Reportedly, MIE procedures such as thoracoscopic esophagectomy are increasingly performed worldwide.[25,26] In this study, we compared the outcomes of MIE with OE using the NCD and found that although there were no significant differences in 30-day or operative mortality rates between the OE and MIE groups, the incidence of anastomotic leakage and the rate of reoperation within 30 days because of surgical complications were significantly higher in the MIE group than in the OE group. However, the patient clinical background were markedly different between the 2 groups in the current study; therefore, in future studies, it is necessary to adjust the preoperative biases to objectively compare MIE and OE groups using other statistical methods such as propensity score matching. Nevertheless, our results were compatible with those from a previous study conducted in the United Kingdom by Mamidanna et al,[21] who reported the comparison of MIE with OE in the largest series of patients and confirmed the safety of MIE, even though MIE was associated with higher reoperation rates because of surgical complications and there were no marked benefits in operative mortality.

In this study, several patient and perioperative factors, including preoperative requirement of assistance in ADL; weight loss of more than 10% within 6 months before surgery; history of smoking within 1 year before surgery; history of respiratory distress within 1 month before surgery; history of COPD; congestive heart failure; and cerebrovascular disease before surgery; and ASA physical status were related to increased mortality as per univariate analysis. These results were relatively consistent with those of a previous analysis using the ACS NSQIP esophagectomy database.[22] It is likely that the preoperative requirement of assistance in ADL was because of various reasons such as comorbidities, advanced-stage esophageal cancer, and patient age.

The risk models developed in our study indicated that preoperative requirement of assistance in ADL, weight loss of more than 10% within 6 months before surgery, and age group were significant factors in both the 30-day and operative mortality models. History of smoking within 1 year before surgery, male sex, history of preoperative COPD, and abnormal preoperative laboratory test results were also identified as independent variables in the 30-day and operative mortality groups. Furthermore, presence of metastatic or relapsed cancer was significantly correlated with operative mortality. It is likely that preoperative poor general condition, as indicated by preoperative requirement of assistance in ADL, weight loss, and advanced age, were significantly correlated with mortality after esophagectomy. In addition, current smoking status and COPD are established strong predictors of pulmonary complications after esophagectomy.[22,27] Our results were compatible with those of previous analyses using large nationwide databases.[21,22] In contrast, presence of metastatic or relapsed esophageal cancer may be related to not only shorter cancer-specific survival but also high morbidity and mortality rates that have been reported in association with surgery for noncurative esophageal cancer.[6,28]

Several independent variables in the preoperative laboratory data, such as white blood cell and platelet counts; serum albumin, sodium, and blood urea nitrogen levels; and PT-INR have not been reported in previous risk models of mortality following esophagectomy.[14,21,22,24] However, abnormal laboratory test results are generally associated with poor overall health. A white blood cell (WBC) count of more than 12,000/mL and a platelet count of more than 400,000/mL may be linked to the possibility of preoperative infection and/or chronic inflammation. On the other hand, a WBC count of less than 4000/mL and a platelet count of less than 120,000/mL could be largely affected by preoperative chemo/radiotherapy. Hypoalbuminemia, which is a marker of malnutrition, is reportedly correlated with postoperative complications and mortality after esophagectomy.[29] Other abnormal laboratory data such as low sodium and blood urea nitrogen levels and extended PT-INR may result from various comorbidities, but severe liver dysfunction or liver cirrhosis because of excess alcohol use may be responsible for the abnormal laboratory test results in patients with esophageal squamous cell carcinoma.[1] Reportedly, esophagectomy in patients with cirrhosis carries a high risk of mortality and morbidity.[30] The preoperative abnormal laboratory data identified in our study can serve as novel markers for esophagectomy.

The C-indices of the 30-day and operative mortality models in the validation data set were 0.767 and 0.742, respectively. These results suggest that our risk models may be reliable and feasible in clinical practice. Although the usefulness of several scoring systems such as the Physiological and Operative Severity Score for enumeration of Mortality and Morbidity (POSSUM) in predicting the risk of esophagectomy has been reported,[31,32] these scoring systems seem to be unsuitable for prospective esophagectomy patients because the POSSUM model frequently overpredicts mortality after esophagectomy.[31,32] Therefore, we developed a novel scoring system suitable for patients with esophagectomy through these risk models, which will be evaluated in future studies.

Limitations

The use of the national database, derived from all types of patients and hospitals, would be expected to contribute to improvements in quality control of surgical procedures. However, the outcomes obtained in this study were influenced by hospital volume, training status and compliance, surgical specialization, resource utilization, and procedure-specific variables, which may change in the future.[33] However, variables pertaining to the risk of mortality in this study should be evaluated in a future study using these basic risk models. The NCD did not include information regarding clinical staging of esophageal cancer and preoperative clearance based on several clinical evaluations or the exclusion criteria of each institution. Furthermore, we could not obtain information regarding patients who avoided esophagectomy based on preoperative evaluations, and the NCD did not contain information regarding patients with prior operative histories.

We recognize that 2-field lymphadenectomy using the Ivor Lewis procedure or transhiatal esophagectomy is more commonly performed for esophageal adenocarcinoma in Western countries. Because differences in pathology may result in differences in surgical procedures, it remains unclear whether the mortality risk models developed in this study are applicable to assess patients in western countries.

Our results demonstrated favorable C-indices for 30-day and operative mortalities in the OE and MIE groups, suggesting that our risk models may not be markedly influenced by the choice of OE or MIE. However, the safety and benefits of MIE compared with those of conventional OE should be evaluated in more depth in the next study using this nationwide database.

The NCD commenced in January 2011 and has continued until 2013. To improve the contents of the NCD, we have decided to add the information of the TNM staging to the latest NCD, and we also plan to revise the NCD to add several important data for further studies.

CONCLUSIONS

We reported the first risk stratification esophagectomy study, as per our knowledge, based on a Japanese nationwide Web-based database. The 30-day and operative mortality rates in this study population were 1.2% and 3.4%, respectively, which were very satisfactory. We also developed risk models pertaining to esophagectomy, which should contribute to improvements in procedural quality control and creation of a novel scoring system suitable for esophagectomy.

ACKNOWLEDGMENTS

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Appropriateness Ratings of Percutaneous Coronary Intervention in Japan and Its Association With the Trend of Noninvasive Testing

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ABSTRACT

OBJECTIVES The aim of this study was to evaluate the appropriateness of percutaneous coronary intervention (PCI) in Japan and clarify the association between trends of pre-procedural noninvasive testing and changes in appropriateness ratings.

BACKGROUND Although PCI appropriateness criteria are widely used for quality-of-care improvement, they have not been validated internationally. Furthermore, the correlation of appropriateness ratings with implementation of newly developed noninvasive testing is unclear.

METHODS We assigned an appropriateness rating to 11,258 consecutive PCIs registered in the Japanese Cardiovascular Database according to appropriateness use criteria developed in 2009 (AUC/2009) and the 2012 revised version (AUC/2012). Trends of pre-procedural noninvasive testing and appropriateness ratings were plotted; logistic regression was performed to identify inappropriate PCI predictors.

RESULTS In nonacute settings, 15% of PCIs were rated inappropriate under AUC/2009, and this percent increased to 30.7% under AUC/2012 criteria. This was mostly because of the focused update of AUC, in which the patients were newly classified as inappropriate if they lacked proximal left anterior descending lesions and did not undergo pre-procedural noninvasive testing. However, these cases were simply not rated under AUC/2009. The amount of inappropriate PCIs increased over 5 years, proportional to the increase in coronary computed tomography angiography use. Use of coronary computed tomography angiography was independently associated with inappropriate PCIs (odds ratio: 1.33; $p = 0.027$).

CONCLUSIONS In a multicenter, Japanese PCI registry, approximately one-sixth of nonacute PCIs were rated as inappropriate under AUC/2009, increasing to approximately one-third under the revised AUC/2012. This significant gap may reflect a needed shift in appropriateness recognition of methods for noninvasive pre-procedural evaluation of coronary artery disease. (J Am Coll Cardiol Intv 2014;7:1000–9) © 2014 by the American College of Cardiology Foundation.

The advent of percutaneous coronary intervention (PCI) has significantly changed the treatment strategy for patients with coronary artery disease (CAD). However, although PCI has a significant benefit for reducing mortality and recurrent myocardial infarction among patients presenting

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with acute coronary syndrome (1), its survival benefit has not been clearly established for patients with stable CAD (2). Because the patients who undergo PCI are exposed to the risks of periprocedural complications such as bleeding or procedure-related myocardial infarction, the appropriate indications of PCI are of significant importance.

To promote the appropriate and judicious implementation of PCI, the American College of Cardiology Foundation and 6 other societies published joint appropriateness use criteria (AUC) for PCI in 2009 (AUC/2009) (3). These AUC have been applied to real-world clinical practice along with various registry data, and studies have demonstrated a strong possibility of PCI overuse in real-world practice in Western countries (4–6). However, reports on AUC application to patients outside of North America are sparse.

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In Japan, the number of PCI procedures has been increasing. More than 200,000 procedures in >800 hospitals were performed in 2012; this number is disproportionately large compared with the number of coronary artery bypass grafting (CABG) procedures. The number of PCI procedures is estimated to be >14 times greater than CABG procedures (7). Consequently, whereas the proportion of elective PCIs accounts for < 40% in the United States, as many as three-fourths of PCIs are performed in nonacute settings in Japan (7,8), and a greater number of patients with multivessel diseases are treated with PCI in Japan than in the United States (9). Furthermore, the pre-procedural evaluation is also quite different between the 2 countries: the performance of coronary CT angiography (CTA) is increasing remarkably in Japan, whereas the stress testing remains the main modality in the United States. These unique characteristics in Japan underscore the need for a proper evaluation of PCI appropriateness.

The purpose of our study was to evaluate the appropriateness of PCI indications in Japan on the basis of U.S. criteria and to compare the rate and characteristics of inappropriate PCIs between both countries. At present, 2 versions of AUC have been published in the United States. The original AUC/2009 was updated in 2012 (AUC/2012), emphasizing the importance of performing noninvasive stress testing before elective PCIs (10). The use of coronary CTA as a pre-procedural test is increasing in Japan and may have significantly altered appropriateness ratings. Although the risk of adverse cardiovascular events could be stratified by the extent of anatomic lesions on the basis of coronary CTA, computed tomography (CT)-based PCIs are rarely recognized as appropriate indications under current AUC. Therefore, in addition to reviewing the overall rating of PCI appropriateness, we sought to clarify its association with the trend in performing various noninvasive diagnostic tests.

ABBREVIATIONS AND ACRONYMS

AUC = appropriateness use criteria

CABG = coronary artery bypass grafting

CAD = coronary artery disease

CTA = computed tomography angiography

CT = computed tomography

FFR = fractional flow reserve

JCD = Japan Cardiovascular Database

PCI = percutaneous coronary intervention

PLAD = proximal left anterior descending artery

METHODS

DATA SOURCE. The Japan Cardiovascular Database (JCD) is an ongoing, prospective multicenter registry designed to collect clinical background and outcome data on consecutive PCI patients (11). In this registry, 16 teaching hospitals within the metropolitan Tokyo area participated and registered all PCI procedures performed during the study period, including failure cases, using an Internet-based interface. Approximately 200 variables were collected for each patient; clinical variables and in-hospital outcomes for JCD were defined in accordance with the National Cardiovascular Data Registry version 4.1. This registry, sponsored by the American College of Cardiology (12,13), is the largest national clinical registry program for diagnostic cardiac catheterization and PCI, with >1,500 centers currently participating across the United States. Additionally, in the JCD-PCI registry, the subgroup of patients who underwent an intracoronary infusion of acetylcholine to induce coronary vasospasm was also registered because vasospastic angina accounts for a significant portion of patients with CAD and acute coronary syndromes in Japan (14). Clinical research coordinators specifically trained in registering PCI procedures confirmed the proper registration of each patient. In addition, data reported on the Internet-based system were checked, and investigators visited each hospital quarterly to audit the database for completeness and consistency.

STUDY POPULATION. A total of 11,258 consecutive patients who underwent PCI procedures between September 2008 and March 2013 for acute and nonacute indications were registered in the database. A total of 1,208 patients were excluded because they underwent serial PCIs during the same hospitalization, there were insufficient baseline data, or they only underwent the acetylcholine challenge test. The remaining 10,050 patients were included in our study (**Figure 1**).

DEVELOPMENT OF AUC/2009 AND ITS RATING ASSIGNMENTS. AUC/2009 was developed by a collaboration of 6 American professional organizations

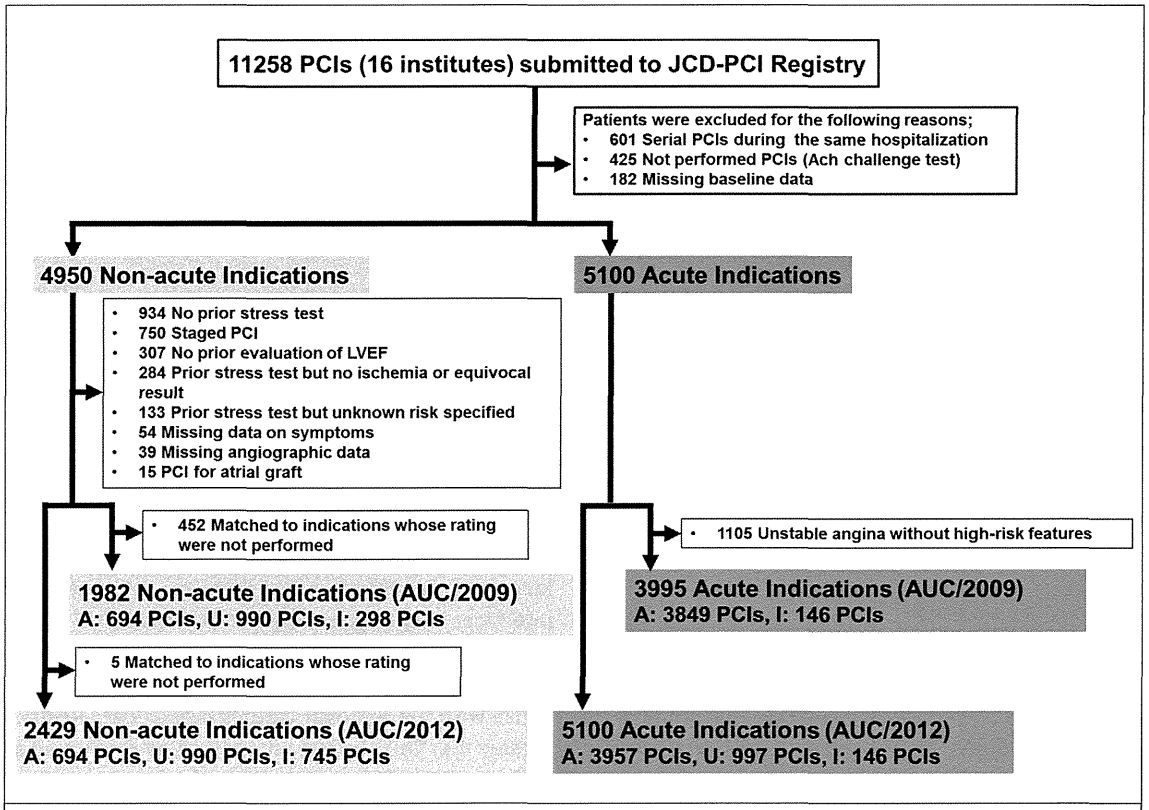

FIGURE 1 Study Cohort Creation

Patients registered in JCD-PCI Registry were divided into 2 groups (nonacute and acute indications). Each group was rated under AUC/2009 and AUC/2012. A = appropriate; Ach = acetylcholine; AUC = appropriateness use criteria; I = inappropriate; JCD-PCI = Japan Cardiovascular Database-Percutaneous Coronary Intervention; LVEF = left ventricular ejection fraction; U = uncertain.

(the American College of Cardiology Foundation, the Society for Cardiovascular Angiography and Intervention, the Society of Thoracic Surgeons, the American Association for Thoracic Surgery, the American Heart Association, and the American Society of Nuclear Radiology) in 2009. The methodology to develop the AUC for coronary revascularization was previously described (3).

We used an algorithm to map PCIs in the JCD-PCI registry to AUC/2009 and rate the procedures as appropriate, uncertain, or inappropriate. This algorithm, which was validated in a previous study (6), enabled the mapping to be performed in an efficient manner. All the definitions in our study were identical to those in AUC/2009. We optimized our mapping algorithm to maximize the use of existing data and minimize the influence of missing data. For example, certain nonacute indications can be assigned the appropriateness rating independent of noninvasive risk results (e.g., 3-vessel CAD with abnormal left ventricular systolic function). In these scenarios, an appropriateness classification could be provided even when noninvasive risk testing was not performed or results were not available.

Among the 10,050 patients, a rating could not be determined for 2,968 nonacute and 1,105 acute PCIs, leaving a total of 1,982 nonacute and 3,995 acute PCIs that could be rated (**Figure 1**). Among the acute indications, unstable angina without high-risk features was the main cause of rating failure. In the nonacute settings, mapping failure was mainly due to one of the following: no previous stress test performed, staged PCI, previous stress test with no ischemia or equivocal result, previous evaluation of left ventricular systolic function, and matched to indications that were not rated.

REVISED AUC/2012 AND ITS RATING ASSIGNMENTS. AUC/2009 was updated in 2012 (AUC/2012) (10). In the revised AUC/2012 version, unstable angina without high-risk features, which was an excluded clinical scenario in AUC/2009, was successfully mapped and divided into 2 indications according to the Thrombolysis In Myocardial Infarction score. In AUC/2009,

the clinical scenario of an asymptomatic patient without previous bypass surgery and with 1- or 2-vessel disease not involving the proximal left anterior descending artery (PLAD) who underwent no noninvasive testing was not evaluated because it was thought to be uncommon. However, in the revised AUC/2012, this clinical scenario was determined to be inappropriate. Accordingly, successfully mapped procedures increased, and 2,429 nonacute and 5,100 acute PCIs were rated (**Figure 1**).

STATISTICAL ANALYSIS. The proportion of PCIs classified as appropriate, uncertain, or inappropriate was determined, after stratification by acute versus nonacute indications on the basis of AUC/2009 and AUC/2012. Baseline characteristics and clinical variables of patients were compared by appropriateness categories. Differences were evaluated using the chi-square or Fisher exact test for categorical variables and the Student unpaired *t* test for continuous variables. Cochran-Armitage analysis was used to evaluate the trends of the proportion of inappropriate PCIs and of the implementation of various tests. Multivariate logistic regression analysis was performed to examine the relationship between the implementation of coronary CTA and inappropriate PCI, adjusting for potential confounders. The covariates included in the model were symptomatic status (symptomatic vs. asymptomatic), extent of ischemic burden (low risk vs. intermediate or high risk), antianginal medication (optimal vs. suboptimal medication), angiographic characteristics (left main trunk, triple-vessel disease, chronic total occlusion, or PLAD), and the time period when the PCI was performed (divided into 8 categories: September 2008 to June 2009, July 2009 to December 2009, January 2010 to June 2010, July 2010 to December 2010, January 2011 to June 2011, July 2011 to December 2011, January 2012 to June 2012, and July 2012 to March 2013). Data were analyzed using SPSS, version 20 (SPSS Inc., Chicago, Illinois). All p values were 2-sided, and significance was defined as $p < 0.05$ for all analyses.

RESULTS

PATIENT CHARACTERISTICS. **Table 1** summarizes the clinical characteristics of patients who underwent PCIs in acute and nonacute settings. The mean age was 67.9 ± 10.9 years; 79.4% were male. Coronary risk factors, including a history of myocardial infarction and PCI, hypertension, hypercholesterolemia, and diabetes mellitus, were common; however, the prevalence of a history of CABG was lower than that in previous reports (4).

TABLE 1 Baseline Characteristics of Acute and Nonacute PCIs

	Total (N = 10,050)	Acute (n = 5100)	Nonacute (n = 4950)
Demographics			
Male	7,978 (79.4)	3,972 (77.9)	4,006 (80.9)
Age, yrs	67.9 ± 10.9	67.5 ± 11.8	68.2 ± 9.7
Clinical factors			
Hypertension	7,462 (74.3)	3,588 (70.4)	3,874 (78.3)
Hypercholesterolemia	6,681 (66.6)	3,109 (61.1)	3,572 (72.2)
Diabetes mellitus	4,229 (42.1)	1,901 (37.4)	2,328 (47.0)
Current and past smoking	3,517 (35.1)	2,022 (39.8)	1,495 (30.3)
History of MI	2,501 (24.9)	799 (15.7)	1,702 (34.4)
Previous PCI	3,613 (36.0)	990 (19.4)	2,623 (53.0)
Previous CABG	532 (5.3)	195 (3.8)	337 (6.8)
Hemodialysis	430 (4.3)	181 (3.6)	249 (5.0)
Cerebrovascular disease	909 (9.1)	454 (8.9)	455 (9.2)
Peripheral arterial disease	817 (8.1)	292 (5.7)	525 (10.6)
Chronic lung disease	309 (3.1)	153 (3.0)	156 (3.2)

Values are n (%) or mean ± SD.

CABG = coronary artery bypass grafting; MI = myocardial infarction; PCI = percutaneous coronary intervention.

ACUTE INDICATIONS. Among the patients with acute indications for PCI, ST-segment elevation myocardial infarction was found in 49.3%, whereas cardiogenic shock was found in 16.9%. All clinical indications for appropriate and inappropriate PCIs in the acute settings are outlined in **Table 2**. Overall, most acute indications (96.3%) were categorized as appropriate under AUC/2009 (**Figure 2**, Online Table 1), whereas all inappropriate procedures were categorized as hemodynamic and electrically stable patients, with

TABLE 2 All the Clinical Scenarios in the Acute Setting

AUC/2009 Indication No.	Indication	n (%)
Appropriate PCI		
1	STEMI, ≤12 h from onset of symptoms Revascularization of the culprit artery	1,397 (35.0)
9	UA/NSTEMI and high-risk features of short-term risk if death or nonfatal MI Revascularization of the presumed culprit artery	1,361 (34.1)
11	Patients with acute myocardial infarction (STEMI or NSTEMI) Evidence of cardiogenic shock Revascularization of ≥1 coronary arteries	755 (18.9)
2	STEMI, onset of symptoms within the previous 12–24 h Severe HF, persistent ischemic symptoms, or hemodynamic or electrical instability present	336 (8.4)
Inappropriate PCI		
3	STEMI, >12 h from symptom onset Asymptomatic; no hemodynamic instability and no electrical instability	146 (3.7)

AUC = appropriateness use criteria; HF = heart failure; MI = myocardial infarction; NSTEMI = non-ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction; UA = unstable angina.

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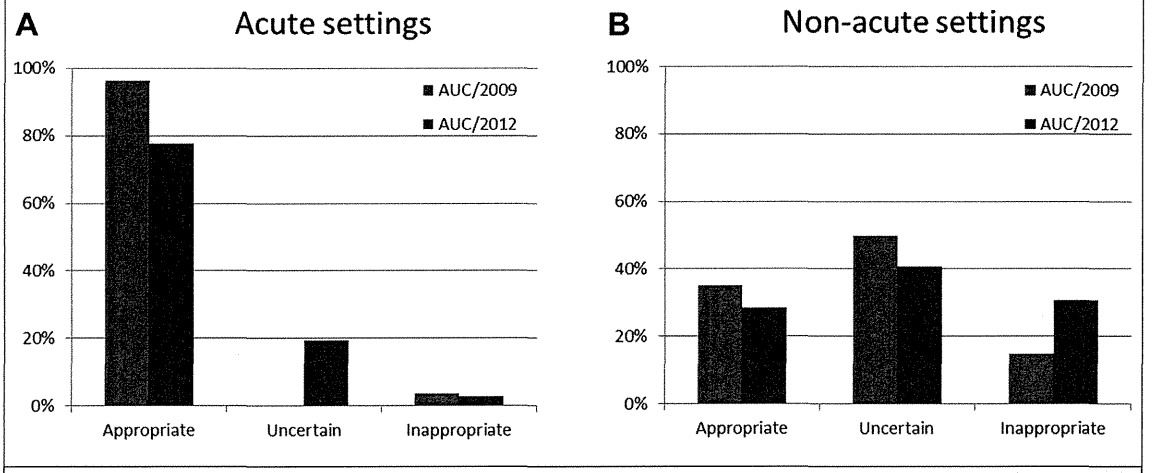

FIGURE 2 Appropriate Ratings Under Each Criterion

Appropriate ratings under each criterion in acute **(A)** settings and nonacute **(B)** settings. AUC = appropriateness use criteria.

PCI performed >12 h after symptom onset after ST-segment elevation myocardial infarction.

On the basis of AUC/2012, almost all cases of unstable angina without high-risk features (997 [90.2%]) were classified as uncertain, whereas 108 (9.8%) were considered appropriate. Overall, nearly 80% of acute procedures were categorized as appropriate (3,957 [77.6%]), whereas 997 (19.5%) were categorized uncertain and 146 (2.9%) were inappropriate (**Figure 2**, Online Table 1). All clinical indications for acute PCIs assessed by AUC/2012 are shown in Online Table 2.

NONACUTE INDICATIONS. In nonacute settings, 35.1% of PCIs were classified as appropriate, 49.9% as uncertain, and 15.0% as inappropriate under AUC/2009 (**Figure 2**, Online Table 1). Compared with procedures classified as appropriate or uncertain,

TABLE 3 Key Variables in Classifying Appropriateness for Nonacute PCIs in AUC/2009

		Procedural Appropriateness			
	Total (N = 1,982)	**Appropriate (n = 694)**	**Uncertain (n = 990)**	**Inappropriate (n = 298)**	**p Value**
Angina					<0.001
No symptoms	555 (32.2)	172 (24.8)	145 (14.6)	238 (79.9)	
CCS angina class					
I	377 (19.0)	67 (9.7)	283 (28.6)	27 (9.1)	
II	750 (37.8)	188 (27.1)	529 (53.4)	33 (11.1)	
III	239 (12.1)	214 (30.8)	25 (2.5)	0 (0)	
IV	38 (1.9)	30 (4.3)	8 (0.8)	0 (0)	
Unknown	23 (1.2)	23 (3.3)	0 (0)	0 (0)	
Noninvasive ischemia evaluation					<0.001
Low risk	228 (11.5)	19 (2.7)	82 (8.3)	127 (42.6)	
Intermediate risk	742 (37.4)	228 (32.9)	343 (34.6)	171 (57.4)	
High risk	195 (9.8)	156 (22.5)	39 (3.9)	0 (0)	
Maximal antianginal medications	117 (5.9)	70 (10.1)	45 (4.5)	2 (0.7)	<0.001
Angiographic characteristics					
Left main trunk	111 (5.6)	109 (15.7)	1 (0.1)	1 (0.3)	<0.001
3VD without left main trunk	345 (17.4)	290 (41.8)	46 (4.6)	9 (3.0)	<0.001
CTO without other coronary stenosis	77 (3.9)	15 (2.2)	44 (4.4)	18 (6.0)	0.007
Presence of proximal LAD stenosis	508 (25.6)	316 (45.5)	183 (18.5)	9 (3.0)	<0.001

Values are n (%).

CCS = Canadian Cardiovascular Society; CTO = chronic total occlusion; LAD = left anterior descending artery; 3VD = 3-vessel disease; all other abbreviations as in Table 2.

TABLE 4 Most Frequent Clinical Scenarios for Nonacute PCIs Classified as Inappropriate and Uncertain by AUC/2009

AUC/2009 Scenario No.	Indication: Anatomy	Previous CABG	Symptoms	Cardiac Risk (Noninvasive Tests)	Antianginal Medication	n (%)
Inappropriate PCIs						298
14a	1- or 2-vessel CAD, no proximal LAD involvement	No	Asymptomatic	Intermediate	None or minimal	146 (7.4)
12a	1- or 2-vessel CAD, no proximal LAD involvement	No	Asymptomatic	Low	None or minimal	60 (3.0)
12b	1- or 2-vessel CAD, no proximal LAD involvement	No	CCS class I or II	Low	None or minimal	57 (2.9)
56a	≥1 stenoses in non-CABG territory all bypass grafts patent	Yes	Asymptomatic	Intermediate	None or minimal	13 (0.7)
24a	CTO of 1 major coronary artery without other coronary stenoses	No	Asymptomatic	Intermediate	None or minimal	12 (0.6)
Uncertain PCIs						990
18b	1- or 2-vessel CAD, no proximal LAD involvement	No	CCS class I or II	Not available	Not available	524 (26.4)
14b	1- or 2-vessel CAD, no proximal LAD involvement	No	CCS class I or II	Intermediate	None or minimal	174 (8.8)
30b	1-vessel CAD involving the proximal LAD	No	CCS class I or II	Intermediate	None or minimal	49 (2.5)
36a	2-vessel CAD involving the proximal LAD	No	Asymptomatic	Intermediate	None or minimal	42 (2.1)
16a	1- or 2-vessel CAD, no proximal LAD involvement	No	Asymptomatic	High	None or minimal	29 (1.5)

CAD = coronary artery disease; all other abbreviations as in Tables 1 to 3.

inappropriate PCIs were more likely to be performed for patients who had no symptoms (appropriate, 24.8%; uncertain, 14.6%; inappropriate, 78.9%; $p < 0.001$), low-risk results from noninvasive testing (appropriate, 2.7%; uncertain, 8.3%; inappropriate, 42.6%; $p < 0.001$), or chronic total occlusion (appropriate, 2.2%; uncertain, 4.4%; inappropriate, 6.0%; $p < 0.007$) (**Table 3**). Overall, almost all of the inappropriate PCIs were confined to 5 scenarios, as summarized in **Table 4**. Frequently encountered scenarios included PCIs with suboptimal antianginal medications or involvement of single or multiple epicardial vessels other than the left main trunk or PLAD.

Under AUC/2012, asymptomatic patients with 1- or 2-vessel CAD with no PLAD involvement and without previous noninvasive testing (indication 18a in AUC/2009, indication 20a in AUC/2012) were rated as inappropriate ($n = 447$). When these scenarios were added, the percent of inappropriate PCIs increased from 15.0% to 30.7% (**Figure 2**, Online Table 1). Of these cases, as many as 120 (26.8%) were evaluated using coronary CTA before the procedures, and the results were positive in almost all the cases (noninterpretable, 4 cases; negative, 1 case). The most frequent clinical scenarios for nonacute PCIs classified as inappropriate and uncertain by AUC/2012 are summarized in **Table 5**.

ASSOCIATION BETWEEN TEMPORAL TRENDS OF NONINVASIVE TESTING AND THE RATE OF INAPPROPRIATE RATINGS. **Figure 3** summarizes the use of several noninvasive tests such as the stress myocardial perfusion imaging and coronary CTA and fractional flow reserve (FFR). FFR is a pressure wire-based ischemic evaluation during coronary angiography. **Figure 3** also demonstrates the temporal trends of the proportion of inappropriate PCIs. Among patients who underwent PCI, the proportion of patients evaluated with coronary CTA and FFR substantially increased (p for trend < 0.001), which coincided with a decrease in use of the stress myocardial perfusion imaging over the course of 5 years (p for trend < 0.001). Contemporaneously, the proportion of inappropriate PCIs increased (p for trend $= 0.003$) in parallel with the increase in coronary CTA use. Implementation of coronary CTA was associated with the rating of inappropriate PCI (odds ratio: 1.33; 95% confidence interval: 1.03 to 1.70; $p = 0.027$). Further, the time variables were not independently associated with the rating of inappropriate PCI (Online Table 3).

Figure 4 presents the change in the proportion of PCIs rated as inappropriate. Although the proportion of inappropriate PCIs accounted for 30.7% of all the elective procedures when the CT-based procedures were classified as inappropriate, this proportion decreased substantially (from 5.0% to 25.7%) when the CT-based procedures were classified as appropriate. Although the proportion of inappropriate PCIs tended to increase even when the CT-based procedures were classified as appropriate, the trend was not statistically significant (p for trend $= 0.09$).

DISCUSSION

In this contemporary, multicenter Japanese PCI registry, almost all acute PCIs were acceptable regardless of the criteria applied. However, approximately one-sixth of nonacute PCIs were rated as inappropriate under the original criteria. Under the updated AUC/

TABLE 5 Most Frequent Clinical Scenarios for Nonacute PCIs Classified as Inappropriate and Uncertain by AUC/2012

AUC/2012 Scenario No.	Indication: Anatomy	Previous CABG	Symptoms	Cardiac Risk	Antianginal Medication	n (%)
Inappropriate PCIs						745
20a	1- or 2-vessel CAD, no proximal LAD involvement	No	Asymptomatic	Not performed	Not available	447 (18.4)
16a	1- or 2-vessel CAD, no proximal LAD involvement	No	Asymptomatic	Intermediate	None or minimal	146 (6.0)
14a	1- or 2-vessel CAD, no proximal LAD involvement	No	Asymptomatic	Low	None or minimal	60 (2.5)
14b	1- or 2-vessel CAD, no proximal LAD involvement	No	CCS class I or II	Low	None or minimal	57 (2.3)
58a	≥1 stenoses in non-CABG territory, all bypass grafts patent	Yes	Asymptomatic	Intermediate	None or minimal	13 (0.6)
26a	CTO of 1 major coronary artery without other coronary stenoses	No	Asymptomatic	Intermediate	None or minimal	12 (0.5)
Uncertain PCIs						990
20b	1- or 2-vessel CAD, no proximal LAD involvement	No	CCS class I or II	Not available	Not available	524 (21.6)
16b	1- or 2-vessel CAD, no proximal LAD involvement	No	CCS class I or II	Intermediate	None or minimal	174 (7.2)
32b	1-vessel CAD involving the proximal LAD	No	CCS class I or II	Intermediate	None or minimal	49 (2.0)
38a	2-vessel CAD involving the proximal LAD	No	Asymptomatic	Intermediate	None or minimal	42 (1.7)
18a	1- or 2-vessel CAD, no proximal LAD involvement	No	Asymptomatic	High	None or minimal	29 (1.2)

Abbreviations as in Tables 1 to 4.

2012, the rate of inappropriate PCIs increased to nearly one-third because noninvasive stress testing was not performed before a large number of elective PCIs in Japan and was seemingly affected by the increasing trend of coronary CTA.

Under the original criteria (AUC/2009), the proportion of inappropriate procedures in our study was almost within the range reported in previous studies. Similar to our study, previous reports have shown that almost all coronary revascularization procedures performed in the acute setting were appropriate (4,6), whereas ratings in nonacute settings varied widely, from 11.6% to 17% depending on the study (4-6,15). Additionally, the characteristics of the nonacute procedures that we classified as inappropriate were also concordant with those reported in previous studies. Inappropriate PCIs were likely to be performed in patients who were either asymptomatic or mildly symptomatic (Canadian Cardiovascular Society class I or II), were receiving suboptimal antianginal medication, and had no PLAD coronary artery stenosis. In our study, the proportion and indications of inappropriate PCIs in Japan were similar to the results of previous studies from North America, which indicates that AUC/2009 may be useful for assessing the appropriateness of PCIs internationally. The same approach, including the education of physicians regarding procedural appropriateness, is needed to improve patient selection in nonacute settings globally.

Between the 2009 and 2012 criteria, the proportion of inappropriate procedures increased substantially from 15.0% to 30.7% in our registry, whereas Hannan et al. (5) reported that the percent of inappropriate PCIs using New York State's Cardiac Surgery Reporting System and the Percutaneous Coronary Interventions Reporting System would increase from 14.3% with AUC/2009 to 23.2% when AUC/2012 was applied. These increases were mainly explained by the following scenario: asymptomatic patients who did not undergo previous noninvasive testing, presence of 1- or 2-vessel CAD, and no PLAD involvement (indication 18a in AUC/2009, indication 20a in AUC/2012). In AUC/2009, this clinical scenario was not rated because the panel members thought that its likelihood was very low. However, these cases would appear to be particularly inappropriate for revascularization because there is no expectation of survival benefit and no possibility of improvement in quality of life. Accordingly, in the revised version AUC/2012, such cases were rated as inappropriate (10). Therefore, the greater increase in inappropriate procedures in our registry compared with the Hannan et al. (5) study is a reflection of the unwillingness to perform previous noninvasive stress testing in Japan.

Less frequent use of noninvasive stress testing may be due to the advent of coronary CTA, which has become recognized as a useful prognostic modality (16). In fact, approximately one-third of the patients in our registry who did not undergo noninvasive stress testing underwent coronary CTA. Furthermore, the proportion of inappropriate PCIs increased substantially in parallel with the increase in the use of coronary CTA. Because appropriateness criteria assign much value to functional information in reflection of a strong tilt toward physiological assessment of ischemia in the United States, coronary CTA, which

only provides anatomic information, is not recognized as one of the previous noninvasive tests under these criteria. In recent studies, the excellent negative predictive value and acceptable positive predictive value with diagnostic use of coronary CTA have been documented (17,18), and the analyses from the CONFIRM registry have demonstrated the prognostic value of coronary CTA. Those patients with nonobstructive or obstructive CAD detected by coronary CTA had an increased risk of long-term mortality compared with those without (16), which might indicate that the risk of adverse cardiovascular events could be stratified by the extent of anatomic lesions. Additionally, subanalysis of the COURAGE trial demonstrated that the anatomic burden of coronary disease, but not ischemic burden, predicted the risk of adverse cardiovascular events (19), which emphasized the importance of anatomic as well as ischemic assessment in patients with CAD. Because such a potential impact of anatomic assessment on adverse cardiovascular outcomes has been demonstrated, we can argue that CT-based procedures can be hypothetically graded as appropriate instead of inappropriate. In our analysis, the proportion of inappropriate PCI decreased by 5% when CT-based procedures were classified not as inappropriate but as appropriate. This proportion of inappropriate PCIs was similar to the findings of earlier reports assessed using revised 2012 criteria (5). This result might demonstrate that the appropriateness of PCIs in Japan was not properly assessed according to the current criteria because the recognition of CAD was totally different from that in the United States. Further studies are needed to evaluate the appropriateness of CT-guided PCIs, which may suggest that a revision of AUC is needed.

Although revascularization for patients who show no signs of functional ischemia is not the standard of care under current guidelines (20), ischemic evaluation is likely to be performed using FFR without a previous stress test, on the basis of the results of the FAME2 (Fractional Flow Reserve versus Angiography for Multi-vessel Evaluation II) study (21). Actually in our registry, the prevalence of PCIs using FFR substantially increased, which coincided with an increase in coronary CTA use. The number of inappropriate PCIs showed an increasing trend even when the CT-based procedures were excluded (or considered appropriate). This may due to the increase in the use of FFR. Because FFR enables the evaluation of the significance of CAD in the cardiac catheterization laboratory, pre-procedural tests might have been omitted in some of the patients. Among the patients mapped to scenario 20a under

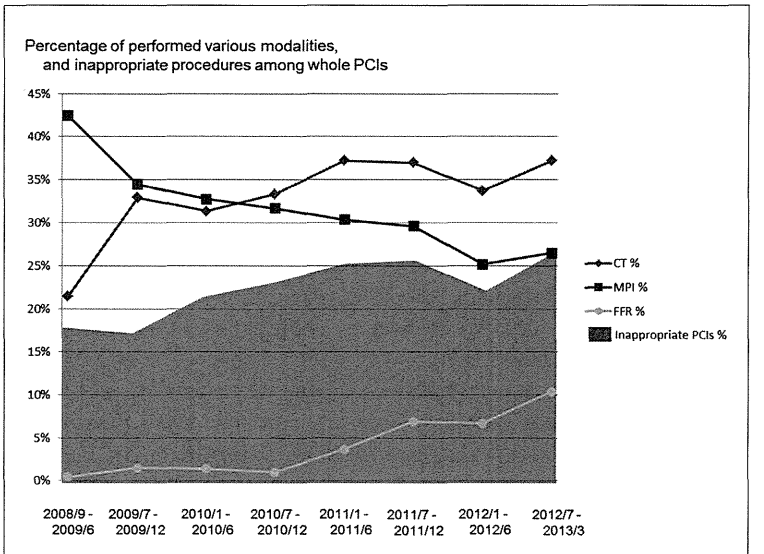

FIGURE 3 Association Between Temporal Trends of Noninvasive Testing and Frequency of Inappropriate Ratings

Gray area indicates the percentages of inappropriate procedures on the basis of original appropriateness criteria (AUC/2009). CT = computed tomography; FFR = functional flow reserve; MPI = myocardial perfusion imaging; PCI = percutaneous coronary intervention.

AUC/2012, almost one-tenth underwent FFR. This trend may indicate that methods for evaluating ischemia have been changing. However, in AUC/2009 or AUC/2012, ischemic evaluation by FFR is

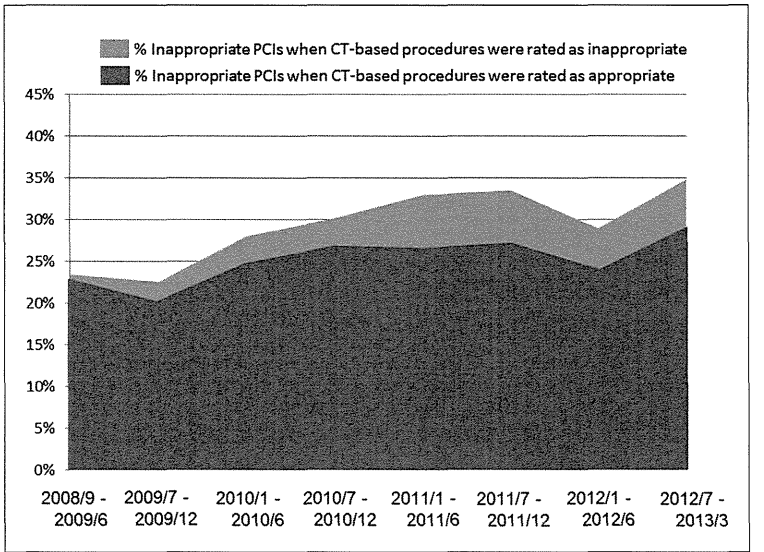

FIGURE 4 Change in the Proportion of PCIs Rated as Inappropriate When CT-Based Procedures Were Classified Not as Inappropriate but as Appropriate

Light brown indicates the trend of proportion of inappropriate PCIs when CT-based procedures were rated as inappropriate. **Dark brown** indicates the trend of proportion of inappropriate PCIs when CT-based procedures were rated as appropriate. Abbreviations as in **Figure 3**.

accepted only for 1- or 2-vessel CAD with borderline stenosis of 50% to 60%. The use of FFR in coronary artery stenosis >60% was not adjudicated, which was also mentioned in the previous study (4). In view of this, there is room for improvement in AUC/2009 or AUC/2012 to permit a more precise evaluation of appropriateness.

There are several reasons for the wide implementation of coronary CTA in Japan. First, high-technology medical equipment including CT and magnetic resonance imaging is widely available in Japan; the number of CT scanners per million people in Japan is estimated to be >7 times more than that in the United States (22). Second, there is universal health coverage in Japan, which makes it easier for patients to access medical resources. In 1961, Japan managed to extend social health insurance to the entire population and achieved universal health coverage (23). This health policy is equally applied to all healthcare facilities, and the provision of equal medical services is achieved across the entire nation. Further studies focused specifically on coronary CTA are needed to close this scientific gap in PCI indications.

STUDY LIMITATIONS. For a thorough understanding of our results, several limitations should be acknowledged. First, not all hospitals that perform PCI in Japan participate in our registry. Our registry, however, is multicenter and includes a relatively large number of procedures. We believe that this is one of the representative Japanese databases on PCI patients and that our results comprise the most complete assessment of practice patterns throughout Japan currently.

Second, the use of coronary CTA has become more widespread in Japan compared with the United States. In 2010, the percent of PCI patients evaluated with coronary CTA was >30% in Japan, whereas it was only 2.7% in the United States (8). Although there is a significant gap in the use of coronary CTA, the temporal trends of noninvasive testing, in which previous anatomic assessment has been increasing, are similar in both countries. This means that similar trends regarding appropriateness of PCIs will be highlighted in the near future in the United States.

CONCLUSIONS

In a multicenter Japanese PCI registry, approximately one-sixth of PCIs were rated as inappropriate under the AUC/2009 in nonacute settings, and the rate of inappropriate PCIs increased to approximately one-third on the basis of the revised AUC/2012. The significant changes in the inappropriate PCI rating between the 2009 and 2012 criteria may be due to the technological evolution of cardiovascular imaging, which continues to evolve in everyday cardiology practice. Further effort is needed to refine and correct the growing disconnection between the AUC and modern pre-PCI evaluation.

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KEY WORDS **appropriateness use criteria, percutaneous coronary intervention, quality of care**

APPENDIX **For supplemental tables and information, please see the online version of this article.**

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ORIGINAL ARTICLE
Cardiovascular Surgery

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

– Nationwide Analysis in Japan –

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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. RCP102±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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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 un-paired t-test or Wilcoxon rank-sum test for continuous covariates. The data are given as mean±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 PaO_2 <60 mmHg or room air $PaCO_2$ >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 confounders[13] (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±3.0°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 atheromatous 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 2weeks)	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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