A study of brain protection during total arch replacement comparing antegrade cerebral perfusion versus hypothermic circulatory arrest, with or without retrograde cerebral perfusion: Analysis based on the Japan Adult Cardiovascular Surgery Database

Yutaka Okita, MD,[a] Hiroaki Miyata, PhD,[b] Noboru Motomura, MD,[c] and Shinichi Takamoto, MD,[d] The Japan Cardiovascular Surgery Database Organization

Objectives: Antegrade cerebral perfusion and hypothermic circulatory arrest, with or without retrograde cerebral perfusion, are 2 major types of brain protection that are used during aortic arch surgery. We conducted a comparative study of these methods in patients undergoing total arch replacement to evaluate the clinical outcomes in Japan, based on the Japan Adult Cardiovascular Surgery Database.

Methods: A total of 16,218 patients underwent total arch replacement between 2009 and 2012. Patients with acute aortic dissection or ruptured aneurysm, or who underwent emergency surgery were excluded, leaving 8169 patients for analysis. For the brain protection method, 7038 patients had antegrade cerebral perfusion and 1141 patients had hypothermic circulatory arrest/retrograde cerebral perfusion. A nonmatched comparison was made between the 2 groups, and propensity score analysis was performed among 1141 patients.

Results: The matched paired analysis showed that the minimum rectal temperature was lower in the hypothermic circulatory arrest/retrograde cerebral perfusion group (21.2°C ± 3.7°C vs 24.2°C ± 3.2°C) and that the duration of cardiopulmonary bypass and cardiac ischemia was longer in the antegrade cerebral perfusion group. There were no significant differences between the antegrade cerebral perfusion and hypothermic circulatory arrest/retrograde cerebral perfusion groups with regard to 30-day mortality (3.2% vs 4.0%), hospital mortality (6.0% vs 7.1%), incidence of stroke (6.7% vs 8.6%), or transient neurologic disorder (4.1% vs 4.4%). There was no difference in a composite outcome of hospital death, bleeding, prolonged ventilation, need for dialysis, stroke, and infection (antegrade cerebral perfusion 28.4% vs hypothermic circulatory arrest 30.1%). However, hypothermic circulatory arrest/retrograde cerebral perfusion resulted in a significantly higher rate of prolonged stay in the intensive care unit (>8 days: 24.2% vs 15.6%).

Conclusions: Hypothermic circulatory arrest/retrograde cerebral perfusion and antegrade cerebral perfusion provide comparable clinical outcomes with regard to mortality and stroke rates, but hypothermic circulatory arrest/retrograde cerebral perfusion resulted in a higher incidence of prolonged intensive care unit stay. Antegrade cerebral perfusion might be preferred as the brain protection method for complicated aortic arch procedures. (J Thorac Cardiovasc Surg 2015;149:S65-73)

See related commentary on pages S74-5.

The present study compared the results of 2 different methods of brain protection used during total arch replacement: hypothermic circulatory arrest (HCA) with retrograde cerebral perfusion (RCP) and selective antegrade cerebral perfusion (ACP). ACP maintains cerebral circulation using cold blood perfusion of 2 or 3 arch branches via separate cannulas, under moderate or hypothermia.[1,2] RCP is an additional method of brain protection used during HCA, whereby the superior vena cava is perfused in a retrograde direction.[3] Both ACP and HCA/RCP have advantages and drawbacks. Although numerous retrospective studies have been performed, there have been few prospective randomized clinical trials that have compared ACP and HCA/RCP. Previous studies indicated no difference between the methods or a slight superiority of ACP. However, the majority of studies conflate hemiarch replacement and total arch replacement, which have different operative risks. This study included only patients who had total arch replacement with reconstruction of the 3 brachiocephalic vessels. We used data from the Japan Adult Cardiovascular Surgery Database (JCVSD), which contains clinical data

From the Department of Cardiovascular Surgery,[a] Kobe University, Kobe, Japan; Health Care Quality Assessment,[b] University of Tokyo, Tokyo, Japan; Department of Cardiovascular Surgery,[c] Toho University Medical Center Sakura Hospital, Chiba, Japan; and Mitsui Memorial Hospital,[d] Tokyo, Japan.

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Address for reprints: Yutaka Okita, MD, Division of Cardiovascular Surgery, Department of Surgery, Kobe University Graduate School of Medicine, 7-5-2 Kusunoki-cho, Chuo-ku, Kobe, Japan 650-0017 (E-mail: yokita@med.kobe-u.ac.jp).

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Abbreviations and Acronyms

ACP = antegrade cerebral perfusion
GI = gastrointestinal
HCA = hypothermic circulatory arrest
ICU = intensive care unit
JCVSD = Japan Adult Cardiovascular Surgery Database
RCP = retrograde cerebral perfusion
TND = transient neurologic dysfunction

from almost all Japanese institutions performing cardiovascular surgery,[4] and performed propensity-matched analysis to best compare groups with comparable risks.

MATERIALS AND METHODS

Study Population

The JCVSD, initiated in 2000, with participation obligatory for surgeons to be certified by the Japanese Board of Cardiovascular Surgery since 2011, captures clinical information from nearly all hospitals of Japanese units performing cardiovascular surgery. The data-collection form has 255 variables[4] that are nearly identical to those in the Society for Thoracic Surgeons National Database, and through September 2013, 260,000 individual data points from 533 institutions were collected.[4]

By using the database, we collected 39,572 thoracic aortic surgery procedures performed between January 1, 2009, and December 31, 2012. Patients with a ruptured aneurysm (n = 818), acute aortic dissection (3861), surgical status of urgent/emergency/salvage (4598), and range of replacement, including descending, thoracoabdominal, or abdominal aorta, were excluded from this study. We also excluded procedures performed at cardiac centers at which the average annual thoracic aortic surgery volume was less than 5 procedures. Cases of chronic dissection were included if treated by total arch replacement. Thus, the subjects analyzed in the present study were confined to those with aneurysms of the ascending aorta and aortic arch who underwent total arch replacement, electively, via a median sternotomy at large-volume centers. Any JCVSD records that had been obtained without the patients' informed consent were excluded from this analysis. Records with missing data also were excluded. Of 16,218 total arch replacements, 8169 were performed using ACP (7038) or HCA/RCP (1141) (Figure 1). This study was approved by the JCVSD board.

Surgical Procedures

All the details of a surgical procedure cannot be represented in a database, but the data show that approximately all patients had a 4-branch arch graft with the arch vessels reconstructed individually. ACP was conducted under some degree of hypothermia, and most patients had bilateral carotid perfusion—the left carotid artery by direct cannulation and the right carotid artery by direct cannulation or by perfusing the right axillary artery (Figure 2).[5] In the 1990s, the distal anastomosis to the descending aorta was generally performed first, followed by anastomosis of the neck vessels and initiation of ACP (Figure 3, *A-C*).[3] More recently, an "arch first" technique[6] has emerged as the procedure of choice in the majority of patients to reduce brain ischemia time (Figure 3, *C-E*). Because this approach entails an increased duration of lower body circulatory arrest, some surgeons have used an occlusion balloon in the descending aorta to perfuse the viscera and spinal cord via the femoral artery.

End Points

The primary outcomes measured from the JCVSD were 30-day mortality and operative mortality. Secondary outcomes were major morbidities: new stroke persisting more than 72 hours; transient neurologic dysfunction (TND), any neurologic dysfunction that recovered completely within 72 hours, including transient ischemic attack, reversible ischemic neurologic deficit, or delirium, regardless of the radiologic findings; reoperation for any reason; need for mechanical ventilation for more than 24 hours after surgery; pneumonia; gastrointestinal (GI) complication, such as bleeding or hepatic failure; renal failure requiring dialysis; deep sternal wound infection; and prolonged postoperative length of hospital stay. Also, a composite outcome, consisting of death, stroke, bleeding requiring reoperation, prolonged ventilation, dialysis, and infection with deep sternal infection, leg wound infection, pneumonia, and septicemia, was evaluated.[4]

Statistical Analysis

We compared the baseline demographics for patients who underwent HCA/RCP surgery with those who underwent ACP surgery, using the chi-square test for categoric variables and the *t* test for continuous variables. For non-normal distribution variables, Kruskal–Wallis 1-way analysis of variance by ranks was used. The trends in HCA/RCP surgery over time were determined using logistic regression analysis, in which the independent variable was the type of brain protection and the dependent variable was the month of surgery. The unadjusted effects of HCA/RCP at 30 days and the operative mortality and 5 major postoperative morbidities were assessed using logistic regression analysis. For risk-adjusted comparisons, a multivariable logistic regression model was used to determine the effect of HCA/RCP. The preoperative risk factors are described in Table 1. The characteristics of 7038 patients who underwent ACP and 1141 patients who underwent HCA/RCP are shown in Table 2. The ACP group showed a significantly higher age, smoking rate, renal failure rate, cerebrovascular accident rate, and hyperlipidemia incidence, but a lower effective glomerular filtration rate compared with the HCA/RCP group. Also, the ACP group had a higher incidence of extracardiac vascular disease, percutaneous coronary intervention, and 2- or 3-vessel coronary artery disease. The HCA/RCP group showed a higher rate of chronic aortic dissection, prior aortic root surgery or valve surgery, left ventricular dysfunction, and aortic valve stenosis. The method of adjustment involved matching patients with a similar probability of undergoing HCA/RCP surgery. We used propensity score matching to adjust for differences and performed a 1-to-1 matched analysis without replacement on the basis of the estimated propensity score, calculated from 28 variables mainly collected from the preoperative factors of each patient (Table 3). The log odds of the probability that a patient received a RCP (the "logit") was modeled as a function of the confounders that we identified and included in our data set. By using the estimated logits, we first randomly selected a patient in the group undergoing RCP and then matched that patient with a patient in the group receiving ACP with the closest estimated logit value. Patients in the group undergoing RCP who had an estimated logit within 0.6 standard deviation of the selected patients in the group receiving ACP were eligible for matching. We selected 0.6 standard deviation because this value has been shown to eliminate approximately 90% of the bias in observed confounders (C-statistic of the propensity model is 0.671 ± 0.009). Differences in clinical variables were tested using the chi-square test for categoric variables and the *t* test for continuous variables. A conditional logistic regression analysis was used to determine the overall effect of HCA/RCP surgery in these matched-pairs groups.

RESULTS

Nonmatched Analysis

In regard to surgery, cardiac ischemia time was longer in the ACP group and the minimum temperature was lower in the HCA/RCP group (Table 3). No significant difference was found between the ACP and HCA/RCP groups in 30-day (3.2% vs 5.9%) and operative mortality (4.1% vs 7.2%)

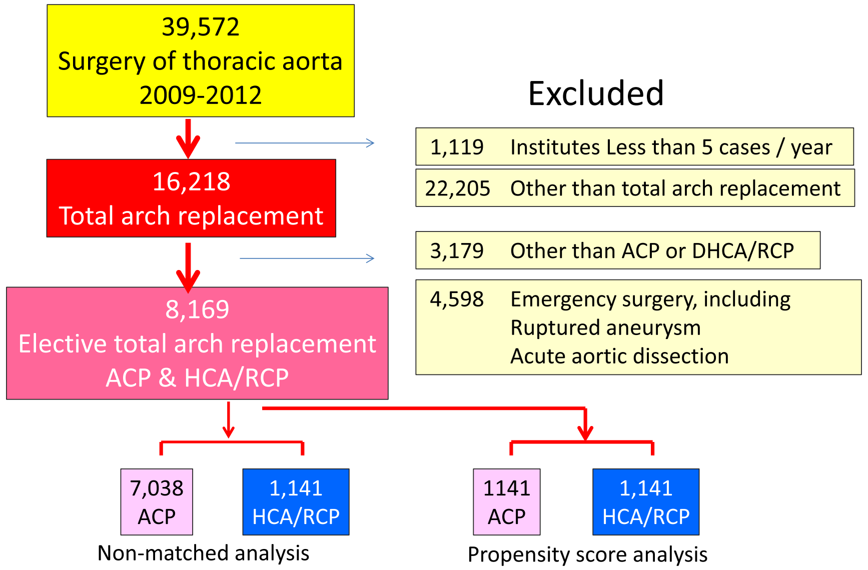

FIGURE 1. Patient selection. *ACP*, Antegrade cerebral perfusion; *HCA*, hypothermic circulatory arrest; *RCP*, retrograde cerebral perfusion; *DHCA*, deep hypothermic circulatory arrest.

rates. Also, there was no difference between groups in the incidence of stroke, TND, bleeding, pneumonia, dialysis, infection, GI complications, and composite outcome. However, the incidence of prolonged ventilation over 24 hours and prolonged intensive care unit (ICU) stay more than 8 days was higher in the HCA/RCP group (Table 2). The incidence of spinal complication, including complete paraplegia and transient paraparesis, was similar in both groups.

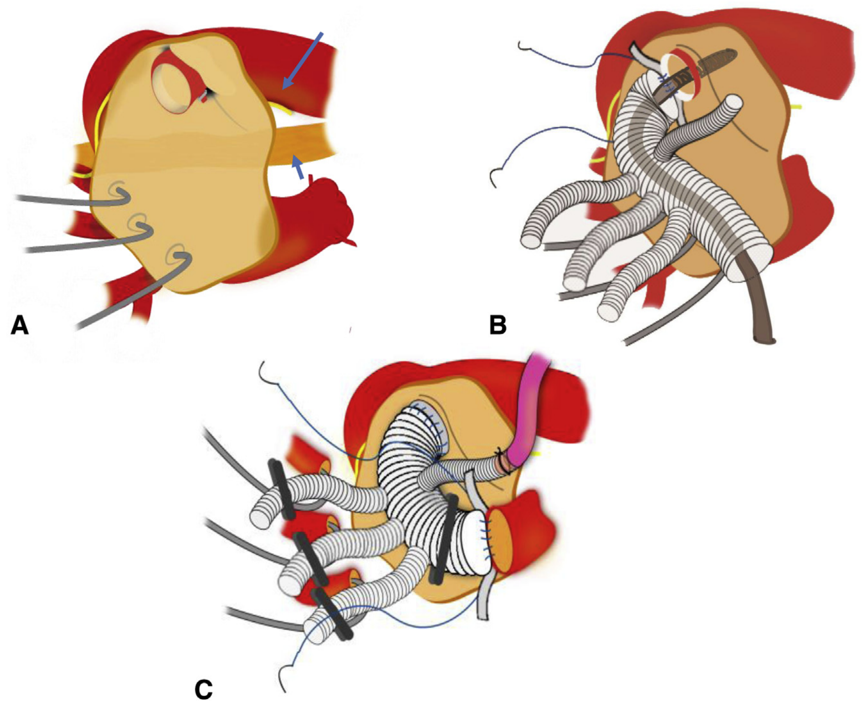

FIGURE 2. ACP. A, Direct cannulation of the neck vessels, without tourniquet, using serrated balloon tipped cannulae. To prevent left recurrent nerve injury, direct enucleation of the proximal end of the descending aorta was performed and dissection of the descending aorta with dividing of the upper intercostal arteries was performed. B, Distal anastomosis using a 4-0 monofilament SH-1 needle with felt strip reinforcement, starting at 9 o'clock and proceeding counterclockwise. A flexible sucker was positioned inside the graft. C, Initiating antegrade lower body perfusion and rewarming. The proximal anastomosis is constructed with a 4-0 monofilament RB-1 needle and felt strip, and the neck vessel anastomoses are performed using 5-0 monofilament sutures.

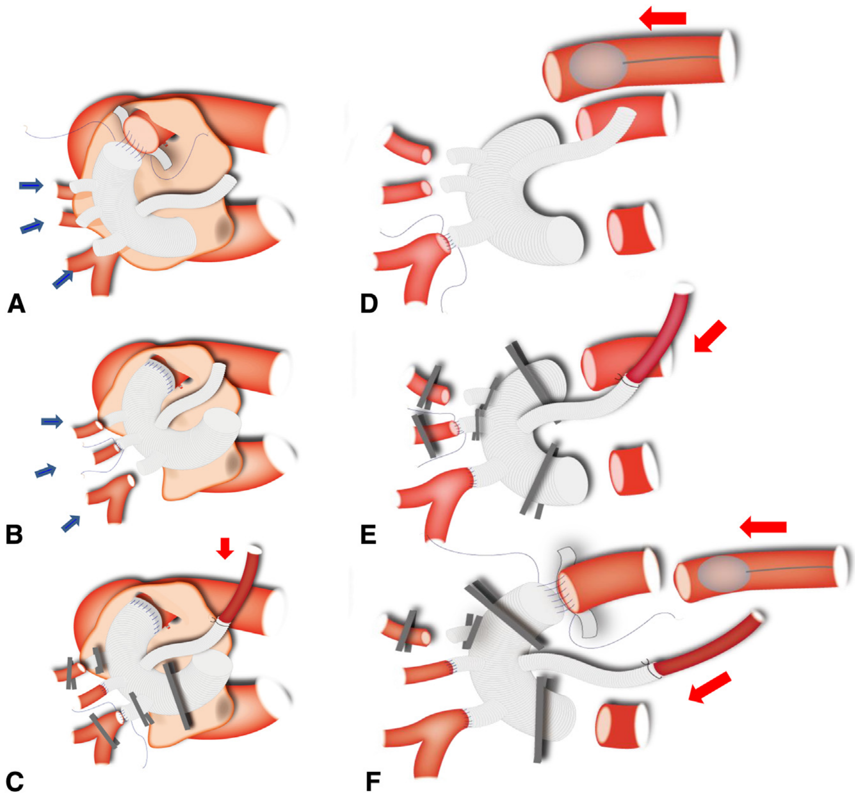

FIGURE 3. A-C, HCA with RCP (old technique). A, Distal anastomosis first. B, Anastomosis to the left common carotid artery. C, Start to reperfuse the brain and lower body. D-F, HCA with RCP (4-branch graft, arch first technique). D, If possible, balloon occlusion of the descending aorta and perfusion from the femoral artery were performed. First, anastomosis to the brachiocephalic artery was performed. E, ACP was initiated from the side branch of the graft. F, Then distal aortic anastomosis, left carotid artery, left subclavian artery, and proximal anastomosis were performed.

Propensity-Matched Analysis

We evaluated 1141 patients receiving ACP and 1141 patients receiving HCA/RCP using case matching with the propensity score (Table 4). After matching, HCA/RCP was more prevalent in the year of 2009. Also, there was a higher incidence of smoking and hyperlipidemia in the ACP group and a higher incidence of aortic valve regurgitation more than grade 2 in the HCA/RCP group. With regard to surgical data, the minimum rectal temperature was lower in the HCA/RCP group, and the duration of cardiopulmonary bypass and cardiac ischemia was longer with ACP.

The 30-day and operative mortality rates were 3.2% and 6.0%, respectively, for patients in the ACP group and 4.0% and 7.1%, respectively, for patients in the HCA/RCP group; no significant differences were observed between the groups. The stroke rate was 6.7% in the ACP group and 8.6% in the HCA/RCP group. There was no significant difference in the incidence of death, stroke, TND, prolonged ventilation, infection, reoperation, spinal complication, GI complications, and composite outcomes when comparing the 2 groups. However, the duration of endotracheal intubation was longer and the incidence of postoperative ICU stay more than 8 days was greater in the HCA/RCP group.

DISCUSSION

The ideal protection method for the brain during surgery for the aortic arch was pursued by DeBakey and colleagues[7] before the era of cardiopulmonary bypass. Some investigators used extra-anatomic bypass as an adjunct for brain protection. Antegrade, pulsatile cerebral perfusion, under normothermia, theoretically provides the best brain protection; however, ACP was accompanied with unsatisfactory clinical outcomes in the 1960s and 1970s, and, with the report of Griepp and colleagues[8] in 1975, HCA came into widespread use for cerebral protection.

HCA requires no additional cannulas or clamps on the aortic arch branches, which might otherwise cause arterial damage or embolic stroke, and no additional extracorporeal circuits, such as those used in ACP. However, HCA has the drawback of a limited safe duration. Svensson and colleagues[9] reported 44 permanent or transient strokes (7%) among 656 patients receiving HCA and found that multivariate predictors were a history of cerebrovascular disease, previous aortic surgery, and cardiopulmonary bypass time; stroke increased after 40 minutes of HCA, and the mortality rate increased markedly after 65 minutes of HCA. Borst and colleagues[10] reported an early mortality

TABLE 1. Preoperative variables in nonmatched analysis

	ACP	HCA/RCP	*P* value
Age (y)	70.5 ± 10.1	68.3 ± 11.6	.000
Sex (male %)	72.5	72	.707
Body surface area (m^2)	1.64 ± 0.18	1.65 ± 0.19	.279
Body mass index (kg/m^2)	23.4 ± 3.5	23.3 ± 3.7	.090
Body mass index >30 kg/m^2 (%)	4.7	4.3	.875
Smoking (%)	61.2	52.8	.000
Hyperlipidemia (%)	39.1	34.9	.006
Hypertension (%)	85.8	84.1	.134
Diabetes (%)	14.4	13	.229
Chronic kidney disease (%)	7.5	6.9	.854
eGFR (mL/min/1.73 m^2)	49.1 ± 20.7	50.7 ± 27.2	.013
Serum creatinine mg/dL	1.13 ± 1.09	1.10 ± 1.15	.511
Liver dysfunction (%)	1.1	0.9	.543
Cerebrovascular accident (%)	14.7	11.8	.011
Carotid lesions (%)	5.2	4.3	.197
COPD moderate to severe (%)	5.5	5.4	.836
Extracardiac vascular disease (%)	82	76.7	.000
CCS II, III, IV (%)	4.8	5.1	.767
Left main trunk disease (%)	2.1	1.9	.654
2- to 3-vessel disease (%)	11.9	9.5	.019
Percutaneous coronary intervention (%)	8.3	5.8	.004
Old myocardial infarction (%)	5.2	4.3	.166
CABG (%)	17.4	15.4	.088
NYHA II, III, IV (%)	2.5	3.1	.180
Congestive heart failure (%)	2.3	3.1	.084
LV dysfunction moderate to severe (%)	21.6	25.4	.004
Aortic dissection (%)	22.7	24.2	.401
Aortic stenosis (%)	6	5.6	.199
Aortic regurgitation >2/4	8.2	7.6	.135
Arrhythmia (%)	8.1	6.4	.058
Reoperation (%)	11	14.2	.002

Numeral with ±; mean ± standard deviation. *ACP*, Antegrade cerebral perfusion; *CABG*, coronary artery bypass grafting; *CCS*, Canadian Cardiovascular Society; *COPD*, chronic obstructive lung disease; *eGFR*, effective glomerular filtration ratio; *HCA*, hypothermic circulatory arrest; *LV*, left ventricle; *NYHA*, New York Heart Association; *RCP*, retrograde cerebral perfusion.

of 10% and 3 ‘‘cerebral deaths’’ among 58 cases of atherosclerotic aneurysm treated using HCA. Ergin and colleagues[11] reported that the mortality rate in patients without any neurologic injury was 6.7%, whereas in patients with permanent neurologic deficit the hospital mortality rate was 46%.

Ueda and colleagues[12] first reported that RCP is a useful adjunct that can augment cerebral protection for aortic arch surgery for up to 80 minutes of HCA. In our previous experience[13] with 148 consecutive patients who received RCP and HCA, 15 (10%) early deaths and 6 (4.0%) new strokes occurred. RCP is clearly effective in maintaining cerebral hypothermia, providing continuous cooling of the whole head, in preventing debris and air from reaching the terminal vessels of the brain, and in washing out some metabolites, thus delaying the onset of acidosis in the ischemic brain. Coselli and LeMaire[14] reported that patients who had RCP during HCA had lower mortality (7.9% vs 14.8%) and stroke rates (2.4% vs 6.5%) than those who did not undergo HCA with RCP among 479 patients. Safi and colleagues[15] demonstrated that RCP had a protective effect against stroke (3% vs 9%) compared with no RCP, and the protective effect was most significant in patients aged more than 70 years; zero of 36 elderly patients who received RCP had a stroke compared with 3 of 13 patients (23%) who did not receive RCP ($P < .003$). Bavaria and Pochettino[16] reported that RCP might extend the safe HCA period and improve morbidity and mortality, especially for HCA exceeding 60 minutes.

However, a higher prevalence of TND indicates the need for caution against overly liberal use of RCP. We[17] demonstrated a correlation between the severity of TND and the duration of HCA by comparative study of ACP and RCP. Hagl and colleagues[18] reported that the incidence of TND increased if the duration of RCP exceeded 25 minutes and that longer ACP increased TND incidence.

After the report by Spielvogel and colleagues,[19] an ‘‘arch first’’ approach using a branched arch graft became a

TABLE 2. Surgical data and the results in nonmatched analysis

	ACP	HCA/RCP	*P* value
Operation duration (min)	471 ± 160	466 ± 150	.178
Cardiopulmonary bypass duration (min)	240 ± 84	237 ± 81	.460
Cardiac ischemia (min)	140 ± 58	138 ± 63	.006
CABG (%)	16.5	15.5	.530
Valve surgery (%)	20.7	21.3	.719
Lowest rectal temperature (°C)	24.2 ± 3.2	21.2 ± 3.7	<.001
30-d death (%)	3.2	4.1	.113
Hospital death (%)	5.9	7.2	.086
Stroke (%)	7	8.5	.071
TND (%)	3.8	4.4	.297
Bleeding (%)	5.7	4.3	.071
Prolonged ventilation >24 h (%)	19.9	22.7	.029
Pneumonia (%)	7.6	7.2	.684
Perioperative myocardial infarction (%)	0.8	0.6	.445
Dialysis (%)	3.9	3.8	.968
Any infection (%)	2.3	1.9	.410
Spinal (%)	3.0	2.9	.927
GI complication (%)	3.2	3.5	.599
Prolonged ICU stay >8 d (%)	17	24.3	<.001
Composite outcome (%)	27.9	30	.152

Numeral with ±; mean ± standard deviation. *ACP*, Antegrade cerebral perfusion; *CABG*, coronary artery bypass grafting; *GI*, gastrointestinal; *HCA*, hypothermic circulatory arrest; *ICU*, intensive care unit; *RCP*, retrograde cerebral perfusion; *TND*, transient neurologic dysfunction.

standard procedure, permitting a marked reduction in cerebral ischemic time compared with the "distal-first anastomosis" technique. However, we continue to use RCP during HCA with this technique because the duration of lower body ischemia is longer with this method.

In 1986, Frist and colleagues[20] revived the concept of ACP and reported 90% survival after arch replacement using unilateral ACP with reduced cerebral blood flow, under moderate hypothermia. In 1989, Bachet and colleagues[21] described "cerebroplegia," a method of cold ACP; their operative mortality was 13%, with 3 serious neurologic complications found among 54 patients. Kazui and colleagues[22] used ACP and a 4-branched graft technique and reported excellent surgical results, with no neurologic sequelae and 3 early deaths in 32 patients with arch aneurysm. A Japanese multicenter, combined study[23] using ACP for atherosclerotic aortic arch aneurysm revealed that age, aneurysmal rupture, and renal dysfunction were significant predictors of mortality and disability.

The most important advantage of ACP is that it provides time for a deliberate repair of complicated arch aneurysms. However, criticisms of ACP include the longer time required for arch repair, cannulation-generated embolism, and uneven distribution of intracranial blood flow. General consensus has been achieved that ACP can provide better and more uniform brain protection than HCA for a long duration of circulatory arrest. Di Eusanio and colleagues[24] demonstrated that ACP for more than 90 minutes is not associated with an increased risk of mortality or a negative neurologic outcome.

Recent studies of brain circulation have prompted physiologic strategies for brain protection. ACP via the brachiocephalic and left common carotid artery, sometimes including the left subclavian artery, under deep, moderate, or even mild hypothermia has achieved safe protection during prolonged cardiopulmonary bypass, although the risk of distal embolization is higher.[25,26] Our recent reports[27-30] demonstrated that risk factors for early death after elective total arch replacement in nondissection aneurysm included prolonged cardiopulmonary bypass time and that risk factors for late death were age 80 years or more, chronic kidney disease (effective glomerular filtration rate <30 mL/min/1.73 m^2), and operation time. Risk factors for postoperative stroke were severity of the leukoaraiosis of the brain white matter and presence of a "shaggy" aorta, whereas risk factors for TND were "shaggy" aorta, leukoaraiosis, carotid artery lesion, and duration of cardiopulmonary bypass. Therefore, postoperative stroke is primarily patient and pathology dependent, and is only marginally affected by cerebral protection technique.

There are a few randomized studies and many retrospective studies comparing HCA and ACP. We[17] evaluated 60 consecutive total arch replacements allocated randomly to HCA or ACP and concluded that both HCA and ACP resulted in acceptable levels of mortality and morbidity, but the prevalence of TND was significantly higher with HCA. Hagl and colleagues[18] retrospectively analyzed the outcomes among 717 survivors of ascending and aortic arch surgery and determined that the method of brain protection did not influence the

TABLE 3. Preoperative variables in matched analysis

	ACP	HCA/RCP	*P* value
Year of surgery			.121
2009 (%)	18.1	22	
2010 (%)	20.9	16.7	
2011 (%)	28.5	30.4	
2012 (%)	32.4	30.9	
Age (y)	68.57 ± 11.29	68.35 ± 11.61	.646
<60	16.7	17.9	.473
60-65	13	14	
65-70	19.2	17.6	
70-75	22.9	23.2	
75-80	19.5	17.2	
80 or >80	8.8	10.1	
Sex (male, %)	70.2	71.8	.406
Body surface area ($m^{2)}$	1.64 ± 0.19	1.65 ± 0.189	.465
Body mass index (kg/m^2)	23.4 ± 3.56	23.3 ± 3.70	.408
Body mass index >30 kg/m^2 (%)	4.4	4.1	.756
Smoking (%)	59.6	52.9	.001
Hyperlipidemia (%)	40.1	35.1	.012
Hypertension (%)	85.2	84	.451
Diabetes (%)	13.8	13.1	.668
Chronic kidney disease (%)	7.8	7.9	.938
eGFR (mL/min/1.73 m^2)	51.6 ± 25.1	50.7 ± 27.2	.435
Serum creatinine (mg/dL)	1.10 ± 1.10	1.12 ± 1.18	.635
Liver dysfunction (%)	1.5	0.9	.175
Cerebrovascular accident (%)	13.1	11.8	.375
Carotid lesion (%)	4.6	4.3	.685
COPD moderate to severe (%)	6.2	5.4	.421
Extracardiac vascular disease (%)	18.7	15.8	.067
CCS II, III, IV (%)	5.1	5.2	.924
Left main trunk disease (%)	2.5	2.0	.784
2- to 3-vessel disease (%)	10.4	9.5	.442
Percutaneous coronary intervention (%)	7.4	5.7	.107
Old myocardial infarction (%)	3.7	4.2	.519
NYHA II, III, IV (%)	14.5	13.2	.364
Congestive heart failure (%)	2.6	3.1	.529
LV dysfunction moderate, severe (%)	24.6	25.2	.735
Arrhythmia (%)	5.4	5.1	.708
Aortic dissection (%)	23.4	25.3	.518
Aortic stenosis (%)	8.5	7.4	.314
Aortic regurgitation >2/4 (%)	25.5	30.4	.009
Redo operation (%)	14.9	14.2	.635

Numeral with ±; mean ± standard deviation. *ACP*, Antegrade cerebral perfusion; *CCS*, Canadian Cardiovascular Society; *COPD*, chronic obstructive lung disease; *eGFR*, effective glomerular filtration ratio; *HCA*, hypothermic circulatory arrest; *LV*, left ventricle; *NYHA*, New York Heart Association; *RCP*, retrograde cerebral perfusion.

incidence of stroke; however, ACP did result in a significant reduction in the incidence of TND. Svensson and colleagues[34] analyzed postoperative neurocognitive function and serum s-100 proteins in a prospective randomized manner and found essentially no differences among the ACP, HCA, and HCA/RCP groups.

Usui and colleagues[35] used the Japanese database to conduct a propensity matched analysis on data from 2792 patients who underwent aortic arch surgery, comparing ACP and RCP, and concluded that there was no difference regarding postoperative survival or neurologic outcome, except for a higher incidence of temporary dialysis and TND in the RCP group; however, they mixed up patients who underwent hemiarch repair and those who had undergone total arch replacement. Barnard and colleagues[36] assessed 408 studies of HCA and ACP and reported that ACP was superior as an adjunct to HCA when compared with HCA or HCA alone, but their clinical evidence was weak. A recent meta-analysis of 5060 patients in 15 studies by Hu and colleagues[37] disclosed that the incidence of postoperative stroke and TND were similar between ACP and RCP.

TABLE 4. Surgical data and the results in nonmatched analysis

	ACP	HCA/RCP	*P* value
Lowest rectal temperature (°C) (100%)	24.2 ± 3.2	21.2 ± 3.7	<.001
<20°C (%)	36.7	9.6	<.001
20°C-25°C (%)	44.4	47.1	
25°C-30°C (%)	42.4	14.6	
30° or >30°C (%)	1.5	3.5	
Operation time (min)	477.8 ± 168.1	465.8 ± 150.0	.073
Cardiopulmonary bypass time (min)	244.6 ± 91.7	237.6 ± 80.5	.043
Cardiac ischemia (min)	144.2 ± 60.4	137.9 ± 62.8	.017
CABG (%)	18.5	17.1	.092
Valve surgery (%)	20.5	20.9	.876
30-d death (%)	36 (3.2%)	46 (4.0%)	.247
Hospital death (%)	69 (6.0%)	81 (7.1%)	.290
Stroke (%)	76 (6.7%)	98 (8.6%)	.083
TND (%)	47 (4.1%)	50 (4.4%)	.756
Intubation time (h)	82 (3-5471)*	121 (7-8760)*	.043
Reoperation for bleeding (%)	5.7	4.4	.151
Dialysis (%)	3.9	3.8	.828
Wound infection (%)	2.5	1.9	.391
Spinal (%)	3.2	3.2	1.000
Perioperative myocardial infarction (%)	1.1	0.6	.249
Acute renal failure (%)	8.2	7.2	.387
GI complication (%)	3.2	3.5	.728
Atrial fibrillation (%)	21.3	21	.878
Septicemia (%)	1.9	3.1	.303
Pneumonia (%)	8	7.2	.477
Readmission (%)	2.1	1.6	.350
ICU stay >8 d (%)	182 (15.6%)	277 (24.2%)	<.001
Composite outcome (%)	325 (28.4%)	344 (30.1%)	.382

Numeral with ±; mean ± standard deviation. *ACP*, Antegrade cerebral perfusion; *CABG*, coronary artery bypass grafting; *GI*, gastrointestinal; *HCA*, hypothermic circulatory arrest; *ICU*, intensive care unit; *RCP*, retrograde cerebral perfusion; *TND*, transient neurologic dysfunction. *Data are median value and range (parentheses).

This study extracted data from 8169 patients registered in the JCVSD who underwent total arch replacement with reconstruction of the 3-head vessels from January 2009 to December 2012, representing most of these procedures performed in Japan during this time period. The results of nonmatched and matched analyses disclosed that no significant differences were detected between patients who had ACP and patients who had HCA/RCP for brain protection with regard to 30-day mortality, operative mortality, stroke, and TND; however, there was a tendency toward a higher incidence of these indices in the RCP group. Also, there was no significant difference in postoperative, in-hospital complications, except for a longer postoperative ventilation time and ICU stay in the HCA/RCP group, perhaps reflecting that these patients take longer to wake up postoperatively. These results are consistent with previous reports observing that HCA/RCP results in an increased incidence of TND. HCA/RCP is a nonphysiologic type of perfusion that provides only a limited protective effect for the brain, and prolonged HCA may cause some neurologic dysfunction.

A relatively higher incidence of spinal complications (3.2%) remains to be a concern. There has been a tendency to increase minimum body temperature in both the ACP and HCA/RCP groups. Even in the HCVA/RCP group, only 9.6% had the lowest temperature less than 20°C and 18% had a body temperature more than 25°C. Approximately half of the patients in the ACP group underwent surgery with a rectal temperature more than 25°C. Warmer body temperature is certainly a risk factor for spinal cord ischemia during circulatory arrest, and the results of the study demonstrated this risk.[31-33]

Study Limitations

This was a retrospective study based on a large-scale database, providing weaker clinical evidence than a randomized prospective study. Because the JCVSD has no data regarding brain perfusion time or circulatory arrest time, we could not analyze the relationship between the severity of the brain injury and the brain ischemia or perfusion time. Also, an intrinsic drawback of multicenter studies, detailed data, such as the degree of atherosclerosis or calcification of the aorta, preoperative brain circulation or ischemia, or conduct of cardiopulmonary bypass, are not available. An imbalance of the number of patients may obscure the virtues of propensity score analysis. Finally, there is no simple method to determine the

incidence or severity of brain injury after a cardiac operation and no consensus definitions of TND after aortic surgery.

CONCLUSIONS

Although ACP was the most frequently used brain protection method among patients undergoing total arch replacement within the JCVSD, the present findings indicated that both HCA and ACP provide excellent and comparable clinical outcomes with regard to mortality, stroke, and TND rates, but HCA resulted in a longer intubation time and ICU stay. ACP might be preferred as the brain protection method for complicated aortic arch procedures.

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