Practice Patterns and Outcomes of Transcatheter Aortic Valve Replacement in the United States and Japan: A Report From Joint Data Harmonization Initiative of STS/ACC TVT and J-TVT

Tsuyoshi Kaneko, MD; Sreekanth Vemulapalli, MD; Shun Kohsaka, MD; Kazuo Shimamura, MD; Amanda Stebbins, MS; Hiraku Kumamaru, MD; Adam J. Nelson, MBBS, PhD; Andrzej Kosinski, PhD; Koichi Maeda, MD; Joseph E. Bavaria, MD; Shigeru Saito, MD; Michael J. Reardon, MD; Toru Kuratani, MD; Jeffrey J. Popma, MD; Taku Inohara, MD; Vinod H. Thourani, MD; John D. Carroll, MD; Hideyuki Shimizu, MD; Morimasa Takayama, MD; Martin B. Leon, MD; Michael J. Mack, MD; Yoshiki Sawa, MD

BACKGROUND: The practice pattern and outcome of medical devices following their regulatory approval may differ by country. The aim of this study is to compare postapproval national clinical registry data on transcatheter aortic valve replacement between the United States and Japan on patient characteristics, periprocedural outcomes, and the variability of outcomes as a part of a partnership program (Harmonization-by-Doing) between the 2 countries.

METHODS AND RESULTS: The patient-level data were extracted from the US Society of Thoracic Surgeons /American College of Cardiology Transcatheter Valve Therapy (STS/ACC TVT) and the J-TVT (Japanese Transcatheter Valvular Therapy) registry, respectively, to analyze transcatheter aortic valve replacement outcomes between 2013 and 2019. Data entry for these registries was mandated by the federal regulators, and the majority of variable definitions were harmonized to allow direct data comparison. A total of 244,722 transcatheter aortic valve replacements from 646 institutions in the United States and 26,673 transcatheter aortic valve replacements from 171 institutions in Japan were analyzed. Median volume per site was 65 (interquartile range, 45–97) in the United States and 28 (interquartile range, 19–41) in Japan. Overall, patients in J-TVT were older (United States: mean-age, 80.1±8.7 versus Japan: 84.4±5.2; P<0.001), were more frequently women (45.9% versus 68.1%; P<0.001), and had higher median Society of Thoracic Surgeons Predicted Risk of Mortality (5.27% versus 6.20%; P<0.001), and had higher median Society of Thoracic Surgeons Predicted Risk of Mortality (5.27% versus 6.20%; P<0.001) than patients in the United States. Japan had lower unadjusted 30-day mortality (1.3% versus 3.2%; P<0.001) and composite outcomes of death, stroke, and bleeding (17.5 versus 22.5%; P<0.001) but had higher conversion to open surgery (0.94% versus 0.56%; P<0.001).

CONCLUSIONS: This collaborative analysis between the United States and Japan demonstrated the feasibility of international comparison using the national registries coded under mutual variable definitions. Both countries obtained excellent outcomes, although the Japanese had lower 30-day mortality and major morbidity. Harmonization-by-Doing is one of the key steps needed to build global-level learning to improve patient outcomes.

Key Words: aortic stenosis ■ bioprosthetic aortic valve ■ TAVR

Correspondence to: Tsuyoshi Kaneko, MD, Division of Cardiac Surgery, Brigham and Women’s Hospital, 15 Francis Street, Boston, MA 02115. E-mail: tkaneko2@partners.org

For Sources of Funding and Disclosures, see page 11.

© 2022 The Authors. Published on behalf of the American Heart Association, Inc., by Wiley. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

JAHA is available at: www.ahajournals.org/journal/jaha
Transcatheter aortic valve replacement (TAVR) has become the cornerstone for the treatment of severe, symptomatic aortic stenosis globally, as reflected in the US and European clinical practice guidelines.\(^1\)-\(^4\) Following the first randomized control study of TAVR in the United States,\(^5\),\(^6\) the TVT (Transcatheter Valve Therapy) registry was initiated by the US Food and Drug Administration, the Society of Thoracic Surgeons (STS), and the American College of Cardiology (ACC) in December 2011.\(^7\)-\(^9\) TAVR in Japan was first performed in 2009, and with subsequent successful clinical trials,\(^10\),\(^11\) the J-TVT (Japanese Transcatheter Valvular Therapy) registry was established in September 2013 by the Japanese TAVR association upon approval by the Pharmaceuticals and Medical Devices Agency. The uniqueness of the J-TVT registry was the alignment of the data elements to the TVT (Transcatheter Valvular Therapy) registry, conducted through mutual activity related to Harmonization by Doing (HBD). HBD was established by regulatory, industry, and academic members from the United States and Japan in December 2003, including the US Food and Drug Administration and the Pharmaceuticals and Medical Devices Agency in Japan, which are responsible for regulation of medical devices in their respective countries. The goal of HBD is to contribute to the promotion of medical device development through convergence in the evaluation and regulatory strategy. The achievements of HBD activity include the conduct of global clinical trials and registries for drug-eluting coronary stents, endovascular devices for limb ischemia, and left ventricular assist devices.\(^12\)-\(^16\)

Since the majority of TVT and J-TVT data elements have been harmonized as a part of the HBD mutual activity, the data captured in these registries afford a rare opportunity to directly compare 2 international TAVR experiences. Use of TAVR to manage severe, symptomatic aortic stenosis typically relies on availability of health care resources, institutional and individual preference for surgical or interventional procedures, and individual perception of quality of life or overall life expectancy; all of these factors may differ considerably in the East and West. Accordingly, the aim of this study was to compare (1) the practice patterns and patient characteristics of patients undergoing TAVR in Japan versus the United States, (2) the procedure details, and (3) periprocedural outcomes and (4) hospital variability in outcomes between the 2 countries using these representative registries.
participation of all US TAVR centers. Participating centers use standardized definitions to collect clinical information—including patient demographics, comorbidities, functional status, quality-of-life indices, and procedural details and outcomes—from consecutive TAVR patients using commercially approved devices. Both the ACC National Cardiovascular Data Registry warehouse and the Duke Clinical Research Institute Data Analysis Center implement data quality checks. Additionally, the data are also audited by an independent third party to assure data quality. The J-TVT registry was established by 4 academic societies (Japanese Circulation Society, Society of Japanese Cardiovascular Surgery, Japanese Association for Thoracic Surgery, and Japanese Association of Cardiovascular Intervention and Therapeutics) in collaboration with the Pharmaceuticals and Medical Devices Agency and industry to develop a database containing information about TAVR procedures in Japan. Data collection started in September 2013, when the registry was established. Consecutive case registration was required for certification of the institutions and operators, and complete case registration is confirmed every 3 years for renewal of institutional certification. Data quality was assured via automatic system validation, reporting of data completeness, training of site data managers, and data auditing (12 institutions annually), which is operated by members of the J-TVT registry Committee. When the 5-year follow-up period is completed, compliance inspection is scheduled for future reassessment/reevaluation. The timelines of the devices approved in each country are shown in Figure 1.

The study was approved by the TVT registry Scientific and Strategic Committee. Steering Committee of the J-TVT, and Institutional Review Board of the Osaka University Graduate School of Medicine (Osaka, Japan). The TVT registry protocol was granted a waiver of informed consent by the Advarra and Duke University Institutional Review Boards. Similarly, the J-TVT registry protocol was granted a waiver of informed consent by Osaka University.

Study Patients
The US and Japanese data were obtained from the STS/ACC TVT and J-TVT Registries, respectively, for all adult patients who underwent TAVR from September 2013 to September 30, 2019. September 2013 was chosen, as this is when the J-TVT registry commenced. Consecutive patients undergoing TAVR were included in the study. We excluded cases from institutions that performed <20 cases annually when modeling site variability to preclude the influence of outliers. The duration of performing TAVR procedures in our study indicates the time between the first and last date of registered TAVR procedures.

Data Definitions and Outcome of Interest
The J-TVT registry collected data elements/definitions that were initially derived from the US TVT registry as a part of a mutual process of HBD. In both the TVT and J-TVT Registries, data elements were selected, corresponding to data reported on the basis of the updated standardized end point definitions for TAVR in the Valve Academic Research Consortium-2 consensus document.17 The majority of the data definitions were mutually harmonized from inception; however, some of the fields relating to patient characteristics and postprocedural outcomes varied between registries. Therefore, the postprocedural outcome comparison was limited to 30-day mortality, 30-day stroke, and 30-day major bleeding. Major bleeding was defined as access-site bleed, access-site hematomata, hemorrhagic stroke, retroperitoneal hemorrhage, gastrointestinal and genitourinary bleeding, other bleeding, or drop in hemoglobin >3 g/dL. STS version 2.73 was used for the calculation of the STS predicted risk of mortality. The following analyses were performed as our outcomes of interest: (1) annual numbers of TAVR procedures and hospitals; (2) patient risk profile including the Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM); (3) intraprocedural details including elective or nonelective, type of valve used, conscious sedation, and conversion to open surgery; (4) postprocedural outcomes: 30-day mortality; 30-day composite of death, stroke, and major bleeding; and (5) assessment of hospital variability in outcomes.

Statistical Analysis
For the unadjusted analyses, continuous variables are presented as mean±SD, or as median with interquartile range (Q1,Q3), and were compared between groups using the 2-sample Student t test or Wilcoxon rank-sum test, respectively. Categorical variables are expressed as frequencies and percentages and were compared using Fisher exact tests or chi-square tests. The ratio of the observed 30-day mortality rates to the expected rates generated using the 2007 STS risk score and the corresponding 95% CI is reported by year of procedure. Observed-to-expected ratio was used for adjusted outcome instead of a multivariable regression model since patient-level data were unable to be shared with the other country and uniform covariates for adjustment were not available between the 2 registries. Hospitals performing <20 TAVRs were excluded from all statistical modeling to eliminate the uncertainty of statistical estimates attributable to the low sample size.
To assess hospital variability of postprocedure outcomes within each country and potential causes for this variability, hierarchical logistic regression models with center-specific random intercepts were performed using SAS GLIMMIX for each country because of the data-sharing limitations. The initial model included no covariates. To assess the impact of hospital and patient characteristics on outcomes, a second model was performed. This included total procedural volume, duration of performing transcatheter valve therapy procedures, number of beds, whether the site is a teaching/university center or not, and STS risk score. Transformations of covariates were carried out when necessary. Median odds ratios (MORs) and $R^2$ measures are reported. The MOR reports the amount of variability between sites for identical patients, where a MOR of 1 indicates no variability between sites. The $R^2$ measure is reported measuring the percentage of outcome variance explained by the models. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

Trend of Cases and Hospitals

From September 2013 to September 2019, a total of 244,722 TAVRs in the TVT registry and 26,673 TAVRs in the J-TVTT registry were reported (Figure 2). The number of cases performed increased in both countries over time: the US cases increased by 347% from 2014 to 2019 (16,337–520,191), and Japanese cases increased by 740% (925–7,778) during the same period. The number of institutions performing TAVR in the United States increased from 272 in 2013 to 646 in 2019, as well as in Japan, from 15 in 2013 to 170 in 2019. Median volume per site was 65 (45–97) in the US and 28 (19–41) in Japan. (Table 1).

Preprocedural Characteristics

There were several key patient characteristics that were different between the 2 countries (Table 2). Japanese patients were older (mean age, United States: 80.1±8.7 versus Japan: 84.4±5.2; $P<0.001$), and more likely to be women (United States: 45.9% versus Japan: 55.0%.$P<0.001$).
versus Japan: 68.1%; \( P<0.001 \)). US patients had more preprocedural permanent pacemaker insertions, hypertension and diabetes, dialysis, New York Heart Association class III/IV, and prior atrial fibrillation (all \( P<0.001 \)). Median STS-PROM was 5.27% (interquartile range, 3.37–8.40) in the United States and 6.20% (interquartile range, 4.41–8.85) in Japan (\( P<0.001 \)). The decrease in STS-PROM was seen in the United States during the study period, whereas the STS-PROM did not change in Japan (Figure 3).

**Intraprocedural Details**

Japan had more elective procedures (97.6% versus 91.1%; \( P<0.001 \)) and less urgent procedures (1.8% versus 8.5%; \( P<0.001 \)) than the United States. The valve sizes used were overall smaller in Japan (Table 3 and 4). The use of conscious sedation was significantly lower in Japan (20.1% versus 42.5%; \( P<0.001 \)). While use of transfemoral access was similar, transapical access was more common in Japan (7.1% versus 3.3%; \( P<0.001 \)). Although limited to a small fraction, conversion to open surgery was higher in Japan (0.94% versus 0.56%; \( P<0.001 \)), mainly driven by higher rates of ventricular and annular ruptures. The use of a mechanical assist device at the start of the procedure and elective/urgent use of cardiopulmonary bypass was higher in Japan (all \( P<0.001 \)).

### Table 1. Site Details

|                      | US TVT | J-TVT |
|----------------------|--------|-------|
| **Annualized site volume** | N=646  | N=171  |
| **Median (25th–75th)** | 65 (45–97) | 28 (19–41) |
| **Means\( \pm \)SD** | 80±53  | 34.7±26.9 |
| **Min–max** | 10–401 | 1–160 |
| **Duration of performing TAVR Procedure, d** | N=652 | N=171 |
| **Median (25th–75th)** | 1813 (993–2202) | 1365 (651–1747) |
| **Means\( \pm \)SD** | 1545±724 | 1230±666 |
| **Min–max** | 0–2218 | 0–2313 |

J-TVT indicates Japanese Transcatheter Valvular Therapy; TAVR, transcatheter aortic valve replacement; and TVT, Transcatheter Valve Therapy.

**Figure 2.** Total numbers and institutions performing TAVR in the United States and Japan. TAVR indicates transcatheter aortic valve replacement; and TVT, Transcatheter Valve Therapy.
Kaneko et al. Practice Patterns Outcomes of TAVR in United States and Japan

Postprocedural Outcomes

In unadjusted analysis, 30-day mortality was lower in Japan compared with the United States (1.3% versus 3.2%; \( P < 0.001 \)). Similarly, unadjusted 30-day stroke and major bleeding rates were lower in Japan (1.4% versus 2.4%, 15.9% versus 21.5%; \( P < 0.001 \), respectively). Overall unadjusted composite outcomes of death, stroke, and major bleeding were lower in Japan compared with the United States (17.5 versus 22.5%; \( P < 0.001 \)). Thirty-day observed-to-expected ratio for mortality was lower in Japan compared with the United States (0.21 versus 0.55) in 2019. The observed-to-expected ratio decreased in Japan from 0.27 in 2013 to 0.21 in 2019 and 1.03 to 0.55 in the United States (Figure 3; Table 5).

Outcome Variation by Hospital in Each Country

For the composite outcome of death, stroke, and major bleeding, there was significant variability in site performance in both the United States (MOR, 1.29; 95% CI, 1.24–1.33) and Japan (MOR, 1.63; 95% CI, 1.32–1.88). Estimates of variability in site performance did not change with the addition of site characteristics (site volume per year, number of beds, teaching hospital status, or duration of institution performing TAVR), or patient characteristics (STS-PROM score), indicating that institutional variability within each country was not explained by these factors (Table 6).

**DISCUSSION**

This first international comparison of TAVR practice using the nationally representative registries between the United States and Japan showed several significant findings. First, the number of TAVR cases and hospitals performing TAVR has dramatically increased in both countries. However, the United States has a much higher proportion of TAVRs performed per capita compared with Japan. Second, the risk profiles were different: Japanese patients were older and predominantly female and had a higher STS-PROM despite US patients having more comorbidities. Third, Japan had more elective cases than the United States.

---

**Table 2. Demographics and Medical History**

| Demographics          | TVT | TVT% | J-TVT | J-TVT% | \( P \) value |
|-----------------------|-----|------|-------|--------|---------------|
| No.                   | N=244 722 | N=26 673 |
| Age, mean (SD), y     | 80.1 (8.7) | 84.4 (5.2) | <0.001 |
| Sex, female           | 112 283 | 45.9 | 18 154 | 68.1 | <0.001 |
| BSA, mean (SD), m²    | 1.89 (0.26) | 1.43 (0.17) | <0.001 |
| Medical history       |     | <0.001 | <0.001 | <0.001 | <0.001 |
| Permanent pacemaker   | 33 156 | 13.5 | 1512 | 5.7 | <0.001 |
| Prior ICD             | 9025 | 3.7 | 76 | 0.3 | <0.001 |
| Prior PCI             | 81 449 | 33.3 | 6108 | 22.9 | <0.001 |
| Prior CABG            | 53 500 | 21.9 | 1239 | 4.6 | <0.001 |
| Prior cardiac surgeries (open heart) | 18 498 | 7.6 | 2239 | 8.4 | <0.001 |
| Prior stroke          | 28 157 | 11.5 | 3209 | 12.0 | 0.018 |
| Transient ischemic attack | 20 300 | 8.3 | 531 | 2.0 | <0.001 |
| Peripheral arterial disease | 67 777 | 27.7 | 2085 | 11.2 | <0.001 |
| Current/recent smoker | 14 955 | 6.1 | 4222 | 15.8 | <0.001 |
| Hypertension          | 221 406 | 90.5 | 21 050 | 78.9 | <0.001 |
| Diabetes              | 93 349 | 38.1 | 7062 | 26.5 | <0.001 |
| Currently on dialysis | 9770 | 4.0 | 131 | 0.5 | <0.001 |
| Creatinine >2.0 mg/dL (excludes dialysis) | 20 138 | 8.3% | 946 | 3.5% | <0.001 |
| Hostile chest         | 16 202 | 6.6 | 324 | 1.2 | <0.001 |
| NYHA class III/IV     | 151 431 | 74.7 | 6952 | 26.1 | <0.001 |
| Porcelain aorta       | 8535 | 3.5 | 2552 | 9.6 | <0.001 |
| Atrial fibrillation   | 93 588 | 38.2 | 4579 | 17.2 | <0.001 |

BSA indicates body surface area; CABG, coronary artery bypass grafting; ICD, implantable cardiac defibrillator; J-TVT, Japanese Transcatheter Valvular Therapy; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; and TVT, Transcatheter Valve Therapy.
Figure 3. STS-PROM and 30-d mortality with calculated O/E ratio by year in the United States (A) and Japan (B).
O/E indicates observed-to-expected; STS, Society of Thoracic Surgeons; STS-PROM, Society of Thoracic Surgeons Predicted Risk of Mortality; TAVR, transcatheter aortic valve replacement; and TVT, Transcatheter Valve Therapy.
used smaller-size valves, and had an increased risk of ventricular/annular rupture and conversion to open surgery. Fourth, the adverse event rate after TAVR (e.g., 30-day mortality, stroke, and bleeding) was lower in Japan. Finally, hospital variability was noted in both countries for composite outcomes and 30-day mortality, and this variability was not explained by differences in the site or patient characteristics. This analysis thus showed the feasibility of international comparison using 2 national registries, and the outcomes should be used to develop further global-level learning to improve patient outcomes and reduce site variability in the quality of TAVR care.

The rapid growth of the US TAVR volume was recently published, and this study confirmed a similar steep increase in TAVR cases in Japan. Based on previous reports from Europe, we can infer that the adoption of this technology is occurring at the global level. Interestingly, despite the growth of TAVR in both countries, the number of TAVRs performed per capita was higher in the United States. The possible explanation for this phenomenon may be the higher prevalence of severe symptomatic aortic stenosis or higher use of TAVR in the United States. Cultural barriers to avoid interventions in the Asian Society is another reason that may explain our findings. Previous randomized control studies in TAVR have included institutions from Asia and Oceania, albeit the patients enrolled in

Table 3. Procedural Details

| Characteristic | TVT | TVT% | J-TV | J-TVT% | P value |
|----------------|-----|------|------|-------|---------|
| No.            | N=244 722 | N=26 673 |       |       |         |
| Procedure status |     |      |      |       |         |
| Elective       | 222 832 | 91.1 | 26 032 | 97.6 | <0.001 |
| Urgent         | 20 887 | 8.5  | 484   | 1.8  | <0.001 |
| Emergency      | 880   | 0.3  | 143   | 0.5  |         |
| Salvage        | 123   | 0.1  | 23    | 0.1  |         |
| Procedure aborted |      | 95   | 0.4  |       |         |
| Type of anesthesia |     |      |      |       |         |
| Moderate sedation | 103 906 | 42.5 | 5367 | 20.1 | <0.001 |
| General anesthesia | 138 536 | 56.6 | 21 306 | 79.9 |         |
| Access site |     |      |      |       |         |
| Femoral        | 222 365 | 90.9 | 23 664 | 88.7 | <0.001 |
| Transapical    | 7989  | 3.3  | 1906  | 7.1  |         |
| Other          | 13 549 | 5.5  | 1103  | 4.1  |         |
| Conversion to open heart surgery | 1370 | 0.56 | 250 | 0.94 | <0.001 |
| Reason converted |     |      |      |       |         |
| Valve dislodged to aorta | 54 | 0.02 | 10 | 0.04 |         |
| Valve dislodged to left ventricle | 123 | 0.05 |     |       |         |
| Ventricular rupture | 287 | 0.11 | 69 | 0.26 |         |
| Annulus rupture | 209 | 0.08 | 52 | 0.19 |         |
| Aortic dissection | 111 | 0.04 | 14 | 0.05 |         |
| Coronary occlusion | 95 | 0.03 | 8 | 0.02 |         |
| Other          | 491   | 0.20 | 97    | 0.36 |         |
| Mechanical assist device in place at start of procedure (any) | 702 | 0.3 | 607 | 2.3 |         |
| Cardiopulmonary bypass |     |      |      |       |         |
| Elective       | 463   | 22.3 | 263   | 1.0  |         |
| Emergent       | 1612  | 77.6 | 271   | 1.0  |         |

J-TV indicates Japanese Transcatheter Valvular Therapy; TAVR, transcatheter aortic valve replacement; and TVT, Transcatheter Valve Therapy.

Table 4. Valve Size

| Characteristic | US TVT | J-TV |
|----------------|--------|------|
| Valve size, n (%) | N=242 226 | N=26 611 |
| ≤20 mm         | 4908 (2.0) | 1368 (5.1) |
| 21–23 mm       | 63 894 (26.3) | 11 806 (44.4) |
| 23–26 mm       | 91 092 (37.6) | 8662 (32.6) |
| 27–29 mm       | 66 194 (27.3) | 3775 (14.2) |
| >29 mm         | 15 844 (6.5) | 0 (0) |

J-TV indicates Japanese Transcatheter Valvular Therapy; and TVT, Transcatheter Valve Therapy.
Kaneko et al. Practice Patterns Outcomes of TAVR in United States and Japan

these regions were considerably fewer than those in North America and Europe, and further analysis of the prevalence of aortic stenosis and surgical aortic valve replacement (SAVR)/TAVR data will be needed to understand this difference between the 2 countries.

Our analysis showed that the number of hospitals performing TAVR has increased in both countries. The criteria for institutions initiating TAVR programs are different for each country. In the United States, the original Centers for Medicare and Medicaid Services National Coverage Data until June 2019 required a new TAVR program to have ≥50 SAVRs in the previous year, including ≥10 high-risk patients, and ≥1000 catheterizations/year, including ≥400 percutaneous coronary interventions/year. The Japanese requirements are SAVR ≥20/year, percutaneous coronary interventions ≥100/year, thoracic or abdominal endograft ≥10/year, and transesophageal echocardiograms ≥200/year; and equipment of a hybrid operating theater is mandatory. The lower threshold for opening a new program in Japan may explain the higher relative increase in the number of institutions and lower median numbers per institution. On the other hand, population density and the number of hospitals also may impact this trend. Overall, the difference in the rate of TAVR expansion between the 2 countries is an example of the rate of real-world technology dispersion in the regulatory environments of the 2 countries that may involve complex mechanisms.

The Japanese patients were older and predominantly female and had a higher STS-PROM than US patients. The contrasting patient characteristics reflect differences in the approved patient risk profiles between the 2 countries. In Japan, only high-risk patients undergoing SAVR were approved for TAVR as of 2020. Conversely, intermediate-risk patients were approved for TAVR in 2015 and low-risk in 2019 in the United States by the Food and Drug Administration. The approval of lower-risk patients has likely led to a decrease in the STS-PROM in the United States.18 The discrepancy in the higher comorbidity rate but lower STS-PROM in the US group may be explained by the older and female group in Japan, which increased the score. Additionally, the Japanese have a smaller body habitus and lean stature, both of which are known to elevate the STS-PROM.

The Japanese registry had more elective cases, which may reflect the fact that technology was used more cautiously in selected patients. This may have contributed to the lower mortality and morbidity rates in Japan. Another potential explanation for this is the more robust and reliable follow-up in the Japanese system such that fewer patients present with either “de novo” severe, decompensated aortic stenosis or were lost to follow-up from “moderate” aortic stenosis. Health care

### Table 5. Clinical End Points

|                  | US TVT   | J-TVT    | P value |
|------------------|----------|----------|---------|
| N=244 722       | N=25 486 |
| 30-d death, n (%) | 7260 (3.2) | 333 (1.3) | <0.001 |
| 30-d site reported all-cause stroke | 5486 (2.4) | 361 (1.4) | <0.001 |
| In-hospital change in hemoglobin ≥ 3 g/dL | 46 361 (18.9) | 3793 (14.9) | <0.001 |
| Overall 30-d bleeding* | 52 613 (21.5) | 4051 (15.9) | <0.001 |
| Composite of 30-d death, any stroke, and bleeding* | 55 138 (22.5) | 4484 (17.6) | <0.001 |
| 2007 STS score, % | N=244 692 | N=25 434 | <0.001 |
| Median (25th–75th) | 5.27 (3.37–6.40) | 6.20 (4.41–8.85) |
| Mean SD | 6.83 (5.57) | 7.43 (5.07) |
| Min–max | 0.36–91.36 | 0.58–77.9 |

J-TVT indicates Japanese Transcatheter Valvular Therapy; STS, Society of Thoracic Surgeons; and TVT, Transcatheter Valve Therapy.

*Bleeding location includes transapical related, transaortic, access site, access hematoma, retroperitoneal, gastrointestinal bleed, genitourinary bleed, other bleed, and hemorrhagic stroke.

### Table 6. Composite and 30-Day Mortality Models

|                  | Model 1                        | Model 2                        |
|------------------|-------------------------------|-------------------------------|
| United States    |                               |                               |
| Composite (death/stroke or bleeding) models, R², % | Marginal=0, conditional=5.1 | Marginal=1.4, conditional=5.7 |
| Median odds ratio (95% CI) | 1.49 (1.45–1.53) | 1.45 (1.41–1.49) |
| 30-day mortality models, R², % | Marginal=0, conditional=21 | Marginal=10.8, conditional=12.4 |
| Median odds ratio (95% CI) | 1.29 (1.24–1.33) | 1.27 (1.22–1.31) |
| Japan            |                               |                               |
| Composite (death/stroke or bleeding) models, R², % | Marginal=0, conditional=7.1 | Marginal=0.4, conditional=7.41 |
| Median odds ratio (95% CI) | 1.62 (1.49–1.74) | 1.61 (1.48–1.73) |
| 30-day mortality models, R², % | Marginal=0, conditional=3.6 | Marginal=0.4%, conditional=1.8 |
| Median odds ratio (95% CI) | 1.63 (1.32–1.88) | 1.60 (1.26–1.87) |

Model 1: Baseline: no covariate. Model 2: STS Risk Score (2007)+ Site Volume Per Year, Number of Beds, Duration of performing TAVR, Teaching Hospital. STS indicates Society of Thoracic Surgeons; and TAVR, transcatheter aortic valve replacement.
reimbursement or ratio of SAVR used may also affect the use of TAVR in nonelective situations. The conversion to open surgery and the use of cardiopulmonary bypass and other mechanical circulatory support were more prevalent in Japan than in the United States.

The increased incidence of ventricular rupture and annular rupture in the Japanese series may be attributed to the small body size of the Japanese patients and may also result from the initial learning curve of the new operators and preoperative imaging. Despite the higher use of cardiopulmonary bypass, mechanical support, and operative conversion, Japanese mortality was low, potentially attributable to the fact that all cases were performed in the hybrid operative theater. Previous studies have reported low-mortality patients undergoing TAVR in Japanese institutions. Inohara et al reported the 134-patient series from the OCEAN-TAVI (Optimized Transcatheter Valvular Intervention-Transcatheter Aortic Valve Implantation) registry in Japan and reported a 30-day mortality rate of 0%.

We must be cautious about the direct comparison of the mortality even with the adjustment. Although the use of STS-PROM in Japanese patients has been validated previously in the cardiac surgery population, the health care system, ethnic composition, regulatory practices, and hospital systems all differ between the 2 countries and are not accounted for in the analysis. There is also a possibility that the STS-PROM may overestimate the expected score in the Japanese TAVR group, which will lead to lower observed-to-expected ratio. Part of the Japanese success may be attributed to the TAVR certification and the proctoring system, which involves mandatory web-based screening and industry lectures. To perform TAVR independently, 8 transfemoral cases must be performed under the supervision of a certified TAVR instructor. Furthermore, to become a TAVR instructor, operators must complete at least 30 cases. In contrast, the United States does not have an operator certification system for TAVR, despite the strict criteria to qualify and continue as a TAVR institution. The US outcomes are similar to those reported in other countries’ registries based on the era: France, 5.6% (2013–2015); Germany, 5.9% (2011–2017); and Finland, 1.2% (2017) and 4.8% (2008), although these different registries include different risk profiles, different valve types, and various-generation valves.

Another important factor is the racial composition. Japan is unique in that the population is almost exclusively monoracial. Conversely, the United States is a multiracial country, and despite the fact that the 2020 US census showed that Asians and Pacific Islanders comprised 6.1% of the population, only 1.5% were of Asian/Native American/Pacific Islander race who underwent TAVR in the previous TVT registry report.

The outcomes of TAVR in this study showed lower 1-year mortality among patients of the Asian/Native American/Pacific Islander race. The racial disparities may be one of the factors of improved outcomes in the J-TVTR group.

Our analysis showed that there was significant variability in national procedural outcomes between sites in both the United States and Japan. Of note, the degree of explained variability did not change after the addition of site characteristics (site volume per year, number of beds, teaching hospital status, or duration of institution performing TAVR) or patient characteristics (STS-PROM) to the model. The addition of simple structural indicators of quality to patient characteristics did not adequately account for the variability and therefore may not be sufficient as metrics of care quality. The cause of variability is likely to be complex, multifactorial, and interrelated. As TAVR expands to smaller and low-volume institutions, further analysis will be needed to identify and intervene upon sources of variability to maintain the high-quality TAVR outcomes in both countries.

The HBD initiative has provided a unique opportunity to compare the 2 national registries, and it is hoped that the results may identify areas for shared learning and iteration among respective TAVR programs. For Japan, the results may suggest considerate pre-/intraprocedural planning to avoid conversion to open surgery. For the United States, it calls for the need for a US TAVR operator certification system similar to that in Japan. Most importantly, this study shows the importance of common data standards to pave the way for further international quality-of-care comparisons.

**Limitations**

There are several limitations in this study. First, data definitions in some of the variables were not the same despite the efforts for harmonization (eg, data elements in the J-TVTR registry were decided when the device and the procedure were approved in 2013, and data elements related to patient frailty and other potential confounders were not included). For the present analysis, only variables that were comparable were used to avoid misinterpretation. Second, the J-TVTR initiated auditing in 2018. This is relatively recent compared with TVTR. Third, there is a possibility of underreporting in both of the registries. Fourth, unmeasured confounding factors may affect the results of the analysis. For example, detailed echocardiographic or computed tomographic data points were not available for comparison. However, most of the preprocedural data were available for comparison, which allowed this unique comparative analysis between the 2 countries. Finally, because of limitations in sharing the individual patient data, we were unable to perform multivariable, patient-level adjusted analysis for outcome comparison. Other differences between the 2 countries, such
as age composition, ethnic composition, health care system, regulatory practices, hospital systems, that were not adjusted might have affected the outcome.

CONCLUSIONS
This collaborative analysis between the United States and Japan demonstrated the feasibility of international comparison using the national registries coded under mutual variable definitions. The number of TAVR procedures and the number of institutions increased rapidly during the study period in both countries with excellent outcomes. This study paves the way for future international collaboration to improve procedural outcomes and reduce variability in quality in various transcatheter interventions at a global level.

ARTICLE INFORMATION
Received September 8, 2021; accepted January 31, 2022.

Affiliations
Division of Cardiac Surgery, Brigham and Women’s Hospital, Boston, MA (T. Kaneko); Duke Clinical Research Institute, Durham, NC (S.V., A.S., A.J.N., A.K., T.I.); Department of Cardiology (S.K., T.I.); and Department of Cardiovascular Surgery (H.S.), Keio University School of Medicine, Tokyo, Japan; Department of Cardiovascular Surgery, Osaka University Hospital, Osaka, Japan (K.S., T. Kuratani, Y.S.); Department of Healthcare Quality Assessment, Graduate School of Medicine, Faculty of Medicine, The University of Tokyo, Japan (H.K.); Department of Cardiovascular Surgery, Osaka University Graduate School of Medicine, Suita City, Japan (K.M.); Division of Cardiac Surgery, University of Pennsylvania, Philadelphia, PA (J.E.B.); Division of Cardiology, Shonan Kamakura Hospital, Kamakura, Japan (S.S.); Division of Cardiac Surgery, Houston Methodist Hospital, Houston, TX (M.J.R.); Medtronic, Santa Rosa, CA (J.J.P.); Department of Cardiac Surgery, Piedmont Heart Institute, Atlanta, GA (V.H.T.); Division of Cardiology, University of Colorado, Aurora, CO (J.D.C.); Department of Cardiology, Sakakibara Heart Institute, Fuchu, Japan (M.T.); Division of Cardiology, Columbia University Irving Medical Center, New York-Presbyterian Hospital, New York, NY (M.B.L.); and Cardiovascular Service line, Baylor Scott & White Health, Baylor Scott & White Research Institute, Dallas, TX (M.J.M.).

Sources of Funding
None.

Disclosures
Dr Kaneko is a consultant/speaker for Edwards Lifesciences, Medtronic, Abbott Structural Heart, Baylis Medical, and 4C Medical. Dr Bavaria is a consultant and clinical trial principal investigator for Edwards Lifesciences and Medtronic, and is the Data and Safety Monitoring Board chair for Abbott. Dr Reardon is a consultant to Medtronic, Boston Scientific, Abbott Vascular, and Gore Medical. Dr Thourani is a consultant to Abbott Vascular, Boston Scientific, CryoLife, Edwards Lifesciences, JenaValve, and Shockwave. Dr Leon receives institutional grants for clinical research from Abbott, Boston Scientific, Edwards Lifesciences, and Medtronic; and a member of the advisory board (nonpaid) of Edwards Lifesciences and Medtronic. Dr Mack is clinical trial co–principal investigator /study chair for Abbott, Edwards Lifesciences, and Medtronic. The remaining authors have no disclosures to report.

REFERENCES
1. Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP, Gentile F, Jneid H, Krieger EV, Mack M, McLeod C, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2021;143:e267–e2227. doi: 10.1161/CIR.00000000000009923
2. Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, Iung B, Lancellotti P, Lansac E, Rodriguez Muñoz D, et al. 2017 ESC/EACTS guidelines for the management of valvular heart disease. Eur Heart J. 2017;38:2739–2791. doi: 10.1093/eurheartj/ehx391
3. Poppma JJ, Deeb GM, Yakubov SJ, Murtaza M, Gada H, O’Hair D, Bajwa T, Heister JC, Merhi W, Kleiman NS, et al. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. N Engl J Med. 2019;380:1706–1715. doi: 10.1056/NEJMoai1816885
4. Mack MJ, Leon MB, Thomuri VH, Makkar R, Kodali SK, Russo M, Kapadia SR, Malaisrie SC, Cohen DJ, Pibarot P, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med. 2019;380:1695–1705. doi: 10.1056/NEJMoa1914052
5. Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana OP, Makkar RR, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med. 2010;363:1597–1607. doi: 10.1056/NEJMoat0908232
6. Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana OP, Makkar RR, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med. 2011;364:2187–2198. doi: 10.1056/NEJMoat1103510
7. Carroll JD, Edwards FH, Marinac-Dabic D, Brindis RG, Grover FL, Peterson ED, Tuzcu EM, Shahian DM, Rumsfeld JS, Sweeney CM, et al. The STS–ACC transcatheter valve therapy national registry: a new partnership and infrastructure for the introduction and surveillance of medical devices and therapies. J Am Coll Cardiol. 2013;62:1026–1034. doi: 10.1016/j.jacc.2013.03.060
8. Holmes DR Jr, Nishimura RA, Grover FL, Brindis RG, Carroll JD, Edwards FH, Peterson ED, Rumsfeld JS, Shahian DM, Thourani VH, et al. Annual outcomes with transcatheter valve therapy: from the STS/ACC TVT registry. J Am Coll Cardiol. 2015;66:2813–2823. doi: 10.1016/j.jacc.2015.10.049
9. Grover FL, VemulaPalli S, Carroll JD, Edwards FH, Mack MJ, Thourani VH, Brindis RG, Shahian DM, Ruiz CE, Jacobs JP, et al. 2016 annual report of the Society of Thoracic Surgeons/American College of Cardiology transcatheter valve therapy registry. J Am Coll Cardiol. 2017;69:1215–1230. doi: 10.1016/j.jacc.2016.11.032
10. Sawa Y, Takayama M, Goto T, Tanaka Y, Komiya T, Tobaru T, Maeda K, Kuratani T, Sakata Y. Five-year outcomes of the first pivotal clinical trial of balloon-expandable transcatheter aortic valve replacement in Japan (PREVAIL-Japan). Circ J. 2017;81:1102–1107. doi: 10.1253/circj.CJ-17-0111
11. Sawa Y, Saito S, Kobayashi J, Ninomi H, Kuratani T, Maeda K, Kanzaki H, Komiya Y, Tanaka Y, Boyle A, et al. First clinical trial of a self-expandable transcatheter heart valve in Japan with symptomatic severe aortic stenosis. Circ J. 2014;78:1093–1090. doi: 10.1253/circj.CJ-14-0162
12. Toyofuku M, Kimura T, Morimoto T, Hayashi Y, Ueda H, Kawai K, Nozaki Y, Hiramatsu S, Miura A, Yokoi Y, et al. Three-year outcomes after sirolimus-eluting stent implantation for unprotected left main coronary artery disease: insights from the j-Gyster registry. Circulation. 2009;120:1866–1874. doi: 10.1161/CIRCULATIONAHA.109.873349
13. Yokoi H, Ho M, Iwamoto S, Suzuki Y, Ansel GM, Azuma N, Haneda N, Iida O, Ikeda K, Ikeno F, et al. Design strategies for global clinical trials of endovascular devices for critical limb ischemia (CLI) - a Joint USA-Japanese perspective. Circ J. 2018;82:2233–2239. doi: 10.1253/circj.CJ-18-0014
14. Patel MR, Conte MS, Cutlip DE, Dib N, Geraghty P, Gray W, Hiatt WR, Ho M, Ikeda K, Ikeno F, et al. Evaluation and treatment of patients with lower extremity peripheral artery disease: consensus definitions from Peripheral Academic Research Consortium (PARC). J Am Coll Cardiol. 2015;65:931–941. doi: 10.1016/j.jacc.2014.12.036
15. Nakatani T, Sase K, Oshiyama H, Akiyama M, Horie M, Nawata K, Nishinaka T, Tanoue Y, Toda K, Tosa T, et al. Japanese registry for mechanically assisted circulatory support: first report. J Heart Lung Transplant. 2017;36:1087–1096. doi: 10.1016/j.healun.2017.08.002
16. Inohara T, Kohsaka S, Speratus JA, Masoudi FA, Rumsfeld JS, Kennedy KK, Wang TY, Yamaji K, Amano T, Nakamura M. Comparative trends in percutaneous coronary intervention in Japan and the United States, 2013 to 2017. J Am Coll Cardiol. 2020;76:1328–1340. doi: 10.1016/j.jacc.2020.07.037
17. Kappetein AP, Head SJ, Généreux P, Piazza N, van Mierheim NM, Blackstone EH, Brott TG, Cohen DJ, Cury DE, van Es G-A, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the valve academic research consortium-2 consensus document. J Am Coll Cardiol. 2012;60:1438–1454. doi: 10.1016/j.jacc.2012.09.001

18. Carroll JD, Mack MJ, Vemulapalli S, Herrmann HC, Gleason TG, Hanzel G, Deeb GM, Thurani VH, Cohen DJ, Desai N, et al. STS-ACC TVT registry of transcatheter aortic valve replacement. J Am Coll Cardiol. 2020;76:2492–2516. doi: 10.1016/j.jacc.2020.09.595

19. Auffret V, Lefèvre T, Van Belle E, Eltchaninoff H, Iung B, Koning R, Motreff P, Leprince P, Verhoeye JP, Manigold T, et al. Temporal trends in transcatheter aortic valve replacement in France: France 2 to France TAVI. J Am Coll Cardiol. 2017;70:42–55. doi: 10.1016/j.jacc.2017.04.053

20. Pineda AM, Harrison JK, Kleiman NS, Rihal CS, Kodali SK, Kirtane AJ, Leon MB, Sherwood MW, Manandhar P, Vemulapalli S, et al. Incidence and outcomes of surgical bailout during TAVR: insights from the STS/ACC TVT registry. JACC Cardiovasc Interv. 2019;12:1751–1764. doi: 10.1016/j.jcin.2019.04.026

21. Inohara T, Hayashida K, Watanabe Y, Yamamoto M, Takagi K, Yashima F, Arai T, Shimasu H, Chevalier B, Lefèvre T, et al. Streamlining the learning process for TAVI: insight from a comparative analysis of the OCEAN-TAVI and the massy registries. Catheter Cardiovasc Interv. 2016;87:963–970. doi: 10.1002/ccd.26266

22. Yamaoka H, Kuwaki K, Inaba H, Yamamoto T, Kato TS, Dohi S, Matushita S, Amano A. Comparison of modern risk scores in predicting operative mortality for patients undergoing aortic valve replacement for aortic stenosis. J Cardiol. 2016;68:135–140. doi: 10.1016/j.jcc.2015.08.017

23. Yamawaki M, Iwasaki K, Araki M, Ito T, Ito Y, Tada N, Takagi K, Yamanaka F, Watanabe Y, Yamamoto M, et al. A proctoring system to manage the learning curve associated with the introduction of transcatheter aortic valve implantation in Japan. Heart Vessels. 2018;33:630–639. doi: 10.1007/s00380-017-1098-9

24. Van Belle E, Vincent F, Labreuche J, Auffret V, Debry N, Lefèvre T, Eltchaninoff H, Manigold T, Gilard M, Verhoeye J-P, et al. Balloon-expandable versus self-expanding transcatheter aortic valve replacement: a propensity-matched comparison from the France-TAVI registry. Circulation. 2020;141:243–259. doi: 10.1161/CIRCULATIONAHA.119.043785

25. Hamm CW, Mollmann H, Holzhey D, Beckmann A, Veit C, Figulla H-R, Cremer J, Kuck K-H, Lange R, Zahn R, et al. The German aortic valve registry (GARY): in-hospital outcome. Eur Heart J. 2014;35:1588–1598. doi: 10.1093/eurheartj/ehu381

26. Abdel-Wahab M, Fujita B, Frerker C, Bauer T, Beckmann A, Bekereldjian R, Bleiziffer S, Mollmann H, Walthier T, Hamm C, et al. Transcatheter versus rapid-deployment aortic valve replacement: a propensity-matched analysis from the German aortic valve registry. ACC Cardiovasc Interv. 2020;13:2642–2654. doi: 10.1016/j.jcin.2020.09.018

27. Mäkikallio T, Jälava MP, Hussu A, Virtanen M, Laakso T, Ahvenvaara T, Taurianen T, Maarinen P, Kimonen E-M, Dahlbacka S, et al. Ten-year experience with transcatheter and surgical aortic valve replacement in Finland. Ann Med. 2019;51:270–279. doi: 10.1080/07853890.2019.1614657

28. U.S. Census Bureau QuickFacts. Available at: https://www.census.gov/quickfacts/fact/table/US/PST045219. Accessed February 25, 2022.

29. Akhouli M, Holmes DR Jr, Carroll JD, Li Z, Inohara T, Kosinski AS, Szerlip M, Thurani VH, Mack MJ, Vemulapalli S. Racial disparities in the utilization and outcomes of TAVR: TVT registry report. JACC Cardiovasc Interv. 2019;12:936–948. doi: 10.1016/j.jcin.2019.03.007