SURGERY FOR ACQUIRED HEART DISEASE

MORTALITY AND CEREBRAL OUTCOME IN PATIENTS WHO UNDERWENT AORTIC ARCH OPERATIONS USING DEEP HYPOTHERMIC CIRCULATORY ARREST WITH RETROGRADE CEREBRAL PERFUSION: NO RELATION OF EARLY DEATH, STROKE, AND DELIRIUM TO THE DURATION OF CIRCULATORY ARREST

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Objective: Our goal was to investigate factors for mortality and cerebral outcome in patients with aneurysm of the aortic arch. **Methods:** From 1993 to 1996, 148 patients with aortic arch aneurysm underwent operations involving deep hypothermic circulatory arrest with retrograde cerebral perfusion. Age was 63.9 ± 11.6 years (mean $\pm$ standard deviation) and 52 patients were older than 70 years. Twenty-eight had acute aortic dissection. Twelve had ruptured aneurysms. Fourteen had redo operations. Seventy had aortic dissection. The aneurysms were caused by atherosclerosis in 123 patients and by other causes in 25. Median sternotomy was used in 92 and left thoracotomy in 56. Twenty-eight patients underwent replacement of the ascending aorta to the proximal arch, 62 had total arch replacement, 38 had distal arch replacement, 12 had simultaneous replacement of the distal arch and the descending aorta or thoracoabdominal aorta, and 8 had patch repair. **Results:** Fifteen (10.1%) early deaths occurred. New stroke occurred in six (4.0%) patients and transient delirium in 37 (25.0%). The duration of deep hypothermic circulatory arrest plus retrograde cerebral perfusion was 49 ± 17 minutes, and it was more than 60 minutes in 36 patients. Patients awoke 7.5 ± 8.2 hours after the operation. Logistic regression analysis demonstrated that risk factors for mortality were ruptured aneurysm, chronic obstructive pulmonary disease, arterial cannulation in the ascending aorta, and stroke. Risks for stroke were ruptured aneurysm and replacement of the distal arch. Risks for delirium were age older than 70 years and atherosclerotic aneurysm. Duration of circulatory arrest plus cerebral perfusion did not correlate with length of time before the patient regained consciousness. No difference was found in mortality, stroke, and delirium between patients with and those without more than 60 minutes of circulatory arrest and cerebral perfusion. **Conclusion:** Prolonged (>60 minutes) deep hypothermic circulatory arrest with retrograde cerebral perfusion was not a risk factor for mortality and stroke in patients who underwent surgery for aneurysms of the aortic arch. However, the prevalence of transient delirium necessitates further investigations. (J Thorac Cardiovasc Surg 1998;115:129-38)

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Although cerebral complication remains a rare event after cardiac surgery,¹ it is a predominant cause of mortality and morbidity after thoracic aortic surgery because of the growing population of elderly patients undergoing such operations.²⁻⁴ Despite recent progress in surgery for thoracic aortic aneurysm, complications involving the central nervous system are still prevalent, especially in patients with aortic arch aneurysm.¹⁻⁴ In 1993, Svensson and associates⁵ reported that the occurrence of stroke was observed to increase after 40 minutes of circulatory arrest, and the mortality rate increased markedly after 65 minutes of circulatory arrest. In 1994, Ergin and coworkers³ reported that the safe limit for circulatory arrest was 60 minutes. However, the retrograde cerebral perfusion (RCP) technique added a new idea that can augment cerebral protection during deep hypothermic circulatory arrest (DHCA).⁶ The current study deals with our surgical experience and the postoperative neurologic outcome in 148 patients who underwent aortic arch operations in which DHCA combined with RCP (DHCA + RCP) was used.

Patients and methods

Patients. From May 1993 to September 1996, 148 consecutive patients with aortic arch aneurysms underwent operations performed with DHCA + RCP in the National Cardiovascular Center, Osaka, Japan (Table I). Mean age was 63.9 ± 11.6 years ($\pm$ standard deviation) and 52 patients were more than 70 years old. Seventy-eight had nondissecting aortic aneurysms and 70 had aortic dissection. Twenty-eight had acute dissection that occurred within 14 days before the operation and 42 had chronic dissection. Twelve patients had ruptured aneurysms and were in shock. Thirty-five patients had surgery on an emergency basis. Fourteen patients had a previous operation on the thoracic aorta. Causes of the aneurysms were atherosclerosis in 123 patients, cystic medial necrosis in 12, Marfan syndrome in 6, and aortitis in 7. Preoperative complications consisted in aneurysm of the ascending aorta in 24 patients, coronary arterial disease in 19, cerebrovascular lesions in 17, valvular heart disease in 15, chronic obstructive pulmonary disease (COPD) in 9, renal failure necessitating dialysis or diet restriction in 9, and peripheral vascular obstruction in 5.

Methods. Preoperative brain computed tomography, carotid echography, and nonselective cerebral four-vessel angiography were done in all patients except those treated on an emergency basis. The patient with preoperative risk factors for brain ischemia, that is, history of transient ischemic attack or infarction and stenotic carotid arteries, had a brain perfusion scan with acetazolamide loading.

The chest was entered through a median sternotomy in 92 patients and through a left thoracotomy in 56. Intraoperative echography, direct epi-aortic scan, and trans-esophageal echography were routinely used in every pa-

Table I. Patients with aortic arch aneurysms who underwent surgery with DHCA + RCP

<i>n</i>	148
Age (yr)	
Mean	63.9 $\pm$ 11.6
Range	27-88
Aortic lesions	
Nondissecting	78
Dissecting	70
Acute	28
Chronic	42
Emergency surgery	34
Ruptured aneurysms	12
Approach	
Median sternotomy	92
Left thoracotomy	56
Operation	
Hemiarch	28
Total arch	62
Distal arch	38
Distal arch-Desc	12
Patch	8

Desc, Descending aorta.

tients to locate a safe site for aortic cannulation and clamping. In 117 patients (79%), 2 million units of aprotinin was added to the pump prime. An arterial cannula was inserted in the ascending aorta in 45 patients and in the femoral artery or descending aorta in 103. Soft aortic cannulas were used to prevent thromboemboli.

Through a median sternotomy,⁶ RCP was implemented with the use of the bypass bridge connecting the arterial and venous lines of the extracorporeal circuit to reverse the flow into the superior vena cava cannula after the initiation of total DHCA at a nasopharyngeal temperature of less than 18° C. Continuous RCP flow was necessary to maintain an internal jugular vein pressure of 15 to 20 mm Hg. Blood draining into the aortic arch was aspirated. Cardiopulmonary bypass was instituted through a left thoracotomy with left atrial venting.⁷ The descending aorta was clamped proximal to the arterial cannula and the distal aortic arch aneurysm was incised after the patient had been cooled to 18° C. RCP was initiated at a central venous pressure of 15 to 18 mm Hg. Proximal anastomosis of a graft with the distal aortic arch was performed during RCP.

Topical external cooling of the brain with an ice jacket is a prerequisite to maintain cerebral hypothermia. Intracranial content of oxygenated hemoglobin was monitored by means of near-infrared spectroscopy. Clamping of the aortic arch was avoided and an open aortic anastomosis technique was used in all patients. Selective cerebral perfusion was available on standby when the duration of DHCA exceeded 80 minutes; however, it was not necessary. After revascularization of cerebral vessels, antegrade perfusion of the brain was initiated as early as possible. Slow rewarming was preferred.

Operative procedures consisted of replacement from the ascending aorta and proximal aortic arch in 28 patients, total arch replacement in 62, distal arch replace-

Table II. Thirty-five perioperative variables affecting postoperative mortality and morbidity

Variables	Yes		No	
	n	%	n	%
1. Age: older than 70 years	52	35.1	96	64.9
2. Sex				
Male	100	67.5		
Female	48	32.5		
3. Etiology				
Atherosclerosis	123	83.1		
Degenerative	18	12.1		
Aortitis	7	4.8		
Preoperative complications				
4. CI, carotid stenosis	17	11.4	131	88.6
5. CAD	19	12.8	129	87.2
6. VHD	15	10.1	133	89.9
7. COLD	9	6.0	139	94.0
8. CRF	9	6.0	139	94.0
9. AAA, ASO	29	19.5	119	80.5
10. Approach				
Midline	92	62.1		
Left lateral	56	37.9		
11. Redo	14	9.4	134	90.6
12. Emergency	34	22.9	114	77.1
13. Rupture	12	8.1	136	91.9
14. Acute aortic dissection	28	18.9	120	81.1
15. Aortic dissection	70	47.2	78	42.8
16. Arterial cannulation				
Ascending aorta	45	30.4		
Femoral artery	103	69.6		
17. ECC over 180 min	53	36.8	112	65.2
18. Cardiac arrest over 120 min	25	16.8	123	83.2
19. RCP over 60 min	36	24.3	112	73.7
20. Aprotinin	117	79.0	31	21.0
21. Procedures				
Hemiarch	28	18.9		
Total arch	62	41.9		
Distal arch (including Desc Ao, TAAA)	50	33.8		
Patch repair	8	5.4		
22. Concomitant procedures	9	6.0	139	94.0
Postoperative complications				
23. Stroke	6	4.0	142	96.0
24. Lung	22	14.8	146	85.2
25. Bleeding	18	12.1	138	87.9
26. LOS	10	6.7	138	93.3
27. ARF	8	5.4	140	94.6
28. Liver	7	4.7	141	95.3
29. Sepsis	3	2.0	145	98.0
30. DIC	2	1.3	146	98.7
31. GI problems	5	3.3	143	96.7

CI, Cerebral infarction; CAD, coronary arterial disease; VHD, valvular heart disease; COLD, chronic obstructive lung disease; CRF, chronic renal failure; AAA, abdominal aortic aneurysm; ASO, arteriosclerosis obliterans; ECC, extracorporeal circulation; Desc Ao, descending aorta; TAAA, thoracoabdominal aortic aneurysm; LOS, low cardiac output syndrome; ARF, acute renal failure; DIC, disseminated intravascular coagulation; GI, gastrointestinal.

Table III. Mortality

Hospital death	15 (10.1%)
Nondissecting aneurysm	11
Acute dissection	4
Early death (–30 days)	12
Age (yr)	
Mean	73.6 ± 7.0
Range	28–88
Emergency surgery	5
Ruptured aneurysm	3
Surgery	
Hemiarch	1
Total arch	7
Distal arch	4
Distal arch–Desc	3
Postoperative stroke (4), but no delirium	
DHCA duration (min)	
Mean	51.8 ± 23.6
Range	30–94
Causes	
Bleeding	3
Mediastinitis	2
Asphyxia	2
Bowel necrosis	2
Stroke	2
Respiratory failure	2
Acute renal failure	1
Low cardiac output	1
Cerebral bleeding	1
Gastrointestinal bleeding	1

Desc, Descending aorta.

Table IV. Comparison of two groups of hospital deaths and survivors

	Deaths (n = 15)	Survivors (n = 133)	p Value
Age	73.6 ± 7.0	62.8 ± 11.5	<0.001
Male	11 (73.3%)	89 (66.9%)	0.61
Emergency	5 (33.3%)	29 (21.8%)	0.31
ECC (min)	272.3 ± 176.7	181.9 ± 68.1	<0.001
Cardiac arrest (min)	92.1 ± 39.0	79.0 ± 37.3	0.71
DHCA + RCP (min)	58.5 ± 15.8	49.6 ± 17.1	0.54
Stroke	4 (26.6%)	2 (1.5%)	<0.001
Delirium	0	37 (27.8%)	0.02

ECC, Extracorporeal circulation; DHCA, deep hypothermic circulatory arrest; RCP, retrograde cerebral perfusion.

ment in 38, simultaneous replacement of the distal arch and the descending aorta or thoracoabdominal aorta in 12, and patch repair of the aneurysms in 8. Thirty concomitant procedures consisted of “elephant trunk” installation in 15 patients, aorta-coronary bypass in 7, Bentall’s operation in 3, carotid endarterectomy in 2, remodeling of the aortic root in 2, and graft replacement of the infrarenal abdominal aorta in 1.

Postoperative stroke was defined as a newly developed neurologic deficit, new lesions diagnosed by computed

Table V. Description statistics

Variables	No. of patients	Univariate analysis		
		Hospital deaths	Stroke	Delirium
		n (% , p)	n (% , p)	n (% , p)
1. Age: older than 70 yr	52	9 (17.3, 0.03)	1 (1.9, 0.33)	25 (58.1, <0.001)
2. Sex				
Male	100	11 (11.0, 0.91)	5 (5.0, 0.39)	26 (29.2, 0.69)
Female	48	5 (10.4)	1 (2.0)	11 (25.5)
3. Etiology				
Atherosclerosis	123	14 (11.3, 0.26)	6 (4.8, 0.26)	35 (32.1, 0.02)
Others	25	1 (4.0)	0 (0)	2 (8.3)
Preoperative complications				
4. CI, carotid stenosis	17	1 (5.8, 0.54)	0 (0, 0.37)	2 (12.5, 0.18)
5. CAD	19	4 (21.0, 0.09)	1 (5.2, 0.77)	6 (40.0, 0.38)
6. VHD	15	1 (6.6, 0.64)	1 (6.6, 0.64)	3 (21.4, 0.32)
7. COLD	9	4 (44.4, <0.001)	0 (0, 0.52)	2 (40.0, 0.91)
8. CRF	5	1 (20.0, 0.46)	1 (20.0, 0.46)	1 (25.0, 0.90)
9. AAA, ASO	29	5 (17.2, 0.16)	1 (3.4, 0.85)	7 (29.1, 0.87)
10. Approach				
Midline	92	10 (10.8, 0.70)	2 (2.1, 0.14)	22 (26.8, 0.75)
Left lateral	56	5 (8.9)	4 (7.1)	15 (29.4)
11. Redo	14	0 (0, 0.19)	0 (0, 0.19)	2 (14.2, 0.23)
12. Emergency	34	5 (14.7, 0.31)	2 (5.8, 0.54)	7 (20.5, 0.28)
13. Rupture	12	5 (41.6, <0.001)	3 (25.0, <0.001)	2 (28.5, 0.37)
14. Acute aortic dissection	28	3 (10.7, 0.91)	2 (7.1, 0.36)	8 (32.0, 0.66)
15. Aortic dissection	70	4 (5.7, 0.09)	2 (2.8, 0.48)	15 (22.7, 0.45)
16. Arterial cannulation				
Ascending aorta	45	8 (17.7, 0.04)	3 (6.6, 0.29)	10 (29.4, 0.81)
Femoral artery	103	7 (6.7)	3 (2.9)	27 (25.4)
17. ECC over 18 min	53	7 (13.2, 0.35)	3 (5.6, 0.46)	10 (21.7, 0.26)
18. Cardiac arrest over 120 min	25	3 (12.0, 0.73)	1 (4.0, 0.99)	3 (13.6, 0.10)
19. RCP over 60 min	36	5 (13.8, 0.39)	1 (2.7, 0.66)	9 (29.0, 0.75)
20. Aprotinin	117	13 (11.1, 0.44)	4 (3.4, 0.45)	30 (28.8, 0.62)
21. Procedures				
Hemiarch	28	1 (3.5, 0.27)	1 (3.5, 0.05)	8 (29.6, 0.25)
Total arch	62	7 (10.6)	0 (0)	12 (20.3)
Distal arch	58	9 (15.5)	5 (8.6)	18 (36.7)
(including Desc Ao., TAAA)				
22. Concomitant procedures	9	2 (22.2, 0.22)	1 (11.1, 0.92)	2 (28.5, 0.96)
Postoperative complications				
23. Stroke	6	4 (66.6, <0.001)		0 (0, 0.38)
24. Lung	22	7 (31.8, <0.001)	3 (13.6, 0.01)	10 (66.6, <0.001)
25. Bleeding	18	9 (27.7, <0.001)	4 (22.2, <0.001)	4 (44.4, 0.25)
26. LOS	10	2 (20.0, 0.28)	2 (20.0, 0.28)	2 (25.0, 0.85)
27. ARF	8	4 (50.0, <0.001)	3 (37.5, <0.001)	2 (50.0, 0.31)
28. Liver	11	1 (9.0, 0.91)	1 (9.0, 0.91)	1 (10.0, 0.19)
29. Sepsis	3	3 (100, <0.001)	0 (0, 0.72)	0 (0)
30. DIC	2	2 (100, <0.001)	1 (33.3, <0.001)	0 (0)
31. GI problems	5	4 (80.0, <0.001)	2 (40.0, <0.001)	1 (100.0, 0.11)

CI, Cerebral infarction; CAD, coronary arterial disease; VHD, valvular heart disease; COLD, chronic obstructive lung disease; CRF, chronic renal failure; AAA, abdominal aortic aneurysm; ASO, arteriosclerosis obliterans; ECC, extracorporeal circulation; Desc Ao, descending aorta; TAAA, thoracoabdominal aortic aneurysm; LOS, low cardiac output syndrome; ARF, acute renal failure; DIC, disseminated intravascular coagulation; GI, gastrointestinal.

tomography, or unresponsiveness 3 days after the operation. *Postoperative delirium* was defined as a transient disorientation and character change with no neurologic sequelae.

Univariate statistical analysis was done by χ^2 test and Student's *t* test. Thirty-one perioperative variables that

were considered to affect postoperative mortality and morbidity (Table II) were entered for analysis by multivariate logistic regression with stepwise addition of variables. A contingent probability of 0.10 or less was used to enter variables into the logistic models in a forward-stepping manner, and a contingent probability of 0.15 or

Table VI. Stepwise logistic regression analysis for mortality and morbidity in patients who underwent surgery for aortic arch aneurysm

Variables	Relative risk	p Value
Hospital death		
Ruptured aneurysm	14.2	0.007
COLD	6.9	0.036
Postoperative stroke	76.9	0.004
Stroke		
Ruptured aneurysm	13.3	0.041
Distal arch aneurysm	5.3	0.053
Delirium		
Over 70 years old	7.1	0.012
Atherosclerotic etiology	10.9	0.022

less was used to remove variables from the model. Postoperative complications were not taken into account as variables in analyzing postoperative brain damage. The estimated relative risk was the likelihood of an event in the presence of a variable compared with its likelihood in the absence of that variable. All statistical significance was assumed at the $p < 0.05$ level.

Results

Fifteen (10.1%, Table III) hospital deaths occurred. Twelve patients died within 30 days after the operation. Eleven patients had nondissecting aneurysms and four patients had acute dissection. The average age was 65.3 years, and that was significantly older than the age of early survivors ($p = 0.004$). Emergency surgery, including operations for aortic rupture, was performed in five patients.

One patient died after hemiarch grafting, seven died after total arch replacement, four died after distal arch replacement, and three died after distal arch and descending aorta replacement. Four patients among those who died in the early postoperative period had a stroke, but duration of DHCA + RCP in this group was not longer than that in the early survivors. Causes of death are listed in Table III. Significant factors for hospital death by univariate analysis were older age (>70 years), preoperative COPD, ruptured aneurysm, arterial cannulation in the ascending aorta, postoperative stroke, respiratory complication, bleeding, acute renal failure, sepsis, disseminated intravascular coagulation, and gastrointestinal problems (Tables IV and V). Stepwise logistic regression analysis of perioperative variables demonstrated that the significant risk factors for hospital death were ruptured aneurysm, preoperative COPD, arterial cannulation in the ascending aorta, and perioperative stroke (Table VI).

Table VII. Stroke

Strokes	6 (40%)
Nondissecting	4
Dissecting	2
Age (yr)	
Mean	65.5 $\pm$ 21.3
Range	60-70
Emergency surgery	2
Ruptured aneurysm	1
Surgery	
Distal arch	3
Patch for distal arch	1
Hemiarch	1
Distal arch + total arch	1
Approach	
Median sternotomy	2
Left thoracotomy	4
Cannulation	
Ascending aorta	3
Femoral artery	3
DHCA duration (min)	
Mean	46.5 $\pm$ 23.5
Range	29-61
Etiology	
Prolonged DHCA	1
Thromboemboli	2
Suture line debris	1
Biologic glue emboli	1
Bilateral carotid obstruction	1
Early death	4
Discharge	2
Disabled	2

DHCA, Deep hypothermic circulatory arrest.

Postoperative stroke was diagnosed in six patients (4.0 %, Table VII). Four patients had nondissecting aneurysm of the distal arch. Operation consisted of replacement or patch repair of the distal arch in four, and ascending aorta replacement for acute type A dissection in one, and subsequent replacement of the total arch after replacement of the descending aorta in one.

One patient required DHCA several times to control bleeding from the aortic cannulation site. He did not awake after a 7-hour pump run, and computed tomographic scans showed global ischemia of the brain. Duration of cardiopulmonary bypass was longer in the stroke group, but this was skewed by extraordinarily prolonged bypass times (457 and 602 minutes) in two patients who had a stroke and died. DHCA + RCP in the stroke group was similar to that in the other group (Table VIII). Computed tomographic scanning clearly demonstrated the embolic characters of these strokes in five patients. Causes of embolization were speculated to be thromboemboli in two, debris from the

Table VIII. Comparison of two groups of patients with stroke and without

	Stroke (n = 6)	No stroke (n = 142)	p Value
Age	65.7 ± 9.6	63.2 ± 12.2	0.30
Male	5 (83.3%)	95 (66.9%)	0.40
Emergency	2 (33.3%)	32 (22.5%)	0.54
ECC (min)	294.3 ± 188.2	181.9 ± 68.1	<0.001
Cardiac arrest (min)	85.2 ± 59.6	79.0 ± 37.3	0.71
DHCA + RCP (min)	46.5 ± 11.2	49.6 ± 17.1	0.54
ICU stay (days)	25.5 ± 17.7	6.4 ± 9.7	<0.001

ECC, Extracorporeal circulation; DHCA; deep hypothermic circulatory arrest; RCP, retrograde cerebral perfusion.

anastomotic suture line in one, and biologic glue emboli in one. Other causes of stroke were considered to be prolonged ischemia in one and obstruction of the bilateral carotid arteries as a result of intraoperative progression of aortic dissection from the descending aorta to the arch in one. Among patients who had a stroke, four died during hospitalization and two became disabled. Univariate analysis demonstrated that risk factors for postoperative stroke were ruptured aneurysm, surgery in the distal aortic arch, and postoperative pulmonary complications, bleeding, acute renal failure, disseminated intravascular coagulation, and gastrointestinal problems (see Table V). Multivariate stepwise logistic regression analysis revealed that risk factors for stroke were ruptured aneurysm and surgery on the distal arch (see Table VI).

Thirty-seven patients (25.0%) had transient delirium (Table IX). Variables of patients who had delirium were compared with variables of those without. No significant difference was noted in age, duration of cardiopulmonary bypass or circulatory arrest, urgency of operation, length of time before the patient regained consciousness after the operation, and intensive care unit (ICU) or hospital stay (Table X). Univariate and stepwise logistic regression analysis demonstrated that age (>70 years) and aneurysm of atherosclerotic etiology are risk factors for postoperative delirium (see Tables V and VI).

Major complications consisted of respiratory problems in 22 patients, bleeding in 18, hoarseness in 13, low cardiac output in 10, acute renal failure in 8, acute myocardial infarction in 7, mediastinitis in 4, gastrointestinal bleeding in 3, septicemia in 3, bowel necrosis in 2, and disseminated intravascular coagulation in 2.

Duration of bypass was 187 ± 78 minutes, ranging from 90 to 696 minutes. Duration of the bypass was

Table IX. Delirium

65.7 ± 21.6	
Delirium	37 (25.0%)
Nondissecting	22
Dissecting	15
Age (yr)	
Mean	65.7 ± 21.6
Range	38-78
Emergency surgery	7
Onset (days after operation)	
Mean	3.1 ± 3.5
Range	1-14
Duration (days)	
Mean	7.7 ± 9.5
Range	1-43
Surgery	
Hemiarch	8
Total arch	12
Distal arch	9
Distal arch-Desc Ao	6
Patch	2
Stroke	0

longer than 180 minutes in 53 patients. Cardiac arrest time was 79 ± 38 minutes, ranging from 22 to 220 minutes, and was more than 120 minutes in 25 patients. Duration of DHCA + RCP was 49 ± 17 minutes, ranging from 21 to 95 minutes, and was more than 60 minutes in 36 patients. Duration of DHCA + RCP did not correlate with incidences of hospital death ($p = 0.635$), stroke ($p = 0.971$), or delirium ($p = 0.972$, Fig. 1).

Patients awoke at a mean of 7.5 ± 8.2 hours (range 1 hour to 49 hours) after the operation. Five patients regained consciousness 24 hours after the operation. Endotracheal extubation was accomplished at 47.1 ± 107.8 hours (range 5 hours to 34 days) after the operation. A delay in extubation (>36 hours after operation) for various reasons occurred in 34 patients. The averaged duration of ICU stay was 6.9 ± 9.8 days, ranging from 1 day to 80 days, and 29 patients had to stay in the ICU 7 days after the operation. Duration of DHCA + RCP did not correlate with length of time before the patient awoke ($r = 0.03$, $p = 0.80$), extubation time ($r = 0.12$, $p = 0.92$), and ICU ($r = 0.11$, $p = 0.37$) or hospital stay ($r = 0.05$, $p = 0.69$). The differences in the incidence of mortality ($p = 0.39$), stroke ($p = 0.65$), and delirium ($p = 1.00$) were not statistically significant between the two groups of patients (Table XI).

Discussion

Over the past 15 years, elucidation of the cerebral circulation and development of new technology has

led to greater improvement in brain protection in aortic arch surgery. Svensson and associates⁶ used logistic regression analysis to evaluate 656 patients after aortic operations in which DHCA was used. They reported that there were 44 permanent or transient strokes (7%) and that the multivariate determined predictors were a history of cerebrovascular disease, previous aortic surgery distal to the left subclavian artery, and cardiopulmonary bypass time. The occurrence of stroke was observed to increase after 40 minutes of circulatory arrest, and the mortality rate increased markedly after 65 minutes of circulatory arrest. Ergin and associates³ showed that temporary neurologic dysfunction occurred in 19% of patients and permanent neurologic deficits were seen in 9% of patients who underwent arch operations with DHCA. Strokes occurred in 11% of their patients but were associated with permanent deficits in 6.9%.

Age and the duration of the arrest period were the only determinants for the occurrence of postoperative neurologic dysfunction. A strong correlation between duration of arrest and cerebral injury, especially the rapid rise in the incidence of temporary dysfunction beyond 50 minutes of arrest time, was demonstrated. Using DHCA + RCP, Coselli and associates⁸ demonstrated that early mortality was 6.1% and no transient or permanent stroke was detected in 111 patients. Duration of DHCA in their series was less than 40 minutes under condition of electroencephalogram silence. Lytle and associates⁹ reported that four hospital deaths, one stroke, and three transient neurologic deficits occurred in 34 patients who had aortic surgery in which DHCA + RCP was used. Periods of DHCA ranged from 4 to 110 minutes (mean 38 minutes) at a bladder temperature of 18° C. For seven patients the period of DHCA was longer than 60 minutes. Lin and associates¹⁰ demonstrated that one of 23 patients died after aortic surgery with DHCA + RCP and no patients had neurologic complications. The DHCA period was 75 ± 12 minutes, ranging from 58 to 104 minutes, at a rectal temperature of 23.3° ± 0.5° C. They also reported that brain cognitive function tests of patients who underwent aortic surgery with DHCA showed no difference compared with a control group 3 months after the operation. In a multicenter study of 228 patients who underwent aortic surgery with DHCA + RCP in 49 institutions in Japan, Usui and associates¹¹ demonstrated that duration of DHCA was the single predictive factor of a cerebral complication. The incidence of perma-

Table X. Comparison of two groups of patients with delirium and without delirium among survivors

	Delirium (n = 37)	No delirium (n = 96)	p Value
Age (yr)	65.7 ± 9.6	63.2 ± 12.2	0.22
Male	26 (70.2%)	74 (77.0%)	0.42
Emergency	7 (18.9%)	27 (28.1%)	0.28
ECC (min)	172.1 ± 51.5	191.3 ± 85.2	0.12
Cardiac arrest (min)	68.9 ± 27.3	82.7 ± 40.7	0.06
DHCA + RCP (min)	49.2 ± 17.1	49.6 ± 16.9	0.90
Stroke	0	2 (2.0%)	0.39
Wake-up (hr)	7.1 ± 5.3	7.6 ± 9.0	0.69
Extubation (hr)	42.3 ± 55.4	49.3 ± 117.9	0.64
ICU stay (days)	5.3 ± 4.0	7.2 ± 11.4	0.16
Discharge (days)	33.7 ± 12.9	45.8 ± 41.5	0.08

ECC, Extracorporeal circulation; DHCA, deep hypothermic circulatory arrest; RCP, Retrograde cerebral perfusion; ICU, intensive care unit.

nent neurologic dysfunction was less than 10% when the DHCA period was shorter than 60 minutes but increased abruptly when this period exceeded 100 minutes, and it remained 15% between 60 and 99 minutes. In the current study, duration of DHCA was 49 ± 17 minutes, ranging from 21 to 95 minutes, and for 36 patients the period of DHCA was longer than 60 minutes. The incidence of hospital death, postoperative stroke, and transient delirium was not correlated to the periods of DHCA. Among six patients with postoperative stroke, only one patient had a stroke as a result of prolonged ischemia and other patients had strokes of a clear embolic origin. We empirically consider that a DHCA + RCP period of up to 80 minutes under a nasopharyngeal temperature of 18° C is safe.

The RCP technique⁶ added a new idea that can augment cerebral protection during DHCA,¹² but the actual mechanism by which RCP provides cerebral protection is still obscure. Pagano and associates¹³ demonstrated that radioisotope tracers accumulated throughout the white and gray matter of the brain during RCP in human beings. In canine experiments, Watanabe and associates¹⁴ demonstrated that RCP through the sagittal sinus and superior vena cava protected the brain during 90 minutes of DHCA. It is clearly effective in maintaining cerebral hypothermia, providing continuous cooling of the whole head, preventing debris and air from reaching the terminal vessels of the brain,^{15, 16} and in washing out some metabolites, to delay the onset of acidosis in the ischemic brain.¹⁷

Multiple mechanisms of stroke are speculated as causes, including hypoperfusion or hyperperfusion during or after the operation and embolization from

Fig. 1. Incidence of hospital death, stroke, and delirium related to duration of DHCA + RCP. *Diagonal bar*, Delirium; *cross-hatched bar*, stroke including two deaths in columns 40-50 minutes and 50-60 minutes; *black bar*, hospital death; *gray bar*, others; *RCP*, retrograde cerebral perfusion.

Table XI. Comparison of two groups of patients with duration of DHCA + RCP more than 60 minutes and less than 60 minute

	DHCA + RCP		p Value
	Over 60 min	Under 60 min	
n	36	112	
Age (yr)	65.4 ± 11.4	63.9 ± 11.5	0.51
RCP (min)	72.3 ± 9.8	41.6 ± 10.0	p < 0.01
Hospital death	5 (13.8%)	10 (8.9%)	0.39
Stroke	1 (2.9%)	5 (4.4%)	0.65
Delirium	9 (25.0%)	28 (25.0%)	1.00
Wake-up (hr)	7.1 ± 6.3	7.7 ± 9.0	0.86
Extubation (hr)	77.0 ± 166.3	38.5 ± 77.6	0.19
ICU stay (days)	13.4 ± 27.4	7.3 ± 18.3	0.24

DHCA, Deep hypothermic circulatory arrest; RCP, retrograde cerebral perfusion; ICU, intensive care unit.

a variety of sources, including the extracorporeal circuit, left side of the heart, aorta itself, iliac artery, or carotid bifurcation. Despite the recent advent of diagnostic modalities, it is often difficult to determine which of these mechanisms are implicated in a particular patient.¹⁸ However, a recent report indi-

cated that the majority of permanent neurologic injuries were due to strokes resulting from embolic phenomena and were not directly related to the method of cerebral protection used.¹⁹

Postoperative transient delirium has been defined as a transient minor neurologic deficit such as disorientation and character change with no neurologic sequelae. However, delirium can result in increased morbidity, delayed functional recovery, and prolonged hospital stay. In a review, Dubin, Field, and Gastfriend²⁰ concluded that cardiac status, the severity of physical illness, the complexity of the surgical procedure, preoperative anxiety, denial depression, and preoperative organic brain disease were the determining factors in postcardiotomy delirium. Vasquez and Chitwood²¹ demonstrated that pathologic brain injuries that were apparently anatomic correlates of neurologic deficits in delirium included anoxic lesions of the hippocampus and infarcted foci. They also showed that contributing physiologic factors included long periods of extracorporeal circulation, arterial hypotension during the operation, emboli, low cardiac output, age, and

severity of cardiac dysfunction. In the current study, no significant correlation was demonstrated between incidence of the delirium and type of aortic lesions, duration of cardiopulmonary bypass or DHCA, age, and sex. Usually delirium occurs after patients have left the ICU and continues for a week or so. Prognosis is always benign.

Our main principle for avoiding postoperative stroke focused on not clamping the arch and performing anastomoses in an open manner. Normal aorta for cannulation is carefully evaluated by direct scan echo in every patient. In patients with severe atheromatous disease of the descending aorta, abdominal aortic aneurysm, and occlusive disease in the iliac arteries, RCP from the femoral cannula is avoided. If femoral cannulation is unavoidable, antegrade cardiac output is maintained at least over the first 10 minutes of bypass to prevent debris from the descending or abdominal aorta from reaching the brain. An additional arterial return line is always inserted for pump rewarming by antegrade flow through a side branch of the arch graft. Cerebral embolization cannot be predicted or prevented by electroencephalography, near-infrared oximetry, or monitoring of oxygen saturation of the jugular vein. The brain is cooled topically with ice packs. If intraoperative echography indicates that a nonaneurysmal portion of the arch is coated with thick atheromatous plaque, the whole arch should be replaced without hesitation. Open aortic anastomosis after complete transection of the aorta is the preferred method for secure anastomosis. A quadritruncated Dacron graft is usually chosen for total arch replacement with reconstruction of the arch vessels. Clearing debris from the suture line by flushing with saline solution and cautious handling of the air and debris are extremely important to prevent brain embolism.

Conclusion

Hospital mortality was 10.1% (15 patients), and six patients (4.0%) had a new stroke among 148 patients with aortic arch aneurysm. Stepwise logistic regression analysis of perioperative variables demonstrated that the significant risk factors for mortality were ruptured aneurysm, preoperative COPD, arterial cannulation in the ascending aorta, and perioperative stroke. Risk factors for stroke were ruptured aneurysm and replacement of the distal arch. Risk factors for delirium were age older than 70 years and atherosclerotic etiology. More than 60 minutes' duration of DHCA + RCP was not a risk

factor for early mortality, stroke, and delirium in patients who underwent operations for aneurysms of the aortic arch.

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Discussion

Dr. M. Arisan Ergin (*New York, N.Y.*). I appreciate the opportunity to discuss this paper. Unfortunately, Dr. Okita and I disagree. We strongly believe that the clinical syndrome that we have called "temporary dysfunction" and Dr. Okita calls "delirium" is a manifestation of ischemic cellular injury. It is most likely related to inadequate or suboptimal brain preservation. I believe its incidence should be reported in all series such as this one so that intelligent comparisons can be made in the future.

The prevalence of this severe and prolonged dysfunctional state in this series of patients leaves me wondering how much of this is related to relatively prolonged periods of DHCA at 18° C. RCP apparently did not prevent it. One could argue that it may in fact have compounded the injury by increasing cerebral edema. We know that *effective* prolonged RCP invariably is associated with cerebral edema. This should raise a caution flag for all who believe that RCP gives one the luxury of time that one would not have with DHCA alone.

We should concentrate on limiting the arrest time rather than relying on prolonged RCP to extend it, because of the increasing potential for harm with RCP. Limiting arrest times to less than 50 minutes is a readily achievable goal in virtually every case if one plans the operation well.

Prevention of embolic strokes is a daunting problem, and RCP may prove to be more useful in solving that. Dr. Okita reported a low 4% incidence of stroke. In our experience, older age, "dirty" aorta, and descending aortic involvement are the major determinants of postoperative stroke. When we use RCP selectively in this high-risk group for prevention of stroke, RCP emerges as a marker for neurologic injury.

Dr. Okita, I notice that you also reported a substantially higher, 2% versus 7%, stroke rate in patients who were operated on through a left thoracotomy. Your difference would also reach statistical significance if you merely double your sample size.

I would argue that the RCP in this high-risk group has not prevented the occurrence of these strokes. Therefore, I would say that the RCP falls short in just the situation in which it may be most useful and necessary. In my opinion, RCP remains a promise yet unfulfilled.

I have three questions. First, when operating through a left thoracotomy, do you use any additional measures to improve the delivery of RCP?

Second, have you taken active measures to prevent, detect, and treat cerebral edema?

Third, how would you reconcile your current results with the multicenter study of RCP in Japan that Dr. Usui presented last year and in which Dr. Takamoto was a participant? They showed a progressively prohibitive increase in risk between 60 and 99 minutes, whereas you show that there is really no risk in extending the RCP beyond 60 minutes.

Dr. Akira T. Kawaguchi (*Isehara, Japan*). Since you have been assessing injury to the central nervous system by extubation time, occurrence of delirium, and incidence of stroke, I would like to know whether you have any evidence for the preservation of functional and organic and/or morphologic integrity of the central nervous system, in addition to those clinical parameters.

We found that rats undergoing 80 minutes of total circulatory arrest have learning disability (functional damage) and pyramidal cell loss in the hippocampus and cerebral cortex (organic injury) despite prompt recovery of somatic growth, exercise capacity, and normal behavior. Therefore, one cannot exclude possible functional or organic injuries to the central nervous system by assessing such clinical parameters alone.

Dr. Okita. Thank you very much for your nice comments and your questions, Dr. Ergin. When we use a left thoracotomy, we use the near-infrared spectroscopy oxygen monitoring system during the operation. The incidence of stroke or delirium in patients who had a left thoracotomy was not statistically higher than that in patients with median sternotomy. However, this technique inherently includes the risk of allowing debris to enter the arch and ascending aorta. We are very cautious about that.

We use no special techniques to prevent cerebral edema during RCP. We do try to keep the DHCA time as short as possible.

Dr. Usui's article is a multicenter study including more than 50 institutions in Japan. His conclusion was that more than 60 minutes of DHCA is a significant risk factor for brain dysfunction. I do not know why our single-institution data differed from Dr. Usui's results.

Dr. Kawaguchi, thank you for your question. We routinely do preoperative and postoperative computed tomography and electroencephalography to detect lesions for imaging, but we did not find any organic change in the brain. I think something happened in the patient who had postoperative delirium, even though he was well after 1 week or so. A different modality is needed to investigate that.