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

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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

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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%)