Comparison of Outcomes of Transcatheter Aortic Valve Implantation in Patients Aged >90 Years Versus <90 Years

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Limited data exist regarding transcatheter aortic valve implantation (TAVI) in nonagenarians. This study evaluates the short- and mid-term outcomes of nonagenarians after TAVI. Between 2008 and 2017, all patients who underwent TAVI in 2 centers in Australia were prospectively included in a registry and followed-up for 5 years. Outcomes were based on VARC-2 criteria. Additionally, the patient's reliance on daily living support at 1 year was evaluated. Of the 588 patients, 71 (12.1%) were ≥90 years old (mean age 92.2 ± 2 vs 83.2 ± 6 years in <90-year-old patients), with a median STS-PROM score of 5.7 (vs 3.9 in <90-year-old patients, odds ratio [OR] 1.07, 95% confidence interval 1.01 to 1.13, p = 0.02) and a median clinical frailty score of 4 (vs 4 <90-year-old patients, OR 0.88, p = 0.44). Mortality was 0% in ≥90-year-old patients at 30 days (vs 1.4% in <90-year-old patients; p = 0.82) and 12% at 1 year (vs 7.4%, in <90-year-old patients; hazard ratio 1.64, p = 0.20). There were no significant differences in periprocedural complications and mortality at 5 years between the 2 groups. At 1 year, nonagenarians were significantly more likely to live in an aged-care facility compared with <90-year-old patients (25% vs 16%, OR 5.99, 95% confidence interval 2.62 to 13.67, p <0.001). In conclusion, carefully selected nonagenarians have excellent short- and mid-term outcomes post-TAVI and should therefore not be refused based on age alone. Nevertheless, the significantly higher rate of transfer to an aged-care facility highlights the importance of a more refined frailty assessment before TAVI than the currently widely used clinical frailty score. **© 2019 Elsevier Inc. All rights reserved.** **(Am J Cardiol 2019;124:1085−1090)**

Nonagenarians represent a small but significant proportion of the population.[1] In 2017, 13% of the Australian population were ≥85 years old (497,000 people) and it is projected that in 30 years' time, this will account for 20% (1.5 million people).[2] Importantly, a sizable proportion of nonagenarians continue to have good survival prognosis,[3] with up to 6.0% of men and 11.4% of women living past 100 years old.[4] The average life expectancy of a 90-year-old person in Australia is 4 years.[5] Consequently, it is no longer justifiable to deny medical procedures using age as the sole reason. With aortic stenosis (AS) being, predominantly, a disease of the elderly, its prevalence has increased significantly over recent years.[6] Transcatheter aortic valve implantation (TAVI) has revolutionized the treatment of AS in this high- and intermediate-risk population by enabling patients to undergo a less-invasive treatment.[7−9] The PARTNER-I subgroup analysis was the first to demonstrate safety and feasibility among very elderly patients, with event rates similar to younger patients.[7] Subsequent analyses confirmed similar 30-day and 1-year mortality.[10−14] Nevertheless, nonagenarians are often denied TAVI. We sought to elucidate outcomes after TAVI of nonagenarians compared with <90-year-old patients.

Methods

Between August 2008 and June 2017, all patients who underwent TAVI in 2 experienced centers in Melbourne, Australia with the CoreValve and Evolut R (Medtronic Inc., Minneapolis, Minnesota), Edwards Sapien XT, Sapien 3 and Centera (Edwards Lifesciences, Irvine, California) or Portico (Abbott, Abbott Park, Illinois) bioprostheses were included in a prospective registry. Ethics approval for this study was gained from the Alfred and Epworth hospital research and ethics committees with an opt-out consent.

AS was considered severe with an aortic valve area <1 cm^2 or an aortic valve mean pressure gradient (MPG) >40 mm Hg. Patients were deemed suitable for TAVI on consensus by the local heart team that included cardiothoracic surgeons and

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interventional cardiologists. All patients underwent preprocedural work-up with coronary and peripheral angiograms, and transthoracic echocardiogram (TTE). After 2011, this work-up involved as well a computed tomography of the aorta and aortic valve.

Follow-up appointments were scheduled at 30 days, 1 year, and then yearly up to 5 years after the intervention with clinical assessment and TTE.

Outcomes were defined based on the Valve Academic Research Consortium-2 consensus document.[15] They were assessed as in-hospital, 30 days, and 1 year. These included myocardial infarction, cerebrovascular event, major bleeding (according to the Bleeding Academic Research Consortium classification[16]), acute kidney injury, conduction disturbances requiring permanent pacemaker (PPM) implantation and vascular complications, as well as aortic valve failure requiring reintervention, device success, and mortality. The patients' length of stay and requirement for ICU admission, and NYHA class were also assessed. Additionally, for a measurement of functional ability and frailty, the clinical frailty score, according to Rockwood et al,[17] and their "living support status" were evaluated at 1 year. The latter was defined as reliance on daily life assistance and stratified to "independent in activities of daily living" (ADL-i), "dependent on another person in the same household in activities of daily living" (ADL-d), or "living in an aged care facility" (ACF). New aged care facility admission was measured as a change from ADL-i or ADL-d preprocedural to ACF at 1 year.

Normally distributed variables were expressed as mean ± standard deviation. For non-normally distributed variables, the median and interquartile range were calculated. Logistic regression was used to analyze binary demographic and periprocedure data except when numbers were small, where Fisher's exact test was used. Mixed-effects logistic regression was used to analyze binary data over time. An interaction term between predictor variables and time was incorporated into each model to assess the comparison of nonagenarians and non-nonagenarians over time. Survival analysis was used to assess mortality at 30 days and at 1 year. Proportional hazard assumption assessed by Stata's phtest and graphical stphplot commands. A p value of less than 0.05 was considered significant. All statistical analyses were performed using Stata version 14.

Results

In total, 588 patients (12.1% nonagenarians) underwent TAVI between 2008 and 2017. One-year follow-up was completed in 70 (98.6%) nonagenarians and 492 (95.2%) <90-year-old patients. The mean age of the nonagenarian cohort was 92.2 ± 1.8 years (83.2 ± 5.5 in <90-year-old patients). Their median STS-PROM score was 5.7 (vs 3.9 in <90-year-old patients, odds ratio [OR] 1.07, 95% confidence interval [CI] 1.01 to 1.13, p = 0.02) and frailty score 4 (vs 4 in <90-year-old patients, OR 0.88, p = 0.44). Nonagenarians had significantly more co-morbidities than <90-year-old patients and had a higher echocardiographic severity of AS (MPG [mm Hg] 54.1 ± 17.4 vs 48.3 ± 14.0 in <90-year-old patients, p = 0.002). Baseline characteristics are shown in Table 1.

The CoreValve and Evolut R valves were most commonly used for both cohorts through femoral access. Notably, there were no significant differences in terms of the length of stay or requirement for ICU admission postprocedural. Periprocedural characteristics are shown in Table 2.

In-hospital and 30-day mortality for nonagenarians were 0% versus 1.6% for <90-year-old patients (p = 0.82). In-hospital complications, including major adverse cardiovascular events and device success occurred at a similar rate in the 2 cohorts. There was no significant difference in mortality at 1 year (11.6% in ≥90-year-old patients vs 7.4% in <90-year-old patients, hazard ratio 1.64, 95% CI 0.76 to 3.55, p = 0.20) and during the 5-year follow-up (p = 0.12, Kaplan-Meier curve in Figure 1).

Nevertheless, there were significantly more nonagenarians who changed from ADL-i and ADL-d to living in an ACF at 1 year compared with <90-year-old patients (24.5% vs 16%, OR 5.99, 95% CI 2.62 to 13.67, p < 0.001). All outcomes are displayed in Table 3.

Paravalvular AR grade 2 or higher was present in 13.2% of nonagenarians at the end of the procedure compared with 6.4% of <90-year-old patients (p = 0.07). There were no significant changes post-TAVI in both patient cohorts with regards to average MPG and AR over time. Table 4 demonstrates the echocardiographic valve parameters and NYHA class during follow-up.

Discussion

This study, which is the first in Australia, demonstrates that nonagenarians have excellent periprocedural, short- and mid-term outcomes post-TAVI. The in-hospital and 30-day mortality rate of our nonagenarian cohort was 0%, which was statistically not different to the <90-year-old patients' cohort (1.4%). Mortality at 1 year was numerically slightly higher in the nonagenarian cohort (11.6% vs 7.4% in <90-year-old patients), although this difference was not statistically significant (p = 0.20), but, potentially, reflects the average shorter life-expectancy of nonagenarians.

Notably, our nonagenarian cohort had a similar incidence of periprocedural complications, device success rate, and length of stay in-hospital compared with <90-year-old patients. With respect to PPM requirement, we found no significant difference between the ≥90-year-old and <90-year-old patients, which is important in light of the associated increased risk of heart failure rehospitalization with the need for a PPM.[18]

The STS-PROM and EuroSCORE I were significantly higher for the nonagenarian cohort and markedly overestimated the mortality of nonagenarians. Because nonagenarians had generally less co-morbidities than <90-year-old patients, this discrepancy can only be attributed to age being a dominant factor. This may be explained by the fact that STS-PROM and the EuroSCORE[19] as well as the newer prognostic scoring systems specific to TAVI such as TAVI2-SCORe.[20] Survival posT TAVI score[21] and OBSERVANT score[22] have contained only small portions of nonagenarians and are therefore of little use in this cohort.

Comparing our results with the other recent observational studies of TAVI in nonagenarians, we found that the

Table 1
Baseline characteristics

Variable	Age (years) ≥90 (n = 71)	Age (years) <90 (n = 517)	OR	95% CI	p Value
Age (years)	92.2±1.8	83.2±5.5			
Men	32 (45%)	261 (51%)	0.80	0.49-1.32	0.39
Estimated glomerular filtration rate	58.1±19.6	57.2±16.8	0.997	0.98-1.01	0.71
Coronary artery disease	22 (31%)	227 (45%)	0.55	0.33-0.94	0.03
Triple vessel coronary artery disease	2 (9.1%)	79 (35%)	0.19	0.04-0.82	0.03
Prior percutaneous coronary intervention	13 (59%)	80 (35%)	2.65	1.09-6.48	0.03
Prior cardiac surgery	26 (37%)	216 (43%)	0.78	0.47-1.30	0.34
Atrial fibrillation	19 (27%)	162 (32%)	0.78	0.45-1.37	0.39
Cerebrovascular disease	12 (17%)	76 (15%)	1.16	0.59 - 2.26	0.67
Hypertension	49 (69%)	367 (73%)	0.84	0.49-1.45	0.54
Diabetes mellitus	15 (21%)	131 (26%)	0.81	0.42-1.53	0.51
Peripheral arterial disease	2 (2.8%)	93 (20%)	0.12	0.03-0.49	0.003
Chronic obstructive pulmonary disease	3 (4.2%)	90 (20%)	0.18	0.06-0.59	0.005
Existing permanent pacemaker	12 (17%)	59 (11%)	1.58	0.80-3.11	0.19
New York Heart Association classification					
I/II	17 (24%)	188 (36%)	1		
III	44 (62%)	264 (51%)	1.80	0.999-3.25	0.05
IV	10 (14%)	65 (13%)	1.67	0.73-3.82	0.23
Frailty score	4.0 [3.0-5.0]	4.0 [4.0-5.0]	0.88	0.64-1.22	0.44
Living support status					
Activities of daily living- independent	43 (62%)	220 (62%)	1		
Activities of daily living- dependent	20 (29%)	126 (35%)	0.81	0.46-1.44	0.48
Aged care facility	6 (8.7%)	11 (3.1%)	2.79	0.98-7.95	0.06
STS-PROM score	5.7 [4.0-7.6]	3.9 [2.8-6.0]	1.07	1.01-1.13	0.02
<4%	16 (23%)	262 (51%)	1		
4 - <8%	43 (61%)	196 (38%)	3.59	1.97-6.57	<0.001
≥8%	12 (17%)	57 (11%)	3.45	1.55-7.68	0.002
EuroSCORE I	16.5 [14.5-23.4]	13.0 [9.4-19.8]	1.03	1.01-1.05	0.01
EuroSCORE II	4.1 [3.0-5.6]	3.5 [2.4-5.7]	0.995	0.94-1.05	0.88
Mean pressure gradient (mm Hg)	54.1±17.4	48.3±14.0	1.03	1.01-1.04	0.002
Aortic valve area (cm^2)	0.65±0.20	0.73±0.03	0.09	0.02-0.37	0.001
Left ventricle ejection fraction (%)	59.6±9.5	58.5±11.5	1.01	0.99-1.03	0.46
Left ventricle ejection fraction < 35%	0	17 (3.6%)	-		
Moderate or severe mitral regurgitation	18 (25%)	62 (12%)	2.48	1.36-4.50	0.003
Pulmonary artery pressure >55 mm Hg	14 (22%)	50 (13%)	1.90	0.98-3.68	0.06
Moderate or severe aortic regurgitation	5 (7.4%)	43 (8.5%)	0.85	0.32-2.23	0.74

Data presented as mean ± SD, number (%), or median [IQR].

mortality rate of our nonagenarian cohort was favorable in-hospital, at 30 days (0% in our cohort vs 2% to 10% in other cohorts) and at 1 year (12% in our cohort vs 10% to 25% in other cohorts).[11,13,14,23,24] Our nonagenarian cohort had significantly less co-morbidities, particularly less-peripheral vascular disease (3% vs 11% to 27%) and chronic obstructive pulmonary disease (4% vs 15% to 24%).[11,13,14,23,24]

Consequently, our nonagenarian cohort had a lower STS-PROM score compared with the other nonagenarian cohorts from existing literature (6 vs 8 to 11). Periprocedural characteristics in our cohorts were comparable and the complication rates similar or even slightly higher than in all the aforementioned cohorts.[11,13,14,23]

The results of our study could have several explanations. TAVI numbers in the public hospitals in Australia are limited due to funding constraints, and, therefore, more stringent patient selection may apply. Notably, 83% of our nonagenarian cohort were of either low or intermediate risk (STS-PROM score <8%). This observation may have translated into better outcomes for our nonagenarians compared with other nonagenarian cohorts. Further, our nonagenarian patients were referred later in the disease process, as evidenced by the higher average MPG than other nonagenarian cohorts (54 mm Hg vs 46 to 47 mm Hg),[11,13,14,23] and compared with our own <90-year-old cohort (54 mm Hg vs 48 mm Hg), therefore undergoing a certain selection process before they are considered for TAVI.

Previous studies have demonstrated the cost-effectiveness of TAVI, by keeping patients with severe symptomatic AS out of hospital and functioning independently in the community.[25] In our nonagenarian cohort, the NYHA status of patients did improve post-TAVI to a similar extent compared with our <90-year-old cohort. Nevertheless, despite this improvement, 25% of the nonagenarian cohort had to transition to an ACF within 1 year after TAVI, which was significantly more compared with the <90-year-old patients. These findings were surprising, given the similar frailty score in the nonagenarian cohort compared with the younger patients before the intervention. However, they are similar to the results published from the STS/ACC TVT

Table 2
Periprocedural characteristics

Variable	Age (years) ≥90 (n = 71)	Age (years) <90 (n = 517)	OR	95% CI	p Value
Access*					
Trans-femoral	68 (96%)	476 (93%)	1		
Subclavian	1 (1.4%)	13 (2.5%)	0.55	0.17-1.84	0.33
Direct-aorta	2 (2.8%)	17 (3.3%)			
Trans-apical	0	2 (0.4%)			
Femoral cutdown	0	6 (1.2%)			
Type of valves					
Corevalve	35 (49%)	287 (56%)	1		
Evolut R	26 (37%)	127 (25%)	1.7	0.97-2.91	0.06
Sapien XT	2 (2.8%)	35 (6.8%)	0.47	0.11-2.03	0.31
Sapien 3	6 (8.5%)	40 (7.7%)	1.23	0.49-3.11	0.66
Portico/Centera	2 (2.8%)	27 (5.3%)	0.61	0.14-2.66	0.51
Valve size (mm)					
20-27	34 (48%)	175 (34%)	1		
29-34	37 (52%)	339 (66%)	0.56	0.34-0.93	0.02
Valve in valve	2 (2.8%)	18 (3.5%)	0.80	0.18-3.54	0.77
Intensive care unit admission	1 (1.4%)	30 (5.8%)	0.23	0.03-1.73	0.15
Length of stay (days)	5.0 [4.0, 7.0]	5.0 [4.0, 7.0]	1.03	0.97-1.09	0.37

Data presented as number (%) or median [IQR].
* Subclavian, direct-aorta, transapical, and femoral cutdown were combined for analysis and compared with transfemoral.

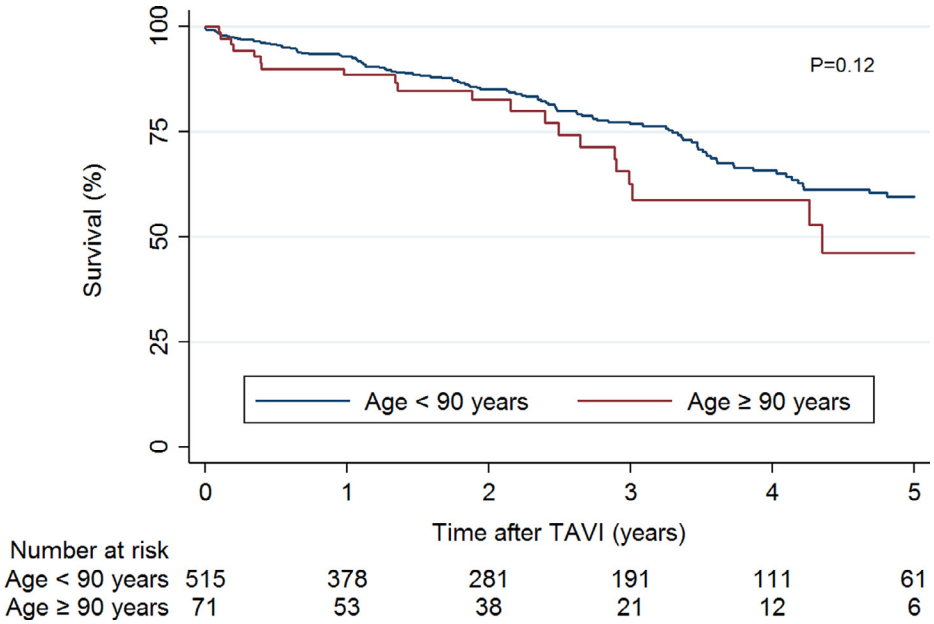

Figure 1. Kaplan-Meier analysis of 5-year survival for ≥90-year-old versus <90-year-old patients. There was no significant difference in mortality during the 5-year follow-up in ≥90-year-old versus <90-year-old patients.

registry, which reported that only 52% of patients were discharged to their home location, whereas 37% were transferred to a rehabilitation center and 8% permanently stayed in a nursing home.[23] This slower recovery from a TAVI procedure in the nonagenarian cohort highlights the importance of a more refined frailty assessment than the clinical frailty score that was performed in our cohort.[17] Several frailty scores have been explored in the recent past, among them the essential frailty toolset, which outperformed other frailty scores in the prediction of short- and mid-term outcomes in Afilalo et al's FRAILTY AVR study.[26]

Being a nonrandomized, noncontrolled prospective observational study, there are intrinsic shortcomings. Systematic selection and allocation bias cannot be excluded given the lack of a comparison patient cohort who underwent SAVR. Nonetheless, these results are robust for a prospective cohort study, given the comprehensive and timely collection of follow-up data.

Selected nonagenarians have excellent short- and mid-term outcomes post-TAVI. There is no significant difference between nonagenarians and <90-year-old patients in terms of periprocedural and short-term complications despite an

Table 3
In-hospital, 30-day, and 1-year outcomes

Variable	Age (years) ≥90	Age (years) <90	OR	95% CI	p Value
In-hospital complications	**n = 71**	**n = 517**			
Myocardial infarction	2 (2.8%)	2 (0.4%)	–	–	0.07
Cerebrovascular event	1 (1.4%)	8 (1.6%)	–	–	0.99
Major bleeding (3a, 3b and 5)	0	9 (1.7%)	–	–	0.61
Access site complications	5 (7.0%)	31 (6.0%)	1.19	0.45 - 3.16	0.71
Acute kidney injury stage 2 and 3	1 (1.4%)	15 (2.9%)	0.47	0.06 - 3.66	0.48
Mortality	0 (0%)	7 (1.4%)	–	–	0.82
30-day outcomes	**n = 71**	**n = 517**			
Device success	68 (96%)	483 (94%)	1.50	0.45 - 5.04	0.51
Major adverse cardiovascular events	3 (4.2%)	15 (2.9%)	1.47	0.42 - 5.20	0.55
Mortality	0 (0%)	7 (1.4%)	–	–	0.82
One-year outcomes	**n = 70**	**n = 492**			
Valve failure requiring re-intervention	1 (1.4%)	11 (2.1%)	0.66	0.08 - 5.17	0.69
Need for permanent pacemaker	19 (27%)	127 (25%)	1.12	0.64 - 1.97	0.69
New aged care facility	13 (25%)	19 (3.8%)	5.99	2.62 - 13.67	<0.001
Device success	60 (85%)	435 (88%)	0.74	0.37 - 1.49	0.40
Mortality (HR)*	8 (12%)	35 (7.4%)	1.64	0.76 - 3.55	0.20

Data displayed as number (%) or median [IQR].
* Mortality is displayed as hazard ratio, proportional hazard assumption tested and met.

Table 4
Change in NYHA and valve parameters over time

Variable	Postprocedure		1 year		p Value
	Age (years) ≥90	Age (years) <90	Age (years) ≥90	Age (years) <90	
Left ventricle ejection fraction (%)	59.7±9.3	59.6±10.6	55.9±9.8	58.4±9.7	0.16
Paravalvular aortic regurgitation ≥ grade II	9 (13%)	32 (6.4%)	7 (13%)	27 (6.5%)	0.88
Mean pressure gradient (mm Hg)	8.9±3.1	10.3±5.4	8.9±3.2	10.2±4.57	0.90
New York Heart Association classification					
I	50 (71%)	338 (71%)	40 (76%)	271 (72%)	0.99
II	17 (24%)	128 (27%)	8 (15%)	89 (24%)	
III/IV	3 (4.3%)	13 (2.7%)	5 (9.4%)	15 (4.0%)	

Data presented as mean ± SD or number (%).
p Value test of interaction between nonagenarian status and time.

overall higher risk score. From our cohort and other studies, we can infer that mainly less co-morbidities—in particular chronic obstructive pulmonary disease—and normal renal function, but not lower age, are associated with better outcomes post-TAVI.[11,27] There is, nevertheless, a significantly higher proportion of nonagenarians who live in ACF at 1 year. Other than on co-morbidities, focus should especially be put on careful and refined frailty assessment to confine TAVI to those most likely to benefit.

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