**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

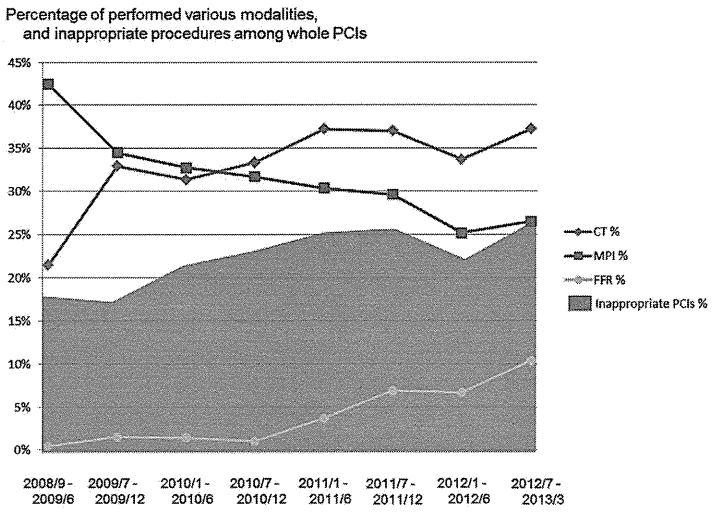


**FIGURE 3 Association Between Temporal Trends of Noninvasive Testing and Frequency of Inappropriate Ratings**

**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

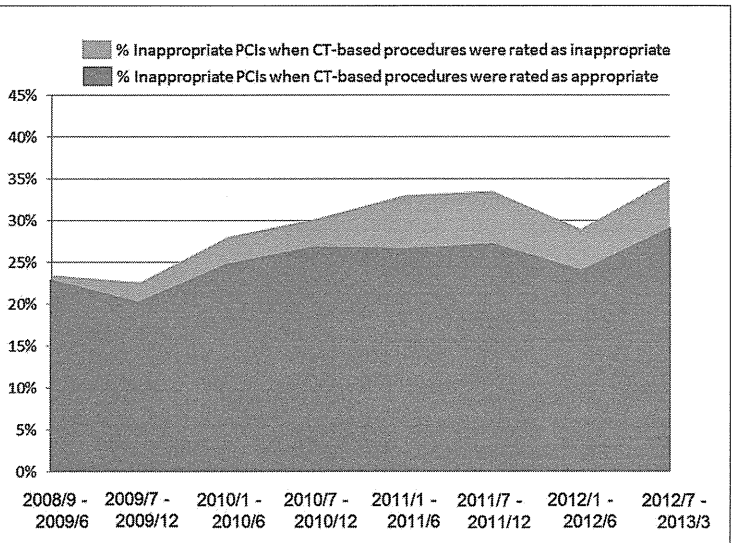


**FIGURE 4 Change in the Proportion of PCIs Rated as Inappropriate When CT-Based Procedures Were Classified Not as Inappropriate but as Appropriate**

**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 –

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. 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 >24 h | 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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REVIEW ARTICLE

# Challenges and prospects of a clinical database linked to the board certification system

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**Abstract** In Japan, the National Clinical Database (NCD) was founded in April 2010 as the parent body of the database system linked to the board certification system. Registration began in 2011, and to date, more than 3,300 facilities have enrolled and more than one million cases are expected to enroll each year. Given the broad impact of this database initiative, considering the social implications of their activities is important. In this study, we identified and addressed issues arising from data collection and analysis, with a primary focus on providing high-quality healthcare to patients and the general public. Improvements resulting from NCD initiatives have been implemented in clinical settings throughout Japan. Clinical research using such database as well as evidence-based policy recommendations can impact businesses, the government and insurance companies. The NCD project is realistic in terms of effort and cost, and its activities are conducted lawfully and ethically with due consideration of its effects on society. Continuous evaluation on the whole system is essential. Such evaluation provides the validity of the framework of healthcare standards as well as ensures the reliability of collected data to guarantee the scientific quality in clinical databases.

**Keywords** Quality improvement · Database · General surgery · Cancer registry · Certification board for expert surgeons

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## Introduction

When evaluating healthcare quality, it is important to consider the structure, process and outcome [1, 2]. However, Japan's healthcare policies have so far been evaluated mainly from the structural viewpoint of offering a system that provides plentiful medical care, i.e., on the number of institutions, physicians, specialists and nurses, on making sure that even a sparsely populated area has a medical facility and on ensuring that patients have access to specialists. This viewpoint of providing widespread medical care has a historical background [3]. In Japan, the fair distribution of medical resources has been politically emphasized in the context of universal health insurance. The equity of healthcare services in Japan is of international value, but when the service quality is referenced, it is important to systematically evaluate not only the structures of the services, but also their processes and outcomes.

To facilitate such evaluations, all surgical societies related to general surgery cooperated to establish the National Clinical Database (NCD), which systematically collects verified data in cooperation with various clinical fields so as to achieve the social responsibility of providing the highest quality healthcare possible in Japan [4, 5]. In order to evaluate the practices and performance of specialists, a committee for each specialty has been set up, and each of them identifies its framework for benchmarking.

As the surgical societies pay for all of the development and operating costs for the database, participating institutions can use the database system for free. Thus, it is mandatory for the institutions to participate in the benchmarking project when applying for the board certification system. Over 3,500 institutions were participating in the NCD in September 2012, and over 1,200,000 cases' data had been registered in 2011. The NCD, in cooperation with the specialist system, will provide important knowledge for future clinical database design and usage [6].

Without a systematic evaluation based on objective information, it is difficult for professionals to achieve social accountability. However, the Japanese healthcare system has been established through profit-sharing among specific groups, including the revision of the fee-for-service system, without fulfilling its social responsibility to weigh social advantage and costs objectively [7]. This system was formed on the basis of rapid economic growth after World War II and a pyramidal population structure.

With the slowdown in economic growth and the coming unprecedented aging society, it will not be possible to keep the current system anymore. Under these circumstances, reconfiguring the system only for a cost reduction will end up affecting its fair accessibility and the quality of the health care. First, whether the values of systematic evaluations based on verified data in the NCD will be suitable for the new society will be validated, and second, resource allocation and the development of a system structure to fulfill the values will be considered. The NCD was built as a platform not only for medical providers, but also for stakeholders, such as administrators, legislators and insurers, to allow them to provide better healthcare and to seek roles in collaboration. Using the nationwide platform, the collaboration among the stakeholders in Japan will also allow them to give useful suggestions to other countries that will face aging societies in the near future. We herein evaluate the significance and issues related to database initiatives that impact various aspects of society.

### Social significance and issues related to the database initiatives

We herein evaluate the social impact of the clinical database initiatives from the perspectives of utility, feasibility and propriety standards [8]. The utility standard involves understanding the values of those involved in the initiatives, as well as those affected by it, determining their needs and evaluating whether services are offered that address these needs. The utility standard is assessed from the perspectives of (a) clarification of the central issue, (b) comprehension of the values of those involved, (c) comprehension of the process and outcomes and (d) consideration of the impact that the initiatives have. The feasibility standard relates to verifying whether the initiatives are realistic and economically reasonable. This standard is discussed herein from the perspectives of (a) political validity, (b) realistic progression, (c) project management and (d) resource use. The propriety standard relates to whether the initiatives are carried out lawfully and ethically and whether they pay due consideration to those affected by the results, as well as those involved in the initiatives. The propriety standard is assessed from the perspectives of (a) respect for basic human rights, (b) transparency and information disclosure and (c) maintaining balance.

## The utility standard

### The central issue

Just as the United States (US) Institute of Medicine identified the concept of "healthcare for the patient" as the chief provision of the twenty-first century medical revolution [9], patient-centric considerations are also an important aspect of future healthcare. Reducing medical costs is often a central policy issue in healthcare. However, the primary aim of healthcare should be to provide the best service to patients, rather than to curb medical costs [10]. High-quality healthcare services must be provided to patients, and considering how to design and coordinate practical approaches and the healthcare provision system, such as that for remuneration, is important to achieve this goal.

A key consideration when discussing the topic of improvements in healthcare quality is to define, understand and evaluate the quality that brings to fruition the values of the patients. The existence of "specialists" in various fields implies that a different result is expected when such specialists are involved in healthcare, compared with when non-specialists are involved. Thus, to fully grasp the quality of healthcare, the different effects that result from specialist involvement must be explained from the patient's perspective. Also important is the understanding of how each specialty is defined and the extent of their involvement. This can be achieved through continuous measurements and evaluations of the structure (e.g., human and material resources, organizational structure and operational management policy), the healthcare process (e.g., diagnosis/examinations, judging treatment indications, patient transport and admission and surgery/treatments) and healthcare outcomes (e.g., short-term mortality, complications, mid- and long-term prognoses and patient quality of life) for each specialty. In this context, the central goal of the NCD is to serve as the foundation for the development of a system that provides long-term, high-quality

healthcare by interfacing with the clinical setting in terms of systematic data collection and practical analyses.

## The value of the NCD to stakeholders

### *Patients and the general public*

The benefits of the NCD for patients and the general public include their ability to receive high-quality healthcare through the improvement of the healthcare service throughout Japan. This is achieved through directives by the NCD for improvement, with the clinical setting at the forefront. By reviewing the NCD data, patients can choose facilities that suit their preferences, whether it be the presence of board certified physicians of a relevant field, or the certification of a particular facility.

### *Health care providers*

By unifying the standards of data management, health care providers in clinical settings can compare their approaches with peers throughout Japan and gain an understanding of where they stand. A risk-adjusted analysis based on nationwide data allows for one to determine and provide feedback on the information of the risks patients have beforehand. On the basis of these objective data, health care providers can then determine treatment indicators and obtain informed consent. Standardized information can be reformulated as case reports and shared at conferences. Moreover, the use of the NCD at individual facilities can reduce the burden of paperwork, for example, by providing clinical organizations with access to data for applications of certification, such as those required for board-certified physicians [11, 12]. By adding additional items and using data from one's own facility, clinical research may progress more efficiently.

### *Participating institutions*

Facility reports, in which the severity-adjusted clinical performance of a facility is contrasted with nationwide data, are periodically sent to the participating institutions. These reports can describe the characteristics of each institution and elucidate the issues that require solution. Moreover, knowing one's position among peers allows for strategic planning and proper staff management. The mere fact that a facility participates in a benchmarking project that uses NCD data is in itself a means to ensure stable quality as a facility [13, 14].

### *Clinical organizations*

Maintaining a clinical database as per the unified standards and definitions allows clinical organizations to improve their understanding of the actual performance of various fields, particularly when unified standards and definitions exist. Not only do unified standards increase the reproducibility of the collected data, they also ensure scientific accuracy. The large sample size offered by the database further paves the way for various types of research designs. Moreover, accurate information, as well as insight into the implementation status of various treatments and their effects, allows clinical organizations to provide policies and recommendations on the evidence-based board certification of physicians, their effective placement, improvement of their work environments and setting remuneration schedules. By serving as the driving force for efforts to improve the quality of healthcare, clinical organizations, as groups of specialists, can broadly appeal to the utility of certified facilities and the significance of board certified physicians to society, and at the same time, achieve accountability to society.

International collaboration is important to evaluate the quality of healthcare and produce meaningful results. The aim of the collaboration is to compare the incidence rates of diseases, the treatment trends and the outcomes and to identify factors that explain the differences. The NCD was developed in collaboration with the leadership of the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP), which adopted a similar goal of developing a standardized surgery database for quality improvement and investigation. The core members of the NCD joined the meetings and seminars of the ACS NSQIP to discuss various issues related to a large clinical database, including the data collection methods, data feedback and public relations. In addition, the NCD implemented the same variables as those of the ACS NSQIP to facilitate future international cooperative studies. This collaboration is expected to lead to potential global benchmarking and further collaborative efforts to evaluate and improve clinical practices.

### *Pharmaceutical/medical device companies*

Research collaborations with clinical organizations will allow pharmaceutical and medical device companies to more rapidly carry out trials and post-marketing surveillance of pharmaceutical products and medical devices. Trials based on the NCD will decrease the costs associated with clinical trials and provide opportunities to obtain information on unregistered patients, thereby improving the scientific quality of the research. Moreover, when randomization is ethically difficult, data from the cases in the clinical database can be used to generate a control group, making it easier to determine the effects of interventions. For post-marketing surveillance, information on the effects and use of medical devices and drugs is valuable

for the development and promotion of more effective drugs and devices.

*Government and insurance companies*

A lack of understanding regarding healthcare quality indicators may result in the provision of low-quality care that increases the overall costs because it results in expensive postoperative adverse effects and higher rates of complications and mortality. Previous studies have reported that decreases in the mortality rates and incidence of adverse events through benchmarking activities can help cut down medical costs [15, 16]. Therefore, taken together, the coordinated efforts of the NCD, which carries out clinically led benchmarking activities, may benefit the government and insurers.

Processing and reporting results

*Benchmarking reports*

As discussed above, a report is periodically distributed to participating facilities and provides data on each facility's severity-adjusted clinical performance in comparison with the national data. The report is formatted in a way that makes the patient characteristics evident. In the cardiac surgery field, a web-based program already provides feedback on severity-adjusted clinical performance [17]. Real-time feedback through the web provides an opportunity to observe changes within facilities and shifts in clinical performance instantaneously.

*NCD and the board certification system*

Data registered with the NCD can be used to design evidence-based board certification systems. In addition to easy tracking of clinical performance, source data acquisition will also become easier, as the system streamlines the need to apply for source data and its usage. Through appropriate data registration, it will also be easier for facilities to become certified or considered an "associated facility" by achieving stable performance. With an effective certification system, the clinical performance data required for the certification process can be readily obtained, and performance comparison and on-site audits using source data can be conducted. For the most part, the current Japanese system focuses on the clinical experience of board-certified physicians. Coordinating with the NCD may enable these organizations to operate on the basis of the parameters that better reflect the clinical reality, including the severity-adjusted clinical performance and the rate of use of appropriate clinical treatments.

*Communication within the clinical settings*

From various perspectives, including reporting the results of the data analyses, status of database operations, policy measures through the NCD, improvements in entry items and interfaces and supporting each facility's efforts, the NCD and facilities of various fields will need to share information and communicate to operate at an advanced level. Periodic meetings, such as symposia and scientific conferences, in addition to the use of the web and e-mail, provide opportunities to share information and increase awareness. Furthermore, the formation of region- or topic-specific groups will promote NCD-related activities. These activities will enable organizations to introduce and share the best practice recommendations in the participating clinical departments.

*Progress reports to patients and the government*

Periodic reports for patients and government officials will ensure the impartiality of NCD-related activities. To this end, the NCD has established a group of outside experts (e.g., patients and specialists of law and information) to provide such reports. Moreover, when outside organizations provide funding, conflicts of interest must be considered. When institutional support is required to provide high-quality healthcare, policy recommendations must be coordinated among the members of the government, legislature and patients.

Considering various influences

In addition to prioritizing and appropriately designing NCD benchmarking efforts in various disciplines, an understanding of the overall clinical performance and the temporal transition of clinical processes is important. For instance, when a new treatment is widely used, the database must be kept current to understand and follow the impact of this treatment. For clinical performance evaluations, if inter-facility differences in perioperative mortality become small, the focus will need to be placed on a different complication with a larger disparity between facilities, and initiatives that consider this new area of investigation will be needed. Negative influences must be considered as well. In other countries, different benchmarking stances have had a major impact on patient selection, for example, the treatment of critically ill patients may be avoided, or patients may be discharged early or transferred to different departments [18, 19]. Continuous assessment of the impact of the NCD may help to prevent such occurrences in Japan. When clinical organizations offer recommendations to the government or other institutions, the consequences and effects of these recommendations must be monitored. This would allow for

before-and-after comparisons of certified facilities with regard to patient transfer and the impact of certification on the clinical performance [20, 21].

## The feasibility standard

### Political validity

The NCD was established in April 2010 as a general incorporated association in partnership with several clinical organizations (http://www.ncd.or.jp). By participating as members of various NCD divisions, leaders of various organizations and those in charge of the board certification system can continuously guarantee partnerships with the leadership of various disciplines and the board certification system. However, NCD operations are free from the influence of other stakeholders, such as the government and businesses. Although donations from businesses and government research grants can help fund NCD-related activities, these are used in a manner that secures the independence of NCD operations.

### Realistic progression

In order for NCD operations to continue successfully, it may be beneficial for the various specialty divisions to divide roles among themselves and to collaborate in performing the day-to-day operations. Independent NCD divisions are already in place for continuous coordination with the board certification system in each field. The data management and analysis secures the scientific quality of the data and analysis, systems management ensures the continuity and security of information systems and investigation of the legality and ethicality of activities aids in securing resources and preparing budget plans.

Particularly important is the development of a system that allows for easy data entry and reduces the burden on those entering the data. To this end, case registration in the NCD is based on an easy-to-use web system. The results of a questionnaire survey of various clinical departments registered with the NCD indicated that 63 % of respondents entered information directly via the web while referring to medical records (i.e., source data: Table 1), and 52 % entered information in real-time or immediately upon finalization of the information without delay (Table 2). Moreover, the survey revealed that data entry was performed at common hospital computer terminals or on individuals' personal computers in most cases. In 3.1 % of clinical departments, data entry was performed at an operating room computer terminal (Table 3); however, entering data onto the web while referring to source data was difficult for some departments. Therefore, information was written on paper first and entered into the system later (Table 1). The Case Report Form developed by the NCD is useful in such situations.

**Table 1** The input method (multiple answers allowed, $n = 2{,}123$)

| | *n* | % |
|---|---|---|
| Direct data entry via the Web while referencing medical records | 1,344 | 63.3 |
| Data entry after first accumulating data in the department's database (e.g., FileMaker, Access) | 458 | 21.6 |
| Data are first written on case report forms (CRFs; data entry manuals) and then registered | 438 | 20.6 |
| Departmental information systems, such as electronic medical charts, are first revised to be compatible with the NCD before data entry | 175 | 8.2 |
| Others | 37 | 1.7 |

**Table 2** Timing of data entry ($n = 2{,}123$; as of January 13, 2012)

| | *n* | % |
|---|---|---|
| Register case information in real-time to the extent possible | 503 | 24 |
| Register case information upon finalization of information | 598 | 28 |
| Case information is collected and entered periodically | 1,022 | 48 |

**Table 3** Location of data entry (multiple answers allowed, $n = 2{,}123$)

| | *n* | % |
|---|---|---|
| Common terminal other than a hospital terminal | 1,156 | 54.5 |
| Personal computer | 1,081 | 50.9 |
| Hospital terminal outside the operating room | 325 | 15.3 |
| Operating room terminal | 65 | 3.1 |
| Others | 50 | 2.4 |

In order to avoid the burden on physicians, the NCD allows data entry by various medical staff members in each department. NCD data entry privileges allow people other than physicians to enter the data. Table 4 lists the data entry workers utilizing the NCD as of January 13, 2012. Although the department chair entered information in 58 % of the departments, a medical information manager entered information in 10.2 % and a medical administrative assistant did so in 35.1 % of departments. Importantly, either the department chair or a physician designated by the department chair must approve each case for data entry when somebody other than a physician enters the data to secure the data accuracy. Before the initiation of the database, tests were conducted in various relevant areas to determine the user needs. As a result, an easy-to-use

**Table 4** Data enterer (multiple answers allowed, $n = 2,123$)

| | *n* | % |
|---|---|---|
| Department chair | 1,125 | 53.0 |
| Department-affiliated physician (other than department chair) | 1,232 | 58.0 |
| Department-affiliated resident | 113 | 5.3 |
| Physician affiliated with different department | 7 | 0.3 |
| Nurse | 13 | 0.6 |
| Medical information manager | 216 | 10.2 |
| Medical administrative assistant | 745 | 35.1 |
| Others | 60 | 2.8 |

system with an error identification component was developed. Efforts to improve the system continue today in the form of a questionnaire on the web that solicits comments on how to improve the system.

Management plan

A database cannot operate on its own if no data are entered, regardless of whether the system is ready for operation. As its name suggests, a clinical database requires the entry of technical and clinical information, which can be time-consuming. Securing funds for labor costs associated with data entry for each department is no simple task in Japan. Therefore, consistent with this, data are often entered by the physicians themselves. In the NCD, data entry is performed by workers of various backgrounds (Table 4). Continuous sharing of high-quality data requires the securing of funding and personnel to enter the data. In addition, the data must be verified. To address this issue, NCD-registered hospitals throughout Japan have been requested to provide continuous support and understanding of the processes involved in maintaining such a huge database. For example, large hospitals may perform examinations that might not be carried out at small-scale facilities. Therefore, data from such examinations cannot be included as entry items in the database. Thus, an important consideration is the verification of whether entry items and the entry system are realistic for each participating institution. Moreover, because the clinical database documents medical treatments, database items and options inevitably change with advances in surgery and changes in treatment. Depending on when the entry items are revised, the entered data may no longer be used; therefore, frequent revisions without careful planning must be avoided. This underscores the importance of entry item management.

Resource use

By unifying the standards and digitizing the medical record systems in each participating facility, the costs related to data collection may be minimized. In addition, incorporating a program that extracts clinical information other than that requiring a physician's judgment into the database would decrease the burden associated with data entry. In this way, the clinical database may be most efficiently developed in conjunction with developments in medical record systems.

## The propriety standard

Respecting basic human rights and consensus building

*Ethical guidelines and study types*

The NCD is grounded on the framework of observational studies. Therefore, no additional tests or surgery, or even a prolonged length of stay, are required for the institution to participate, and the registration of patient information does not influence the treatments. Projects that do not involve documenting actual events are bound by the Ethical Guidelines for Epidemiological Research developed by the Japanese Ministry of Education, Culture, Sports, Science, and Technology and the Ministry of Health, Labour and Welfare [22]. For interventional studies, such as randomized-controlled trials, comprehensive registration in the NCD may be desirable [23]. In such cases, a new review based on the Ethical Guidelines for Clinical Research must be conducted [24]. Even within the framework of observational studies, broadening registration details and targeting certain disorders can change the nature of the management and operation of clinical databases. Changes that are particularly pronounced may warrant further ethical review, and project implementation may be reconsidered in light of independent valuations.

*Patient consent*

The patient intentions must be respected when considering the pros and cons of data registration. This can involve obtaining explicit verbal or written consent from participants (opt-in) [23], or not obtaining consent, but accepting a patient's explicit refusal to participate (opt-out) [25]. Only when these conditions are satisfied can clinical databases adopt the opt-out system. A few points are worth noting in this regard. First, clinical databases operate for the purpose of medical and public health research [26]. Second, clinical databases operate under the principle that the risk to participating patients is minimal [27]. Finally, clinical databases must guarantee that patients are given the opportunity to learn about the purpose of registration and the type of information registered [28]. The NCD has adopted the opt-out system and broadly discloses the

purpose of registration and the type of registered information. Moreover, to support the efforts of various clinical departments, the NCD provides web-based templates and explanatory material. However, when interventional studies (e.g., clinical trials) are conducted using the NCD infrastructure, a sufficient explanation must be provided to patients, and their explicit consent must be obtained.

*Information security*

The NCD data entry system is managed and operated via the web. Occasionally, a tradeoff may exist between the benefits of using the web and the associated risks, such as information leakage. The NCD data entry system uses an ID and password system, and the department chair of every participating facility has the authority to issue IDs. Users are notified about the password management policy; however, given that desirable security standards change as technology advances, the possibility that the evaluation standards at one point may not necessarily be valid in the future must be considered. In such situations, clearly articulating new policies on information management and operations is important. By complying with the disclosed policies, and the contents and measures therein, when issues arise, information system managers and operators can achieve a certain degree of accountability.

*Use of personal information*

Clinical databases must adhere to laws related to the protection of personal information. Various types of personal information, including (1) identifiable non-anonymous data, (2) identifiable anonymous data and (3) non-identifiable anonymous data require different considerations. In addition to patient information, the NCD includes information on participating facilities, as well as the health care providers involved in the treatment. Thus, the data management system and data use must be carefully considered. The American Association of Thoracic Surgery accepts analysis plans from applicants, and rather than source data, it principally feeds back the results of the analyses [29]. The Japanese Association of Thoracic Surgery has adopted a similar policy.

In view of the sensitivity of such information, the parent operating body of the NCD has established an ethics committee comprising outside experts. This committee includes members of the Japanese Surgical Society ethics board, lawyers, patient representatives and experts on information security. This ethics committee was requested to consider the ethical propriety of the entire initiative, and the progress of the review process was made public on the Japan Surgical Society website [30]. Thus, rather than merely undergoing a review, the contents of the discussion were made public, clarifying for the public the measures taken to address ethical issues. In addition, the NCD requested that the participating facilities undergo a review of ethical propriety regarding case registration in the form of facility director approval or a review from the facility's ethics committee. Because some participating facilities may not have ethics committees, the NCD made it possible to submit to a review by the NCD ethics committee. Since the review of ethical propriety must occur without delay, an application template was designed for ethics committee review and is available on the NCD website. As of January 2012, most participating facilities had received approval from a facility director.

Transparency and disclosure

*Data usage*

It becomes necessary to accept/adopt a fair stance for data usage. For example, in particular, covering up information that would be disadvantageous for certain facilities or businesses, or disclosing only advantageous information, may lead to conflicts of interest. Transparency must be guaranteed. Therefore, disclosure of information regarding the standards for data usage and rule of publication are important.

*Publicizing the results of the data analyses*

Further, the standards for publicizing the results of the data analyses need to be established. When performing severity adjustments, as in the US, where additional remuneration is provided on the basis of a department's clinical performance, the details and how severity adjustment is carried out must be disclosed [31]. In some cases, applicants who wish to use data may retain the results as internal documents without publicizing them. It is difficult to determine whether such decisions are made because secrecy would be advantageous, or whether the results are simply not worthy of public disclosure. However, certain standards need to be in place from the perspective of fairness.

Maintaining balance

*Unifying the standards for evaluating clinical performance*

Standards must be applied for evaluating the clinical performance of departments whose data are registered with the NCD. For instance, when choosing "mortality rate" as a clinical performance indicator, one facility may narrowly define the mortality rate as intraoperative mortality, whereas others may broadly define it as the 30-day postoperative mortality. Some facilities may even exclude periods in which an abnormally high number of deaths

**Table 5** Participating facilities/number of departments (as of April 5, 2012)

| | Facilities | |
|---|---|---|
| | *n* | % |
| Hokkaido/Tohoku | 437 | 13.0 |
| Kanto | 942 | 27.9 |
| Chubu | 495 | 14.7 |
| Kinki | 650 | 19.3 |
| Chugoku | 252 | 7.5 |
| Shikoku | 142 | 4.2 |
| Kyushu/Okinawa | 454 | 13.5 |
| Total | 3,372 | |

occur. Even with raw mortality rates, the meaning differs between facilities that treat severe illnesses and those that only treat mild ailments. Therefore, the clinical performance must be fairly evaluated to avoid distrust among the participating facilities. Balanced information sharing can achieve this goal.

*Fairness of participation*

The NCD intends to improve the quality of healthcare throughout Japan. Because data registration is a condition for obtaining board certification, securing fairness is particularly important. In the US, many businesses pay millions of dollars each year to participate in clinical databases. However, in payment-based systems, the fairness of participation cannot be guaranteed, and coordination with board certification systems is difficult as well. Given the large number of small facilities in Japan, purchasing software for each department within a participating facility is not economically feasible. The NCD data entry software program was developed for use by all facilities and is distributed for free. Therefore, since the beginning of registration on January 1, 2011, more than 3,300 participating facilities have registered with the NCD as of April 2012 (Table 5).According to an administrative cross-country study of medical facilities by the Ministry of Health, Labour and Welfare, surgery under general anesthesia was conducted in 4,519 facilities in Japan [32]. The number of registered facilities by the Japan Surgical Society was 2,143 as of March 2012. [33] Therefore, a large proportion of the Japanese facilities in which surgeries are conducted participate in the NCD.

## Conclusions

The coordination of a nation-wide clinical registry, such as the NCD in Japan, with board certification systems in various medical disciplines will positively impact society through their activities. The social implications of the activities must be considered. By identifying and addressing issues that arise from analyzing data, the clinical setting will drive improvements in healthcare quality. The central theme of clinical database activities is the provision of high-quality healthcare to patients and the general public. Clinical research and evidence-based policy recommendations based on the data from this database may positively impact businesses, the government and insurers. Initiatives may be evaluated to assess whether they are realistic and reasonably economical in comparison with the previous initiatives, in order to guarantee that they are conducted lawfully and ethically and to ensure that they pay due consideration to all the stakeholders involved. To ensure this, the continuity and responsibility of activities require continuous evaluation.

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