Brain Protection During Ascending Aortic Repair for Stanford Type A Acute Aortic Dissection Surgery

– Nationwide Analysis in Japan –

Yoshiyuki Tokuda, MD, PhD; Hiroaki Miyata, MD, PhD; Noboru Motomura, MD, PhD;
Hideki Oshima, MD, PhD; Akihiko Usui, MD, PhD; Shinichi Takamoto, MD, PhD;
Japan Adult Cardiovascular Database Organization

Background: The optimal brain protection strategy for use during acute type A aortic dissection surgery is controversial.

Methods and Results: We reviewed the results for 2 different methods: antegrade cerebral perfusion (ACP) and retrograde cerebral perfusion (RCP), during ascending aortic repair for acute type A aortic dissection for the period between 2008 and 2012 nationwide. Cases involving root repair, arch vessel reconstruction and/or concomitant procedures were excluded. Using the Japan Adult Cardiovascular Surgery Database, a total of 4,128 patients (ACP, n=2,769; RCP, n=1,359; mean age, 69.1±11.8 years; male 41.9%) were identified. The overall operative mortality was 8.6%. Following propensity score matching, among 1,320 matched pairs, differences in baseline characteristics between the 2 patient groups diminished. Cardiac arrest time (ACP 116±36 vs. RCP 102±38 min, P<0.001), perfusion time (192±54 vs. 174±53 min, P<0.001) and operative time (378±117 vs. 340±108 min, P<0.001) were significantly shorter in the RCP group. There were no significant differences between the 2 groups regarding the incidence of operative mortality or neurological complications, including stroke (ACP 11.2% vs. RCP 9.7%). Postoperative ventilation time was significantly longer in the ACP group (ACP 128.9±355.7 vs. RCP 98.5±301.7 h, P=0.018). There were no differences in other early postoperative complications, such as re-exploration, renal failure, and mediastinitis.

Conclusions: Among patients undergoing dissection repair without arch vessel reconstruction, RCP had similar mortality and neurological outcome to ACP. (*Circ J* 2014; **78**: 2431–2438)

Key Words: Aorta; Cardiopulmonary bypass; Dissection

Acute type A aortic dissection is a life-threatening emergency associated with major morbidity and mortality requiring immediate surgical treatment.^{1,2} With respect to improving surgical outcomes, the optimal selection of a brain protection strategy is of critical importance. In recent decades, various brain protection methods have been used in the field of surgery of the thoracic aorta based on the concept of hypothermic circulatory arrest (HCA).³ In addition to the use of HCA alone, various cerebral perfusion strategies have been developed to prolong the safe duration of circulatory arrest. In particular, 2 major methods are generally utilized as adjuncts to HCA: selective antegrade cerebral perfusion (ACP), which maintains the cerebral circulation using cold blood perfusion via the arch vessels with separate cannulas;⁴ and retrograde cerebral perfusion (RCP), an alternative method for brain

protection during deep hypothermic circulation arrest achieved using the perfusion of a small volume of blood via the superior vena cava in a retrograde manner.⁵

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In the setting of acute aortic dissection surgery, because there is a possibility of involvement of dissection in the arch vessels, selecting the brain protection strategy is particularly difficult and complex. In such cases, ACP can cause brain ischemia due to worsening of malperfusion despite a sufficient blood supply through the perfusion cannula.⁶ No consensus, therefore, has been reached among cardiac surgeons concerning the optimal strategy for brain protection during acute type A aortic dissection surgery.

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Department of Cardiac Surgery, Nagoya University Graduate School of Medicine, Nagoya (Y.T., H.O., A.U.); Japan Cardiovascular Surgery Database Organization, Tokyo (H.M., N.M., S.T.), Japan

Mailing address: Yoshiyuki Tokuda, MD, PhD, Department of Cardiac Surgery, Nagoya University Graduate School of Medicine, 65 Tsurumai, Showa-ku, Nagoya 466-8550, Japan. E-mail: tokuda@mx.mesh.ne.jp

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Given that acute type A dissection repair is usually performed on an emergency or urgent basis, conducting a randomized control trial to compare brain protection methods, although desirable, is difficult in practice. For this reason, a comparative clinical study using a large-scale database is a good alternative for assessing the superiority of methods of brain protection, while achieving a higher level of evidence.

The primary purpose of the present study was to compare brain protection methods in order to identify the optimal brain protection strategy for use in acute type A aortic dissection surgery. The broad range of preoperative conditions, anatomic features and surgical procedures observed in this setting has hampered comparisons of postoperative outcomes. We used the Japan Adult Cardiovascular Surgery Database (JACVSD) in order to obtain a sufficient number of cases to enable risk-adjusted analysis. The surgical treatment of type A aortic dissection primarily consists of the replacement of the ascending aorta in order to excise the entry tears and prevent an expansion of the area of dissection toward the aortic root with consequent rupture into the pericardial sac. In order to minimize procedure-related bias, the present study focused on the outcome of the most common and simple form of acute type A aortic dissection repair: isolated replacement of the area of the ascending aorta. The present study therefore excluded patients who underwent repair with root or arch vessel reconstruction and/or repair performed in association with other concomitant procedures.

Methods

JACVSD

The JACVSD was established in 2000 to assess the surgical outcomes of cardiovascular procedures on a multicenter basis throughout Japan. The JACVSD currently collects clinical information from 520 Japanese hospitals performing cardiovascular surgery, as of April 2013. The form used for data collection includes a total of more than 250 variables (the definitions are available online at <http://www.jacvsd.umin.jp>) that are almost identical to those used in the Society of Thoracic Surgeons (STS) National Database (the definitions are available online at <http://sts.org>). The methods used for data collection in the JACVSD are described in a previous publication.⁷ The data collection protocol was approved by the Institutional Review Board of each participating hospital. The use of data for the present study was approved by the Data Utilization Committee of the Japan Cardiovascular Surgery Database Organization. The committee waived the individual consent for the present study. The data collection process achieved a high level of completion, with missing data representing <2% of all assembled data. The accuracy of the submitted data was maintained using a data audit achieved via random, monthly visits by administrative office members to participating hospitals in which the data were verified using clinical records.

Subjects

We examined isolated primary repair operations of Stanford type A acute aortic dissection (performed within 14 days after onset) performed between 1 January 2008 and 31 December 2012 in which the range of repair was confined to the ascending aorta. Cases involving repair with root or arch vessel reconstruction (partial or total) or repair associated with other concomitant major surgical procedures, such as valve surgery or coronary artery bypass grafting, were excluded. So-called hemi arch replacement (replacement of the proximal aorta with resection of some portion of the concavity of the aortic arch,

leaving the convexity and origin of the arch vessels intact) was not deemed to constitute replacement of the aortic arch, and such cases were therefore included in the present study.

Cases involving records with missing or out of range data for age, sex or the 30-day status, as well as those in which the brain protection method was not specified, were excluded. With respect to the brain protection method, an initial 2,769 patients were treated with ACP, 1,359 were treated with RCP, 832 were treated with isolated HCA alone and 14 were treated with other methods. Among these patients, those treated with ACP or RCP were selected for the present analysis. After cleaning the data, the subject group included in the analysis consisted of 4,128 cases (ACP, $n=2,769$; RCP, $n=1,359$) of isolated type A acute aortic dissection repair without arch vessel or root reconstruction in Japan.

Endpoints

The primary outcome measured from the JACVSD was the operative mortality rate. Operative mortality was defined as death occurring within the index hospitalization, regardless of the length of hospital stay, and including any deaths occurring after discharge from the hospital up to 30 days from the date of surgery. A hospital-to-hospital transfer was not considered discharge.⁸ The definitions of postoperative outcomes were determined based on the JACVSD definitions. Using a definition obtained from previous studies, major morbidity was defined as the occurrence of any of 5 postoperative in-hospital complications: stroke; reoperation for bleeding; need for mechanical ventilation >24 h postoperatively due to respiratory failure; renal failure associated with newly required dialysis; or mediastinitis.⁹ In addition to evaluating stroke as a new neurological dysfunction, we assessed the incidence of transient neurological dysfunction, continuous coma >24 h and paraparesis/paraplegia as neurological complications, as per the JACVSD protocol.¹⁰ Transient neurological dysfunction was defined as a focal neurologic deficit lasting <72 h or postoperative delirium, agitation, confusion and/or a decreased level of consciousness without the detection of any new structural abnormalities on imaging.¹¹

Statistical Analysis

We compared the baseline demographics of the patients who underwent RCP surgery with those who underwent ACP surgery. Differences between the 2 brain protection strategy groups were determined using bivariate tests, including Fisher's exact test and the chi-squared test for categorical covariates and the unpaired t-test or Wilcoxon rank-sum test for continuous covariates. The data are given as mean $\pm$ SD.

For risk-adjusted comparisons, a multivariate logistic regression model was applied to determine the effects of RCP. Using stepwise regression with backward elimination, the baseline characteristics were listed as independent variables, while mortality and major morbidities were established as the dependent variable for the multivariate logistic regression analysis.

The second method of adjustment involved matching patients with a similar probability of receiving RCP. Because the patients were not randomly assigned to receive RCP, we used propensity score matching to adjust for differences in the preoperative factors.¹² We performed a 1-to-1 matched analysis without replacement based on the estimated propensity score, calculated from variables for each patient collected from the baseline characteristics listed in Table 1. The log odds of the probability that a patient received RCP (the "logit") was modeled as a function of the confounders identified and included in the dataset. Using the estimated logits, we first randomly

Table 1. Baseline Subject Characteristics

Characteristics	ACP (n=2,769)	RCP (n=1,359)	P-value
Age (years)			0.034
≤60	559 (20.2)	327 (24.1)	
61–65	360 (13.0)	189 (13.9)	
66–70	403 (14.6)	191 (14.1)	
71–75	446 (16.1)	216 (15.9)	
75–80	523 (18.9)	238 (17.5)	
≥81	478 (17.3)	198 (14.6)	
Mean age (years)	69.6±11.6	68.2±12.1	0.001
Male gender	1,146 (41.4)	583 (42.9)	0.365
Smoking history	962 (34.7)	510 (37.5)	0.084
CLD (moderate-severe)	49 (1.8)	21 (1.5)	0.701
Diabetes	160 (5.8)	100 (7.4)	0.056
Diabetes requiring medication	91 (3.3)	50 (3.7)	0.524
Hypertension	2,166 (78.2)	1,064 (78.3)	0.968
Renal dysfunction	172 (6.2)	74 (5.4)	0.363
Hepatic dysfunction	139 (5.0)	52 (3.8)	0.098
History of CBV event	375 (13.5)	185 (13.6)	0.961
Recent CBV event (within the past 2 weeks)	216 (7.8)	102 (7.5)	0.757
Carotid stenosis	86 (3.1)	26 (1.9)	0.032
Peripheral vascular disease	354 (12.8)	115 (8.5)	<0.001
≥2-vessel CAD	11 (0.4)	6 (0.4)	0.801
Cardiac symptom			
NYHA III or IV	794 (28.7)	302 (22.2)	<0.001
NYHA IV	599 (21.6)	227 (16.7)	<0.001
CHF (within the past 2 weeks)	127 (4.6)	85 (6.3)	0.024
Cardiogenic shock	538 (19.4)	262 (19.3)	0.933
Angina symptom (CCS class ≥2)	207 (7.5)	63 (4.6)	<0.001
LV function			
Good (EF ≥60%)	1,999 (72.2)	910 (67.0)	0.001
Medium (EF 30–60%)	698 (25.2)	401 (29.5)	0.003
Low (EF <30%)	52 (1.9)	20 (1.5)	0.378
Heart valve disorder			
Aortic insufficiency (≥II/IV)	641 (23.1)	253 (18.6)	0.001
Mitral insufficiency (≥II/IV)	107 (3.9)	47 (3.5)	0.542
Tricuspid insufficiency (≥II/IV)	126 (4.6)	56 (4.1)	0.573
Arrhythmia	199 (7.2)	79 (5.8)	0.099
Atrial fibrillation	142 (5.1)	48 (3.5)	0.022
Obesity (BMI ≥30)	139 (5.0)	91 (6.7)	0.030
Previous cardiac surgery	15 (0.5)	2 (0.1)	0.072
Priority of surgery			
Urgent	307 (11.1)	187 (13.8)	0.014
Emergency	2,338 (84.4)	1,120 (82.4)	0.106

Data given as n (%) or mean ± standard deviation (SD). Moderate chronic lung disease defined as FEV1 50–59% of the predicted value and/or the use of chronic steroid therapy to treat lung disease. Severe chronic lung disease defined as FEV1 <50% predicted and/or a room air PaO₂ <60 mmHg or room air PaCO₂ >50 mmHg.

ACP, antegrade cerebral perfusion; BMI, body mass index; CAD, coronary artery disease; CBV, cerebrovascular; CCS, Canadian Cardiovascular Society; CHF, congestive heart failure; CLD, chronic lung disease; EF, ejection fraction; LV, left ventricular; NYHA, New York Heart Association; RCP, retrograde cerebral perfusion.

selected a patient in the RCP group and then matched that patient with a patient in the ACP group with the closest estimated logit value. Patients in the RCP group with an estimated logit within 0.6 SD of the selected patients in the ACP group were eligible for matching. We selected 0.6 SD because this has been shown to eliminate approximately 90% of the bias present in observed confounders¹³ (C-statistic of the propensity model, 0.614). The differences in clinical variables

were tested on univariate analysis.

Results

Baseline Characteristics and Clinical Outcome

Among the subject group, 2,769 patients underwent ACP and 1,359 patients underwent RCP. The characteristics of the 2 groups are listed in **Table 1**. Overall, the mean patient age was

Table 2. Morbidity and Mortality

	ACP (n=2,769)	RCP (n=1,359)	Overall (n=4,128)	P-value
Intraoperative variables				
Operative time (min)	379.0±115.8	341.2±108.8	366.5±114.9	<0.001
Perfusion time (min)	192.3±53.5	174.3±53.0	186.4±54.0	<0.001
Cardiac arrest time (min)	115.9±37.6	102.1±38.3	111.4±38.4	<0.001
Minimal core temperature (°C)	24.5±2.9	22.6±3.0	23.9±3.1	<0.001
Operative mortality	246 (8.9)	109 (8.1)	355 (8.6)	0.41
Composite operative mortality and major complication	1,092 (39.4)	482 (35.5)	1,574 (38.1)	0.01
Reoperation for bleeding	137 (4.9)	75 (5.5)	212 (5.1)	0.45
Renal failure	314 (11.3)	144 (10.6)	458 (11.1)	0.49
De novo hemodialysis	175 (6.3)	69 (5.1)	244 (5.9)	0.12
Cardiac complications				
Cardiac arrest	50 (1.8)	27 (2.0)	77 (1.9)	0.71
Cardiac tamponade	122 (4.4)	50 (3.7)	172 (4.2)	0.28
Heart block requiring pacemaker	15 (0.5)	8 (0.6)	23 (0.6)	0.83
Atrial fibrillation	589 (21.3)	298 (21.9)	887 (21.5)	0.63
Perioperative MI	30 (1.1)	8 (0.6)	38 (0.9)	0.16
Infection				
Mediastinitis	53 (1.9)	24 (1.8)	77 (1.9)	0.81
Septicemia	90 (3.3)	33 (2.4)	123 (3.0)	0.17
Pneumonia	185 (6.7)	95 (7.0)	280 (6.8)	0.74
Prolonged ventilation	834 (30.1)	339 (24.9)	1,173 (28.4)	<0.001
Neurological complications, any	514 (18.6)	248 (18.2)	762 (18.5)	0.83
Stroke	311 (11.2)	132 (9.7)	443 (10.7)	0.15
Transient neurological dysfunction	121 (4.4)	61 (4.5)	182 (4.4)	0.87
Coma	149 (5.4)	74 (5.4)	223 (5.4)	0.94
Paraparesis/Paraplegia	109 (3.9)	62 (4.6)	171 (4.1)	0.36
GI tract complication	99 (3.6)	37 (2.7)	136 (3.3)	0.16
Multiple organ failure	86 (3.1)	43 (3.2)	129 (3.1)	0.92
Transfusion	2,730 (98.6)	1,332 (98.0)	4,062 (98.4)	0.19
Length of stay ICU >8 days	809 (29.2)	364 (26.8)	1,173 (28.4)	0.11
Postoperative ventilation time (h)	134.8±360.0	100.3±304.0	123.5±343.0	0.001
Re-admission	38 (1.4)	19 (1.4)	57 (1.4)	1.00

Data given as n (%) or mean±SD. GI, gastrointestinal; ICU, intensive care unit; MI, myocardial infarction. Other abbreviations as in Table 1.

69.1±11.8 years, and 41.9% of the patients were male. Emergency procedures were required in 83.8% of cases (defined as a procedure that began immediately after surgical intervention was selected), while 12.0% of the patients required urgent procedures (defined as a procedure that began within 24 h of the decision to perform surgery).

The overall operative mortality was 8.6%. The specific morbidity rates in both groups are given in **Table 2**. There were no differences in operative mortality between the ACP (8.9%) and RCP (8.1%) groups. Moreover, there were no significant differences in the stroke rate between the 2 groups: 11.2% in the ACP group and 9.7% in the RCP group. The postoperative ventilation time was significantly longer in the ACP group (ACP 134.8±360.0 vs. RCP 100.3±304.0 h, $P=0.001$). The need for prolonged ventilation (>24 h due to respiratory reasons) was therefore more frequent in the ACP group (ACP 30.1% vs. RCP 24.9%, $P<0.001$). Given that prolonged ventilation was categorized as a major complication, the composite mortality and major complication rate was higher in the ACP group (ACP 39.4% vs. RCP 35.5%, $P=0.01$). Otherwise, there were no differences in the rates of early postoperative complications.

Risk-Adjusted Analysis

As to the risk-adjusted analysis, the effects of RCP were assessed using logistic regression analysis, the results of which are given in **Table 3**. Among the 5 major postoperative morbidities (stroke; reoperation due to bleeding; prolonged ventilation; de novo dialysis; or mediastinitis), operative mortality and neurological complications, only the need for prolonged ventilation was significantly different, with a higher rate in the ACP group.

The odds ratio of RCP over ACP for prolonged ventilation was 0.77 (95% confidence interval: 0.66–0.90, $P=0.001$; the odds ratio of ACP over RCP was 1.30).

Propensity-Matched Pairs Analysis

Based on the results given in the previous section, we evaluated 1,320 ACP patients and 1,320 RCP patients based on case matching using the propensity score. As a result, the differences in the preoperative factors decreased substantially. There were no significant differences in the various preoperative factors between the 2 post-matching groups (**Table 4**).

Similar to that observed for the overall cohort data, the

Table 3. Major and Neurological Complications

Outcome	OR (RCP over ACP) (95% CI)	P-value
Operative mortality	0.91 (0.71–1.17)	
Reoperation for bleeding	1.18 (0.88–1.58)	0.28
De novo hemodialysis	0.81 (0.60–1.10)	0.17
Prolonged ventilation	0.77 (0.66–0.90)	0.001
Mediastinitis	0.92 (0.57–1.52)	0.76
Neurological complications, any	1.02 (0.86–1.22)	0.81
Stroke	0.87 (0.70–1.08)	0.21
Transient neurological dysfunction	1.03 (0.75–1.42)	0.85
Coma	1.1 (0.81–1.50)	0.53
Paraparesis/Paraplegia	1.17 (0.84–1.61)	0.35

CI, confidence interval; OR, odds ratio. Other abbreviations as in Table 1.

operative time (ACP 378 ± 117 vs. RCP 340 ± 108 min, $P < 0.001$), perfusion time (ACP 192 ± 54 vs. 174 ± 53 min, $P < 0.001$) and cardiac arrest time (ACP 116 ± 36 vs. RCP 102 ± 38 min, $P < 0.001$) were significantly longer and the minimal core temperature was higher (ACP 24.5 ± 2.9 vs. RCP $22.6 \pm 3.0^\circ\text{C}$) in the ACP group. The postoperative outcomes of the propensity matched pairs are given in Table 5. There were no significant differences between the 2 groups regarding operative mortality (ACP 8.8% vs. RCP 7.7%) or the various neurological complications. Specifically, there were no significant differences in the rate of stroke (ACP 11.2% vs. RCP 9.7%), coma (ACP 4.9% vs. RCP 5.4%), paraparesis/paraplegia (ACP 4.2% vs. RCP 4.5%), transient neurological dysfunction (ACP 4.9% vs. RCP 4.5%) or any other neurological complications (ACP 18.7% vs. RCP 18.1%). A higher rate of prolonged ventilation was again observed in the ACP group (ACP 29.9% vs. RCP 24.7%, $P = 0.003$), and the postoperative ventilation time was also significantly longer in the ACP group (ACP 128.9 ± 355.7 vs. RCP 98.5 ± 301.7 h, $P = 0.018$). Otherwise, there were no differences in the rate of early postoperative complications, including other major complications, such as re-exploration, renal failure and mediastinitis.

Discussion

The present study found that if arch vessel reconstruction is not involved in the dissection repair procedure, RCP provides similar clinical outcomes regarding both mortality and neurological complication rates in comparison to ACP. Moreover, the cardiac arrest time, perfusion time and operative time were all significantly shorter in the RCP group whereas the minimal core temperature was lower in the RCP group. In addition, the need for prolonged ventilation (>24 h) occurred more frequently in the ACP group. An analysis of the overall cohort, as well as a risk-adjusted analysis and propensity matching analysis, confirmed these results.

Currently, there is no consensus regarding the optimal strategy for providing brain protection during acute type A aortic dissection surgery. There have been several reports comparing the effectiveness of ACP and RCP in cases involving atherosclerotic thoracic aortic aneurysms.^{10,14–17} These studies found either no obvious differences between the methods, or a slight superiority of ACP. The superiority of ACP with respect to neurological outcomes is especially clear among patients undergoing arch replacement with separate arch vessel reconstruction using branched grafts. The rate of transient neurological dysfunction is generally lower if ACP is applied in such

cases.^{15,16} In the present study, the rate of transient neurological dysfunction was similar between the ACP group and the RCP group, but it should be noted that inter-observer differences in evaluating the transient neurological dysfunction may have been present, because the criteria for delirium or agitation are not clear in the JACVSD system.

The situation is more complex, however, in the setting of dissection repair, in that brain protection must be provided in the presence of possible branch dissection and malperfusion of the cerebral vessels. There have also been a few previous studies comparing the efficacy of different brain protection methods in dissection repair, specifically. For example, Wiedemann et al reported that patients who receive ACP have somewhat better neurological and survival outcomes, although the difference was not significant on multivariate analysis.¹⁸ Importantly, their subjects included patients who underwent arch vessel reconstruction. The background of their study was therefore more favorable for ACP use and differs from the present setting. A similar study by Comas et al found that the use of ACP in the setting of dissection repair results in similar neurological outcome compared to that obtained with other techniques. The authors emphasized that performing aortic clamping prior to circulatory arrest carries a risk of stroke.¹⁹ Both the brain protection method and perfusion strategy (antegrade or retrograde perfusion) or cannulation site strategy can affect outcome. In particular, antegrade perfusion through the true lumen (via axillary cannulation or central aortic cannulation) has been reported to be associated with better survival.²⁰

In general, both ACP and RCP have advantages and disadvantages with regard to brain protection. ACP could be used to provide a reliable cerebral circulation, but it requires the placement of additional cannulas on the arch branches, which potentially increases the chance of embolism or worsening of malperfusion.⁶ Furthermore, the use of additional pump circuits and cannulas clutters the operative field. In the presence of such cannulas, performing anastomosis becomes more complex, which may possibly elongate the time required to complete anastomosis. In the present study, cardiac arrest time, which was approximately equivalent to the sum of the time required for distal and proximal anastomosis, was significantly elongated in the ACP group. Previous studies have similarly noted a tendency toward a longer distal circulatory arrest time (lower body visceral ischemic time) in patients treated with ACP compared to those treated with RCP.¹⁴ The shorter anastomosis time in the RCP group may have been mainly related to the simpler anastomosis performed, but it could also have been surgeon related, because RCP used to be an established

Table 4. Baseline Characteristics of Propensity-Matched Pairs

Characteristics	ACP (n=1,320)	RCP (n=1,320)	P-value
Age (years)			0.998
≤60	305 (23.1)	301 (22.8)	
61–65	182 (13.8)	185 (14.0)	
66–70	193 (14.6)	187 (14.2)	
71–75	206 (15.6)	214 (16.2)	
75–80	238 (18.0)	237 (18.0)	
≥81	196 (14.8)	196 (14.8)	
Mean age (years)	68.5±12.0	68.6±11.9	0.880
Male gender	577 (43.7)	559 (42.3)	0.504
Smoking history	491 (37.2)	491 (37.2)	1.000
CLD (moderate-severe)	21 (1.6)	19 (1.4)	0.874
Diabetes	84 (6.4)	90 (6.8)	0.695
Diabetes requiring medication	54 (4.1)	47 (3.6)	0.543
Hypertension	1,039 (78.7)	1,031 (78.1)	0.741
Renal dysfunction	94 (7.1)	72 (5.5)	0.092
Hepatic dysfunction	61 (4.6)	52 (3.9)	0.442
History of CBV event	164 (12.4)	181 (13.7)	0.356
Recent CBV event (within the past 2 weeks)	105 (8.0)	101 (7.7)	0.828
Carotid stenosis	36 (2.7)	26 (2.0)	0.247
Peripheral vascular disease	97 (7.3)	114 (8.6)	0.251
Extent of CAD			
≥2 vessel CAD	8 (0.6)	7 (0.5)	1.000
Cardiac symptom			
NYHA III or IV	305 (23.1)	294 (22.3)	0.642
NYHA IV	225 (17.0)	219 (16.6)	0.795
CHF (within the past 2 weeks)	75 (5.7)	73 (5.5)	0.933
Cardiogenic shock	242 (18.3)	249 (18.9)	0.605
Angina symptom (CCS class ≥2)	66 (5.0)	63 (4.8)	0.857
LV function			
Good (EF ≥60%)	911 (69.0)	897 (68.0)	0.586
Medium (EF 30–60%)	372 (28.2)	379 (28.7)	0.796
Low (EF <30%)	27 (2.0)	17 (1.3)	0.171
Heart valve disorder			
Aortic insufficiency (≥II/IV)	235 (17.8)	251 (19.0)	0.451
Mitral insufficiency (≥II/IV)	31 (2.3)	47 (3.6)	0.084
Tricuspid insufficiency (≥II/IV)	48 (3.6)	56 (4.2)	0.484
Arrhythmia	64 (4.8)	78 (5.9)	0.262
Atrial fibrillation	36 (2.7)	48 (3.6)	0.222
Obesity (BMI ≥30)	81 (6.1)	75 (5.7)	0.680
Previous cardiac surgery	3 (0.2)	2 (0.2)	1.000
Priority of surgery			
Urgent	146 (11.1)	179 (13.6)	0.058
Emergency	1,111 (84.2)	1,093 (82.8)	0.373

Data given as n (%) or mean±SD. Abbreviations as in Table 1.

procedure only at major aortic centers and by well-experienced surgeons.

In contrast, RCP has the drawback of a limited safe duration. In general, the RCP procedure should not exceed 60 min, and a longer RCP duration has been reported to be associated with the incidence of stroke.²¹ In the present study, however, the anastomosis time normally did not exceed the safe duration of RCP, given that cases involving branch vessel reconstruction were excluded. As another drawback, there is a theoretical controversy regarding the blood supply effects of RCP.²² If arch vessel dissection is present, however, RCP is a reliable

method of providing brain protection because the antegrade perfusion of blood through such vessels potentially results in serious malperfusion and ischemia.

In addition to the data regarding neurological outcome, another finding of the present study is that ACP was found to carry a risk of prolonged ventilation. The pathophysiology of cardiopulmonary bypass (CPB)-induced lung injury is primarily associated with the activation of a systemic inflammatory response via contact of blood with the artificial material of the CPB circuit.^{23–25} In addition, a decreased bronchial artery flow during CPB has been thought to induce ischemic damage to

Table 5. Propensity-Matched Analysis of Outcome

	ACP (n=1,320)	RCP (n=1,320)	P-value
Intraoperative variables			
Operative time (min)	378±117	340±108	<0.001
Perfusion time (min)	192±54	174±53	<0.001
Cardiac arrest time (min)	116±36	102±38	<0.001
Minimal core temperature (°C)	24.5±2.9	22.6±3.0	<0.001
Operative mortality	116 (8.8)	101 (7.7)	0.321
Composite operative mortality and major complication	509 (38.6)	464 (35.2)	0.076
Reoperation for bleeding	58 (4.4)	72 (5.5)	0.242
Renal failure	150 (11.4)	135 (10.2)	0.380
De novo hemodialysis	80 (6.1)	63 (4.8)	0.169
Cardiac complications			
Cardiac arrest	29 (2.2)	26 (2.0)	0.786
Cardiac tamponade	63 (4.8)	49 (3.7)	0.209
Heart block requiring pacemaker	8 (0.6)	8 (0.6)	1.000
Atrial fibrillation	270 (20.5)	289 (21.9)	0.391
Perioperative MI	9 (0.7)	8 (0.6)	1.000
Infection			
Mediastinitis	24 (1.8)	23 (1.7)	1.000
Septicemia	49 (3.7)	29 (2.2)	0.028
Pneumonia	80 (6.1)	93 (7.0)	0.345
Prolonged ventilation >24h	395 (29.9)	326 (24.7)	0.003
Neurological complications, any	247 (18.7)	239 (18.1)	0.725
Stroke	148 (11.2)	128 (9.7)	0.227
Transient neurological dysfunction	65 (4.9)	59 (4.5)	0.646
Coma	65 (4.9)	71 (5.4)	0.660
Paraparesis/Paraplegia	56 (4.2)	60 (4.5)	0.776
GI tract complication	41 (3.1)	34 (2.6)	0.482
Multiple organ failure	38 (2.9)	39 (3.0)	1.000
Transfusion	1,301 (98.6)	1,294 (98.0)	0.367
Length of stay ICU >8 days	370 (28.0)	350 (26.5)	0.406
Postoperative ventilation time (h)	128.9±355.7	98.5±301.7	0.018
Re-admission	12 (0.9)	19 (1.4)	0.278

Data given as n (%) or mean±SD. Abbreviations as in Tables 1,2.

the lungs,²⁶ which should be particularly severe during the distal circulatory arrest period of aortic surgery.²⁷ Furthermore, in recent years, with the use of ACP, deep hypothermia is not deemed necessary for brain protection, and higher temperatures are often used to shorten the CPB time and maintain coagulation.²⁸ End organs that receive no perfusion during the distal circulatory arrest period potentially suffer from “warm” ischemia injury.^{29–31} We speculate that the combination of a longer procedure time and higher temperature observed in the ACP group could result in poor lung protection, thus possibly leading to postoperative respiratory dysfunction.

In the present study, among the patients undergoing dissection repair without arch vessel reconstruction, RCP had similar mortality and neurological outcome to ACP despite insufficient blood supply. Moreover, RCP was found to be associated with a shorter procedure time and a smaller chance of prolonged ventilation. Nevertheless, the selection of the brain protection method should be tailored to the individual patient, taking into consideration several factors, including the possibility of malperfusion, expected distal circulatory arrest time, and preoperative respiratory function. The decision can be modified later if needed, even during the operation. For example,

in cases in which a longer distal procedure time is subsequently required, RCP can always be switched to ACP.

Study Limitations

The present study has certain limitations owing to the nature of the JACVSD. First, no long-term follow-up data for survival were obtained, and all outcomes were restricted to in-hospital outcomes. Second, regarding the present subjects, in order to avoid procedure-related bias, we excluded patients undergoing repair with root or arch vessel reconstruction. Therefore, the present findings are not applicable to all dissection repair patients, but rather confined to those undergoing replacement of areas of the ascending aorta. Moreover, because some centers routinely perform arch replacement for acute dissection repair, the present data may not reflect the situation throughout Japan.

Third, the JACVSD lacks several important types of information related to this topic. For example, there is no available information regarding the rate of malperfusion of the cerebral vessels, the cannulation site or the systemic perfusion strategy (antegrade or retrograde) and the duration of brain protection or distal circulatory arrest. In particular, the lack of informa-

tion on the duration of brain circulatory arrest or the selective cerebral perfusion time is a major weak point. Fourth, the possibility of a selection bias was not completely excluded. There might have been some differences in the selection of the brain protection method according to the case-volume of the centers and the experience of the surgeons. These points were not analyzed.

Despite these limitations, the present study is thus far the most extensive nationwide analysis of the outcome of aortic dissection repair in the modern surgical era in Japan. We thus believe that the present study provides important insight into managing this challenging clinical situation.

Conclusions

Aortic dissection repair remains a procedure associated with relatively high morbidity and mortality. In the present study, ACP and RCP had similar mortality rates and neurological outcome among the patients undergoing dissection repair without arch vessel reconstruction. Given that ACP and RCP have their own advantages and drawbacks, surgeons should therefore select the most appropriate brain protection method depending on the individual needs of each patient.

Disclosures

The authors have no conflict of interest to disclose.

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