ORIGINAL RESEARCH

Temporal Trends and Clinical Outcomes of Transcatheter Aortic Valve Replacement in Nonagenarians

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Background—Contemporary outcomes of transcatheter aortic valve replacement (TAVR) in nonagenarians are unknown.

Methods and Results—We identified 13 544 nonagenarians (aged 90–100 years) who underwent TAVR between 2012 and 2016 using Medicare claims. Generalized estimating equations were used to study the change in short-term outcomes among nonagenarians over time. We compared outcomes between nonagenarians and non-nonagenarians undergoing TAVR in 2016. A mixed-effect multivariable logistic regression was performed to determine predictors of 30-day mortality in nonagenarians in 2016. A center was defined as a *high-volume center* if it performed ≥100 TAVR procedures per year. After adjusting for changes in patients' characteristics, risk-adjusted 30-day mortality declined in nonagenarians from 9.8% in 2012 to 4.4% in 2016 ($P<0.001$), whereas mortality for patients <90 years decreased from 6.4% to 3.5%. In 2016, 35 712 TAVR procedures were performed, of which 12.7% were in nonagenarians. Overall, in-hospital mortality in 2016 was higher in nonagenarians compared with younger patients (2.4% versus 1.7%, $P<0.05$) but did not differ in analysis limited to high-volume centers (2.2% versus 1.7%; odds ratio: 1.33; 95% CI, 0.97–1.81; $P=0.07$). Important predictors of 30-day mortality in nonagenarians included in-hospital stroke (adjusted odds ratio [aOR]: 8.67; 95% CI, 5.03–15.00), acute kidney injury (aOR: 4.11; 95% CI, 2.90–5.83), blood transfusion (aOR: 2.66; 95% CI, 1.81–3.90), respiratory complications (aOR: 2.96; 95% CI, 1.52–5.76), heart failure (aOR: 1.86; 95% CI, 1.04–3.34), coagulopathy (aOR: 1.59; 95% CI, 1.12–2.26; $P<0.05$ for all).

Conclusions—Short-term outcomes after TAVR have improved in nonagenarians. Several procedural complications were associated with increased 30-day mortality among nonagenarians. **(*J Am Heart Assoc*. 2019;8:e013685. DOI: 10.1161/JAHA.119.013685.)**

Key Words: elderly • nonagenarians • outcome • transcatheter aortic valve implantation

Since its approval by the US Food and Drug Administration in 2011, transcatheter aortic valve replacement (TAVR) has been a breakthrough in the treatment of patients with severe symptomatic aortic stenosis (AS), especially in high-risk and elderly patients.[1,2] Because of improvement in health care, the nonagenarian population continues to expand and is expected to reach >8.5 million nonagenarians in the United States by 2050.[3] Because AS is a disease of aging, it is expected that the number of nonagenarians with severe AS will rise proportionally.[4]

Nonagenarians were underrepresented in the pivotal TAVR trials, where the mean age of the study population was early 80s.[2,5] Although a few studies demonstrated the feasibility of TAVR in nonagenarians,[6,7] the available data regarding TAVR

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Accompanying Data S1, Tables S1 through S5, and Figure S1 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.013685

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Clinical Perspective

What Is New?

- Thirty-day mortality after transcatheter aortic valve replacement in nonagenarians has improved significantly over the past few years.
- Procedural complications such as in-hospital stroke, acute kidney injury, and need for blood transfusion remain associated with increased risk of short-term mortality.

What Are the Clinical Implications?

- In nonagenarians with severe symptomatic aortic stenosis, transcatheter aortic valve replacement is a safe and feasible option.
- Appropriate preprocedural planning should be focused on reducing periprocedural complications to improve short- and long-term outcomes.

outcomes in this population are limited. Prior studies were either limited by small sample sizes from single centers[8,9] or by reporting outcomes from the earlier years of TAVR experience,[6,10] making the extrapolation of these results to the contemporary era of TAVR suboptimal. Although age is an important element of the Society of Thoracic Surgery risk score, which determines mortality risk with surgical aortic valve replacement, its utility in determining 30-day mortality with TAVR is unclear.[11,12]

The goals of this study are (1) to evaluate changes over time in short-term outcomes of TAVR nonagenarians; (2) to compare trends in 30-day mortality among nonagenarians and patients aged 65 to 89 and other short-term outcomes among patients undergoing TAVR in the last year of the study (2016); and (3) to evaluate factors associated with 30-day mortality among nonagenarians in 2016, including postprocedural complications and facility TAVR volume. Our findings may help nonagenarian patients and their clinicians reach informed decisions regarding TAVR in this relatively high-risk population.

Methods

Study Population

Data used for the study are covered under a data use agreement with the Centers for Medicare and Medicaid Services (CMS) and are not available for distribution by the authors but may be obtained from CMS with an approved data use agreement. Requests for statistical and analytic SAS programs used to create the analytic data set may be sent to first author Amgad Mentias (amgad-mentias@uiowa.edu). The study cohort was derived from 100% Medicare Provider and Analysis Review (MEDPAR) Part A files for the years 2011–2016, obtained from CMS. We utilized MEDPAR Part A files, which include all hospital discharges for Medicare fee-for-service beneficiaries to identify individuals aged ≥65 years who underwent TAVR during 2012–2016 using *International Classification of Diseases, Ninth Revision* (*ICD-9*) procedure codes for the period through September 2015 (35.05 and 35.06) and *ICD-10* procedure codes for the period after September 2015 (02RF37Z, 02RF38Z, 02RF3JZ, 02RF3KZ, 02RF37H, 02RF38H, 02RF3JH, 02RF3KH, or X2RF332). In patients who got a second TAVR procedure in follow-up, only the first procedure was included in our study. Dates of beneficiary Medicare fee-for-service enrollment and death were obtained from the 100% Beneficiary Summary and enrollment files for the same period. Patients were excluded if they had been enrolled in Medicare fee-for-service for <12 months before TAVR. Patient characteristics and comorbidities were derived from Medicare enrollment data and inpatient claims during the year before and during the TAVR admission. Patient characteristics included patient age, sex, and race (from the discharge record); dual eligibility for Medicaid (from the Beneficiary Summary file); and preexisting clinical conditions defined using *ICD-9* or *ICD-10* codes. Comorbid diseases included 30 conditions defined by Elixhauser et al[13] and additional conditions relevant to patient outcomes (Table S1).

Outcomes

The study cohort was divided into 2 groups based on age: nonagenarians (90–100 years) and non-nonagenarians (65–89 years). Patients aged >100 years were excluded (n=68). We explored 3 outcomes with TAVR in the nonagenarian group across the study period (2012–2016). One outcome was trends of postprocedure complications such as in-hospital stroke, acute kidney injury (AKI), blood transfusion, respiratory complications, vascular complications, and new permanent pacemaker implantation. The *ICD-9* and *ICD-10* codes used to define complications are outlined in Table S2. For in-hospital complications, a "Present on Admission" indicator was used to identify complications that developed during the TAVR hospitalization.[14] New pacemaker was defined using procedure codes on the same TAVR admission with no prior history of pacemaker. Other outcomes explored were trends of short-term outcomes (in-hospital and 30-day mortality and 30-day heart failure [HF] admissions) and trends in risk-adjusted rate of 30-day mortality using generalized estimating equations (GEE) modeling.

Subsequently, we conducted separate analyses of TAVRs performed in 2016 to compare short-term outcomes among nonagenarians and younger patients undergoing TAVR in 2016; to explore predictors of 30-day mortality in

nonagenarians in 2016; and to evaluate subsequent risk of stroke, bleeding, or heart failure admissions among nonagenarians. In addition to patient characteristics described previously, these analyses also used a validated *ICD-10*–based frailty index score to study prevalence of frailty in TAVR patients.[15] A score ≥5 is indicative of frailty. *ICD-9* and *ICD-10* codes used to define the study outcomes are reported in Table S2. These codes have been validated in prior studies and showed consistent validity.[16,17] The institutional review board of the University of Iowa approved this study with a waiver for individual informed consent, given the retrospective nature of the study.

Statistical Analysis

To evaluate trends in short-term outcomes among nonagenarians, continuous outcomes (eg, length of stay) were described as mean and standard deviation or median and interquartile range, as appropriate, and the trend was assessed with linear regression. Categorical outcomes were described as percentages, and trends were assessed using the Cochran–Armitage test for trend. To assess temporal trends in both groups, we performed the Mantel–Haenszel test for categorical variables.

Subsequently, we used GEE to estimate risk-adjusted trends in 30-day mortality among nonagenarians while accounting for clustering of patients in hospitals. Models were adjusted for patient demographics and comorbidities to determine the adjusted relative risk (aRR) and risk-adjusted 30-day mortality for each subsequent year compared with 2012. We further included other important factors that are known to affect post-TAVR mortality and that have changed over time, including procedure characteristics (eg, apical access), and postprocedural complications such as blood transfusion, respiratory complications, vascular complications, and in-hospital stroke. Because we hypothesized that hospital experience with TAVR is related to improvements in outcomes, we also included a facility-level measure of TAVR volume, calculated by summarizing all TAVR procedures across hospitals for each given year. A center was considered high-volume if it performed >100 TAVR cases per year.[18] To determine magnitude of different factors that might explain the improvement in 30-day mortality in nonagenarians, we performed the GEE model analysis in a stepwise fashion, adjusting first to change in patient characteristics and then to hospital volumes and change in postprocedure complications. The size of our sample and the number of events recorded permitted the utilization of a modified Poisson regression distribution model and the log link function to estimate RR ratios, as described previously.[19]

We then compared several short-term outcomes and postprocedure complications among nonagenarians and younger patients (aged 65–90 years) undergoing TAVR in the final study year (2016). Continuous outcomes (eg, length of stay) were compared between the 2 groups using ANOVA or the Mann–Whitney test; categorical outcomes were compared using the χ^2 test or Fisher exact test, as appropriate. In addition, we compared all-cause mortality among nonagenarians and younger patients through the end of the follow-up period (December 2016) using multivariable Cox proportional hazards regression to adjust for age, sex, preexisting comorbidities, TAVR access (apical versus nonapical), and hospital volume. A stepwise backward selection process, guided by the lowest Akaike information criterion to determine the best model fit combined with insight from clinical experience and previous literature, was performed.[20] To assess whether the proportional hazards assumption was violated, a Kolmogorov-type supremum test and graphical inspection of Schoenfeld residuals plotted against time were performed. Hazard ratios with 95% CIs were calculated. Kaplan–Meier curves with 95% CIs were generated to determine the cumulative proportion of patients who died as a function over time and were compared using log-rank or generalized Wilcoxon statistics. We then compared 1-year mortality outcome in nonagenarians with expected survival in an age- and sex-matched US cohort through indirect standardization using actuarial life tables published by the US Social Security Administration.[21] In supplementary analyses, we compared the RR of subsequent stroke, bleeding event, or heart failure admission among nonagenarians and younger patients in 2016 using proportional hazards regression, as detailed in Data S1. For these analyses, patients were censored due to death, Medicare disenrollment, or end of the study period (December 31, 2016).

Finally, we determined predictors of 30-day mortality in nonagenarians in the last year (2016) using a mixed-effects multivariable logistic regression with hospitals as a random-effects variable to account for clustering of patients within hospitals. Patient baseline characteristics were included in multivariable models, with additional analysis that also evaluated the impact of procedural complications on mortality (eg, in-hospital stroke). Adjusted odds ratios (aORs) are reported with 95% CIs derived from sandwich estimates of standard errors. Goodness of fit was determined with the Hosmer and Lemeshow test, and collinearity was assessed using the variance inflation factor with a cutoff of 2.0.

We performed a sensitivity analysis after excluding apical TAVR procedures. A *P* value of 0.05 was chosen for statistical significance. The analysis was done with SAS v9.4 (SAS Institute) and R 3.4.3 (R Foundation for Statistical Computing).

Results

Overall, 95 763 TAVR procedures were performed from 2012 to 2016 with nonagenarians comprising 14% (n=13 544) of

the population. The number of nonagenarians who underwent TAVR increased from 1209 in 2012 to 4546 in 2016, representing 17.8% and 12.7% of the total TAVR procedures performed in 2012 and 2016, respectively. Table 1 shows changes in nonagenarians' characteristics and comorbidities over the study years, and Table S3 shows the changes in younger patients (aged 65–89).

Trend in Outcomes Over the Study Period

In-hospital and short-term outcomes in nonagenarians

Table 2 shows the change in unadjusted outcomes in nonagenarians compared with younger patients across the 5 years of the study period. We observed a significant reduction in multiple adverse short-term outcomes in nonagenarians, including unadjusted rates of in-hospital mortality (7.5% in 2012, 4.7% in 2014, and 2.4% in 2016; P_{trend}<0.0001), in-hospital stroke (4.1% in 2012 versus 2.2% in 2016; P_{trend}=0.005), 30-day mortality (9.8% in 2012 versus 3.6% in 2016; P_{trend}<0.0001), and HF admissions (4.1% in 2012 versus 3.0% in 2016; P_{trend}=0.02). Length of intensive care unit and hospital stay also declined in nonagenarians, as did the percentage of patients discharged within 72 hours after TAVR increased (7.2% versus 56.4%; *P*<0.001). Similarly, postprocedure AKI and vascular and respiratory complications declined significantly in nonagenarians over the study period. Although 30-day mortality also decreased among younger patients (from 6.4% to 2.7%; *P*<0.001), the relative decrease in mortality among younger patients was roughly 10% smaller than the decrease experienced by nonagenarians (Figure 1A).

Table 1. Trends in Nonagenarians' Comorbidities Over the Study Years

Variable	2012	2013	2014	2015	2016	*P* Value
n	1209	1847	2549	3393	4546	
White race	94.3	94.6	94.8	94.6	94.5	0.9
Black race	2.5	2.9	2.6	2.7	2.7	
Male sex	49.7	47.2	49.0	47.5	49.5	0.3
Deficiency anemia	51.4	48.2	46.9	46.7	40.8	<0.001
Congestive heart failure	84.8	85.2	84.9	83.9	81.8	<0.001
Chronic lung disease	35.2	32.2	30.4	29.5	26.6	<0.001
Coagulopathy	31.8	28.8	28.3	25.3	20.8	<0.001
Depression	12.8	11.0	11.7	11.9	10.7	0.2
Diabetes mellitus	23.0	24.0	23.0	24.3	24.3	0.6
Hypertension	93.5	93.0	93.2	93.5	94.4	0.2
Hypothyroidism	29.0	31.0	29.8	29.4	30.1	0.7
Liver disease	1.3	0.5	0.8	1.0	1.4	0.007
Lymphoma	1.3	1.6	1.7	1.1	1.3	0.4
Electrolyte abnormality	52.1	51.7	50.0	46.9	42.5	<0.001
Obesity	4.8	6.8	7.4	7.7	7.7	0.008
Peripheral vascular disease	43.3	38.9	35.2	34.9	32.1	<0.001
Kidney disease	46.0	45.3	45.1	44.7	43.4	0.3
Underweight	11.8	11.0	10.5	9.5	8.4	<0.001
Atrial fibrillation	37.8	38.3	36.5	34.5	29.3	<0.001

Data represented in percentage.

Risk-adjusted rate of 30-day mortality in nonagenarians

After using GEE modeling to adjust for nonagenarians' demographics and comorbidities, risk-adjusted 30-day mortality in nonagenarians declined by 54% over the study period (9.8% in 2012 versus 4.4% in 2016; aRR: 0.44; 95% CI, 0.35–0.58; *P*<0.0001) and was lower in 2016 compared with each individual year in the study (2015: aRR: 0.73; 95% CI, 0.60–0.89; *P*=0.002; 2014: aRR: 0.60; 95% CI, 0.49–0.73; *P*<0.0001; 2013: aRR: 0.59; 95% CI, 0.47–0.74; *P*<0.0001; Figure 1B). Among younger patients, risk-adjusted 30-day mortality decreased by ≈46% (from 6.4% to 3.5%, *P*<0.001)—a roughly 15% smaller decrease than experienced by nonagenarians after adjusting for demographics and comorbidities. Table S4 shows the full GEE model for change in 30-day mortality. When changes in postprocedure complications (in-hospital stroke, blood transfusion, AKI, vascular and respiratory complications) and center volume were accounted for in the model, the RR of 2016 compared with prior years in nonagenarians was attenuated but remained significant (aRR: 0.54; 95% CI, 0.42–0.70; *P*<0.001 compared with 2012; aRR: 0.80; 95% CI, 0.66–0.96; *P*=0.02 compared with 2015), whereas high-volume centers showed a trend with lower 30-day mortality in the full GEE model (aRR: 0.88; 95% CI, 0.73–1.02; *P*=0.08).

Outcomes With TAVR in Nonagenarians Versus Non-Nonagenarians in 2016

Table 3 shows baseline characteristics and comorbidities in nonagenarians and non-nonagenarians in 2016. Nonagenarians had higher prevalence of HF, preexisting atrial fibrillation, and chronic kidney disease and lower prevalence of diabetes mellitus, liver disease, and chronic lung disease. Nonagenarians had slightly higher prevalence of frailty compared with younger patients (31.7% versus 30.0%; *P*=0.02) (Table S5).

In-hospital and short-term outcomes

In 2016, in-hospital mortality was higher in nonagenarians compared with non-nonagenarians (2.4% versus 1.7%; OR: 1.41; 95% CI, 1.15–1.74; *P*=0.001). However, in separate

Table 2. Trends in Nonagenarians' Procedure Characteristics and Outcomes Over the Study Period

Variable	2012	2013	2014	2015	2016	*P* Value
n (n=13 544)	1209	1847	2549	3393	4546	
Blood transfusion	32	31.9	22.4	16.1	9.6	<0.001
Length of ICU stay, d, mean±SD	3.3±5.2	3.4±5.0	3.2±5.0	2.6±4.3	2.0±3.5	<0.001
Length of hospital stay, d, median (IQR)	5 (4–8)	5 (4–8)	5 (3–7)	4 (3–6)	3 (2–5)	<0.001
Early discharge ≤72 h	7.2	11.4	20.4	35.2	56.4	<0.001
Next-day discharge	0.4	0.3	1.2	3.9	10.4	<0.001
AKI	19.8	21.7	19.3	16.1	12.3	<0.001
Respiratory complications	2.8	2.4	1.8	1.6	2.1	0.05
Vascular complications	15.6	10.7	10.7	8.3	3.7	<0.001
Discharge destination						
Home	22.1	19.6	23.4	31.3	42.5	<0.001
Skilled nursing facility	30.9	35.0	31.1	25.8	20.4	
Home health care	29.1	29.9	31.7	31.0	29.0	
Inpatient rehabilitation	7.5	6.7	6.5	6.0	4.0	
New pacemaker implantation	26.6	25.8	25.0	26.3	25.1	0.6
In-hospital mortality	7.5	5.6	4.7	3.7	2.4	<0.0001
In-hospital stroke	4.1	2.7	2.9	2.4	2.2	0.0005
30-d mortality	9.8	7.4	7.1	5.5	3.6	<0.0001
30-d stroke	4.6	3.0	3.2	2.9	2.7	0.001
30-d HF readmissions	4.1	4.9	3.7	4.2	3.0	0.003
6-mo mortality	21.3	17.4	16.6	14.3	9.8	<0.0001

Data are shown as percentage except as noted. AKI indicates acute kidney injury; HF, heart failure; ICU, intensive care unit; IQR, interquartile range.

analysis of high- and low-volume centers, we found no significant mortality difference among 2358 nonagenarians and 15 641 younger patients treated in high-volume centers (2.2% versus 1.7%; OR: 1.33; 95% CI, 0.97–1.81; *P*=0.07), whereas the risk of death was 1.50 times higher in nonagenarians compared with younger patients treated in

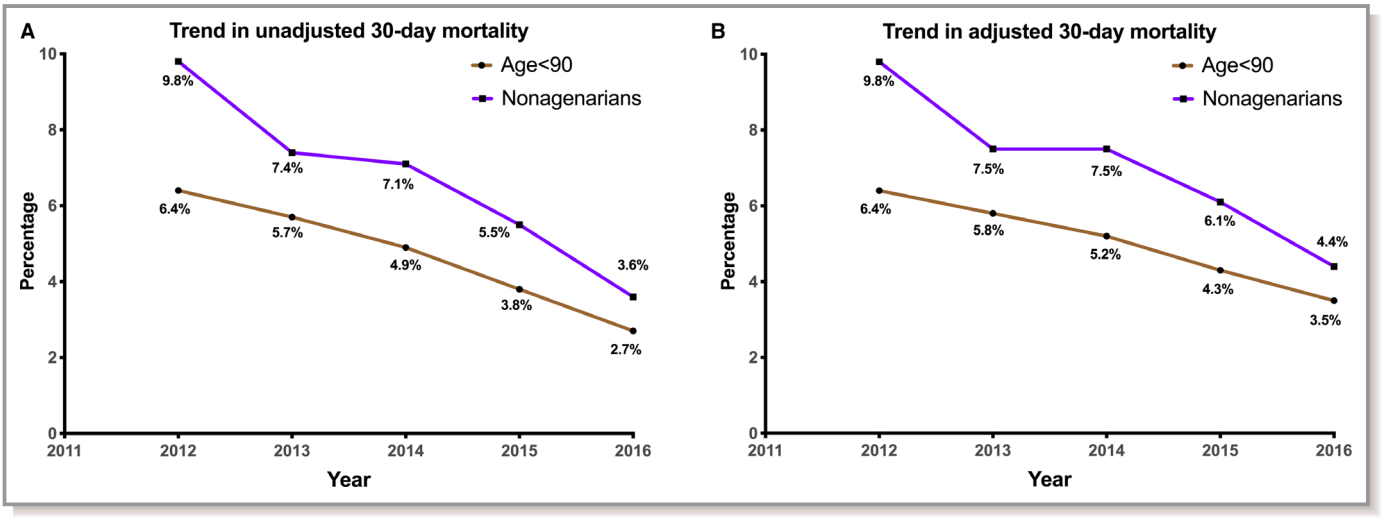

Figure 1. **A**, Trend in unadjusted 30-day mortality rates in nonagenarians and patients aged <90 years after transcatheter aortic valve replacement. P_{trend}<0.0001. **B**, Trend in risk-adjusted 30-day mortality rates in nonagenarians and patients aged <90 years after transcatheter aortic valve replacement. P_{trend}<0.0001.

Table 3. Baseline Characteristics of Patients in the 2 Groups in 2016

Variable	Patients <90 y	Nonagenarians	*P* Value
n	31 166	4546	
Age, y, mean (SD)	79.6 (7.4)	92.1 (2.0)	
White race	91.8	94.5	<0.0001
Black race	4.2	2.7	
Male	53.8	49.5	<0.0001
Alcohol use	2.8	0.8	<0.0001
Deficiency anemia	40.2	40.8	0.43
Connective tissue disease	7.0	5.4	<0.0001
Blood loss anemia	4.8	4.1	0.03
Congestive heart failure	78.5	81.8	<0.0001
Chronic lung disease	38.9	26.6	<0.0001
Coagulopathy	21.0	20.8	0.87
Depression	15.9	10.7	<0.0001
Diabetes mellitus	43.9	24.3	<0.0001
Hypertension	94.2	94.4	0.6
Hypothyroidism	24.7	30.1	<0.0001
Liver disease	4.4	1.4	<0.0001
Lymphoma	1.8	1.3	0.003
Fluid and electrolyte abnormality	42.5	42.5	0.9
Obesity	27.3	7.7	<0.0001
Peripheral vascular disease	35.3	32.1	0.0001
Psychosis	2.4	1.2	<0.0001
Pulmonary circulatory disease	8.7	7.8	0.1
Kidney disease	41.2	43.4	0.08
Tumor without metastasis	5.2	5.0	0.3
Weight loss	8.1	8.4	0.55
Atrial fibrillation	26.6	29.3	0.0002
Prior stroke	17.3	15.5	0.002
Obstructive sleep apnea	20.6	6.8	<0.0001
Prior smoking	19.0	12.5	<0.0001
Prior revascularization	33.1	24.4	<0.0001
Coronary artery disease	32.9	29.4	<0.0001
Prior bleeding	48.7	46.9	0.03
Prior pacemaker	12.9	19.7	<0.0001
Prior implanted defibrillator	4.4	2.2	<0.0001
Apical access	3.4	2.2	0.001
High volume TAVR center	65.6	66.4	0.33
Frailty score, mean (SD)	3.9 (6.0)	4.1 (5.8)	0.001
Low-risk score for frailty (score <5)	70.0	68.3	0.02
Intermediate-risk score for frailty (score 5–15)	23.6	25.7	0.002
High-risk score for frailty (score >15)	6.4	6.0	0.25
CHA_2DS_2VASc score			
≤3	9.5	6.9	<0.001
4	21.1	21.3	
5	31.6	36.4	
6	21.1	20.4	
≥7	16.7	15.0	

Data are shown as percentage except as noted. TAVR indicates transcatheter aortic valve replacement.

low-volume centers (2.6% versus 1.8%; OR: 1.50; 95% CI, 1.13–1.2.00; *P*=0.005). Overall, in-hospital stroke (2.2% versus 1.8%; *P*=0.04), 30-day mortality (3.6% versus 2.7%; *P*=0.0002), and 30-day HF readmissions (3.0% versus 2.1%; *P*<0.0001) were higher in nonagenarians compared with younger patients. Duration of intensive care unit stay, incidence of AKI, vascular complications, respiratory complications, and new permanent pacemaker implantation were similar in both groups. However, nonagenarians had higher incidence of blood transfusion and longer hospital stay and were less likely to be discharged within 72 hours or discharged home compared with non-nonagenarians (Table 4).

All-cause mortality and secondary outcomes

In time-to-event analysis comparing all-cause mortality among nonagenarians and younger patients while controlling for patient characteristics, apical access, and facility volume, being a nonagenarian was associated with higher risk of mortality (26.1 versus 17.7 deaths per 100 person-years; adjusted hazard ratio; 1.50; 95% CI, 1.36–1.66; *P*<0.001; Figure 2). When we used data from 2015 for indirect standardization to compare 1-year mortality with an age- and sex-matched US population,[21] nonagenarians who underwent TAVR in 2015 had 1-year mortality of 20.4% overall and 20% in high-volume centers, whereas the age- and sex-matched US population without AS would have expected 1-year mortality of 18.4%. Results of time-to-event analysis for secondary outcomes of stroke, bleeding events, and heart failure in 2016 are shown in Figure S1A through S1C.

Table 4. Procedure Measures and Outcomes in Nonagenarians and Patients Aged <90 Years With TAVR in 2016

Variable	Patients <90 y	Nonagenarians	*P* Value
n	31 166	4546	
Length of ICU stay, d, median (IQR)	1 (0–2)	1 (0–2)	0.2
Length of hospital stay, d, median (IQR)	3 (2–4)	3 (2–5)	<0.01
Early discharge ≤72 h	62.7	56.4	<0.001
Next-day discharge	13.2	10.4	<0.001
Blood transfusion	7.9	9.6	<0.001
AKI	11.9	12.3	0.42
Respiratory complications	2.4	2.1	0.26
Vascular complications	3.8	3.7	0.9
Discharge destination			
Home	56.4	42.5	<0.001
Skilled nursing facility	12.1	20.4	
Home health care	25.2	29.0	
Rehabilitation	3.1	4.0	
New pacemaker implantation	24.4	25.1	0.29
In-hospital mortality	1.7	2.4	0.001
In-hospital stroke	1.8	2.2	0.04
30-d mortality	2.7	3.6	0.003
30-d HF readmissions	2.1	3.0	<0.001
30-d stroke	2.2	2.7	0.06

Data are shown as percentage except as noted. AKI indicates acute kidney injury; HF, heart failure; ICU, intensive care unit; IQR, interquartile range; TAVR, transcatheter aortic valve replacement.

Predictors of 30-day mortality in nonagenarians in 2016

In the multivariable mixed-effect logistic regression accounting for clustering of patients, important predictors of 30-day mortality in nonagenarians included in-hospital stroke (aOR: 8.67; 95% CI, 5.03–15.00), AKI (aOR: 4.11; 95% CI, 2.90–5.83), blood transfusion (aOR: 2.66; 95% CI, 1.81–3.90), respiratory complications (aOR: 2.96; 95% CI, 1.52–5.76), heart failure (aOR: 1.86; 95% CI, 1.04–3.34), and coagulopathy (aOR: 1.59; 95% CI, 1.12–2.26; $P<0.05$ for all), whereas high-volume center was not associated with 30-day mortality in nonagenarians (aOR: 0.77; 95% CI, 0.55–1.07; Figure 3). Neither frailty nor age was associated with 30-day mortality in nonagenarians in 2016.

Sensitivity Analysis

In a sensitivity analysis, when apical TAVR procedures were excluded, the results of the study remained the same. For example, risk-adjusted 30-day mortality in nonagenarians declined from 9.2% in 2012 to 4.3% in 2016, $P_{trend}<0.001$. In GEE mode, the aRR was the lowest in 2016 compared with each previous year (2012: aRR: 0.47; 95% CI, 0.37–0.61; $P<0.001$; 2015: aRR: 0.74; 95% CI, 0.61–0.90; $P=0.003$). High-volume TAVR centers were still associated with lower 30-day mortality compared with lower volume centers (aRR: 0.84; 95% CI, 0.72–0.99; $P=0.04$). In 2016, in-hospital mortality was higher in nonagenarians compared with younger patients (2.4% versus 1.6%; $P<0.01$) but was not different when the analysis was limited to high-volume centers (2.1% versus 1.6%; $P=0.053$).

Discussion

In this study using Medicare data, we showed several important findings. First, the number of TAVR procedures done in nonagenarians has increased exponentially over the past few years accompanied by a significant decline in the rate of procedural complications in this population. Second, in-hospital and 30-day mortality rates have improved significantly in nonagenarians compared with the earlier years. In fact, in high-volume centers in 2016, there was no significant difference in in-hospital mortality between nonagenarians and patients aged <90 years. Third, we showed that among nonagenarians who underwent TAVR in the last available year, age was not associated with 30-day mortality. Important procedural outcomes such as in-hospital stroke, AKI, blood transfusion, and respiratory complications were associated with higher 30-day mortality and thus may represent potential opportunities to improve overall outcomes in this population.

According to the Social Security Administration, 1 of every 4 people aged 65 years in the United States will live past 90 years, and 1 of every 10 will live past 95 years.[22] As nonagenarians become an expanding cohort in our daily practice, the prevalence of AS in this population will continue to rise. The relatively high frailty in these patients significantly affects the decision of both patients and physicians regarding optimal treatment strategies. Consequently, our study represents an important addition to the literature regarding the most recently available outcomes with TAVR in this high-risk population.

In our study, we noted a significant decline in vascular complications in nonagenarians from 2012 to 2016. This change is probably related to improvement in the valve profile and smaller delivery systems used in recent years[23] and can explain the decline in blood transfusion rates in nonagenarians in the current study—this complication has always been linked to worse outcomes after TAVR.[24] We also noticed a significant decline in respiratory complications including mechanical ventilation, which is probably a reflection of the

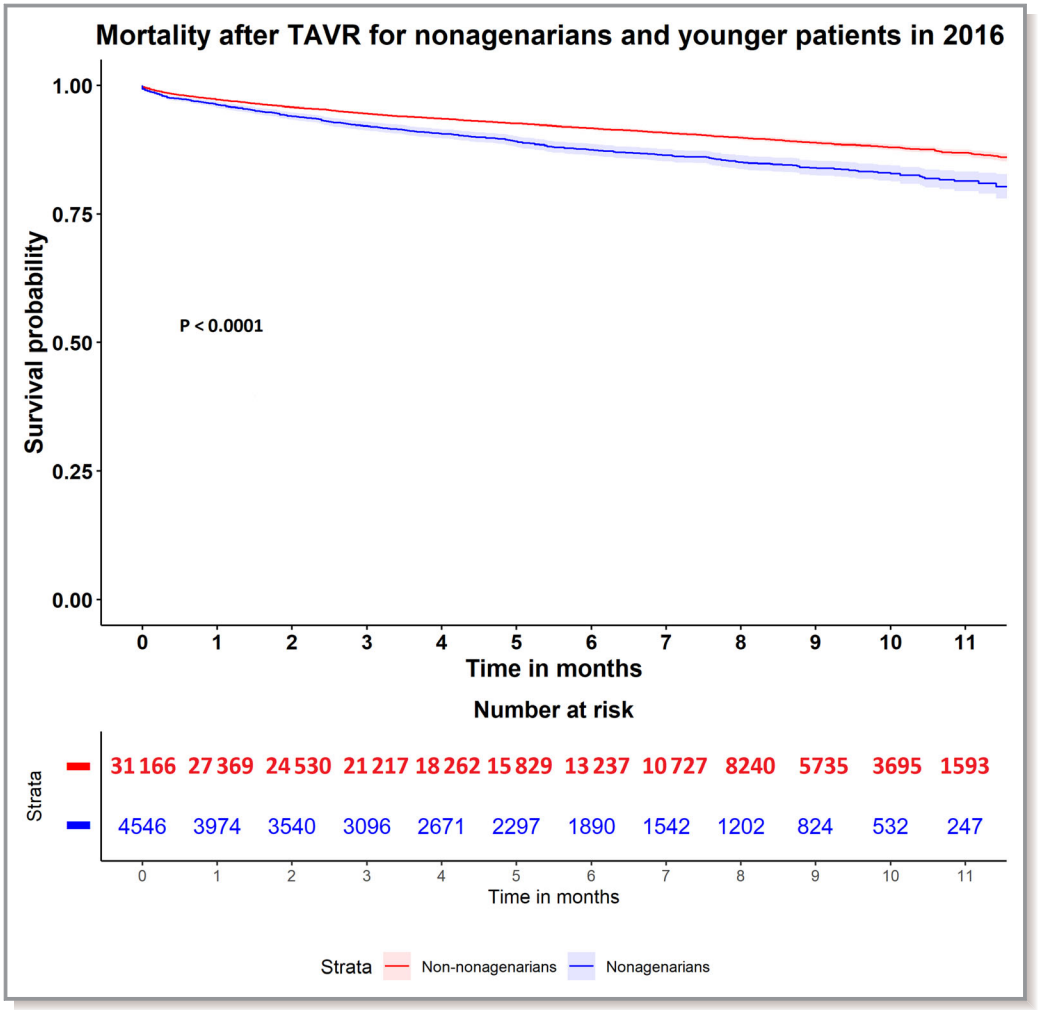

Figure 2. Kaplan–Meier curves for all-cause mortality after transcatheter aortic valve replacement in nonagenarians and patients aged <90 years in 2016. Log-rank test $P<0.0001$.

increase in the use of conscious sedation versus general anesthesia with TAVR.[25] The improvement in these perioperative complications translated into shorter durations of ICU and hospital stay and an increase in the percentage of patients with early discharge (<72 hours) after TAVR and with direct discharge home rather than to a skilled care or rehabilitation facility in 2016. Recent studies have shown that earlier discharge for TAVR patients is associated with less morbidity and mortality.[26,27] In our GEE model, when we adjusted for changes in nonagenarians' comorbidities across the years, adjusted 30-day mortality remained significantly lower in 2016 compared with all prior years. Nevertheless, it is possible that these findings could be partially explained by performing TAVR in less frail nonagenarians in recent years.

Procedural volume plays an integral role in influencing outcomes of complex structural procedures like TAVR. In prior studies, both the operator learning curve and the center volume effect had impacts on outcomes with TAVR.[28–30] A recent study showed that center volume remained a significant predictor of mortality even after excluding the TAVR "startup period" for the first 12-month period in a center.[30] This high-volume effect might extend to nonagenarians. High-volume centers in our model were associated with nonsignificant 14% risk reduction in 30-day mortality after adjusting for all procedural complications in our final GEE model. These procedural complications are indirect mediators through which high-volume centers might have reduced mortality further, and true risk reduction could be even greater. It is important to note that when we limited the comparison to high-volume centers only in 2016, there was no significant difference in in-hospital mortality between nonagenarians and younger patients.

When we used data from 2015, nonagenarians had 1-year mortality of 20.4% overall and 20% in high-volume centers. With an indirect standardization method using actuarial life tables published by the Social Security Administration for 2015,[21] an age- and sex-matched US population without AS would have expected 1-year mortality of 18.4%. Although

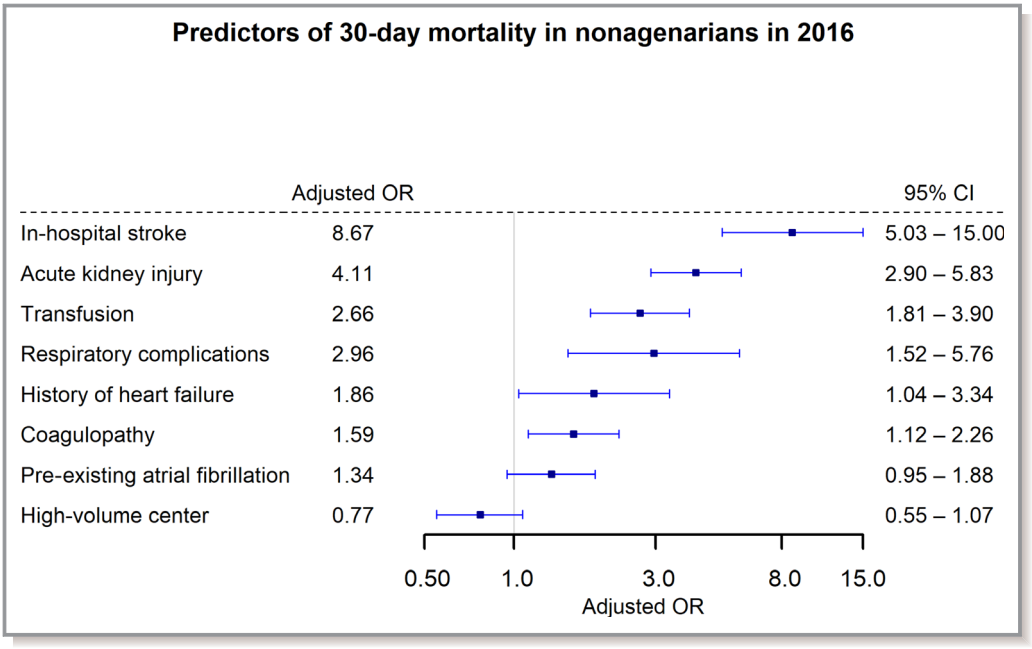

Figure 3. Adjusted odds ratios (ORs) from mixed-effects multivariable logistic regression for important predictors of 30-day mortality after transcatheter aortic valve replacement in nonagenarians in 2016.

untreated severe AS at any age is associated with a significant increase in mortality, our study showed that TAVR in nonagenarians with severe AS was associated with a reduction in 1-year mortality to a percentage that is comparable with an age- and sex-matched US population without AS. This intervention is probably one of the most promising to be performed in such an age group to reduce mortality.

It is worth mentioning that with mixed-effects logistic regression, none of the patient characteristics or comorbidities other than HF and coagulopathy were associated with 30-day mortality. Instead, 30-day mortality was primarily influenced by procedural complications. Periprocedural stroke and AKI were the 2 most important factors that affected short-term mortality in nonagenarians. In a recent analysis from the PARTNER (Placement of Aortic Transcatheter Valve Trial) study, investigators found that periprocedural stroke and AKI were associated with adjusted hazard ratios of 5.4 and 4.9, respectively, for 1-year mortality.[31] The mean age in that analysis was 82 years. Stroke and AKI seem to be even more strongly associated with in-hospital mortality in nonagenarians. Careful monitoring of these potential complications would represent a paramount opportunity to further improve short-term outcomes, and future innovations should focus on reducing the risk of stroke in the periprocedural period.

Limitations

The current study represents the largest and most comprehensive analysis examining outcomes with TAVR in nonagenarian and younger populations and reporting the temporal trend of outcomes over the year using the Medicare database. However, our study has some limitations. First, the most recent CMS data available were from 2016. It will be of great interest to examine the data from more recent years, when available, for more accurate reflection of the contemporary era. Second, frailty and nutritional status are important measures in elderly patients who undergo TAVR, and they affect mortality and outcomes.[32,33] We used a recently validated score for frailty using *ICD-10* codes in 2016 TAVR patients.[15] However, we did not utilize frailty indexes validated using *ICD-9* codes because it would not be accurate to compare 2 different indexes based on *ICD-9* and *ICD-10* codes in different years of the study. Third, despite robust statistical adjustments for comorbidities, there is the possibility of residual confounding from other unmeasured factors. Last, most of the secondary outcomes were derived from *ICD-9* and *ICD-10* codes, which are vulnerable to miscoding and misclassification.

Conclusions

TAVR is increasingly being performed in nonagenarians and elderly patients in the United States, and short-term outcomes have improved significantly. High-volume TAVR centers were associated with significant reductions in 30-day mortality over the years and in periprocedural complications. In-hospital stroke and AKI remain associated with significant 30-day hospital mortality in this population.

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SUPPLEMENTAL MATERIAL

Data S1.

Supplemental Outcomes Analysis: Proportional Hazards Regression on time to death, stroke, bleeding, or heart failure admission:

Supplemental Methods

For the secondary outcomes of stroke, bleeding and HF admissions, multivariable survival analyses were performed by competing risk regression analysis to account for death using the Fine-Gray proportional sub hazards model, and subdistribution hazard ratios (sHRs) were calculated, along with 95% CIs. (1)

Supplemental Results

Time to event analysis for outcomes in 2016

For the 2016 cohort, the total follow up was 15,873 person-years. Being a nonagenarian was associated with higher risk of mortality (26.1 versus 17.7 death per 100 person-year, adjusted hazard ratio (aHR) 1.48, 95% CI 1.35-1.64, p<0.001), bleeding (9.7 versus 8.1 event per 100 person-year, subdistribution HR 1.25, 95% CI 1.05-1.50, p=0.01), and HF admissions (15.7 versus 11.3 event per 100 person-year, sHR 1.33, 95% CI 1.14-1.54, P<0.001) but similar risk of stroke (4.5 versus 3.9 event per 100 person-year, sHR 1.14, 95% CI 0.90-1.43, p=0.3) compared to non-nonagenarians (Supplemental figures 1A-C).

Table S1. ICD codes for comorbidities.

	ICD-9 code	ICD-10 code
Atrial fibrillation	42731	I480*, I481*, I482*, I489*
GI hemorrhage	5307, 53081-53089, 53100, 53101, 53110, 53120 53121, 53140, 53141, 53160 53161, 53200, 53201, 53220 53221, 53240, 53241, 53260 53261, 53300, 53301, 53320 53321, 53340, 53341, 53360 53361, 53400, 53401, 53420 53421, 53440, 53441, 53460 53461, 56200-56203, 56210-56213, 5693, 56985	K644 K648 I8501 I8511 I8510 R58 K226 K219 K228 J860 K2270 K9432 K9433 K250 K5660 K251 K252 K254 K256 K260 K262 K264 K266 K270 K272 K274 K276 K280 K282 K284 K286 K5710 K5712 K5711 K5713 K5730 K5732 K5731 K5733 K625 K5521 K920 K921 K922
Sleep apnea	78057, 32723	G4730, G4733
Underweight	78322	V850, Z681, R636
Kidney disease	5853, 5854, 5855, 5856, V4511	N183, N184, N185, N186, N189, Z992
Obesity	2780, 27800, 7802, 27803, 27801	E668, E669, E661, E6609 E663, E669, V853, V853, V8531, V8532, V8533, V8534, V8535, V8536, V8537, V8538, V8539, Z683, Z6831, Z683, Z6833, Z6834, Z6835, Z6836, Z6837, Z6838, Z6839, E662, E6601, V854, V8541, V8542, V8543, V8544, V8545, Z684, Z6841, Z6842, Z6843, Z6844, Z6845

Table S2. ICD codes for study outcomes.

	ICD-9 code	ICD-10 code
Heart failure	39891, 40201, 40211, 40291, 40401, 40411, 40491, 4280-4289	I5020, I5021, I5022, I5023, I5030, I5031, I5032, I5033, I5040, I5041, I5042, I5043
GI hemorrhage	4552, 4555, 4558, 4560, 45620, 5307, 53082, 5310-5316, 5320-5326, 5330-5336, 5340-5346, 53501-53561, 56202-56203, 56212-56213, 5693, 56985, 5780, 5781, 5789, 53783, 56881	I8501, I8511, K644*, K648* K226*, K228*, K250*-K256*, K260*-K266*, K270*-K276*, K280*-K286*, K2901, K2911, K2921, K2931, K2941, K2951, K2961, K2971, K2981, K2991 K5701, K5711, K5713, K5721, K5731, K5733, K5741, K5751, K5753, K5781, K5791, K5793 K625, K5521, K920*, K921*, K922*, K31811, K661*
Cerebral hemorrhage	430*, 431*, 432*	I60*, I61*, I62*
Other major bleeding	59970, 59971, 59972, 71911, 7847*, 7848x, 7863*, 4230*, 4590*, 852*, 853*	R310*, R311*, R312*, R319*, M25019, R040*, R041*, R042*, R0481, R0489, R049, I312*, R58* S064X0A, S064X1A, S064X2A, S064X3A, S064X4A, S064X5A, S064X6A, S064X7A, S064X8A, S064X9A, S065X0A, S065X1A, S065X2A, S065X3A, S065X4A, S065X5A, S065X6A, S065X7A, S065X8A, S065X9A, S066X0A, S066X1A, S066X2A, S066X3A, S066X4A, S066X5A, S066X6A, S066X7A, S066X8A, S066X9A.
Ischemic Stroke	433*, 434*, 436*, 4371, 4378, 4379	I63, I65, I66, I6781, I6782, I6789, I679
Pacemaker implantation	ICD9 procedure codes: 0050, 0051, 0052, 0053, 0054, 4260, 42612, 42613, 3770, 3771, 3772, 3773, 3774, 3778, 3780, 3781, 3782, 3783, 3785	ICD10 Procedure Codes: 02H40JZ, 02H40MZ, 02H43JZ, 02H43KZ, 02H43MZ, 02H44JZ, 02H60JZ, 02H60MZ, 02H63JZ, 02H64JZ, 02H64MZ, 02H70JZ, 02H70MZ, 02H73JZ, 02H74JZ, 02H74MZ, 02HK0JZ, 02HK0KZ, 02HK0MZ, 02HK3JZ, 02HK3KZ, 02HK3MZ, 02HK4JZ, 02HK4KZ, 02HK4MZ, 02HL0JZ, 02HL0KZ, 02HL0MZ, 02HL3JZ, 02HL3KZ, 02HL3MZ, 02HL4JZ, 02HL4KZ, 02HL4MZ, 0JH604Z, 0JH605Z, 0JH606Z, 0JH607Z, 0JH609Z, 0JH60PZ, 0JH634Z, 0JH635Z, 0JH636Z, 0JH637Z, 0JH639Z, 0JH63PZ, 0JH804Z, 0JH805Z, 0JH806Z, 0JH807Z, 0JH809Z, 0JH80PZ, 0JH834Z, 0JH835Z, 0JH836Z, 0JH837Z, 0JH839Z, 0JH83PZ, 0JPT0PZ, 0JPT3PZ, 5A1213Z, 5A1223Z, I442

Table S3. Trends in non-nonagenarians' procedure characteristics and outcomes overtime.

Variable	2012	2013	2014	2015	2016	P value
White race Black race	92.8 4.1	93.1 4.0	92.1 4.3	92.3 4.1	91.8 4.2	<0.001
Male sex	52.4	50.8	53.4	52.8	53.8	<0.001
Anemia deficiency	49.3	47.1	45.8	43.0	40.2	<0.001
Congestive heart failure	80.7	81.4	82.6	80.0	78.5	<0.001
Chronic lung disease	48.0	47.8	44.2	42.4	38.9	<0.001
Coagulopathy	29.8	28.9	27.7	24.3	21.0	<0.001
Depression	16.3	16.6	16.8	16.3	15.9	0.15
Diabetes mellitus	45.0	44.1	45.1	44.6	43.9	0.14
Hypertension	93.1	94.3	93.9	94.1	94.2	0.2
Hypothyroidism	27.2	27.3	26.0	25.9	24.7	<0.001
Liver disease	3.6	3.3	4.2	4.2	4.4	<0.001
Lymphoma	2.4	2.3	2.2	2.1	1.8	0.01
Electrolytes abnormality	54.3	52.7	50.5	46.3	42.5	<0.001
Obesity	23.4	24.7	26.2	26.7	27.3	<0.001
Peripheral vascular disease	44.5	43.9	41.9	38.3	35.3	<0.001
Kidney disease	46.3	45.4	45.6	43.2	41.2	<0.001
Underweight	11.2	10.8	10.4	9.1	8.1	<0.001
Atrial fibrillation	36.7	36.2	34.6	32.3	26.6	<0.001

Table S4. Generalized estimating equation marginal model accounting for clustering in centers for 30-day mortality in nonagenarians over the study period.

Variable	Adjusted RR	95% CI	p value
Age	1.03	1.00-1.07	0.04
2013	0.76	0.61-0.96	0.02
2014	0.78	0.62-0.97	0.03
2015	0.68	0.54-0.87	0.002
2016	0.54	0.42-0.70	<.0001
Prior stroke	1.20	1.01-1.42	0.03
pulmonary circulatory disease	1.22	1.03-1.44	0.02
Coagulopathy	1.22	1.06-1.40	0.005
female sex	1.05	0.92-1.21	0.46
Anemia deficiency disease	0.81	0.71-0.94	0.004
Congestive heart failure	1.16	0.92-1.45	0.21
Chronic lung disease	1.17	1.03-1.32	0.01
Diabetes	0.95	0.82-1.10	0.52
Hypertension	0.82	0.61-1.09	0.17
Peripheral vascular disease	1.14	0.99-1.30	0.07
Kidney disease	1.30	1.13-1.48	<0.001
Prior Atrial fibrillation	1.18	1.02-1.37	0.03
Liver disease	0.97	0.54-1.72	0.91
Electrolytes abnormality	1.56	1.33-1.83	<.0001
Obesity	0.96	0.74-1.24	0.74
Underweight	1.47	1.09-1.98	0.01
Prior GI hemorrhage	0.96	0.84-1.10	0.55
Prior cerebral hemorrhage	1.56	0.90-2.69	0.11
High volume center	0.88	0.73-1.02	0.08
In-hospital stroke	3.16	2.35-4.24	<.0001
Acute kidney injury	3.78	3.24-4.40	<.0001
Respiratory complications	1.56	1.17-2.07	0.00
Vascular complications	1.24	1.00-1.54	0.05

Comparison	Adjusted risk ratio	95% confidence interval	P value
2014 vs.2013	1.02	0.83-1.25	0.87
2015 vs.2013	0.89	0.73-1.10	0.28
2016 vs.2013	0.71	0.57-0.89	<0.01
2015 vs.2014	0.88	0.73-1.06	0.18
2016 vs.2014	0.70	0.58-0.85	<0.01
2016 vs.2015	0.80	0.66-0.96	0.02

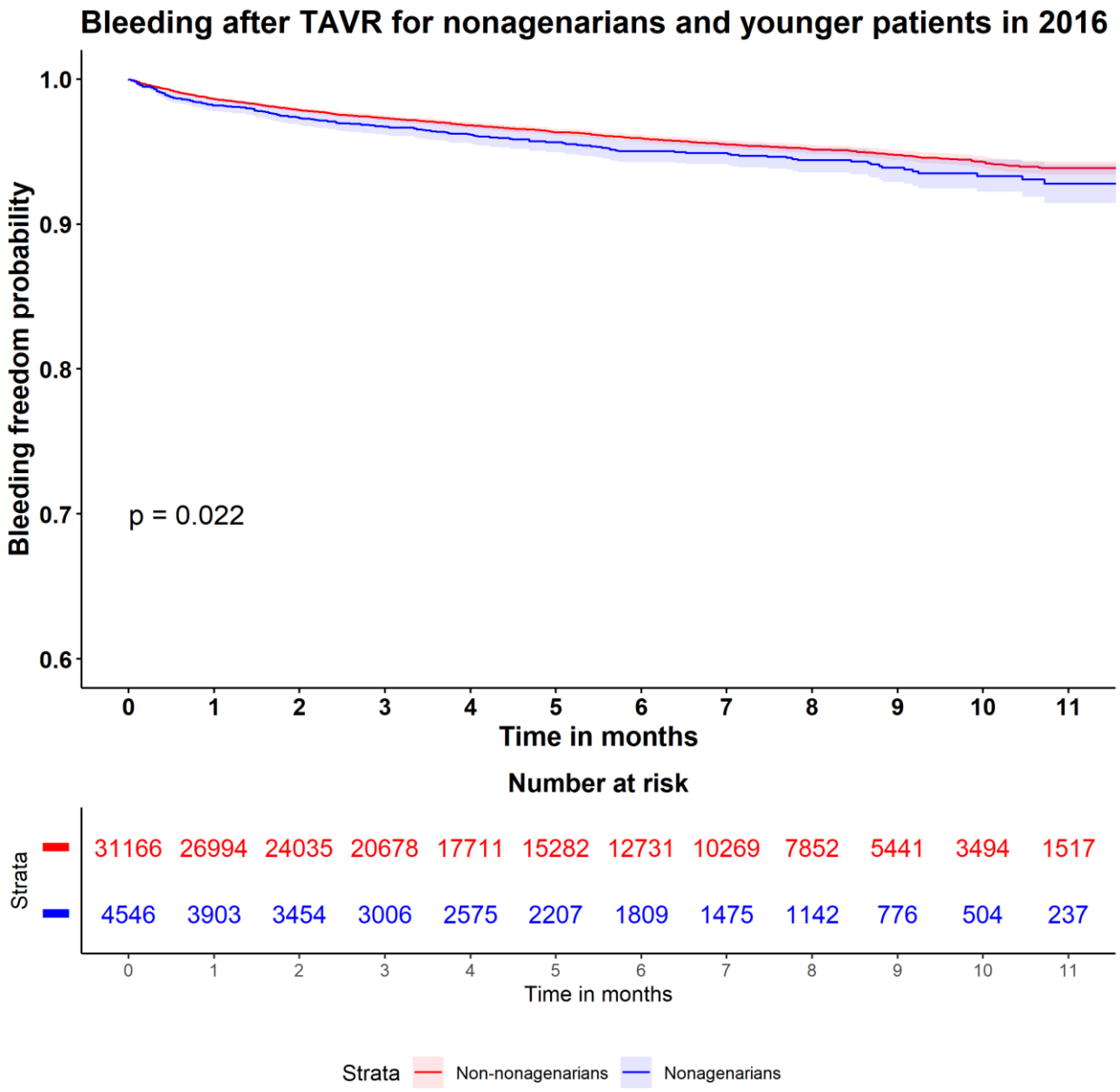
Table S5. Individual components of the frailty score with weight scores and prevalence in the 2016 TAVR cohort.

ICD code	Diagnosis	Prevalence (%)	Score
G81	Hemiplegia	0.6	4.4
G30	Alzheimer's disease	0.6	4.0
I69	Sequelae of cerebrovascular disease	2.0	3.7
R29	Other symptoms and signs involving the nervous and musculoskeletal systems	1.4	3.6
N39	Other disorders of urinary system	7.1	3.2
F05	Delirium, not induced by alcohol and other psychoactive substances	0.5	3.2
W19	Unspecified fall	0.2	3.2
S00	Superficial injury of head	0.5	3.2
R31	Unspecified hematuria	1.4	3.0
B96	Other bacterial agents as the cause of diseases classified to other chapters (secondary code)	3.2	2.9
R41	Other symptoms and signs involving cognitive functions and awareness	2.0	2.7
R26	Abnormalities of gait and mobility	5.8	2.6
I67	Other cerebrovascular diseases	0.6	2.6
R56	Convulsions, not elsewhere classified	0.4	2.6
R40	Somnolence, stupor, and coma	0.3	2.5
T83	Complications of genitourinary prosthetic devices, implants, and grafts	0.4	2.4
S06	Intracranial injury	0.4	2.4
S42	Fracture of shoulder and upper arm	0.3	2.3
E87	Other disorders of fluid, electrolyte, and acid-base balance	18.1	2.3
M25	Other joint disorders, not elsewhere classified	1.4	2.3
E86	Volume depletion	5.3	2.3
R54	Senility	0.7	2.2
F03	Unspecified dementia	3.0	2.1
W18	Other fall on same level	0.2	2.1
Z75	Problems related to medical facilities and other health care	**	2.0
F01	Vascular dementia	0.3	2.0
S80	Superficial injury of lower leg	0.3	2.0
L03	Cellulitis	2.4	2.0
H54	Blindness and low vision	1.0	1.9
E53	Deficiency of other B group vitamins	0.8	1.9
Z60	Problems related to social environment	0.3	1.8
G20	Parkinson's disease	0.8	1.8
R55	Syncope and collapse	2.9	1.8
S22	Fracture of rib(s), sternum and thoracic spine	0.6	1.8
K59	Other functional intestinal disorders	5.2	1.8

N17	Acute renal failure	15.1	1.8
L89	Decubitus ulcer	1.2	1.7
Z22	Carrier of infectious disease	0.3	1.7
B95	Streptococcus and staphylococcus as the cause of diseases classified to other chapters	1.4	1.7
L97	Ulcer of lower limb, not elsewhere classified	1.2	1.6
R44	Other symptoms and signs involving general sensations and perceptions	0.2	1.6
K26	Duodenal ulcer	0.5	1.6
I95	Hypotension	7.3	1.6
N19	Unspecified renal failure	0.2	1·6
A41	Other septicemia	3.8	1·6
Z87	Personal history of other diseases and conditions	22.6	1·5
J96	Respiratory failure, not elsewhere classified	11.7	1·5
M19	Other arthrosis	9.8	1·5
G40	Epilepsy	1.0	1·5
M81	Osteoporosis without pathological fracture	3.5	1·4
S72	Fracture of femur	0.9	1·4
S32	Fracture of lumbar spine and pelvis	0.4	1·4
E16	Other disorders of pancreatic internal secretion	0.2	1·4
R94	Abnormal results of function studies	0.6	1·4
N18	Chronic renal failure	21.4	1·4
R33	Retention of urine	2.4	1·3
R69	Unknown and unspecified causes of morbidity	**	1·3
N28	Other disorders of kidney and ureter, not elsewhere classified	2.4	1·3
R32	Unspecified urinary incontinence	1.0	1·2
G31	Other degenerative diseases of nervous system, not elsewhere classified	0.6	1·2
Y95	Nosocomial condition	**	1·2
S09	Other and unspecified injuries of head	0.2	1·2
R45	Symptoms and signs involving emotional state	0.3	1·2
G45	Transient cerebral ischemic attacks and related syndromes	0.7	1·2
Z74	Problems related to care-provider dependency	0.3	1·1
M79	Other soft tissue disorders, not elsewhere classified	1.6	1·1
W06	Fall involving bed	**	1.1
S01	Open wound of head	0.5	1.1
A04	Other bacterial intestinal infections	0.7	1·1
A09	Diarrhea and gastroenteritis of presumed infectious origin	0.2	1.1
J18	Pneumonia, organism unspecified	7.8	1·1
J69	Pneumonitis due to solids and liquids	1.1	1·0
R47	Speech disturbances, not elsewhere classified	1.1	1·0
E55	Vitamin D deficiency	1.7	1·0

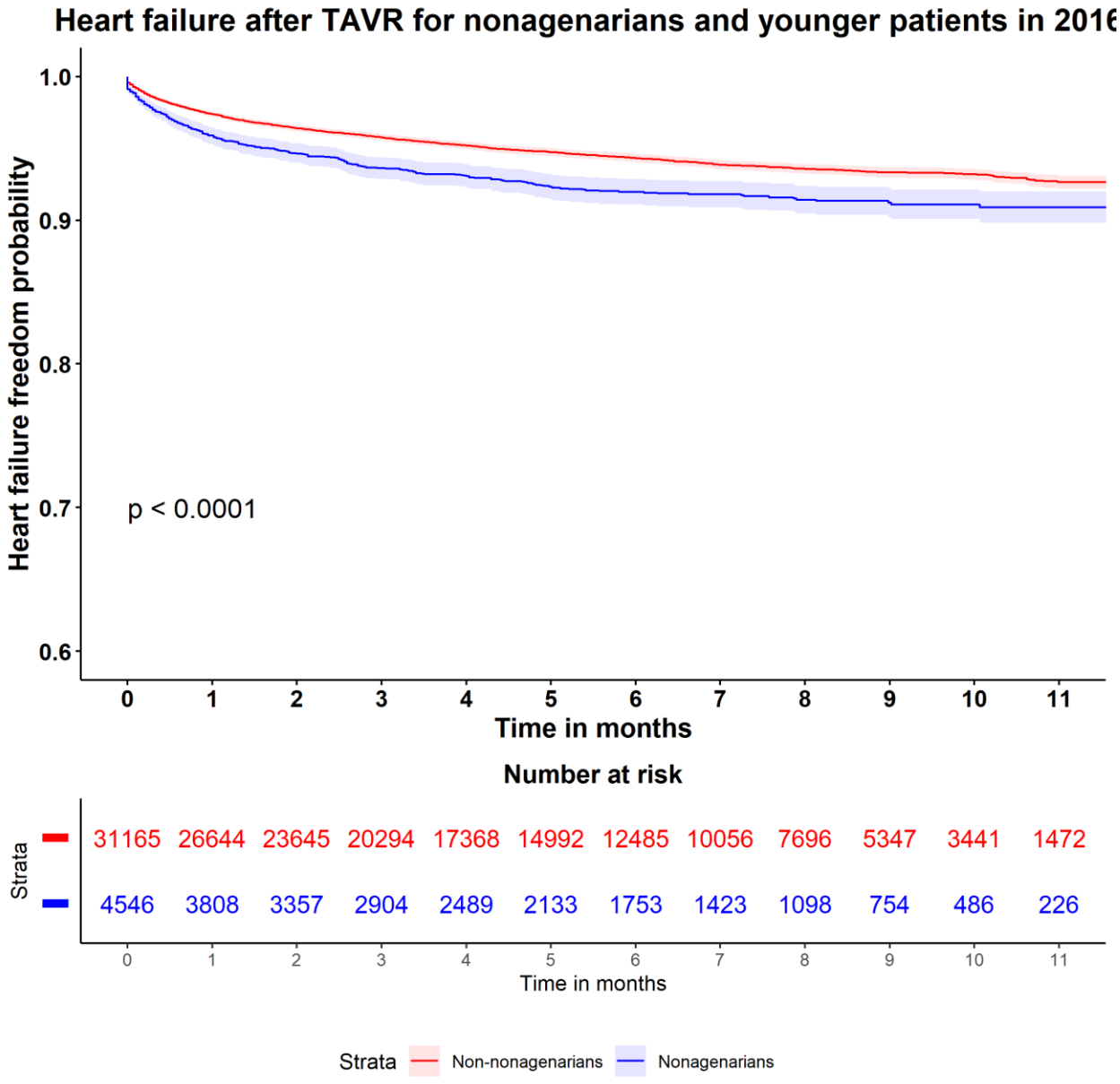
Z93	Artificial opening status	0.6	1·0
R63	Symptoms and signs concerning food and fluid intake	1.0	0·9
H91	Other hearing loss	2.4	0·9
W10	Fall on and from stairs and steps	**	0·9
W01	Fall on same level from slipping, tripping and stumbling	0.1	0·9
E05	Thyrotoxicosis [hyperthyroidism]	0.5	0·9
M41	Scoliosis	0.4	0·9
R13	Dysphagia	2.3	0·8
Z99	Dependence on enabling machines and devices	7.0	0·8
M80	Osteoporosis with pathological fracture	0.2	0·8
K92	Other diseases of digestive system	3.5	0·8
I63	Cerebral Infarction	1.4	0·8
N20	Calculus of kidney and ureter	0.5	0·7
F10	Mental and behavioral disorders due to use of alcohol	1.2	0·7
Y84	Other medical procedures as the cause of abnormal reaction of the patient	0.1	0·7
R00	Abnormalities of heart beat	3.7	0·7
J22	Unspecified acute lower respiratory infection	**	0·7
Z73	Problems related to life-management difficulty	**	0·6
R79	Other abnormal findings of blood chemistry	2.5	0·6
Z91	Personal history of risk-factors, not elsewhere classified	6.4	0·5
S51	Open wound of forearm	0.1	0·5
F32	Depressive episode	6.5	0·5
M48	Spinal stenosis (secondary code only)	2.2	0·5
E83	Disorders of mineral metabolism	4.8	0·4
M15	Polyarthrosis	0.6	0·4
D64	Other anemias	11.7	0·4
L08	Other local infections of skin and subcutaneous tissue	0.1	0·4
R11	Nausea and vomiting	1.0	0·3
K52	Other noninfective gastroenteritis and colitis	0.9	0·3
R50	Fever of unknown origin	0.7	0·1

Figure S1A. Kaplan Meier curves for the secondary outcome of bleeding after transcatheter aortic valve replacement in nonagenarians and patients younger than 90 years in 2016.



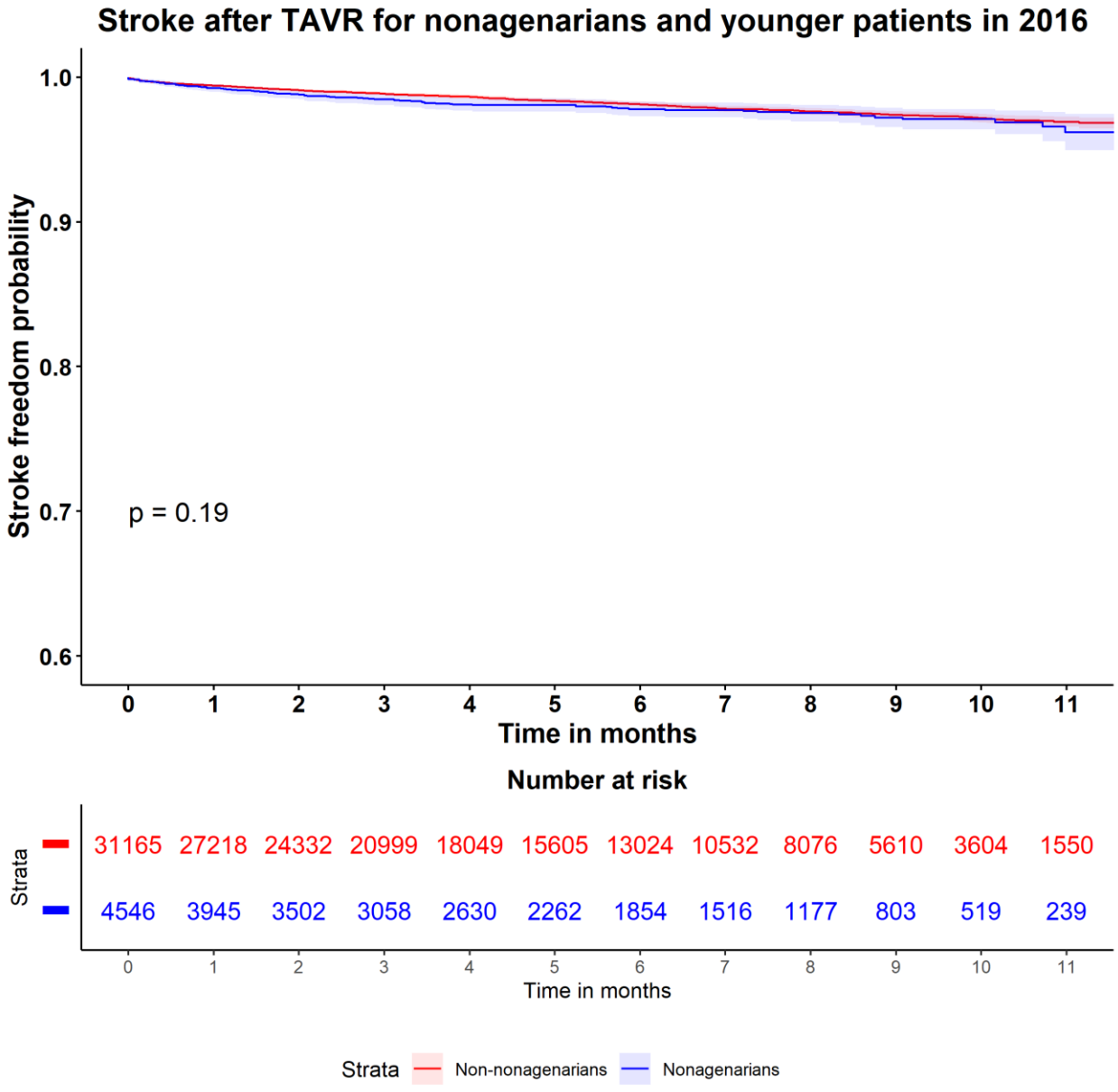
Log-rank test p=0.019.

Figure S1B. Kaplan Meier curves for the secondary outcome of heart failure admissions after transcatheter aortic valve replacement in nonagenarians and patients younger than 90 years in 2016.



Log-rank test p <0.0001.

Figure S1C. Kaplan Meier curves for the secondary outcome of stroke after transcatheter aortic valve replacement in nonagenarians and patients younger than 90 years in 2016.



Log-rank test p=0.17.

Supplemental Reference:

1. Fine JP, Gray RJ. A Proportional Hazards Model for the Subdistribution of a Competing Risk. *J Am Stat Assoc.* 1999.