Brief Report

Transcatheter Aortic Valve Replacement in Nonagenarians: A Finnish Multicenter Study

Matti Riihiniemi, BM[a,*], Jarkko Piuhola, MD, PhD[a,b], Matti Niemelä, MD, PhD[a,b], Yoichi Sugiyama, MD, PhD[c], Heidi Kiviniemi, MD, PhD[d], Fausto Biancari, MD, PhD[e], Mika Laine, MD, PhD[c], Mikko Savontaus, MD, PhD[d], and Juhani Junttila, MD, PhD[a,b]

Keywords: TAVR, TAVI, nonagenarian, aortic stenosis

Transcatheter aortic valve replacement (TAVR) has emerged as a treatment for aortic stenosis (AS), proving to be a valid alternative to surgical aortic valve replacement, which is often denied in older patients because of prohibitive operative risk.[1] With an aging population and a growing prevalence of AS, an increasing number of nonagenarians requiring TAVR is expected and clinicians are going to face the clinical dilemma of offering an invasive treatment in these high-risk patients more often.[2] However, nonagenarian patients have been underrepresented in previous research. With their increasing clinical significance, we aimed to assess the characteristics and outcomes of nonagenarians who underwent TAVR.

This was an observational, retrospective, multicenter study including consecutive nonagenarians who underwent TAVR in 3 Finnish tertiary hospitals (Helsinki, Oulu, and Turku University Hospitals). The 30-day and 1-year mortality were the primary outcomes of this study. The secondary outcomes were stroke, major/life-threatening bleeding, major vascular complication, and permanent pacemaker implantation occurring within 30 days from the procedure, as defined by the Valve Academic Research Consortium-2 criteria.[3] The study protocol was approved by the Finnish Social and Health Data Permit Authority and complies with the Declaration of Helsinki. Patient written informed consent was waived because of the retrospective and observational design of this study.

A univariable analysis was performed using the Mann−Whitney, chi-square, and Fisher's exact tests to identify baseline characteristics associated with 30-day mortality. The linear-by-linear association test was used to evaluate the prognostic impact of ordinal variables in predicting the 30-day mortality. The discrimination ability of the EuroSCORE II in predicting 30-day mortality was assessed by estimating the area under the receiver operating characteristics curve. Calibration plots, the expected/observed ratio, calibration-in-the-large, and slope for the EuroSCORE II in predicting 30-day mortality were estimated using the *pmcalplot* module for Stata software (StataCorp LLC, College Station, TX). Survival analysis was performed using the Kaplan−Meier method. Multivariable analysis was not performed because of the small size of this series. Cumulative observed survival; year-, age-, and gender-matched cumulative expected survival; and cumulative relative survival were estimated using the Ederer II method with the *strs* module for Stata. The mortality rates of the general Finnish population were retrieved from the Human Mortality Database (https://www.mortality.org/). Analyses were performed using Stata v. 15.1 (StataCorp LLC, College Station, TX) and SPSS v. 29.0 (IBM Corporation, NY) statistical softwares.

Overall, 183 nonagenarians underwent TAVR at participating hospitals between August 2009 and September 2021. Baseline characteristics, procedural details, and clinical outcomes are listed in Table 1. The mean age was 91.3 ± 1.3 years and 62.8% of the patients were women. The mean EuroSCORE II was 6.0 ± 4.0% and most of the patients (83.1%) had symptoms equivalent to New York Heart Association Classification classes III or IV. Transfemoral access was used in all but 2 patients who underwent transaortic and subclavian TAVR.

The 30-day mortality and stroke rates were 5.5% and 3.8%, respectively. Major or life-threatening bleeding occurred in 22 patients (12.0%), whereas 32 patients (17.5%) had a major vascular complication during the 30-day follow-up. Permanent pacemaker was implanted in 19 patients (10.4%) during the 30-day follow-up.

The predictive ability of the EuroSCORE II in predicting 30-day mortality was herein evaluated. The expected/observed ratio of 30-day mortality was 1.103, calibration-in-the-large was −0.107, slope was 1.096, geometric mean was 5.1% (95% confidence interval 4.7% to 5.5%), and area under the curve was 0.734 (95% confidence interval 0.560 to 0.908). The calibration plot suggested that the EuroSCORE II had excellent predictive ability in patients with an EuroSCORE II <10% but tended to underestimate the operative risk in higher risk patients. Increasing quartiles of the EuroSCORE II (<3.6, 3.6 to 5.1, 5.2 to 7.4, and >7.4) were associated with significantly increasing 30-day mortality (2.2% vs 0.0% vs 8.9% vs 10.9%, respectively, p = 0.020). In the univariable analysis, atrial fibrillation (30-day mortality 10.0%

[a]Research Unit of Biomedicine and Internal Medicine, Medical Research Center Oulu, University of Oulu, Oulu, Finland; [b]Department of Cardiology, Oulu University Hospital, Oulu, Finland; [c]Heart and Lung Center, Helsinki University Hospital, Helsinki, Finland; [d]Heart Center, Turku University Hospital, Turku, Finland; and [e]Department of Cardiovascular Surgery, Centro Cardiologico Monzino IRCCS, Milan, Italy. Manuscript received May 26, 2024; revised manuscript received and accepted August 28, 2024.

Funding: none.

See page 84 for Declaration of Competing Interest.

*Corresponding author: Tel: +358 442717820.

E-mail address: matti.riihiniemi@student.oulu.fi (M. Riihiniemi).

https://doi.org/10.1016/j.amjcard.2024.08.030

Table 1
Baseline characteristics, procedural details and clinical outcomes.

Variables	N=183	Univariable analysis P-value
Baseline characteristics		
Age (years)	91.3 ± 1.3	0.355
Female	115 (62.8%)	0.746
Body mass index (kg/m^2)	25.2 ± 3.5	0.324
Hemoglobin (g/l)	123 ± 15	0.638
Anemia	85 (46.4%)	0.343
eGFR < 60	119 (65.0%)	0.498
NYHA classes III/IV	152 (83.1%)	0.216
Hypertension	157 (85.8%)	1.000
Dyslipidemia	116 (63.4%)	0.095
Diabetes	32 (17.5%)	0.688
Atrial fibrillation	80 (43.7%)	0.022
Prior hospitalisation for heart failure	42 (23.0%)	0.241
COPD or asthma	25 (13.7%)	1.000
Prior myocardial infarction	19 (10.9%)	0.562
Prior PCI	42 (23.0%)	1.000
Prior CABG	16 (8.7%)	1.000
Lower limb atherosclerosis	23 (12.6%)	0.365
Prior stroke	21 (11.5%)	0.608
Prior permanent pacemaker implantation	21 (11.5%)	1.000
Alzheimer's disease	5 (2.8%)	0.020
EuroSCORE II (%)	6.0 ± 4.0	0.011
Medication		
Aspirin	64 (35.2%)	0.743
Clopidogrel	21 (11.5%)	1.000
Warfarin	49 (26.8%)	0.461
DOAC	31 (16.9%)	0.678
ACE-inhibitor/ARB	107 (58.5%)	0.323
β-blocker	108 (59.0%)	1.000
Echocardiographic data		
Left ventricular ejection fraction (%)	57 ± 11	0.520
AVA (cm^2)	0.61 ± 0.17	0.235
Max. aortic valve gradient (mmHg)	77 ± 22	0.673
Mean aortic valve gradient (mmHg)	49 ± 15	0.634
Procedural details		
Study period		
2009-2017	72 (39.3%)	
2018-2021	111 (60.7%)	
Vascular access sites		
Transfemoral	181 (98.9%)	
Surgical cutdown	9 (4.9%)	
Trans-aortic	1 (0.5%)	
Trans-subclavian	1 (0.5%)	
Aortic valve pre-procedural dilatation	138 (75.4%)	
Transcatheter aortic valve device*		
Sapien	64 (35.8%)	
Acurate	54 (30.2%)	
Evolut	40 (22.3%)	
Lotus	13 (7.3%)	
Allegra	7 (3.9%)	
Portico	1 (0.6%)	
Prosthesis size (mm) *		
≤ 23	38 (21.1%)	
25-27	99 (55.0%)	
≥ 29	43 (23.9%)	
Post-procedural prosthesis dilatation	35 (19.1%)	
Clinical outcomes		
In-hospital outcomes		
Intraprocedural death	2 (1.1%)	
Device success†	168 (93.3%)	
Cardiac tamponade	1 (0.5%)	
Coronary occlusion	0 (0.0%)	
Annular rupture	0 (0.0%)	
Device embolization	0 (0.0%)	
RBC transfusion	23 (12.6%)	
Paravalvular regurgitation‡		
Mild	46 (25.8%)	
Moderate	7 (3.9%)	
Severe	0 (0.0%)	
Length of hospital stay (days)	5.5 ± 4.4	
30-day outcomes		
Mortality	10 (5.5%)	
Stroke	7 (3.8%)	
Major bleeding	22 (12.0%)	
Major vascular complication	32 (17.5%)	
Permanent pacemaker implantation	19 (10.4%)	
1-year mortality	21 (11.6%)	

(*continued*)

Table 1 (***Continued***)

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; AVA = aortic valve area; CABG = coronary artery bypass grafting; COPD = chronic obstructive pulmonary disease; DOAC = direct oral anticoagulant; eGFR = estimated glomerular filtration rate; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; RBC = red blood cell.

Univariable analysis was performed to identify baseline characteristics associated with 30-day mortality.

Sapien (Edwards Lifesciences, Irvine, CA, USA), Evolut (Medtronic, Minneapolis, MN, USA), Acurate (Boston Scientific, Marlborough, MA, USA), Portico (Abbott Vascular, Santa Clara, CA, USA), Allegra (NVT AG, Morges, Switzerland and Biosensors, Singapore, Singapore) and Lotus (Boston Scientific, Marlborough, MA, USA).

* Device was not implanted in 2 patients due to intraoperative death. Information on valve type was missing in 2 patients and size was missing in one patient.

† Defined according to the VARC-2 criteria: missing information in 3 patients.

‡ Information on paravalvular regurgitation was missing in 3 patients.

Values are counts and percentages (in parentheses) and means and standard deviations.

vs 1.9%, p = 0.022) and Alzheimer's disease (30-day mortality 40.0% vs 4.0%, p = 0.020) were associated with increased early mortality.

A total of 2 patients (1.1%) who were discharged from the hospital 4 and 6 days after the procedure were lost to follow-up. Preoperative EuroSCORE II were 3.7% and 2.2% in these patients, respectively. The 1-year mortality was 11.6%. With an expected survival of 82.4%, the relative survival was 1.07, as estimated comparing year-, age-, and gender-matched general Finnish population (Figure 1). Despite an initial negative trend in survival related to early postprocedural mortality, the relative survival increased a few months after the procedure, suggesting a possible fast recovery after TAVR.

The present findings demonstrated that TAVR in carefully selected nonagenarians is a safe and effective therapy, which should not be discarded solely by age. In our series, the 1-year survival of nonagenarians who underwent TAVR was comparable to the year-, age-, and gender-matched general Finnish population, which can be held as an excellent outcome considering the high mortality associated with untreated severe symptomatic AS.[4] Although the rates of early stroke and permanent pacemaker implantation were low, a rather high incidence of major vascular and bleeding complications were observed. There have been previous reports about nonagenarians being more prone than their younger counterparts to vascular and bleeding complications, possibly attributed to higher prevalence of peripheral vascular disease and fragility of tissues common to the older aged patients.[5–7] In addition, majority of our patients were women who have a higher risk for such complications,

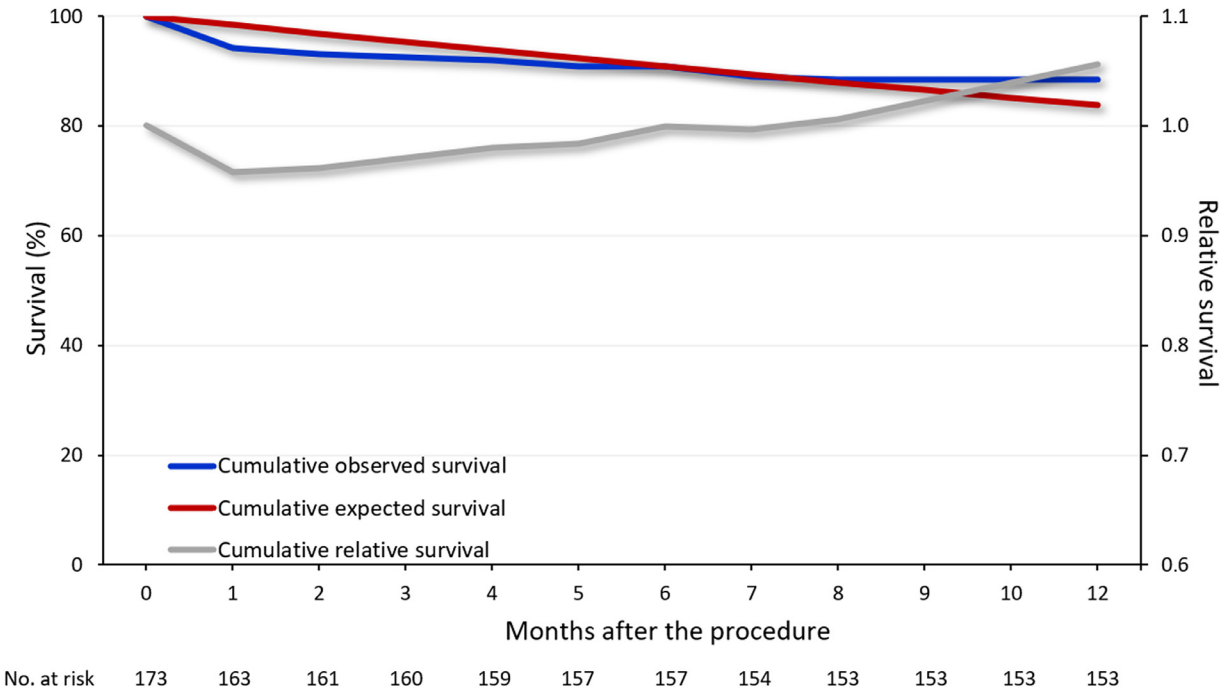

Figure 1. Cumulative observed survival, expected survival, and relative survival at 1-year after the procedure compared with year-, age-, and sex-matched general Finnish population.

presumably because of their more complex vascular anatomy.[8] However, advances in devices, procedural technique, operator experience, and perioperative care have reportedly improved outcomes after TAVR.[9,10] Indeed, in the present series, where majority of the procedures (60.7%) were performed after 2018, the incidence of major vascular complication (14.4% vs 22.2%) and major bleeding (8.1% vs 18.1%) decreased when comparing rates before and after 2018. Nonetheless, the incidence remained high also during the more recent period, warranting further investigation.

Lastly, thorough preoperative risk assessment and identification of nonagenarian patients who may gain most from TAVR remains important. In our series, mortality increased significantly according to the EuroSCORE II quartiles. This relation was seemingly nonlinear, highlighting the safety of TAVR in low-risk nonagenarians. Overall, the EuroSCORE II demonstrated rather good predictive ability, suggesting that estimation of operative risk with the EuroSCORE II may be useful in the preoperative decision-making process of older aged patients.

Declaration of competing interest

Dr. Savontaus received advisory fees from Medtronic and Boston Scientific. The remaining authors have no competing interest to declare.

CRediT authorship contribution statement

Matti Riihiniemi: Writing – review & editing, Writing – original draft, Visualization, Formal analysis, Data curation. **Jarkko Piuhola:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Matti Niemelä:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Yoichi Sugiyama:** Writing – review & editing, Data curation. **Heidi Kiviniemi:** Writing – review & editing, Data curation. **Fausto Biancari:** Writing – review & editing, Visualization, Formal analysis. **Mika Laine:** Writing – review & editing, Conceptualization. **Mikko Savontaus:** Writing – review & editing, Data curation. **Juhani Junttila:** Writing – review & editing, Supervision, Methodology, Conceptualization.

Data Availability

The data supporting the results may be accessed from the corresponding author upon reasonable request and permission from relevant authorities.

1. Iung B, Cachier A, Baron G, Messika-Zeitoun D, Delahaye F, Tornos P, Gohlke-Bärwolf C, Boersma E, Ravaud P, Vahanian A. Decision-making in elderly patients with severe aortic stenosis: why are so many denied surgery? *Eur Heart J* 2005;26:2714–2720.
2. Messika-Zeitoun D, Baumgartner H, Burwash IG, Vahanian A, Bax J, Pibarot P, Chan V, Leon M, Enriquez-Sarano M, Mesana T, Iung B. Unmet needs in valvular heart disease. *Eur Heart J* 2023;44:1862–1873.
3. Kappetein AP, Head SJ, Généreux P, Piazza N, NM Van Mieghem, Blackstone EH, Brott TG, Cohen DJ, Cutlip DE, GA Van Es, Hahn RT, Kirtane AJ, Krucoff MW, Kodali S, Mack MJ, Mehran R, Rodés-Cabau J, Vranckx P, Webb JG, Windecker S, Serruys PW, Leon MB, Valve Academic Research Consortium (VARC)-2. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document (VARC-2). *Eur J Cardiothorac Surg* 2012;4:S45–S60.
4. Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Brown DL, Block PC, Guyton RA, Pichard AD, Bavaria JE, Herrmann HC, Douglas PS, Petersen JL, Akin JJ, Anderson WN, Wang D, Pocock S, PARTNER Trial Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med* 2010;363:1597–1607.

5. Yamamoto M, Meguro K, Mouillet G, Bergoend E, Monin JL, Lim P, Dubois-Rande JL, Teiger E. Comparison of effectiveness and safety of transcatheter aortic valve implantation in patients aged ≥90 years versus <90 years. *Am J Cardiol* 2012;110:1156–1163.
6. Matta A, Lhermusier T, Bouisset F, Parada FC, ELBaz M, Nader V, Blanco S, Roncalli J, Carrié D. Outcomes of transcatheter aortic valve implantation in nonagenarians compared to younger than 90 year old patients. *Am J Med* 2022;135:745–751.
7. Arsalan M, Szerlip M, Vemulapalli S, Holper EM, Arnold SV, Li Z, Dimaio MJ, Rumsfeld JS, Brown DL, Mack MJ. Should transcatheter aortic valve replacement be performed in nonagenarians?: insights from the STS/ACC TVT registry. *J Am Coll Cardiol* 2016;67:1387–1395.
8. Vlastra W, Chandrasekhar J, García Del Blanco B, Tchétché D, Brito FS de, Barbanti M, Kornowski R, Latib A, D'Onofrio A, Ribichini F, Baan J, Tijssen JGP, Moreno R, Dumonteil N, Tarasoutchi F, Sartori S, D'Errigo P, Tarantini G, Lunardi M, Orvin K, Pagnesi M, Berenguer A, Modine T, Dangas G, Mehran R, Piek JJ, Delewi R. Sex differences in transfemoral transcatheter aortic valve replacement. *J Am Coll Cardiol* 2019;74:2758–2767.
9. Mentias A, Saad M, Desai MY, Horwitz PA, Rossen JD, Panaich S, Elbadawi A, Qazi A, Sorajja P, Jneid H, Kapadia S, London B, Vaughan Sarrazin MS. Temporal trends and clinical outcomes of transcatheter aortic valve replacement in nonagenarians. *J Am Heart Assoc* 2019;8:e013685.
10. Ismayl M, Aboud Abbasi M, Al-Abcha A, Robertson S, El-Am E, Goldsweig AM, Alkhouli M, Guerrero M, Anavekar NS. Outcomes of transcatheter aortic valve implantation in nonagenarians and octogenarians (analysis from the national inpatient sample database). *Am J Cardiol* 2023;199:59–70.