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ORIGINAL RESEARCH

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%; $P<0.001$) 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

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CLINICAL PERSPECTIVE

What Is New?

- Transcatheter aortic valve replacement outcomes in the 2 national registries were compared for the first time using harmonized data from Japan and the United States.
- The number of transcatheter aortic valve replacement procedures and institutions increased in both Japan and the United States.
- In Japan, the outcomes after transcatheter aortic valve replacement measured by 30-day mortality, stroke, and bleeding were better, but the risk of conversion to open surgery was higher.

What Are the Clinical Implications?

- This first international comparative analysis showed the feasibility of international procedures and helps identify areas for shared learning and iteration among respective transcatheter aortic valve replacement programs.
- Most importantly, this study shows the importance of common data standards to pave the way for further international quality-of-care comparisons.

Nonstandard Abbreviations and Acronyms

ACC	American College of Cardiology
HBD	Harmonization by Doing
J-TVT	Japanese Transcatheter Valvular Therapy
MOR	median odds ratio
SAVR	surgical aortic valve replacement
STS	Society of Thoracic Surgeons
STS-PROM	Society of Thoracic Surgeons Predicted Risk of Mortality
TAVR	transcatheter aortic valve replacement
TVT	Transcatheter Valve Therapy

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.

METHODS

The authors will not make the data, methods used in the analysis, and materials used to conduct the research available to any researcher for purposes of reproducing the results or replicating the procedure.

Data Source

The 2 cohorts analyzed in this study originated from the 2 national registries: the STS/ACC TVT and the J-TVT registry. The STS/ACC TVT registry is a collaborative clinical registry program developed by the STS and the ACC in response to the Centers for Medicare and Medicaid Services national coverage decision (May 2012) requirement for national registry

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 hematoma, 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.

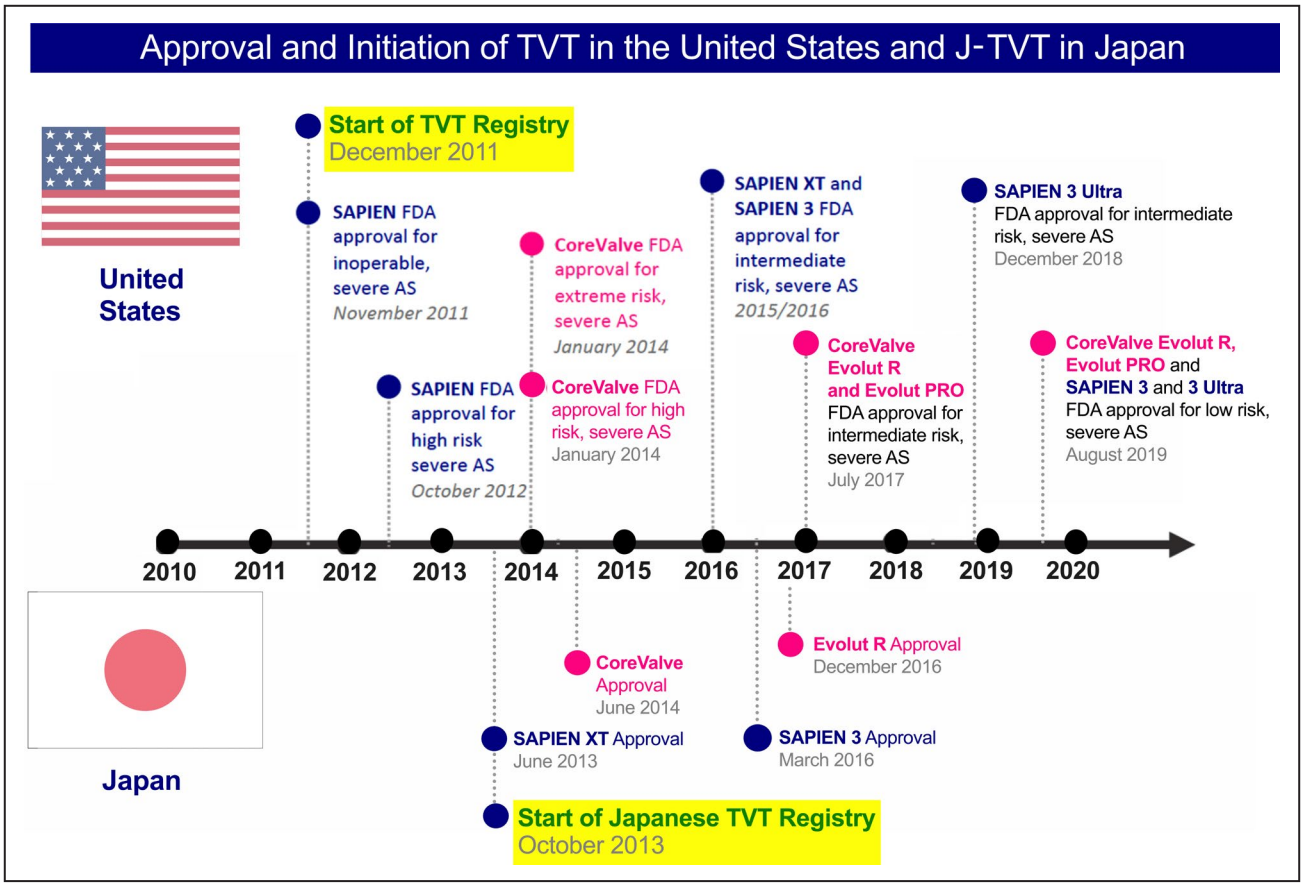


Figure 1. Timeline of governmental approval of TAVR devices and initiation of the Registries in the United States and Japan. AS indicates aortic stenosis; FDA, Food and Drug Administration; J-TVT, Japanese Transcatheter Valvular Therapy; TAVR transcatheter aortic valve replacement; and TVT, Transcatheter Valve Therapy.

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).

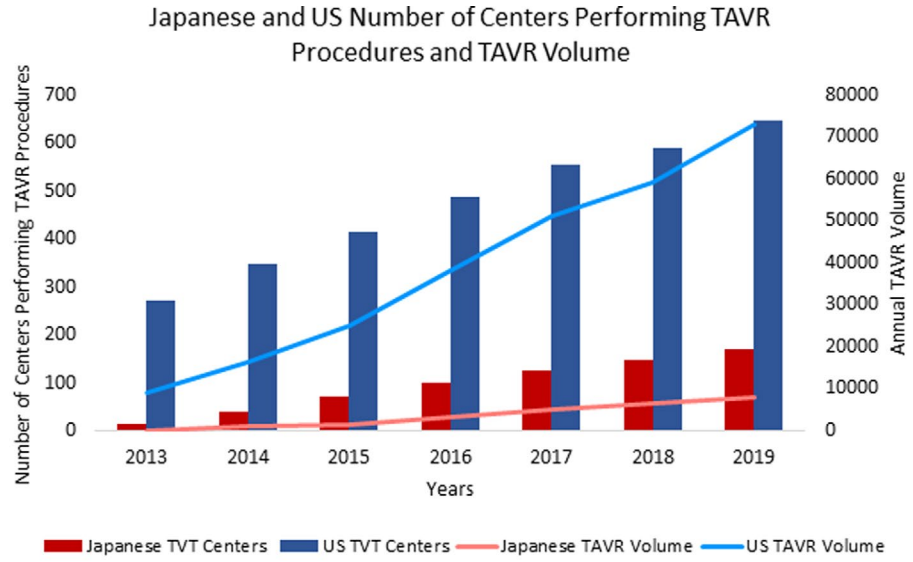
RESULTS

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-TVT 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% (925–7778) 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%



Years	2013	2014	2015	2016	2017	2018	2019
Japanese TVT Centers	15	39	70	100	126	147	170
US TVT Centers	272	347	414	488	554	590	646
Japanese TAVR Volume	98	925	1,538	3,103	5,110	6,601	7,778
US TAVR Volume	3039	16337	25096	38049	51001	59181	52019

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.

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).

Table 1. Site Details

	US TVT	J-TVT
Annualized site volume	N=646	N=171
Median (25th–75th)	65 (45–97)	28 (19–41)
Mean±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)
Mean±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.

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 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), m^2	1.89 (0.26)		1.43 (0.17)		<0.001
Medical history					<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	2985	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	181 431	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.

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, 1.49; 95% CI, 1.45–1.53) and Japan (MOR, 1.62; 1.49–1.74). Similarly, when 30-day mortality was used as an outcome, significant variability in site performance existed 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,

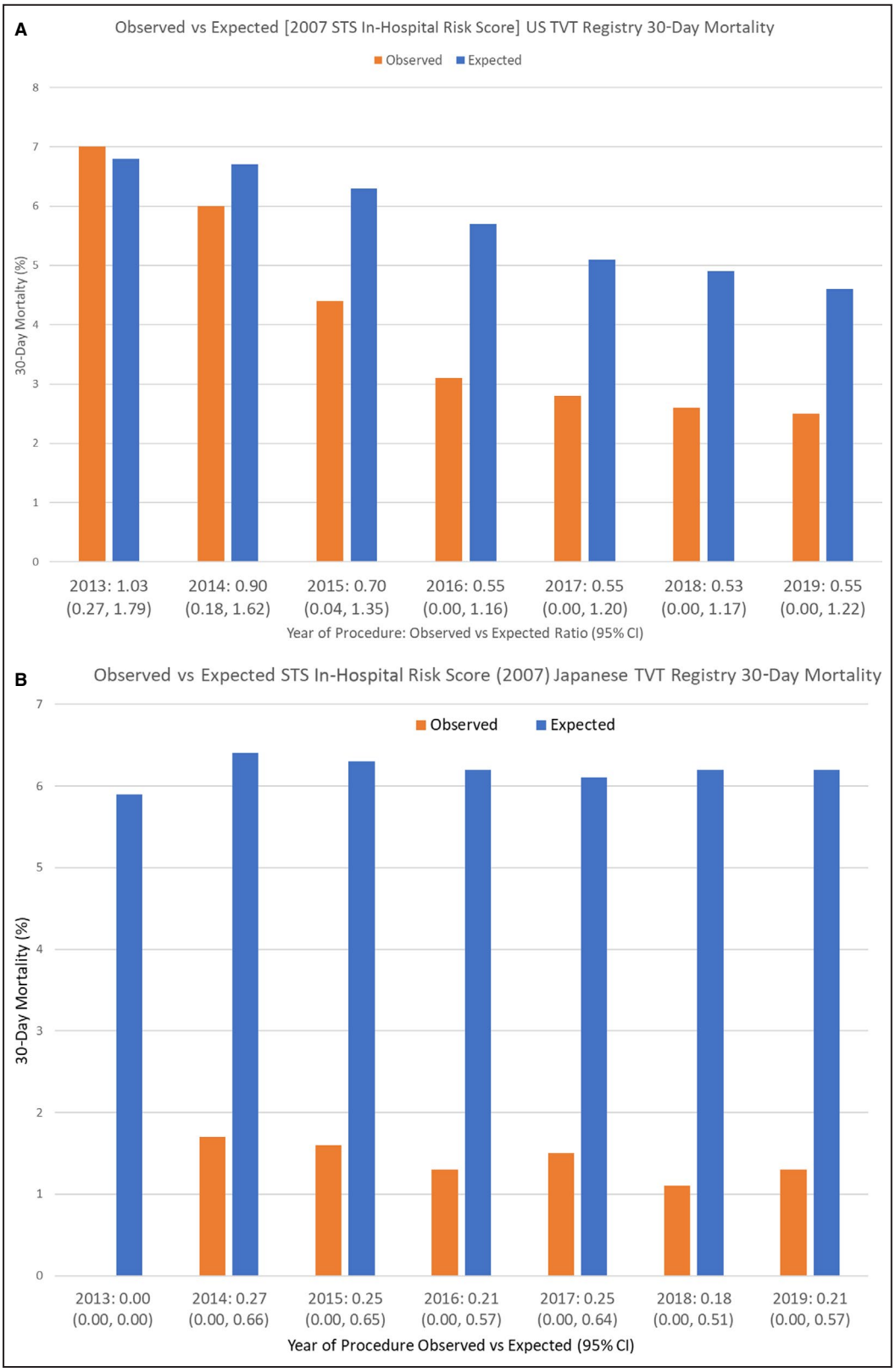


Figure 3. STS-PROM and 30-d mortality with calculated O/E ratio by year in the United States (A) and Japan (B).
O/E indicates observed-to-expected; STS, Society of Thoracic Surgeons; STS-PROM, Society of Thoracic Surgeons Predicted Risk of Mortality; TAVR, transcatheter aortic valve replacement; and TVT, Transcatheter Valve Therapy.

Table 3. Procedural Details

	TVT	TVT%	J-TVT	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	680	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-TVT indicates Japanese Transcatheter Valvular Therapy; 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 (eg, 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.

Table 4. Valve Size

Characteritic	US TVT	J-TVT
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-TVT indicates Japanese Transcatheter Valvular Therapy; and TVT, Transcatheter Valve Therapy.

The rapid growth of the US TAVR volume was recently published,[18] and this study confirmed a similar steep increase in TAVR cases in Japan. Based on previous reports from Europe,[19] 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 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 (3.37–8.40)	6.20 (4.41–8.85)	
Mean SD	6.83 (5.57)	7.43 (5.07)	
Min–max	0.35–91.35	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.

these regions were considerably fewer than those in North America and Europe,[3,4] 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 6. Composite and 30-Day Mortality Models

	Model 1	Model 2
United States		
Composite (death/stroke or bleeding) models, R^2, %	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, R^2, %	Marginal=0, conditional=2.1	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, R^2, %	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, R^2, %	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.[20] 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[21] 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,[22] 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.[23] 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), 1.8% (2011–2017); and Finland, 1.2% (2017) and 4.8% (2008),[19,24–27] 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.[28,29] 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-TVT 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-TVT 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-TVT 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.

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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.).

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