Contemporary Outcomes of Surgical Aortic Valve Replacement in Japan

Yoshiyuki Tokuda, MD, PhD; Hiroyuki Yamamoto, MD, PhD; Hiroaki Miyata, PhD; Akihiko Usui, MD, PhD; Noboru Motomura, MD, PhD; The Japan Cardiovascular Surgery Database Organization

Background: Given the rapid expansion in the use of transcatheter aortic valve implantation (TAVI), recent outcomes of surgical aortic valve replacement (SAVR) should be re-evaluated.

Methods and Results: Using the data from the Japan Cardiovascular Surgery Database of 160 enrolled hospitals, trends in elective isolated SAVR were evaluated until the introduction of TAVI in Japan. Trend analyses were performed over 4 periods: period 1, 2008–2009 (4,415 cases); period 2, 2010–2011 (4,861 cases); period 3, 2012–2013 (5,674 cases); and period 4, 2014–2015 (5,563 cases). Baseline risk, evaluated on JapanSCORE, increased significantly over the 4 periods, from a median of 1.56 (IQR, 0.99–2.61) in period 1 to 2.08 (IQR, 1.33–3.96) in period 4 (P<0.001, trend test). Despite the increased risk, the composite major complication and operative mortality rate decreased significantly (10.7% in period 1 to 9.2% in period 4, P=0.01). Using a risk-adjusted model, the OR of operative mortality was 1.61 (95% CI: 1.29–2.02) in period 1 (P<0.0001) compared with period 4. An increase in the use of bioprostheses was also observed, from 60.4% to 76.8% (P<0.001) over the 4 periods.

Conclusions: Even in a short 8-year period, SAVR outcomes improved in Japan. This should be taken into account when discussing the indications for aortic valve intervention.

Key Words: Aortic valve replacement; Japan Cardiovascular Surgery Database; JapanSCORE; Transcatheter aortic valve implantation

In recent years, transcatheter aortic valve implantation (TAVI) has been established as a less invasive alternative to surgical aortic valve replacement (SAVR).1,2 Although TAVI has been used predominantly for patients at high risk or with old age who were not considered optimal candidates for SAVR, its indication is now expanding toward a low-risk profile and younger age.3,4 Progress in SAVR has also been made. Cardiopulmonary bypass-related complications have been well recognized, and concepts of fast track recovery have been widely introduced. Knowledge of the potentially lethal complications (i.e., deep sternal wound complications, acute kidney injury, stroke, bleeding) has increased, thus ensuring better postoperative results.

To adequately assess appropriate indications for aortic valve intervention, it is necessary to know the contemporary results of SAVR procedures. Recent data on outcomes after SAVR, however, are limited and were mainly obtained from reports on randomized, controlled trials comparing SAVR and TAVI, with many exclusion criteria.5 Possible changes in recent outcomes need to be re-evaluated. The aim of this study was to analyze recent trends in patient characteristics and outcomes of SAVR in the real-world situation in Japan. The Japan Cardiovascular Surgery Database (JCVSD), a national registry in Japan, was used to evaluate the outcomes.

Methods

JCVSD

The JCVSD is a national database used to assess surgical outcomes after cardiovascular procedures on a multicenter basis throughout Japan. The JCVSD adult division currently captures clinical information from 99% of Japanese hospitals performing cardiovascular surgery (as of 2017).6 The data collection form has a total of >250 variables (definitions available online at http://www.jacvsd.umin.jp), which are derived from those in the Society of Thoracic Surgeons (STS) National Database (definitions available online at http://sts.org). The methods used for data collection for the JCVSD have been described previously.7 Data collection achieved a high completion level, with missing
### Table. Patient Background Characteristics and Surgery Outcomes

| Period 1 | Period 2 | Period 3 | Period 4 | Trend test P-value |
|----------|----------|----------|----------|--------------------|
| 2008–2009 | 2010–2011 | 2012–2013 | 2014–2015 | n=4,415 | n=4,861 | n=5,674 | n=5,564 | n=4,415 | n=4,861 | n=5,674 | n=5,564 |
| **Background characteristics** | **Period 1** | **Period 2** | **Period 3** | **Period 4** | **Period 1** | **Period 2** | **Period 3** | **Period 4** | **Period 1** | **Period 2** | **Period 3** | **Period 4** |
| JapanSCORE | 1.56 (0.99–2.61) | 1.70 (1.05–2.81) | 1.80 (1.20–3.22) | 2.08 (1.33–3.96) | <0.001 |
| Age category (years) | | | | |
| ≤59 | 766 (17.3) | 640 (13.2) | 670 (11.8) | 574 (10.3) | | | | | | | | |
| 60–64 | 461 (10.4) | 515 (10.6) | 445 (7.8) | 409 (7.4) | | | | | | | | | |
| 65–69 | 630 (14.3) | 580 (11.9) | 698 (12.3) | 669 (12.0) | | | | | | | | | |
| 70–74 | 928 (21.0) | 928 (19.1) | 1,037 (18.3) | 1,057 (19.0) | | | | | | | | | |
| 75–79 | 942 (21.3) | 1,150 (23.7) | 1,360 (24.0) | 1,399 (25.1) | | | | | | | | | |
| ≥80 | 688 (15.6) | 1,048 (21.6) | 1,464 (25.8) | 1,456 (26.2) | | | | | | | | | |
| Sex (male) | 2,325 (52.7) | 2,536 (52.2) | 2,819 (49.7) | 2,806 (50.4) | 0.004 |
| DM treatment | 757 (17.1) | 904 (18.6) | 1,209 (21.3) | 1,249 (22.4) | <0.001 |
| Renal failure | 409 (9.3) | 537 (11.0) | 858 (15.1) | 1,291 (23.2) | <0.001 |
| Chronic dialysis | 268 (6.1) | 356 (7.3) | 440 (7.8) | 561 (10.1) | 0.154 |
| Cardiogenic shock | 90 (2.0) | 76 (1.6) | 88 (1.6) | 111 (2.0) | 0.003 |
| NYHA functional class | | | | |
| III | 690 (15.6) | 745 (15.3) | 698 (12.3) | 711 (12.8) | <0.001 |
| IV | 85 (1.9) | 103 (2.1) | 105 (1.9) | 133 (2.4) | 0.201 |
| Three-vessel CAD | 39 (0.9) | 60 (1.2) | 131 (2.3) | 142 (2.6) | <0.001 |
| EF >60% | 2,753 (62.4) | 3,104 (63.9) | 3,754 (66.2) | 3,740 (67.2) | <0.001 |
| EF 30–60% | 1,536 (34.8) | 1,644 (33.8) | 1,803 (31.8) | 1,721 (30.9) | <0.001 |
| EF <30% | 122 (2.8) | 153 (3.1) | 164 (2.9) | 160 (2.9) | 0.866 |
| Mitral regurgitation ≥2 | 1,027 (23.3) | 1,086 (22.3) | 1,294 (22.8) | 1,398 (25.1) | <0.001 |
| Mitral regurgitation ≥3 | 113 (2.6) | 158 (3.3) | 163 (2.9) | 203 (3.6) | 0.009 |
| Tricuspid regurgitation ≥2 | 663 (15.0) | 716 (14.7) | 892 (15.7) | 923 (16.6) | 0.010 |
| Tricuspid regurgitation ≥3 | 67 (1.5) | 94 (1.9) | 77 (1.4) | 86 (1.5) | 0.487 |
| Aortic stenosis | 2,900 (65.7) | 3,461 (71.2) | 4,265 (75.2) | 4,198 (75.4) | <0.001 |
| Rheumatic valvular disease | 214 (4.8) | 188 (3.9) | 246 (4.3) | 235 (4.2) | 0.33 |
| Atrial fibrillation | 252 (5.7) | 273 (5.6) | 353 (6.2) | 286 (5.1) | 0.413 |

**Postoperative Outcomes**

| **Operative mortality** | 95 (2.2) | 97 (2.0) | 125 (2.2) | 97 (1.7) | 0.241 |
| **Composite major complication and operative mortality** | 473 (10.7) | 532 (10.9) | 528 (9.3) | 512 (9.2) | 0.001 |

**Major complications**

| **Stroke** | 58 (1.3) | 76 (1.6) | 88 (1.6) | 100 (1.8) | 0.070 |
| **Newly required dialysis** | 65 (1.5) | 82 (1.7) | 82 (1.4) | 81 (1.5) | 0.671 |
| **Prolonged ventilation** | 244 (5.5) | 267 (5.5) | 199 (3.5) | 179 (3.2) | <0.001 |
| **Deep sternal wound infection** | 62 (1.4) | 54 (1.1) | 57 (1.0) | 52 (0.9) | 0.025 |
| **Reoperation for bleeding** | 134 (3.0) | 151 (3.1) | 164 (2.9) | 158 (2.8) | 0.442 |

Data given as median (IQR) or n (%). CAD, coronary artery disease; CLD, chronic lung disease; DM, diabetes mellitus; EF, ejection fraction; IE, infective endocarditis; NYHA, New York Heart Association; PCI, percutaneous coronary intervention.
data representing <2% of all assembled data. The accuracy of submitted data was maintained by a data audit; this was achieved by random, monthly visits by administrative office members to a participating hospital to check data against clinical records.

### Subjects

For the present study, use of data from the period 2008–2015 was approved by the Data Utilization Committee of the JCVSD. Following JCVSD approval in November 2016, data analysis was undertaken and completed in December 2017. Elective isolated SAVR performed between 1 January 2008 and 31 December 2015 was examined. SAVR with other concomitant procedures were excluded, but SAVR with additional aortic root enlargement techniques (such as Nicks or Manouguian procedures) were included, because such techniques are part of SAVR. Throughout the study period, the number of institutes participating in JCVSD increased dramatically. For an appropriate trend analysis, only SAVR performed at institutes participating in JCVSD from the initial period, before January 2008 (160 hospitals), were included; thus, this was not a complete nationwide analysis. Records missing critical information such as 30-day status were also excluded. After cleaning the data, the population for analysis consisted of 20,514 cases of elective isolated SAVR. To evaluate the trend in preoperative characteristics and outcomes during the period, patients were divided into 4 groups based on the timing of operation: period 1, January 2008–December 2009; period 2, 2010–2011; period 3, 2012–2013; and period 4, 2014–2015.

### Endpoints

The definitions of postoperative outcome, including various postoperative complications, were based on the JCVSD protocol. Operative mortality was the primary endpoint and defined as in-hospital mortality or death ≤30 days after operation (whichever was longer). The composite endpoint of surgical mortality or major morbidity was also used in the risk analysis of surgical outcomes. Using a definition from previous studies, major morbidity was defined as any of 5 postoperative in-hospital complications: stroke; reoperation for bleeding; need for mechanical ventilation >24h postoperatively due to respiratory failure; renal failure with newly required dialysis; or deep sternal wound infection (mediastinitis).8–10

### Statistical Analysis

Statistical analysis was performed using STATA 15 (STATA Corp., College Station, TX, USA). Continuous variables are presented as median (IQR). Categorical variables are presented as n (%). Two-tailed P<0.05 was considered significant. Cochran-Armitage trend test was used for the trend analysis.

Preoperative risk was also evaluated for expected operative mortality using the JapanSCORE.11 The risk-adjusted OR for operative mortality over the study periods were evaluated on multivariable logistic regression modeling using a generalized estimation equation. To adjust for patient-level risk factors, the variables used in JapanSCORE were utilized.11 The variables selected based on JapanSCORE for risk adjustment were as follows: age category (5-year age group); diabetes mellitus (DM) treatment; renal dysfunction; chronic dialysis; active infective endocarditis; chronic lung disease (CLD); cerebrovascular disease; carotid stenosis; peripheral vascular disease; thoracic aortic lesion; history of percutaneous coronary intervention; history of valve operation; inotropic agent required; congestive heart failure; cardiogenic shock; unstable angina symptoms; New York Heart Association functional class (≥3); 3-vessel coronary artery disease; impaired left ventricular function (ejection fraction <60%); and tricuspid insufficiency (≥2).
Discussion

The present study showed that the background risks in SAVR patients have increased during this short 8-year period to 2015. Despite the increased risk, the composite major complication and operative mortality rate decreased. In particular, decreases in deep sternal infection and prolonged ventilation were noted. Decreases in risk-adjusted mortality were also significant.

Early valvular intervention is strongly recommended in symptomatic patients with severe aortic stenosis (AS) because of the dismal spontaneous prognosis. AS severity is best described by the specific numerical measures of maximum velocity, mean gradient, and valve area as assessed on echocardiography. Occasionally, the assessment of the severity of AS in patients with a low mean gradient may be challenging. In general, however, valve area of 1.0cm², maximum jet velocity of 4m/s, and mean gradient of 40mmHg can be used as the clear-cut definitions of severe AS in adults. The current guideline of the American Heart Association includes a class IIa recommendation for TAVI for intermediate-risk patients and class Ia for patients with symptomatic severe AS with high or prohibitive risk for SAVR. Additionally, recent trials showed similar or even better outcomes for low–intermediate-risk patients who underwent TAVI compared with SAVR. The present study has confirmed the recent continuous improvement of SAVR outcomes.

Although a rapid expansion in the use of TAVI occurred worldwide, according to the present study, SAVR can still represent the primary treatment modality of choice in patients with AS. Especially for intermediate-low-risk patients, the risk–benefit balance of each procedure (SAVR and TAVI) should be thoroughly evaluated for each individual patient. The procedural risk of TAVI depends greatly on patient anatomy. Potential risks of rare but lethal complications of TAVI need always to be investigated, usually on computed tomography. For example, the risk of coronary obstruction depends on coronary arterial height, the size of the sinus of Valsalva (narrow root), and the degree of calcification of the valve leaflets (presence of bulky cusps). The risk of annular rupture is known to be related to sub-annular calcification. Moreover, procedural difficulty increases if patients have the following access problems: horizontal aorta, tortuous aorta, or poor peripheral access. In cases of such TAVI-specific anatomic risks, SAVR becomes the preferred option.

In contrast, there were certain cases in which TAVI was preferred regardless of surgical risk score. For example, there were known risk factors of SAVR not included in the surgical risk models. Such factors included previous cardiac surgery with patent mammary artery grafts, porcelain aorta, or the presence of malignant disease or immunocompromised status. In such cases, TAVI will be the preferred option. Although the midterm durability of transcatheter bioprostheses is encouraging, the long-term durability remains largely unknown. Mechanisms that contribute to TAVI degeneration include valve crimpling, balloon expansion, stent under-expansion, and valve thrombosis.
With expected improvements in TAVI valve construction and deployment techniques, the long-term durability may improve as well; but until the long-term outcomes are better understood, TAVI should be performed with caution. Procedural risks of both types of procedure should be well evaluated by experienced heart teams from the technical viewpoint, and the evaluation should not be based solely on the conventional surgical risk score models.

The present study noted a significant improvement in outcomes of SAVR during an 8-year period, but did not clearly identify the reasons for the improved outcomes. The surgical mortality of SAVR in the varying background-risk patients, including high-risk patients, became 1.7% in period 4 in the present study. In recent international trials, 30-day surgical mortality of isolated SAVR in low-risk patients was between 1.1 and 1.3%. Presumably, the improvement in outcomes is due to multiple improvement bundles, rather than to a single factor. Concepts of fast track recovery and early ventilator weaning have been widely introduced. Guideline-based multiple measures to prevent wound complications have also been recognized. Knowledge of other postoperative pathophysiologies including coagulopathy, kidney injury, and neurologic injury have increased. Moreover, the Japanese Society for Cardiovascular Surgery started an education program in 2014 for quality improvement of operative techniques using JCVSD, and this improved the outcomes of period 4 to some extent. These multiple factors have potentially contributed to the improvements in patient care. We therefore note that progress in SAVR could occur faster than expected, given the improvement observed even in this short 8-year period.

**Study Limitations**

The present study had certain limitations owing to the nature of the JCVSD. First, no long-term follow-up data on survival or valve-related events could be obtained. All outcomes were restricted to in-hospital outcomes or death ≤30 days after operation. Furthermore, TAVI was officially approved in Japan at the end of 2013. According to the annual Japan Transcatheter Valve Therapies report (available online at http://www2.convention.co.jp/jtvt), the number of TAVI performed nationwide was 98 during period 3, 1,231 in period 4. Thus, TAVI was virtually unavailable prior to period 4 in the present study. As such, the present study did not largely reflect the potential changes in the risk profiles and outcomes of SAVR patients after the introduction of TAVI.

**Conclusions**

Despite the limitations in the present study, contemporary outcomes of SAVR have improved. Continuous improvement in this short-term 8-year period suggest possible further improvement of outcomes in the future. The present results should be taken into account when discussing the indications for aortic valve intervention.

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**References**

1. Mack MJ, Leon MB, Smith CR, Miller DC, Moses JW, Tupe EM, et al. 5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): A randomised controlled trial. Lancet 2015; 385: 2477–2484.
2. Leon MB, Smith CR, Mack MJ, Makkar RR, Svensson LG, Kodali SK, et al. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. N Engl J Med 2016; 374: 1609–1620.
3. Thyregod HG, Steinbrüchel DA, Ihlemann N, Nissen H, Kjeldsen BJ, Petursson P, et al. Transcatheter versus surgical aortic valve replacement in patients with severe aortic valve stenosis: 1-year results from the All-Comers NOTION Randomized Clinical Trial. J Am Coll Cardiol 2015; 65: 2184–2194.
4. Mack MJ, Leon MB, Thourani V, Makkar R, Kodali SK, Russo M, et al. Transcatheter aortic valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med 2019; 380: 1695–1705.
5. Fujita B, Ensinger S, Bauer T, Möllmann H, Beckmann A, Bekeredjian R, et al. Trends in practice and outcomes from 2011 to 2015 for surgical aortic valve replacement: An update from the German Aortic Valve Registry on 42,776 patients. Eur J Cardiothorac Surg 2018; 53: 552–559.
6. Daimon M, Miyata H, Motomura N, Okita Y, Takamoto S, Kinki S, et al. Outcomes of thoracic aortic surgery in patients with coronary artery disease: Based on the Japanese Adult Cardiovascular Surgery Database. Circ J 2019; 83: 978–984.
7. Murakami A, Hiraoka Y, Motomura N, Miyata H, Iwanaka T, Takamoto S. The national clinical database as an initiative for quality improvement in Japan. Korean J Thorac Cardiovasc Surg 2014; 47: 437–443.
8. Tokuda Y, Miyata H, Motomura N, Araki Y, Oshima H, Usui A, et al. Outcome of percutaneous for constrictive pericarditis in Japan: A nationwide outcome study. Ann Thorac Surg 2013; 95: 571–576.
9. Motomura N, Miyata H, Tsukihara H, Okada M, Takamoto S. Japan Cardiovascular Surgery Database Organization. First report on 30-day and operative mortality in risk model of isolated coronary artery bypass grafting in Japan. Ann Thorac Surg 2008; 86: 1866–1872.
10. Tokuda Y, Miyata H, Motomura N, Oshima H, Usui A, Takamoto S, et al. Brain protection during ascending aortic repair for Stanford type A acute aortic dissection surgery: Nationwide analysis in Japan. Circ J 2014; 78: 2431–2438.
11. Miyata H, Tomotoki A, Motomura N, Takamoto S. Operative mortality and complication risk model for all major cardiovascular operations in Japan. Ann Thorac Surg 2015; 99: 130–139.
12. Baumgartner H, Falk V, Bach J, De Bonis M, Hamm C, Holm PJ, et al. ESC/EACTS guidelines for the management of valvular heart disease. Eur Heart J 2017; 38: 2739–2791.
13. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Fleisher LA, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2017; 135: e1159–e1195.
14. Popma JJ, Deeb GM, Yakubov SJ, Mumtaz M, Gada H, O’Hair D, et al. Transcatheter aortic valve replacement with a self-expanding valve in low-risk patients. N Engl J Med 2019; 380: 1706–1715.
15. Blanke P, Weir-McCall JR, Achenbach S, Delgado V, Hausleiter J, Jilaihawi H, et al. Computed tomography imaging in the context of transcatheter aortic valve implantation (TAVI)/transcatheter aortic valve replacement (TAVR): An expert consensus document of the Society of Cardiovascular Computed Tomography. JACC Cardiovasc Imaging 2019; 12: 1–24.
BJ, Petursson P, et al. Five-year clinical and echocardiographic outcomes from the Nordic Aortic Valve Intervention NOTION randomized clinical trial in patients at lower surgical risk. *Circulation* 2019; **139**:2714–2723.

17. Toraman F, Evrenkaya S, Yuce M, Gökşel O, Karabulut H, Alhan C. Fast-track recovery in noncoronary cardiac surgery patients. *Heart Surg Forum* 2005; **8**:E61–E64.

18. Berrios-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR, et al. Centers for Disease Control and Prevention guideline for the prevention of surgical site infection, 2017. *JAMA Surg* 2017; **152**:784–791.

19. Miyahara K, Matsuura A, Takemura H, Mizutani S, Saito S, Toyama M. Implementation of bundled interventions greatly decreases deep sternal wound infection following cardiovascular surgery. *J Thorac Cardiovasc Surg* 2014; **148**:2381 – 2388.

20. Sharma S, Kumar S, Tewari P, Pande S, Murari M. Utility of thromboelastography versus routine coagulation tests for assessment of hypocoagulable state in patients undergoing cardiac bypass surgery. *Ann Card Anaesth* 2018; **21**:151 – 157.

21. Meersch M, Zarbock A. Prevention of cardiac surgery-associated acute kidney injury. *Curr Opin Anesthesiol* 2017; **30**:76 – 83.

22. Cropsey C, Kennedy J, Han J, Pandharipande P. Cognitive dysfunction, delirium, and stroke in cardiac surgery patients. *Semin Cardiothorac Vasc Anesth* 2015; **19**:309 – 317.