantly greater than that for the remaining patients ($P = .001$).²⁰ Furthermore, we noted an unequal distribution of patients with acute type A dissection within the 3 subgroups of varying isolated ACP times, which hampered interpretation of the safe limits of the perfusion strategy itself: 21% (133/643) in the less than 30-minute group versus 56% (165/297) in the 30- to 60-minute group versus 79% (49/62) in the 60- to 90-minute group. No difference was seen in early mortality among the 3 groups of increasing ACP times when focusing on indications for surgery other than acute type A dissection ($P \geq .6$). Also, the number of patients ($n = 13$) left in the 60- to 90-minute group was limited, hindering a definite recommendation. The increasing overall mortality for the entire series (including acute type A dissection), with a longer duration of selective ACP statistically supporting the findings recently published by the work force of the German Registry for Acute Aortic Dissection Type A (GERAADA).²¹ In that report, the investigators reported an increase in 30-day mortality (overall 16%) with prolonged aortic arch reconstructive times, independent of the perfusion and temperature management applied. In the GERAADA experience, the 30-day mortality and PND rate (11% overall) in the subgroup of patients undergoing surgery during selective ACP was independent of the lowest core temperature. This also included patients from the 2 contributing centers of the present series with core temperatures of 30°C or greater.

We also observed a low incidence of permanent and transient neurologic deficits. The rate of PND was 3%. This is at the lower level of normal compared with previous reports. In the 5 major series cited, the risk of PND averaged 8%.^{1,15-18} The 3 patients who developed paraplegia all belonged to the subset of patients with acute type A dissection. All 3 patients came into the operating room on the ventilator and had an unclear preoperative neurologic status. With regard to the operative course, the 3 cases had a wide range of ACP times (24, 41, and 127 minutes, respectively). To minimize the risk of this devastating complication, it is important to stress that in both centers we adapt the level of systemic cooling to the anticipated extent of arch reconstructive

time according to the preoperative computed tomography scan (approximately 32°C–34°C for 15 minutes, 30°C–32°C for 30 minutes, and 28°C for ≥ 45 minutes). In a porcine model, Etz and colleagues²² demonstrated that paraplegia was probable after 90 minutes and inevitable after 120 minutes of cerebral perfusion and systemic circulatory arrest at 28°C. From these findings, one might expect a greater incidence of paraplegia than the 0.3% rate we have reported. However, the technical details of ACP applied in that experimental study showed relevant variations, including a perfusion pressure of only 50 mm Hg. This was much lower than the 86 ± 14 mm Hg in the present series. We believe that the warm ACP perfusate (28°C–30°C) combined with the high perfusion pressure allows for an important collateral flow from the brain to the spinal cord that is clinically evidenced as a substantial backflow of blood from the descending aorta requiring continuous suction to maintain a bloodless operating field during open arch repair. Using bifurcated arterial lines and branched vascular prostheses, such as is also practiced by Kouchoukos and Massetti,²³ enables the gradual (here described in detail) re-establishment of perfusion after completing the particular anastomoses (Figure 2). This gradual re-establishment of perfusion is a very important adjunct to refine the perfusion and surgical technique and shorten the isolated ACP time, especially in complex aortic pathologic features. However, because, in our experience, the mean isolated ACP time did not exceed 40 minutes, we have not routinely used gradual perfusion re-establishment. Another important finding was that a trend was seen toward a decreased PND rate after unilateral ACP compared with the PND rate after bilateral ACP ($P = .06$). Unilateral ACP might be advantageous in that it reduces the incidence of embolism arising from surgical manipulation on arch vessels. Different ACP times did not affect the PND or TND rates ($P \geq .4$) in our series. The reported TND rate of 4% was similar to the TND rate of 4% for atherosclerotic arch aneurysms reported by Kazui and colleagues.²

In addition to operative mortality and sufficient cerebral protection, adequate distal organ protection during extended selective ACP times in patients requiring aortic arch replacement remains a major issue. The risk of developing ARF after aortic arch surgery has been reported to be 5% to 14%.²⁰ Reviewing the reported data on renal damage after cardiac surgery, it becomes evident that a wide variation of definitions for ARF has been used. Thus, similar to most previous reports, we focused on the incidence of a transient renal replacement therapy requirement. In a recent series of 4707 patients undergoing thoracic aortic surgery in Japan with a wide range of different surgical techniques, the incidence of ARF requiring dialysis was 7%.²⁴ That report included a mixed cohort of patients, with 47% who had undergone ascending aortic replacement. In our series of hemiarch and total arch replacement,

the incidence of ARF requiring dialysis was only 4%. Multivariate analysis identified advanced age and the presence of an acute type A dissection as independent predictors of ARF. Even after an intensive data search, we were not able to find substantial data on hepatic outcomes after aortic arch surgery. Given our data of only 3 patients developing acute postoperative hepatic failure, we can speculate that hepatic injury should not be a limiting factor to using this perfusion and temperature management protocol.

CONCLUSIONS

When corrected for the unequal distribution of acute type A dissection, early mortality and the need for temporary dialysis were independent of the duration of selective ACP for up to 90 minutes. For the entire series, neurologic outcome was independent of the isolated ACP time. Despite an increase in mortality and ARF with prolonged isolated ACP times in patients, including those with acute type A dissections, the results achieved within this high-risk subgroup (including an incidence of paraplegia of only 0.3%) can still be considered good compared with the literature. Unilateral ACP offers brain and visceral organ protection at least equal to that of bilateral ACP and might be advantageous in that it reduces the incidence of embolism arising from surgical manipulation on arch vessels. Thus, the concept of selective ACP for aortic arch surgery using a warm perfusate and a core temperature of $\sim 30^\circ\text{C}$ as described in the present study from 2 institutions can be considered safe, straightforward, and reproducible and might help reduce the CPB time and hypothermia-related side effects. A definite recommendation regarding the safe limits of this approach from the present data was hampered by the limited number of patients with an ACP time longer than 60 minutes.

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Discussion

Dr Nicholas T. Kouchoukos (St Louis, Mo). This study from Dr Zierer and his colleagues reports an experience with aortic arch replacement from 2 separate institutions using a general technique of selective antegrade perfusion at 28°C to 30°C for brain protection. It is not a homogeneous study in that different protocols for establishing antegrade perfusion were used. In Frankfurt, in the early and late periods of the study, unilateral brain perfusion through the right axillary artery was used, and in the middle interval, the left carotid artery was also perfused. In Bad Neustadt, unilateral perfusion through either the right or left common carotid artery was used in most patients. These and other perhaps less important differences between the 2 institutions, such as a perfusion temperature of 28°C in Frankfurt and 30°C in Bad Neustadt and slightly differing core temperatures and flow rates to the brain, have introduced confounding variables that might have had

some influence on the outcome and the conclusions drawn by the authors.

That being said, the overall results are highly satisfactory, with acceptably low rates of early death, stroke, paraplegia, renal failure, and reoperation. They add support to the general strategy of antegrade perfusion at moderate hypothermia and maintenance of body temperature at comparable levels.

The stated objectives of the study were to assess the efficacy of this approach in the setting of acute dissection and prolonged brain perfusion, for which less information is available. Although the authors conclude that the strategy is effective even with brain perfusion intervals of up to 90 minutes, they observed substantial early mortality, 14%, and a significantly greater prevalence of renal failure in the subset of patients with acute dissection and brain perfusion longer than 60 minutes. High rates of these 2 complications were also observed in a subset of acute dissection and perfusion times of 30 to 59 minutes. I have 3 questions, and you can answer them separately.

You state that in both centers you adapted the level of systemic cooling to the anticipated extent of the arch reconstructive time. Are you willing, based on your findings, to lower the brain perfusate and body temperatures below the levels that you used in the study to reduce complications in high-risk substrates? That is, do you believe lower temperatures will make a difference?

Dr Zierer. Thank you very much, Dr Kouchoukos, for your thorough comments and interesting question. You are certainly right, that the number of patients with a prolonged ACP time is limited, which hampers interpretation of the data. However, as previously shown on the slide of the surgical techniques, we have the additional tool of perfusing the body once the distal anastomosis has been completed, by either cannulating the graft with a flexible cannula or using a graft with a side branch.

You mentioned the outcome in patients with acute type A dissection. I would like to make a comment on this, because I read the report from the German registry that was published in *Circulation* just last year. They had 1600 patients with a broad range of different protection strategies, and the overall mortality for the entire series was 16%. Also, in the current series in the subgroup of patients with prolonged ACP times with 80% of patients having type A dissections, the mortality was 11%, although you are right that it was 15% for type A dissections only. However, we still think these are acceptable results.

So we would suggest performing a stepwise reconstitution of body perfusion rather than to cool down the patient further; however, as also mentioned, cooling is adapted to the anticipated duration of arch repair. So, for acute type A dissection, we always cool down to at least 28°C.

Dr Kouchoukos. Did you find any differences between the patients having perfusion only of the left carotid versus those who had perfusion of the right axillary or right carotid, which would permit perfusion of the right vertebral and right carotid, and are you concerned about the possibility of hyperperfusion with unilateral perfusion?

Dr Zierer. Actually, regarding the neurologic morbidity, no difference was found when we analyzed the different cannulation sites. All patients with left carotid artery cannulation were from Bad Neustadt, but I reviewed the data and discussed them with Dr Urbanski, and in both institutions there was no problem with hyperperfusion.

Dr Kouchoukos. You observed a significantly lower prevalence of permanent neurologic injury among the patients who had unilateral versus bilateral perfusion, at least that is what appeared in the report, presumably with no adverse effects. Are you willing to abandon bilateral perfusion?

Dr Zierer. Well, actually most of the patients with bilateral antegrade cerebral perfusion were from our institution in Frankfurt. I have to admit that we initially started with unilateral cerebral perfusion, and then we, as a unit, switched to bilateral perfusion. However, most recently since we reviewed the data, and we interpreted the data this way that there might be an increased risk of cerebral emboli by manipulating on the arch vessels for bilateral perfusion, we do, in fact, prefer unilateral ACP again.

Dr Kouchoukos. Thank you. It was a very nice report on a very important topic.

Dr Zierer. Thank you very much.

Dr Edward P. Chen (*Atlanta, Ga*). I really enjoyed your presentation and congratulate you on your group's outstanding results. We, at Emory, since 2004, have used a very similar protocol of circulation management and cerebral protection, and in our series of 800 patients, have had very similar permanent and temporary neurologic dysfunction rates.

I did want to ask whether there was a difference in your protocols between the hemiarch and the total arch patients with respect to how much you would cool them and the temperature at which you would perfuse their brains during the period of circulatory arrest and were there differences in the outcomes if you compared the hemiarch versus total arch in terms of neurologic events?

Dr Zierer. Thank you. That is an excellent question. Actually we did not really compare hemiarch versus total arch replacements, but the difference should be reflected in the different arch repair times. Regarding neurologic outcome, no difference was seen between the less than 30-minute group and the 30- to 60-minute group.

Apparently, there is a huge difference if you only plan an elective hemiarch replacement as compared to a full arch replacement in the presence of an acute aortic dissection, and that is why we cool down the patients for a nondissected aneurysm for which we plan a simple hemiarch replacement to 30°C to 32°C and we cool down to at least 28°C for an acute type A dissection. However,

the ACP perfusate temperature we always keep at 28°C to 30°C, because we believe that this maintains cerebral autoregulation and improves collateral flow to the contralateral hemisphere.

Dr Behzad Soleimani (*Hershey, Pa*). Thank you very much for your clear presentation. I have 1 question. You stated that preoperative stroke or neurologic event was predictive of a postoperative neurologic event. Did you find that presence of preoperative stroke was more predictive in unilateral versus bilateral perfusion? That is, do you have any data to support that if there has been a stroke, it is better to do bilateral, or if you do unilateral, do it contralateral to the site of the stroke?

Dr Zierer. Well, actually, that is an excellent question, but I have to admit that we did not specifically look at these data. It is a good idea, but I do not have any answer for this at this point.

Dr Friedhelm Beyersdorf (*Freiberg, Germany*). This is a very nice study, and I have a question concerning the near infrared spectroscopy measurement. Do you have some correlation between unilateral and bilateral perfusion and these measurements for the cerebral oxygen content?

The second question is, have you any experience with using this method for the oxygenation of the spinal cord when you put these patches in the back?

Dr Zierer. Actually, we did not measure the saturation in the spinal cord. Regarding cerebral oxygen measurement, we could hardly ever see a difference in the contralateral hemisphere when using unilateral ACP. In fact, there was only 1 single case in which the saturation of the left hemisphere when perfusing the right common carotid artery decreased substantially because the patient had an occluded vertebral artery and also a stenosis of the left common carotid artery. So this was the only patient in whom we switched to bilateral ACP because of the near infrared spectroscopy measurement.

In our opinion, it is important to consider, on the one hand, the oxygen saturation on near infrared spectroscopy but also to closely watch the pressure measurement on the contralateral radial artery. If this pressure stays within a range of 40 to 60 mm Hg and the cerebral oxygen saturation in the contralateral hemisphere does not decrease to a level less than 70% of what it was in the beginning, this should be correlated with a good clinical outcome.