JACC: ASIA VOL. 2, NO. 7, 2022
© 2022 THE AUTHORS. PUBLISHED BY ELSEVIER ON BEHALF OF THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION. THIS IS AN OPEN ACCESS ARTICLE UNDER THE CC BY-NC-ND LICENSE (http://creativecommons.org/licenses/by-nc-nd/4.0/).

ORIGINAL RESEARCH

Outcome of Nonagenarians Undergoing Transfemoral Transcatheter Aortic Valve Replacement

A Nationwide Registry Analysis From Japan

Ryosuke Higuchi, MD,[a] Hiraku Kumamaru, MD, ScD,[b] Shun Kohsaka, MD, PhD,[c] Mike Saji, MD,[a] Itaru Takamisawa, MD,[a] Mamoru Nanasato, MD, PhD,[a] Tomoki Shimokawa, MD, PhD,[d] Hideyuki Shimizu, MD, PhD,[e] Morimasa Takayama, MD, PhD[a]

ABSTRACT

BACKGROUND Nonagenarians are a growing age group in patients undergoing transcatheter aortic valve replacement (TAVR); however, the appropriate use of TAVR in this population remains discussed because of their limited life expectancy and worse outcome reported.

OBJECTIVES The authors aimed to evaluate clinical characteristics and the prognostic impact of nonagenarians.

METHODS We analyzed consecutive patients undergoing transfemoral TAVR and were registered in the nationwide registry for TAVR in Japan (Japanese Transcatheter Valvular Therapies registry) between 2013 and 2018. The rate of 30-day and 1-year mortality and composite adverse event, comprising all-cause death, all stroke, and life-threatening/major bleeding, were assessed.

RESULTS Of the 15,028 registered patients during the study period, 2,215 (14.7%) were nonagenarians. Although the nonagenarians were less likely to have comorbid conditions (eg, diabetes mellitus and malignancy) than patients aged <90 y, they had a higher Society of Thoracic Surgeons risk score (8.8% vs 5.6%), mainly owing to their advanced age. The procedural characteristics were identical between 2 groups. The rate of 30-day mortality and composite endpoint was similar, whereas 1-year mortality and composite adverse events were increased among nonagenarians (10.3% vs 6.8% and 13.5% vs 9.2%, respectively), and nonagenarians were independently associated with these endpoints (HR: 1.21; 95% CI: 1.03-1.42; $P = 0.023$; HR: 1.24; 95% CI: 1.07-1.42; $P = 0.004$).

CONCLUSIONS Of the 15,028 TAVR procedures performed in Japan between 2013 and 2018, 14.7% were performed in nonagenarians. These patients were carefully selected by a multidisciplinary heart team and showed 21% and 24% increase of 1-year mortality and composite adverse outcome. (JACC: Asia 2022;2:856-864) © 2022 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

From the [a]Department of Cardiology, Sakakibara Heart Institute, Tokyo, Japan; [b]Department of Healthcare Quality Assessment, Graduate School of Medicine, University of Tokyo, Tokyo, Japan; [c]Department of Cardiology, Keio University, Tokyo, Japan; [d]Department of Cardiovascular Surgery, Sakakibara Heart Institute, Tokyo, Japan; and the [e]Department of Cardiovascular Surgery, Keio University, Tokyo, Japan.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received March 21, 2022; revised manuscript received July 27, 2022, accepted August 8, 2022.

ISSN 2772-3747 https://doi.org/10.1016/j.jacasi.2022.08.007

Transcatheter aortic valve replacement (TAVR) has been successfully implemented in the treatment of severe aortic stenosis for more than 2 decades. Traditionally, large-scale clinical trials target patients who have a high or prohibitive surgical risk, and most patients undergoing TAVR are elderly patients, such as octogenarians and septuagenarians.[1,2] The percentage of patients older than 65 years worldwide is 9.1% at present, which is projected to increase to 11.7% in 2030 and to 15.9% in 2050.[3] The increasing percentage of this population is particularly prominent in East Asian countries. According to the Statistics Bureau of Japan, the population of those 65 years and older accounts for 28.4% of the total population in Japan as of October 1, 2019, representing the highest percentage worldwide.[4]

With the aging of the population, the number of TAVRs performed in nonagenarians has also increased. Historically, nonagenarians have represented of 7% to 16% of patients in previous large-scale TAVR studies,[5-8] and this population is likely to continue to account for a substantial number of patients undergoing TAVR. However, randomized clinical trials on the effectiveness of TAVR did not enroll an adequate number of nonagenarian patients, and they are reported to be associated with a higher incidence of postprocedural complications and poor prognosis after TAVR from real-world databases.[5-8] For these reasons, the appropriateness of TAVR use in nonagenarians remains controversial,[9] and their outcome in contemporary TAVR (ie, transfemoral access, second generation valve, moderate anesthesia, high implantation method, and early discharge) is largely unknown.

ABBREVIATION AND ACRONYM

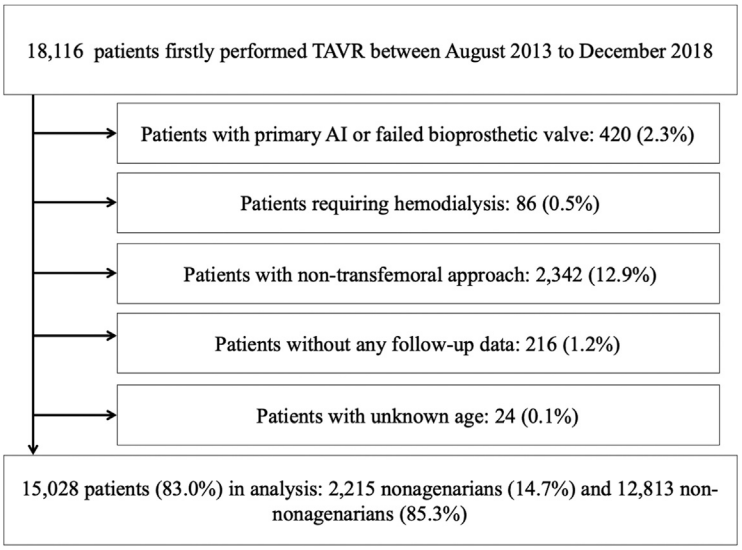
TAVR = transcatheter aortic valve replacement

Using the data of the Japanese nationwide TAVR registry, which encompasses TAVRs performed in Japan as the most aging country, we aimed to: 1) compare nonagenarians with non-nonagenarians in terms of baseline and procedural characteristics; and 2) assess the impact of nonagenarian status on 30-day and 1-year outcomes.

METHODS

The Japanese nationwide TAVR registry (J-TVT [Japan Transcatheter Valve Therapies] registry) was launched in 2013, and consecutive prospective registration is mandated for institutional- or operator-level certification. The J-TVT registry was established by 4 academic societies (Japanese Circulation Society, The Society of Japanese Cardiovascular Surgery, Japanese Association for Thoracic Surgery, and Japanese Association of Cardiovascular Intervention and Therapeutics) in collaboration with

FIGURE 1 Patient Flow in the Study



A total of 15,028 patients (83.0%) of 18,116 patients register in the Japanese Transcatheter Valvular Therapies registry were analyzed in the present study. AI = aortic insufficiency; TAVR = transcatheter aortic valve replacement.

JACC: ASIA, VOL. 2, NO. 7, 2022
DECEMBER 2022:856–864

TABLE 1 Baseline Characteristics of Nonagenarians and Patients Aged <90 Years

	Nonagenarians (n = 2,215)	Patients Aged <90 y (n = 12,813)	SD
Clinical variables			
Age, y			1.58
<65	0 (0.0)	46 (0.4)	
<75	0 (0.0)	531 (4.1)	
<85	0 (0.0)	6,561 (51.2)	
85-89	0 (0.0)	5,675 (44.3)	
90 and older	2,215 (100.0)	0 (0.0)	
Male/female	542 (24.5)/1,673 (75.5)	3,990 (31.1)/8,823 (68.9)	−0.15
BSA, m^2	1.34 (1.25-1.46)	1.43 (1.32-1.56)	−0.50
NYHA functional class III/IV	688 (31.1)	3,103 (24.2)	0.15
Hypertension	1,751 (79.1)	10,034 (78.3)	0.02
Dyslipidemia	860 (38.8)	6,205 (48.4)	−0.20
Diabetes mellitus	378 (17.1)	3,474 (27.1)	−0.24
CLD, moderate or severe	138 (6.2)	1,044 (8.1)	−0.07
CAD	588 (26.5)	4,958 (30.9)	0.10
Previous PCI	433 (19.5)	2,939 (22.9)	−0.08
Previous CABG	38 (1.7)	582 (4.5)	−0.16
Noncardiac artery disease	210 (9.5)	1,184 (9.2)	0.01
Cerebrovascular disease	234 (10.6)	1,490 (11.6)	−0.03
Porcelain aorta	181 (8.2)	1,005 (7.8)	0.01
Previous cardiovascular surgery	119 (5.4)	986 (7.7)	−0.09
Pacemaker	169 (7.6)	692 (5.4)	0.09
Malignancy	114 (5.1)	1,299 (10.1)	−0.19
Laboratory variables			
Hemoglobin, g/dL	10.9 (9.0-11.9)	11.4 (10.3-12.5)	−0.31
Albumin, g/dL	3.6 (3.3-3.9)	3.8 (3.5-4.1)	−0.12
Creatinine, mg/dL	0.9 (0.7-1.2)	0.9 (0.7-1.1)	0.07
AV mean gradient, mm Hg	49 (39-63)	47 (38-60)	0.09
LVEF, %	63 (55-70)	64 (57-70)	−0.07
Aortic insufficiency grade 3-4	138 (6.2)	994 (7.8)	0.003
Mitral insufficiency grade 3-4	222 (10.0)	994 (7.8)	0.08
STS score, %	8.8 (6.8-12.1)	5.6 (4.1-7.8)	0.61

Values are n (%) or median (IQR) unless otherwise indicated.

AV = aortic valve; BSA = body surface area; CABG = coronary artery bypass grafting; CAD = coronary artery disease; CLD = chronic lung disease; LVEF = left ventricle ejection fraction; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; SD = standardized difference; STS = Society of Thoracic Surgeons.

the Pharmaceuticals and Medical Devices Agency and industry to develop a database collecting information about TAVR procedures in Japan.[10,11] The strength of the J-TVT registry is to capture complete and accurate data of all TAVR procedures performed in Japan. Data collection started in August 2013. Complete case registration is confirmed every 3 years for the renewal of institutional certification. The annual number of cases registered in 2014 and 2020 exceeded 1,000 and 9,000, respectively. Data quality is ensured through automatic system validation, reporting of data completeness, training of site data managers, and data auditing (12 institutions annually), operated by members of the J-TVT Steering Committee. With more than 17,000 consecutive patients registered to date, the J-TVT registry provides an opportunity to investigate the procedural characteristics and outcomes of elderly patients who undergo TAVR.[10,11]

This study was conducted in accordance with relevant guidelines[12] and the declaration of Helsinki, and was acknowledged by the institutional review board of Sakakibara Heart Institute (number: 20-065).

STUDY POPULATION. Patient-level data were obtained from the J-TVT registry for all patients who underwent their first TAVR for primary aortic valve stenosis or failed surgical bioprosthesis between August 2013 and December 2018 (**Figure 1**). We excluded patients undergoing hemodialysis at baseline, in whom the use of TAVR was considered as off-label during the study period. Patients were also excluded if they had no follow-up information registered within the first 1-year post procedure or if they were missing age information. Because the transfemoral approach is the preferred access route and occupies the greatest proportion of contemporary TAVR, only transfemoral TAVR was analyzed. Patients included in the database were followed for 365 days after the index TAVR procedure. The modality used to obtain follow-up information on the patients was left to the discretion of the respective hospital participating in the J-TVT registry (eg, recording of the hospital visits, telephone interview, or mail).

DATA SOURCE. Consecutive patients who underwent TAVR were included in this study. During the study period, TAVR valves available for use included the following: SAPIEN XT (Edwards Lifesciences), SAPIEN3 (Edwards Lifesciences), CoreValve (Medtronic), Evolut R (Medtronic), and Evolut PRO (Medtronic). The J-TVT registry collects data elements/definitions that were initially derived from the US TVT Registry as part of a mutual process of harmonization. These elements also corresponded to data reported according to the updated standardized endpoint definitions for TAVR in the Valve Academic Research Consortium-2 consensus document.[13] The individual definitions of clinical variables are described in Supplemental Table 1.

STUDY ENDPOINTS. The outcome of interest was 1-year all-cause mortality following TAVR. We also assessed 1-year composite adverse endpoints comprising all-cause death, all stroke, and life-threatening or major bleeding. The rate of emergent surgical conversion and 30-day mortality and composite endpoints were evaluated as procedural outcomes.

STATISTICAL ANALYSIS. The patients were divided into 2 groups according to age (<90 years [non-nonagenarians] and ≥90 years [nonagenarians]).

We tabulated the patients' characteristics as counts and percentages for categorical variables and as median (IQR) for continuous variables. The baseline and procedural characteristics among nonagenarian and non-nonagenarians were compared using a standardized difference. We assessed the survival of nonagenarians and non-nonagenarians from the primary and secondary outcomes using the Kaplan-Meier method. Survival was compared between groups using the log-rank test. Patients were censored at 1 year after the procedure date or at the last follow-up date registered in the database, whichever occurred earlier. We constructed multivariate Cox proportional hazard regression models from the baseline and procedural factors presented in Table 1 to assess whether nonagenarians remained at an increased risk of event after adjusting for these factors. Statistical significance was set at $P < 0.05$, and all analyses were conducted using SAS (version 9.4, SAS Institute).

TABLE 2 Procedural Characteristics and Results of Nonagenarians and Patients Aged <90 Years

	Nonagenarians (n = 2,215)	Patients Aged <90 y (n = 12,813)	SD
Nonelective procedure	44 (2.0)	194 (1.5)	0.004
Anesthesia: moderate sedation/general anesthesia	447 (20.2)/1,768 (79.8)	2,435 (19.0)/10,378 (81.0)	0.09
Device			0.08
SAPIEN XT	411 (18.6)	2,343 (18.3)	
SAPIEN 3	1,243 (56.1)	7,560 (59.0)	
CoreValve	88 (4.0)	467 (3.6)	
Evolut R	405 (18.3)	2,041 (15.9)	
Evolut PRO	67 (3.0)	376 (2.9)	
None	1 (0.0)	26 (0.2)	
Valve implantation at proper position[a]	2,146 (96.9)	12,314 (96.1)	0.04
Conversion to open heart surgery	18 (0.8)	109 (0.9)	−0.004
Thirty-day mortality, %	38 (1.7)	125 (1.0)	0.06
Thirty-day composite adverse event,[b] %	109 (4.9)	404 (3.2)	0.09

Values are n (%). [a]Valve implantation at proper position denotes a correct positioning of a single prosthetic heart valve without valve embolization or ectopic valve deployment. [b]30-day composite adverse event included all-cause death, all strokes and life-threatening bleeding within 30 days.

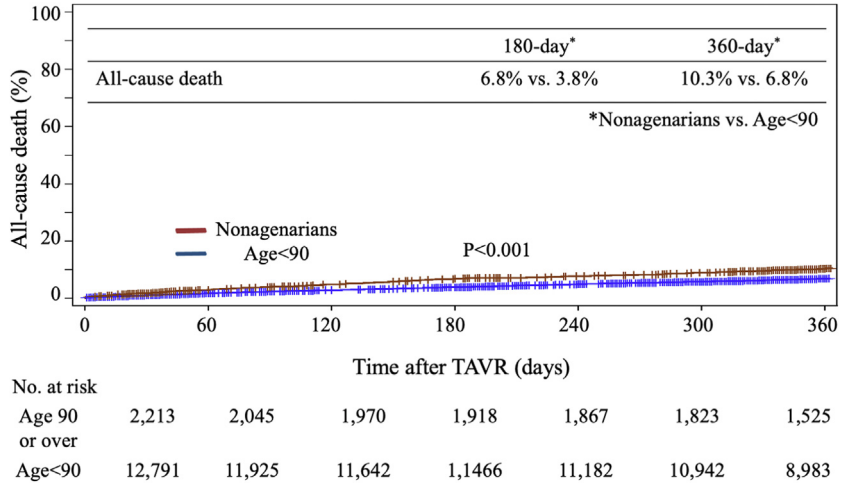
SD = standardized difference.

RESULTS

Overall, 18,116 patients underwent TAVR and were registered in the database between August 2013 and December 2018 in Japan. After excluding patients with primary aortic insufficiency or a failed bioprosthetic valve (n = 420), chronic dialysis (n = 86), non-transfemoral approach (n = 2,342), without follow-up data during 1 year after the procedure (n = 216), and unknown age (n = 24), 15,028 patients (83.0%) remained for analysis (Figure 1).

BASELINE AND PROCEDURAL CHARACTERISTICS, PROCEDURAL OUTCOMES. A total of 2,215 nonagenarians (median age: 91 years) were compared with 12,813 non-nonagenarians (median age: 84 years) in terms of baseline and procedural characteristics and procedural outcome (Tables 1 and 2). In terms of baseline characteristics, nonagenarians included a higher proportion of female patients and less frequently had associated comorbid conditions (eg,

FIGURE 2 All-Cause Mortality After TAVR in Nonagenarians and Non-Nonagenarians



All-cause death in nonagenarians was higher than that in non-nonagenarians. TAVR = transcatheter aortic valve replacement.

TABLE 3 Predictors of Mortality After TAVR: Multivariate Analysis

	HR	95% CI	*P* Value
Nonagenarians	1.21	1.03-1.42	**0.023**
Year of TAVR			
2013	0.64	0.20-2.02	0.45
2014	1.02	0.72-1.45	0.91
2015	reference		
2016	0.90	0.69-1.17	0.43
2017	0.81	0.64-1.04	0.10
2018	0.77	0.61-0.98	**0.036**
Female	0.48	0.41-0.57	**<0.0001**
BSA per 1-m^2 increase	0.98	0.98-0.99	**<0.0001**
NYHA functional class III/IV	1.17	1.02-1.35	**0.030**
Hypertension	0.87	0.75-1.01	0.074
Dyslipidemia	0.74	0.64-0.85	**<0.0001**
Diabetes mellitus	1.21	1.05-1.40	**0.010**
CLD, moderate or severe	1.50	1.24-1.81	**<0.0001**
CAD	0.95	0.74-1.23	0.71
Previous PCI	0.99	0.76-1.29	0.95
Previous CABG	1.17	0.77-1.79	0.46
Noncardiac artery disease	1.24	1.03-1.51	**0.026**
Cerebrovascular disease	0.95	0.78-1.15	0.58
Porcelain aorta	1.09	0.87-1.36	0.46
Previous cardiovascular surgery	1.05	0.77-1.42	0.76
Pacemaker	0.91	0.70-1.17	0.45
Malignancy	1.85	1.56-2.20	**<0.0001**
Hemoglobin per 1-g/dL increase	0.91	0.87-0.95	**<0.0001**
Albumin per 1-g/dL increase	0.60	0.53-0.68	**<0.0001**
Creatinine per 1-mg/dL increase	1.02	0.98-1.06	0.34
AV mean gradient per 1-mm Hg increase	0.99	0.98-0.99	**<0.0001**
AVA per 1-cm^2 increase	0.83	0.66-1.06	0.13
LVEF per 1% increase	1.01	1.00-1.01	0.073
Aortic insufficiency grade 3-4	1.03	0.82-1.28	0.83
Mitral insufficiency grade 3-4	1.01	0.81-1.25	0.96
STS score per 1% increase	1.03	1.02-1.04	**<0.0001**
Nonelective procedure	1.69	1.20-2.39	**0.003**

The **bold** values indicate statistical significance.
AVA = aortic valve area; TAVR = transcatheter aortic valve replacement; other abbreviations as in Table 1.

diabetes mellitus, coronary artery disease, and malignancy) than non-nonagenarians. With respect to laboratory values, hemoglobin values and albumin level were lower among nonagenarians, and a higher average Society of Thoracic Surgeons score was observed (8.8% vs 5.6%) mainly because of their older age. The procedural characteristics, including method of anesthesia and type of transcatheter heart valve used, did not differ between the 2 groups.

Emergent surgical conversion occurred in 0.8% of nonagenarians. Composite adverse events, including all-cause death, all strokes, and life-threatening/major bleeding events, occurred equivalently in both groups (4.9% vs 3.2%). The 30-day mortality rate was similar in both groups (1.7% vs 1.0%).

PRIMARY ENDPOINT. Figure 2 and Table 3 show the rates of all-cause death after TAVR. At 180 and 360 days, the mortality was 6.8% and 3.8%, and 10.3% and 6.8% in nonagenarians and non-nonagenarians, respectively (log-rank $P < 0.001$). After adjustment for baseline conditions and laboratory values, the relative increase in the risk of death in nonagenarians was 21% compared with that in non-nonagenarians (HR: 1.21; 95% CI: 1.03-1.42; $P = 0.023$).

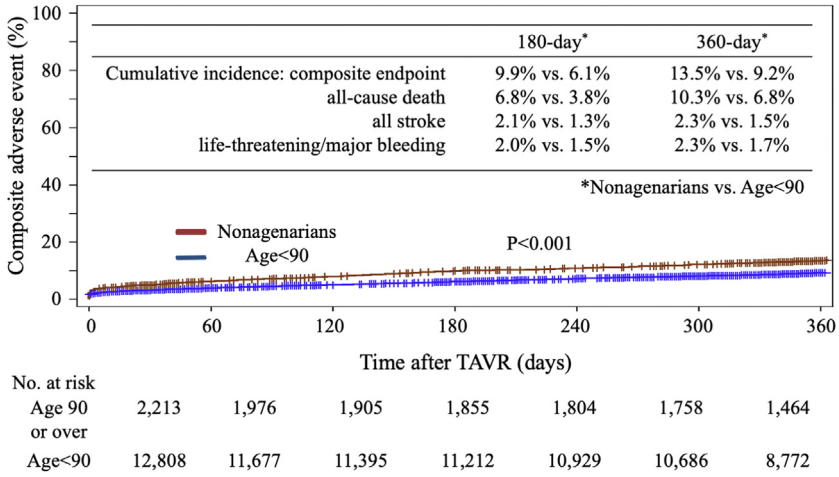
SECONDARY ENDPOINT. The Kaplan-Meier curve of composite adverse event after TAVR is shown in Figure 3 (see also Table 4). The rates of composite events in nonagenarians/non-nonagenarians were 9.9% and 6.1%, and 13.5% and 9.2% at 180 and 360 days, respectively (log-rank $P < 0.001$). In the multivariate regression model, a nonagenarian was a predictor of the composite adverse endpoint (HR: 1.24; 95% CI: 1.07-1.42; $P = 0.004$), along with other variables known to be associated with adverse outcomes, such as female sex, body size, symptom status, and other comorbid conditions (dyslipidemia, chronic lung disease, noncardiac artery disease, malignancy, anemia, malnutrition), mean pressure gradient, and Society of Thoracic Surgeons score. More recent procedure was inversely associated with mortality and composite outcome.

DISCUSSION

We analyzed the prevalence, clinical characteristics, complications, and long-term outcomes of nonagenarian patients who underwent TAVR by using a national J-TVT database in Japan (Central Illustration). To date, this is one of the largest cohorts of nonagenarians who underwent TAVR, representing a rapidly growing patient subgroup requiring treatment for severe aortic stenosis. Nonagenarians accounted for 14.7% of 15,028 patients registered in the J-TVT registry during the study period. Nonagenarians had the higher proportion of female patients, lower body habitus measurements, and higher overall preprocedural surgical score, and their 1-year mortality and composite adverse event rates were modestly increased compared with non-nonagenarians.

CHARACTERISTICS OF PATIENTS WHO UNDERWENT TAVR. In our study, nonagenarians differed from non-nonagenarians in several characteristics. These patients represent an innately distinct population from non-nonagenarians undergoing TAVR. The nonagenarians selected for our study did not simply equal the non-nonagenarians being 10 years older. Some common trends have been reported in nonagenarinans undergoing TAVR. In the largest

FIGURE 3 **Composite Adverse Events After TAVR in Nonagenarians and Non-Nonagenarians**



Composite adverse events in nonagenarians were higher than that in non-nonagenarians. TAVR = transcatheter aortic valve replacement.

registries in United States,[5,6] nonagenarians had a higher proportion of female patients and patients with previous heart failure and lower proportions of patients with diabetes mellitus, atherosclerotic disease, and chronic lung disease than non-nonagenarians. These findings are consistent with those observed in the present study. The possible reasons for the background differences between nonagenarians and non-nonagenarians included survival bias (ie, healthier individuals more frequently reached a nonagenarian), and selection bias (ie, nonagenarians who were estimated to have a better prognosis were selected as candidates for TAVR). Galatas and Afilalo[9] reviewed the outcomes of nonagenarians undergoing TAVR and described a healthy survivor effect and a referral bias. Although advanced age is a major risk factor of cardiac surgeries, the positive background characteristics of nonagenarians may overweigh its effects, considering the reasonable prognosis after TAVR in these patients.

PROCEDURAL CHARACTERISTICS AND IN-HOSPITAL OUTCOMES OF TAVR IN NONAGENARIANS. The procedural factors, including clinical status, anesthesia method, and approach site, were similar between nonagenarians and non-nonagenarians. From the current nationwide data, Japanese clinicians had evenly chosen the therapeutic plan and device among nonagenarians and non-nonagenarians.

In our study, emergent surgical conversion and 30-day mortality were infrequent in nonagenarians, similar to non-nonagenarians. The rate of our surgical conversion in the current study was also identical to that in a study based on the European registry.[14] A bias resulting from the avoidance of emergent surgery in the life-threatening complication may be absent considering the similar 30-day mortality rate between nonagenarians and non-nonagenarians. The 30-day mortality in our study was lower than that in previous reports.[5-7] The possible reasons may be: 1) the study period (ie, our study was performed during the mature phase of TAVR; TAVR was introduced into clinical practice in Japan in the second decade after the first-in-human TAVR [ie, 2002] under a specific program[10]); 2) the high proportion of second-generation devices used (vs first-generation devices); and 3) the exclusion of patients with non-transfemoral access. In addition, Japanese practitioners might be cautious about TAVR interventions to nonagenarians.[15] Indeed, the J-TVT registry had more elective cases compared with previous studies. Another potential explanation for this is the more robust and reliable follow-up in the Japanese system such that fewer patients present with “de novo” severe, decompensated aortic stenosis.

1-YEAR OUTCOME. The J-TVT registry has the advantage of capturing complete data of all TAVR procedures performed in Japan.[10,11] Accordingly, our data represent the real nature of TAVR in Japanese nonagenarians with a universal 1-year follow-up. The 2020 American College of Cardiology/American Heart Association guidelines do not recommend TAVR: 1) in patients with a life expectancy of <1 year even with a

JACC: ASIA, VOL. 2, NO. 7, 2022
DECEMBER 2022:856–864

TABLE 4 Predictors of Composite Adverse Events After TAVR: Multivariate Analysis

	HR	95% CI	*P* Value
Nonagenarians	1.24	1.07-1.42	**0.004**
Year of TAVR			
2013	0.79	0.32-1.94	0.61
2014	1.13	0.85-1.51	0.39
2015	reference		
2016	0.86	0.68-1.08	0.18
2017	0.80	0.65-0.99	**0.038**
2018	0.76	0.62-0.93	**0.009**
Female	0.61	0.52-0.70	**<0.0001**
BSA per 1-m^2 increase	0.99	0.98-0.99	**<0.0001**
NYHA functional class III/IV	1.18	1.04-1.33	**0.010**
Hypertension	0.96	0.84-1.09	0.49
Dyslipidemia	0.84	0.75-0.95	**0.004**
Diabetes mellitus	1.13	0.99-1.28	0.064
CLD, moderate or severe	1.48	1.26-1.75	**<0.0001**
CAD	0.98	0.79-1.22	0.87
Previous PCI	1.02	0.82-1.28	0.85
Previous CABG	1.01	0.70-1.46	0.95
Noncardiac artery disease	1.22	1.03-1.44	**0.021**
Cerebrovascular disease	1.08	0.92-1.27	0.34
Porcelain aorta	1.17	0.98-1.41	0.090
Previous cardiovascular surgery	1.13	0.87-1.47	0.35
Pacemaker	0.97	0.78-1.21	0.78
Malignancy	1.64	1.40-1.91	**<0.0001**
Hemoglobin per 1-g/dL increase	0.94	0.91-0.98	**0.001**
Albumin per 1-g/dL increase	0.72	0.65-0.80	**<0.0001**
Creatinine per 1-mg/dL increase	1.01	0.97-1.05	0.67
AV mean gradient per 1-mm Hg increase	0.99	0.99-0.99	**<0.0001**
AVA per 1-cm^2 increase	0.83	0.67-1.03	0.091
LVEF per 1% increase	1.00	1.00-1.01	0.77
Aortic insufficiency grade 3-4	1.06	0.88-1.29	0.53
Mitral insufficiency grade 3-4	0.93	0.77-1.12	0.45
STS score per 1% increase	1.02	1.01-1.03	**<0.0001**
Nonelective procedure	1.50	1.09-2.07	**0.014**

The **bold** values indicate statistical significance.
Abbreviations as in Tables 1 and 3.

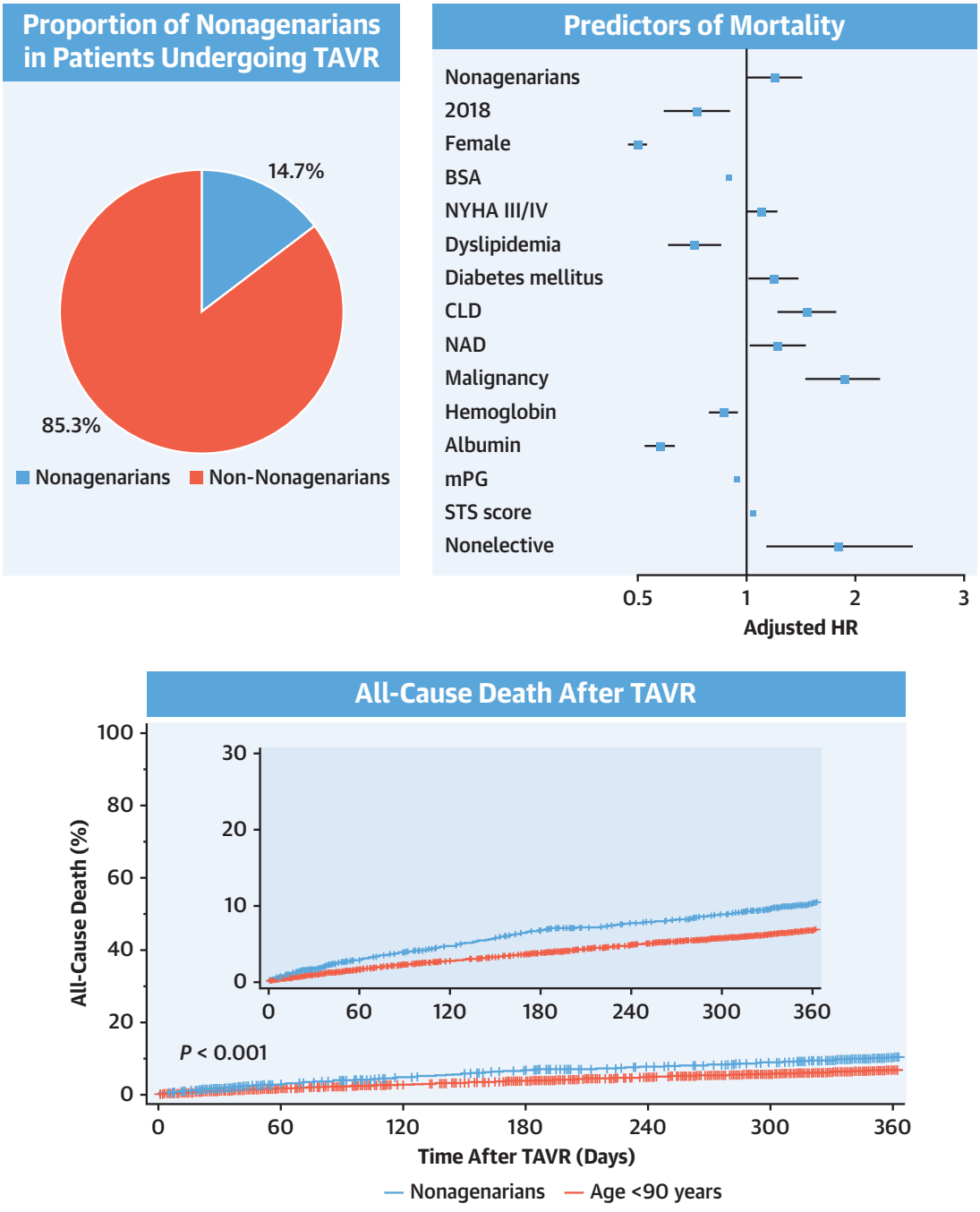
successful procedure; or 2) in those with a chance of survival with benefit of <25% at 2 years.[16] According to the Statistics Bureau of Japan, the average life expectancy of 90-year-old Japanese individuals is 4.33 years for men and 5.66 years for women as of 2018.[17] In line with prior studies reporting inferior mid-term outcome in nonagenarians,[5-8] a nonagenarian status itself was a statistically significant factor for prediction of mortality in our analysis. However, the percentage of 1-year mortality of nonagenarians in the J-TVT registry is approximately one-half of those studies. The possible explanations include longer life expectancy in Japanese nonagenarians,[17] and the fact that TAVR was performed in more recent years for these patients. We included TAVRs performed between 2013 and 2018, whereas prior studies were mostly based on data before the era of novel devices (eg, Society of Thoracic Surgeons/American College of Cardiology TVT registry: 2011 to 2014; German Aortic Valve Registry: 2011 to 2015).[5-8] Mentias et al[6] reported 30-day mortality declined in nonagenarians from 9.8% in 2012 to 4.4% in 2016. In our multivariate analysis, TAVR performed in 2018 was associated with better survival, and this should be attributed to more optimal patient selection, procedure learning curve, the newest device, and appropriate peri-procedural management. For therapeutic decision in nonagenarians, careful attention should be paid to the anatomic compatibility for TAVR, individual life expectancy after the cure of aortic stenosis, and estimated regression of symptom and quality of life after TAVR. To enhance the efficacy of TAVR, a comprehensive approach to frailty, sarcopenia, malnutrition, and comorbidities is needed in nonagenarians.[18-20] Considering the increasing health care cost and limited medical resource, the economics of TAVR in nonagenarians should be investigated in further study.[21]

STUDY LIMITATIONS. First, the database lacked information on Valve Academic Research Consortium-2 criteria defined vascular complication, frailty, and quality of life. Previous study reported the higher incidence of major vascular access site complication in nonagenarians.[5] The comorbidities included in the present study are known to correlate with the degree of individual frailty. Therefore, it is possible that therapeutic gain of quality of life might be smaller in nonagenarians.[5] Second, the follow-up duration was limited, and the long-term influence of a nonagenarian status was not evaluated. Third, we could not perform a cost-effectiveness analysis. Fourth, as the study population was selected from a registry database that mandated registration for institutional and operator certification in Japan, our results may not be applicable to patients undergoing TAVR in other regions or countries. Fifth, additional factors including psychosocial and financial variables and operator preferences could not be fully accounted for in our models.

CONCLUSIONS

Among the Japanese patients who underwent TAVR between 2013 and 2018, 14.7% were nonagenarian. Nonagenarians differed from non-nonagenarians in several backgrounds. The 30-day mortality rate in nonagenarians was similar to that in non-nonagenarians. At the 1-year follow-up, nonagenarians showed 21% and 24% increases of mortality and composite adverse endpoints compared with non-nonagenarians.

CENTRAL ILLUSTRATION **Proportion and Mortality of Nonagenarians After TAVR**



Higuchi R, et al. JACC: Asia. 2022;2(7):856–864.

Of the 15,028 TAVR procedures performed in Japan between 2013 and 2018, 14.7% were performed in nonagenarians. These patients showed 21% increase of 1-year mortality after TAVR. BSA = body surface area; CLD = chronic lung disease; NAD = noncardiac artery disease; NYHA = New York Heart Association; PG = mean pressure gradient; STS = Society of Thoracic Surgeons; TAVR = transcatheter aortic valve replacement.

JACC: ASIA, VOL. 2, NO. 7, 2022
DECEMBER 2022:856–864

ACKNOWLEDGMENTS The authors thank all the participants of J-TVT registry.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

Dr Kumamaru is affiliated with the department of Healthcare Quality Assessment, which is a social collaboration department supported by National Clinical Database, Johnson & Johnson K.K., and Nipro Corporation. Dr Kohsaka has received unrestricted grants from Daiichi Sankyo and Novartis and lecture fees from Bayer, Bristol-Myers Squibb, and Pfizer outside of the submitted work. Dr Takamisawa is a technical proctor of Edwards Lifesciences and Medtronic. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr Ryosuke Higuchi, Department of Cardiology, Sakakibara Heart Institute, 3-16-1 Asahi-cho, Fuchu, Tokyo 183-0003, Japan. E-mail: rhiguchi@shi.heart.or.jp. Twitter: @SHI_Cardiol.

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: The increasing percentage of the elderly population is particularly prominent in East Asian countries. Of the 15,028 transfemoral TAVR procedures performed in Japan between 2013 and 2018, 14.7% were performed in nonagenarians, who present a distinct patient population from non-nonagenarians. The 30-day mortality rate in nonagenarians was similar to that in non-nonagenarians. At the 1-year follow-up, the relative increase in mortality in nonagenarians was limited compared with that in non-nonagenarians.

TRANSLATIONAL OUTLOOK: Further studies with longer follow-up are warranted to evaluate the impact of physical/psychological/social frailty and the cost-effectiveness on TAVR in nonagenarians.

REFERENCES

1. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med*. 2010;363:1597–1607.

2. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med*. 2011;364:2187–2198.

3. Population Division, Department of Economic and Social Affairs, United Nations. World population prospects 2019: highlights. Accessed February 13, 2021. https://population.un.org/wpp/Publications/Files/WPP2019_Highlights.pdf

4. Statistics Bureau. Ministry of Internal Affairs and Communications, Japan. Current population estimates as of October 1, 2019. Accessed February 13, 2021. https://www.stat.go.jp/english/data/jinsui/2019np/index.html

5. Arsalan M, Szerlip M, Vemulapalli S, et al. Should transcatheter aortic valve replacement be performed in nonagenarians? Insights from the STS/ACC TVT Registry. *J Am Coll Cardiol*. 2016;67:1387–1395.

6. Mentias A, Saad M, Desai MY, et al. Temporal trends and clinical outcomes of transcatheter aortic valve replacement in nonagenarians. *J Am Heart Assoc*. 2019;8:e013685.

7. Deharo P, Bisson A, Herbert J, et al. Outcomes in nonagenarians undergoing transcatheter aortic valve implantation: a nationwide analysis. *EuroIntervention*. 2020;15:1489–1496.

8. Blumenstein J, Möllmann H, Bleiziffer S, et al. Transcatheter aortic valve implantation in nonagenarians: insights from the German Aortic Valve Registry (GARY). *Clin Res Cardiol*. 2020;109:1099–1106.

9. Galatas C, Afilalo J. Transcatheter aortic valve replacement over age 90: risks vs benefits. *Clin Cardiol*. 2020;43:156–162.

10. Handa N, Kumamaru H, Torikai K, et al. Learning curve for transcatheter aortic valve implantation under a controlled introduction system - initial analysis of a Japanese nationwide registry. *Circ J*. 2018;82:1951–1958.

11. Meguro K, Kumamaru H, Kohsaka S, et al. Transcatheter aortic valve replacement in patients with a small annulus - from the Japanese Nationwide Registry (J-TVT). *Circ J*. 2021;85:967–976.

12. Ministry of Health, Labour and Welfare, Japan. Ethical guidelines for medical and health research involving human subjects. Accessed February 13, 2021. https://www.mhlw.go.jp/file/06-Seisakujouhou-10600000-Daijinkanboukouseikagakuka/0000080278.pdf

13. Kappetein AP, Head SJ, Généreux P, 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.

14. Eggebrecht H, Vaquerizo B, Moris C, et al. Incidence and outcomes of emergent cardiac surgery during transfemoral transcatheter aortic valve implantation (TAVI): insights from the European Registry on Emergent Cardiac Surgery during TAVI (EuRECS-TAVI). *Eur Heart J*. 2018;39:676–684.

15. Kaneko T, Vemulapalli S, Kohsaka S, et al. 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. *J Am Heart Assoc*. 2022;11:e023848.

16. Otto CM, Nishimura RA, Bonow RO, 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. *J Am Coll Cardiol*. 2021;77:e25–e197.

17. Statistics Bureau. Ministry of Internal Affairs and Communications, Japan. Trends of life expectancies by age. Accessed February 13, 2021. https://www.stat.go.jp/english/data/nenkan/70nenkan/1431-02.html

18. Hioki H, Watanabe Y, Kozuma K, et al. Risk stratification using lean body mass in patients undergoing transcatheter aortic valve replacement. *Catheter Cardiovasc Interv*. 2018;92:1365–1373.

19. Shimura T, Yamamoto M, Kano S, et al. Predictors and prognostic impact of nutritional changes after transcatheter aortic valve replacement. *Cardiovasc Revasc Med*. 2021;23:68–76.

20. Bernal E, Ariza-Solé A, Bayés-Genís A, et al. Management of nonagenarian patients with severe aortic stenosis: the role of comorbidity. *Heart Lung Circ*. 2018;27:219–226.

21. Reynolds MR, Magnuson EA, Lei Y, et al. Cost-effectiveness of transcatheter aortic valve replacement compared with surgical aortic valve replacement in high-risk patients with severe aortic stenosis: results of the PARTNER (Placement of Aortic Transcatheter Valves) trial (Cohort A). *J Am Coll Cardiol*. 2012;60:2683–2692.

KEY WORDS elderly, Japan, J-TVT registry, TAVR

APPENDIX For a supplemental table, please see the online version of this paper.