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Life Expectancy After Surgical Aortic Valve Replacement

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ABSTRACT

BACKGROUND Surgical risk, age, perceived life expectancy, and valve durability influence the choice between surgical aortic valve replacement (SAVR) and transcatheter aortic valve implantation. The contemporaneous life expectancy after SAVR, in relation to surgical risk and age, is unknown.

OBJECTIVES The purpose of this study was to determine median survival time in relation to surgical risk and chronological age in SAVR patients.

METHODS Patients ≥60 years with aortic stenosis who underwent isolated SAVR with a bioprosthesis (n = 8,353) were risk-stratified before surgery into low, intermediate, or high surgical risk using the logistic EuroSCORE (2001-2011) or EuroSCORE II (2012-2017) and divided into age groups. Median survival time and cumulative 5-year mortality were estimated with Kaplan-Meier curves. Cox regression analysis was used to further determine the importance of age.

RESULTS There were 7,123 (85.1%) low-risk patients, 942 (11.3%) intermediate-risk patients, and 288 (3.5%) high-risk patients. Median survival time was 10.9 years (95% confidence interval: 10.6-11.2 years) in low-risk, 7.3 years (7.0-7.9 years) in intermediate-risk, and 5.8 years (5.4-6.5 years) in high-risk patients. The 5-year cumulative mortality was 16.5% (15.5%-17.4%), 30.7% (27.5%-33.7%), and 43.0% (36.8%-48.7%), respectively. In low-risk patients, median survival time ranged from 16.2 years in patients aged 60 to 64 years to 6.1 years in patients aged ≥85 years. Age was associated with 5-year mortality only in low-risk patients (interaction $P < 0.001$).

CONCLUSIONS Eighty-five percent of SAVR patients receiving bioprostheses have low surgical risk. Estimated survival is substantial following SAVR, especially in younger, low-risk patients, which should be considered in Heart Team discussions. (J Am Coll Cardiol 2021;78:2147–2157) © 2021 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/).

European and North American guidelines on valvular heart disease recommend that age, surgical risk, and life expectancy be taken into consideration, together with clinical, anatomic, and procedural factors, when the Heart Team decides between surgical aortic valve replacement (SAVR) and transcatheter aortic valve implantation (TAVI) in patients with severe aortic stenosis (1,2). The

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ABBREVIATIONS AND ACRONYMS

CI = confidence interval

EuroSCORE = European System for Cardiac Operative Risk Evaluation

HR = hazard ratio

ICD-10 = International Classification of Disease-10th Revision

SAVR = surgical aortic valve replacement

STS-PROM = Society of Thoracic Surgery-Predicted Risk of Mortality

TAVI = transcatheter aortic valve implantation

chronological age is evident, whereas the surgical risk can be estimated using the European System for Cardiac Operative Risk Evaluation (EuroSCORE) or the Society of Thoracic Surgery-Predicted Risk of Mortality (STS-PROM) score, based on patient characteristics, comorbidities, and type of surgical procedure (3-5). Surgical risk scores have been widely used to stratify different groups of patients for comparative clinical trials between SAVR and TAVI (6-9). The average life expectancy at different ages within the general population can be calculated from official statistics (10). Life expectancy after SAVR in relation to age, both in absolute numbers and in relation to the general population, has been thoroughly reported (11,12). By contrast, life expectancy in relation to surgical risk and surgical risk combined with chronological age has not previously been published, despite the strong recommendations for assessing these factors during the Heart Team's decision-making process (1,2). Hence, the present study aimed to estimate survival time related to surgical risk and age after SAVR with a bioprosthesis for aortic stenosis, that is, in a population in which both SAVR and TAVI may be considered.

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METHODS

PATIENTS. The study population was identified from the Swedish Cardiac Surgery Register (13), part of the SWEDEHEART registry (14). All patients aged 60 years or older at the time of surgery, who underwent first-time isolated SAVR with implantation of a bioprosthesis for aortic stenosis, or a combination of stenosis and regurgitation, from January 1, 2001, to December 31, 2017, were considered for inclusion in this observational nationwide Register-based study. If patients had previous or concomitant cardiac surgery, they were not considered eligible for inclusion. Follow-up ended on December 31, 2017. Patients without preoperative risk stratification and patients with acute endocarditis (defined as endocarditis within 6 months before surgery) were excluded from further analysis. A flow chart of the included and excluded patients is depicted in **Figure 1**. All patients underwent risk stratification with either the logistic EuroSCORE (2001-2011) or EuroSCORE II (2012-2017). The logistic EuroSCORE was originally developed to improve patient selection and was soon widely adopted (15); however, as peri- and postoperative care improved, the accuracy of logistic EuroSCORE risk estimates decreased, especially for patients undergoing SAVR. Therefore, the updated EuroSCORE II was established, which outperforms the logistic EuroSCORE for risk estimations (16). EuroSCORE II and STS-PROM have comparable discrimination and calibration regarding in-hospital mortality in patients receiving aortic valve replacement (17,18).

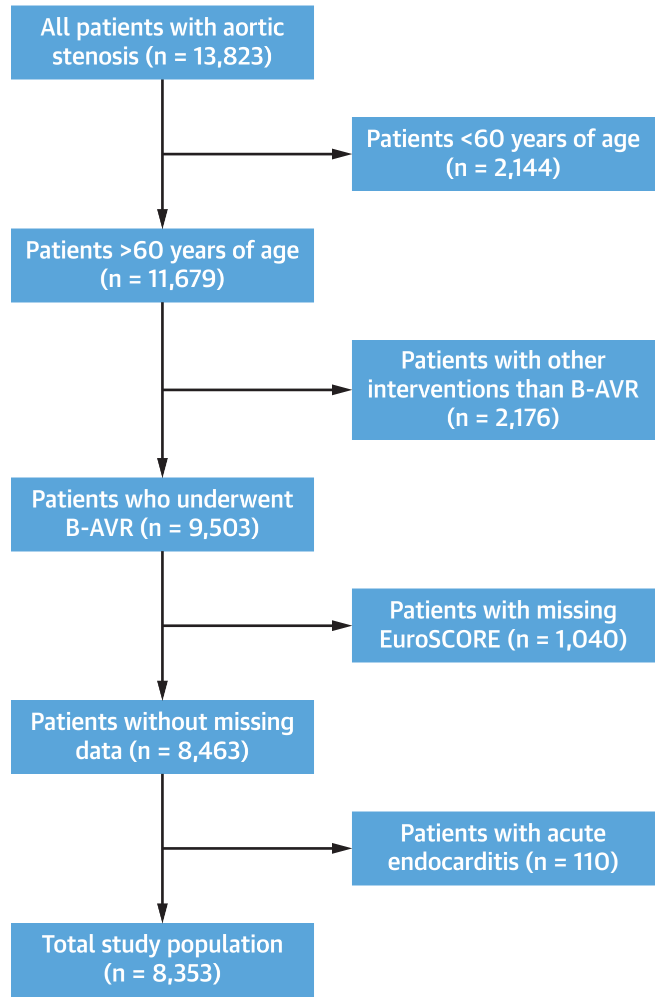
Patients were divided into risk score groups as follows: low-risk, defined as a logistic EuroSCORE of <10% or EuroSCORE II <4%; intermediate-risk (logistic EuroSCORE of 10%-20% or EuroSCORE II of 4%-8%); or high-risk (logistic EuroSCORE of >20% or EuroSCORE II of >8%), following current European guidelines and contemporary studies comparing SAVR and TAVI (1,6-9). In addition, patients were divided into 6 age groups, 60-64, 65-69, 70-74, 75-79, 80-84, and ≥85 years. Patient characteristics stratified by risk group are presented in **Table 1**.

This paper was written according to recommendations in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement (19). The study was performed in accordance with the 1975 Declaration of Helsinki and was approved by the Regional Research Ethics Committee in Gothenburg (registration number 139-16). The need for individual patient consent was waived.

DATA SOURCES. Preoperative status, including risk stratification, was retrieved from the Swedish Cardiac Surgery Register, which contains detailed information on all cardiac operations performed in Sweden since 1992 (13). All types of bioprostheses were included: both stented and stentless prostheses. In addition to those registered in the Swedish Cardiac Surgery Register, comorbidities were collected from the National Patient Register, which has full coverage of diagnoses from all hospital admissions in Sweden (20). Diagnoses in the Register have been reported according to the International Classification of Diseases, 10th revision (ICD-10), since 1997. Mortality data were collected from the National Cause of Death Register, which has information on the date and cause of death, according to the ICD-10, of all deceased Swedish citizens. There is no loss to follow-up as all deaths are, by law, reported to the Register by the responsible physician. The Swedish Population Register was used for basic demographic information, including emigration dates if applicable. Patients were followed up until death, emigration, or until December 31, 2017. The merging of registry data was based on the personal identification number that all Swedish residents are given at birth or shortly after immigration (21).

STATISTICAL ANALYSIS. Continuous variables are presented as mean with standard deviation or median with (interquartile range) if not normally distributed. Categorical variables are presented as frequencies with percentages. For comparison between risk and age groups, the Cochrane-Armitage test for trend was used to compare distribution of binary variables, and linear regression was used to compare distribution of normally distributed continuous variables. Cumulative mortality was calculated and illustrated with Kaplan-Meier curves for the 3 risk groups and patients of different ages within a risk group. The curves were compared with a log-rank test. Median survival time was used as a proxy of life expectancy and calculated using the Kaplan-Meier method with confidence intervals (CIs) calculated using log-transformation (exp[log(p) ± 1.96se(log(p))]). Median survival time was chosen due to the straightforward interpretation of the values. In addition, 5-year and 10-year cumulative mortality, derived from Kaplan-Meier estimates, was reported as a complement to enhance the understanding of early mortality in the different risk and age groups. Median survival time as a function of age, separated into 5-year intervals, and presented separately for each risk group, was calculated and illustrated using locally estimated scatterplot smoothing. The current study did not have any missing data for age, sex, comorbidities at baseline, or mortality during follow-up. Patients who emigrated during follow-up (0.3%) were excluded before study inclusion. EuroSCORE values were missing in 1,040 patients and these were excluded in the primary analysis. An additional sensitivity analysis in which median survival time was estimated after imputation (using multiple imputation, employing bootstrapping and predictive mean matching) of missing EuroSCORE values was performed. Cox regression analyses adjusted for year of operation were used to evaluate age as an additional risk factor for 5-year mortality in low-, intermediate-, and high-risk patients. Results from these analyses are presented as hazard ratios (HRs) with 95% CIs. The proportional hazards assumption was tested using scaled Schoenfeld residuals and visual inspection; the assumptions were fulfilled for the models. In addition, a regression analysis with age- and sex-based matching of low-risk patients to intermediate- and high-risk patients was performed with full optimal matching, as the intermediate- and high-risk patients were significantly older with a right-skewed distribution. In a separate analysis, we calculated median survival time independently for men and women. All tests were 2-tailed and interpreted at the 0.05 significance level. All analyses were performed using R version 4.0.3 (R Foundation for Statistical Computing).

FIGURE 1 **Flow Chart of Excluded SAVR Patients**



Patients who emigrated during follow-up, or had previous or concomitant cardiac surgery were excluded. Patients younger than 60 years were not included. The final study population included 8,353 patients who underwent isolated biological aortic valve replacement (B-AVR). EuroSCORE = European System for Cardiac Operative Risk Evaluation; SAVR = surgical aortic valve replacement.

RESULTS

PATIENTS. A total of 8,353 patients were included in the study. The mean age in the study population was 75.1 ± 6.6 years and 48.8% were women. There were 7,123 (85.1%) patients at low operative risk, 942 (11.3%) at intermediate risk, and 288 (3.5%) at high risk of operative mortality, according to the logistic EuroSCORE or EuroSCORE II. High- and intermediate-risk patients were older, were more often women, and had more comorbidities than low-risk patients (Table 1). Patient characteristics in the 3 risk groups

TABLE 1 Baseline Characteristics in Patients Undergoing SAVR With a Bioprosthesis for Aortic Stenosis

	Low-Risk (n = 7,123)	Intermediate-Risk (n = 942)	High-Risk (n = 288)	*P* Value
Age, y	74.3 ± 6.4	80.0 ± 5.8	79.3 ± 6.2	<0.001
Female	3,342 (46.9)	586 (62.2)	151 (52.4)	<0.001
Previous MI	479 (6.7)	153 (16.2)	62 (21.5)	<0.001
Heart failure	1,100 (15.4)	371 (39.4)	177 (61.5)	<0.001
Hypertension	3,784 (53.1)	551 (58.5)	150 (52.1)	<0.001
Atrial fibrillation	1,052 (14.7)	261 (27.7)	91 (31.6)	<0.001
Previous stroke	466 (6.5)	105 (11.1)	40 (13.9)	<0.001
Diabetes	1,225 (17.2)	217 (23.0)	61 (21.2)	<0.001
Renal failure	195 (2.7)	68 (7.2)	36 (12.5)	<0.001
History of cancer	1,360 (19.1)	189 (20.1)	51 (17.7)	<0.001

Values are mean ± SD or n (%). Patients are stratified into low-, intermediate-, and high-risk groups. *P* values for trend.
SAVR = surgical aortic valve replacement.

clustered by age are presented in **Tables 2, 3, and 4**. Histograms to illustrate the age distribution in low-, intermediate-, and high-risk groups are available in Supplemental Figure 1. The median follow-up was 5.2 years (range 0-17 years). When the logistic EuroSCORE was used (before 2012), a higher percentage of patients were in the intermediate- and high-risk categories, 14.2% and 4.7%, respectively, compared with 7.4% and 1.8% after the introduction of EuroSCORE II in 2012.

SURVIVAL TIME IN RELATION TO SURGICAL RISK. The 30-day mortality for the entire cohort was 2.0% (95% CI: 1.7%-2.3%), 1.2% (95% CI: 1.2%-1.7%) for low-risk, 4.1% (95% CI: 2.9%-5.4%) for intermediate-risk, and 8.3% (95% CI: 5.1%-11.5%) for high-risk patients (Supplemental Figure 2).

Low-risk patients had a median survival time of 10.9 years (95% CI: 10.6-11.2 years), intermediate-risk patients of 7.3 years (95% CI: 7.0-7.9 years), and high-risk patients of 5.8 years (95% CI: 5.4-6.5 years) (**Central Illustration, Table 2**). The continuous survival time for the 3 risk groups is illustrated in **Figure 2**. The cumulative 5-year mortality of patients classified as low risk was 16.5% (95% CI: 15.5%-17.4%), for those classified as intermediate-risk, 30.7% (95% CI: 27.5%-33.7%), and for patients classified as high-risk, 43.0% (95% CI: 36.8%-48.7%). The 10-year cumulative mortality is depicted in Supplemental Table 1. The sensitivity analysis, with imputed EuroSCORE values for patients with missing risk assessment, confirmed the results of the primary analysis (Supplemental Figure 3).

SURVIVAL TIME IN RELATION TO SURGICAL RISK AND AGE. Median survival time and cumulative 5-year mortality after SAVR in low-risk, intermediate-risk, and high-risk patients in relation to chronological age at surgery are presented in 5-year intervals in **Figures 3A to 3C and Table 5**. The median survival time in low-risk patients ranged from 16.2 years (95% CI: 15.6-not defined) years in patients aged 60 to 64 years to 6.1 (95% CI: 5.9-6.6 years) in patients aged ≥85 years. The cumulative 5-year mortality of low-risk patients ranged from 6.8% (95% CI: 4.4%-9.1%) in patients aged 60 to 64 years to 37.7% (95% CI: 30.1%-43.3%) in those aged ≥85 years.

The association between age and mortality risk was significantly different between risk groups (interaction *P* value <0.001). In low-risk patients, there was a significant association between higher age at surgery and 5-year mortality (HR: 1.30 per 5-year increase, 95% CI: 1.23-1.37), whereas no significant association between age and mortality was observed in intermediate-risk patients (HR: 1.04; 95% CI: 0.93-1.16) or in high-risk patients (HR: 1.01; 95% CI: 0.87-1.18) (**Figure 4**). To further evaluate a possible ceiling effect for age in the intermediate- and high-risk group, a regression analysis was performed in low-risk patients, age- and sex-matched to individuals in the high- and intermediate-risk groups. The analysis confirmed the findings of the primary analysis (HR: 1.22; 95% CI: 1.10-1.34; *P* < 0.001).

GENDER PERSPECTIVES. The mean age at SAVR was 74.2 ± 6.6 years for men and 76.1 ± 6.4 years for women (*P* = 0.001). The overall median survival time was somewhat shorter for men than for women, 10.0 years (95% CI: 9.7-10.2 years) and 10.3 years (95% CI 10.1-10.7 years), respectively (*P* = 0.004). The median survival time was 10.5 (95% CI: 10.2-11.0) in the low-risk group of men vs 11.3 years (95% CI: 10.9-11.7 years) in the low-risk group of women (*P* = 0.002). In intermediate-risk patients, the estimated median survival time was 6.6 years (95% CI: 5.9-7.4 years) in men vs 7.9 years (95% CI: 7.2-8.7 years) in women (*P* < 0.001). The median survival time in high-risk patients was 5.7 years (95% CI: 4.3-6.5 years) in men vs 5.8 years (95% CI: 5.5-7.4 years) in women (*P* = 0.10) (Supplemental Figure 4A to 4C). The results did not differ after adjusting for age at operation.

DISCUSSION

The present national study provides essential perspectives on survival time after SAVR with a bioprosthesis in patients with aortic stenosis at various surgical risks and various age categories. The main findings include the following: 1) the EuroSCORE identified 85% of patients undergoing SAVR during 17 years as having low surgical risk; 2) the survival after SAVR was substantial, especially in low-risk patients,

TABLE 2 Baseline Characteristics in Low-Risk Patients Undergoing SAVR With a Bioprosthesis for Aortic Stenosis

	60-64 Years (n = 571)	65-69 Years (n = 1,127)	70-74 Years (n = 1,777)	75-79 Years (n = 1,979)	80-84 Years (n = 1,396)	85+ Years (n = 273)	*P* Value
Age, y	62.3 ± 1.4	67.3 ± 1.4	72.1 ± 1.4	77.0 ± 1.4	81.7 ± 1.4	86.1 ± 1.4	
Female	202 (35.4)	444 (39.4)	801 (45.1)	995 (50.3)	791 (56.7)	109 (39.9)	<0.001
Previous MI	39 (6.8)	81 (7.2)	123 (6.9)	132 (6.7)	95 (6.8)	33 (12.1)	0.67
Heart failure	83 (14.5)	164 (14.6)	273 (15.4)	340 (17.2)	267 (19.1)	73 (26.7)	0.009
Hypertension	275 (48.2)	641 (56.9)	1071 (60.3)	1192 (60.2)	838 (60.0)	156 (57.1)	<0.001
Atrial fibrillation	40 (7.0)	103 (9.1)	224 (12.6)	353 (17.8)	256 (18.3)	76 (27.6)	<0.001
Previous stroke	32 (5.6)	62 (5.5)	131 (7.4)	170 (8.6)	132 (9.5)	29 (10.6)	0.20
Diabetes	90 (15.8)	237 (21.0)	377 (21.2)	362 (18.3)	214 (15.3)	35 (12.8)	<0.001
Renal failure	15 (2.6)	47 (4.2)	70 (3.9)	72 (3.6)	60 (4.3)	18 (6.6)	<0.001
History of cancer	68 (11.9)	171 (15.2)	306 (17.2)	427 (21.6)	325 (23.3)	65 (23.8)	<0.001

Values are mean ± SD or n (%). *P* values for trend.
MI = myocardial infarction; abbreviations as in Table 1.

but also in higher-risk groups and older patients; and 3) the association between chronological age and 5-year mortality was significant for low-risk patients, whereas no association between age and 5-year mortality in intermediate-risk and high-risk patients was observed.

USE OF SURGICAL RISK SCORES IN THE DECISION BETWEEN SAVR AND TAVI. Surgical risk has been the key inclusion criterion in the landmark randomized studies that have compared the safety and efficacy of SAVR vs TAVI in patients with severe aortic stenosis. The first randomized studies between SAVR and TAVI were performed in patients with high surgical risk, defined as an STS-PROM score >10% (8) or based on an estimation of 30-day mortality risk >15% by a Heart Team before surgery (22). The trials in high-risk patients were followed by randomized trials comparing SAVR and TAVI in patients with intermediate-risk using an STS-PROM score of 4%-8% (9) or 3%-15% (7). Finally, recent low-risk trials have used either a <3% 30-day mortality risk, as estimated by the local Heart Team (23), or an STS-PROM score of <4% (6).

Based on available results from the randomized clinical trials comparing TAVI vs SAVR, the 2021 European Society of Cardiology (ESC)/European Association for Cardiothoracic Surgery (EACTS) guidelines (1) recommend SAVR for patients aged <75 years at low surgical risk (STS or EuroSCORE II <4%, Class I, Level of Evidence [LoE]: B). In addition, the guidelines recommend TAVI in patients with high surgical risk (STS or EuroSCORE II >8%) and aged >75 years. For remaining patients, the decision should be made after a risk-benefit assessment by the local Heart Team (1). The 2020 AHA/ACC guidelines emphasize that individual risks should be calculated and discussed before the procedure, as part of a shared decision-making process of the Heart Team (Class I, LoE: C). Still, importantly they do not include risk scores in the explicit recommendations (2). Instead, SAVR is recommended for patients <65 years and patients with >20 years of life expectancy, whereas TAVI is recommended for patients aged >80 years and patients with <10 years of life expectancy. The Heart Team should base decision-making for the remaining patients (ie, those aged 65-80 years) on

TABLE 3 Baseline Characteristics in Intermediate-Risk Patients Undergoing SAVR With a Bioprosthesis for Aortic Stenosis

	60-64 Years (n = 7)	65-69 Years (n = 52)	70-74 Years (n = 114)	75-79 Years (n = 222)	80-84 Years (n = 302)	85+ Years (n = 245)	*P* Value
Age, y	63.1 ± 1.1	67.4 ± 1.3	72.4 ± 1.4	77.5 ± 1.4	82.0 ± 1.4	86.5 ± 1.5	<0.001
Female	2 (28.6)	20 (38.5)	49 (43.0)	144 (64.9)	184 (60.9)	187 (76.3)	0.17
Previous MI	1 (14.3)	18 (34.6)	20 (17.5)	33 (14.9)	61 (20.2)	27 (11.0)	0.042
Heart failure	4 (57.1)	36 (69.2)	64 (56.1)	91 (41.0)	123 (40.7)	89 (36.3)	0.006
Hypertension	3 (42.9)	31 (59.6)	74 (64.9)	145 (65.3)	191 (63.2)	144 (58.8)	<0.001
Atrial fibrillation	2 (28.6)	6 (11.5)	32 (28.1)	66 (29.7)	99 (32.8)	56 (22.9)	<0.001
Previous stroke	2 (28.6)	8 (15.4)	18 (15.8)	32 (14.4)	38 (12.6)	23 (9.4)	0.040
Diabetes	0 (0.0)	21 (40.4)	38 (33.3)	72 (32.4)	62 (20.5)	31 (12.7)	<0.001
Renal failure	0 (0.0)	8 (15.4)	16 (14.0)	21 (9.5)	29 (9.6)	19 (7.8)	<0.001
History of cancer	2 (28.6)	9 (17.3)	26 (22.8)	41 (18.5)	65 (21.5)	46 (18.8)	0.017

Values are mean ± SD or n (%).
Abbreviations as in Tables 1 and 2.

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TABLE 4 Baseline Characteristics in High-Risk Patients Undergoing SAVR With a Biological Prosthesis for Aortic Stenosis

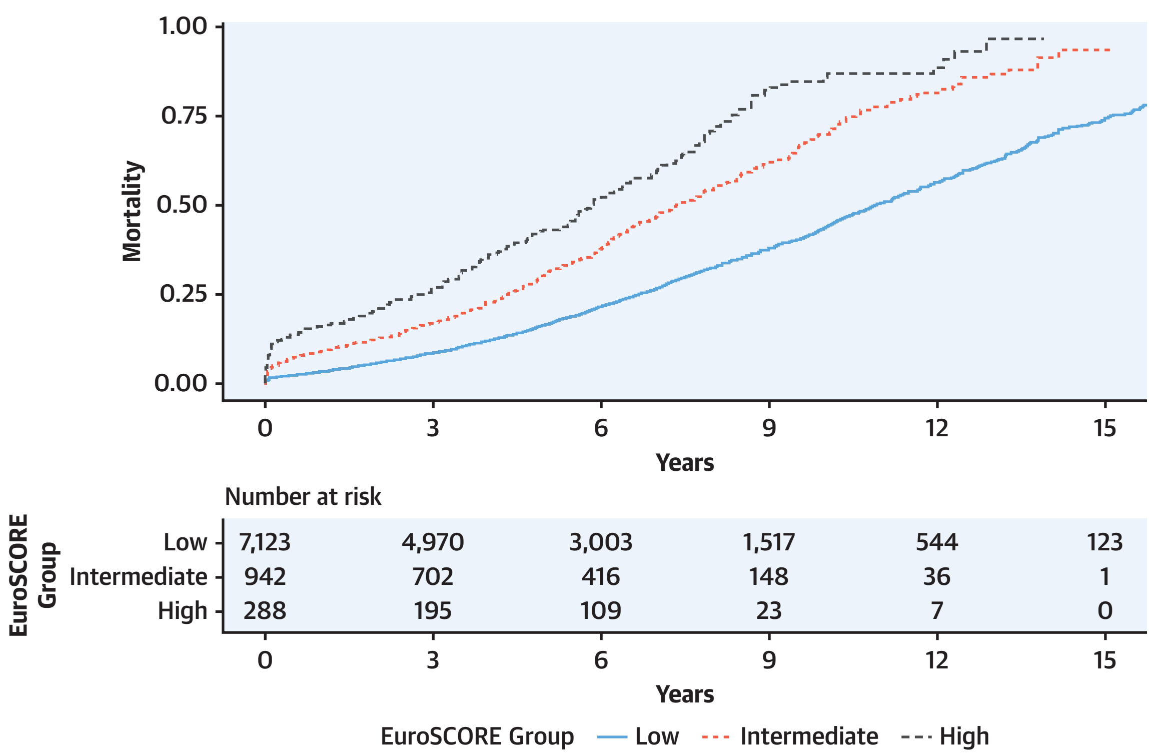
	60-64 Years (n = 9)	65-69 Years (n = 14)	70-74 Years (n = 31)	75-79 Years (n = 71)	80-84 Years (n = 116)	85+ Years (n = 47)	*P* Value
Age, y	62.9 ± 0.9	67.2 ± 1.9	72.0 ± 1.3	76.9 ± 1.4	82.1 ± 1.4	87.3 ± 2.1	
Female	5 (55.6)	4 (28.6)	10 (32.3)	26 (36.6)	78 (67.2)	28 (59.6)	0.35
Previous MI	5 (55.6)	3 (21.4)	9 (29.0)	11 (15.5)	26 (22.4)	11 (23.4)	0.65
Heart failure	7 (77.8)	13 (92.9)	21 (67.7)	51 (71.8)	76 (65.5)	26 (55.3)	0.23
Hypertension	5 (55.6)	10 (71.4)	22 (71.0)	37 (52.1)	60 (51.7)	25 (53.2)	<0.001
Atrial fibrillation	2 (22.2)	3 (21.4)	10 (32.3)	21 (29.6)	42 (36.2)	13 (27.7)	0.003
Previous stroke	1 (11.1)	1 (7.1)	5 (16.1)	16 (22.5)	19 (16.4)	3 (6.4)	0.45
Diabetes	2 (22.2)	6 (42.9)	9 (29.0)	16 (22.5)	28 (24.1)	3 (6.4)	0.002
Renal failure	2 (22.2)	6 (42.9)	10 (32.3)	10 (14.1)	15 (12.9)	5 (10.6)	<0.001
History of cancer	3 (33.3)	2 (14.3)	3 (9.7)	19 (26.8)	18 (15.5)	7 (14.9)	0.084

Values are mean ± SD or n (%).
Abbreviations as in Tables 1 and 2.

individual clinical and anatomic factors, including surgical risk.

LONG-TERM SURVIVAL AFTER SAVR. Long-term survival after SAVR has been reported in several observational studies with long follow-up time. Glaser et al (11) found an overall median survival time after SAVR with or without concomitant coronary artery bypass surgery of approximately 9.5 years

CENTRAL ILLUSTRATION Cumulative Mortality After Surgical Aortic Valve Replacement With a Bioprosthesis for Aortic Stenosis



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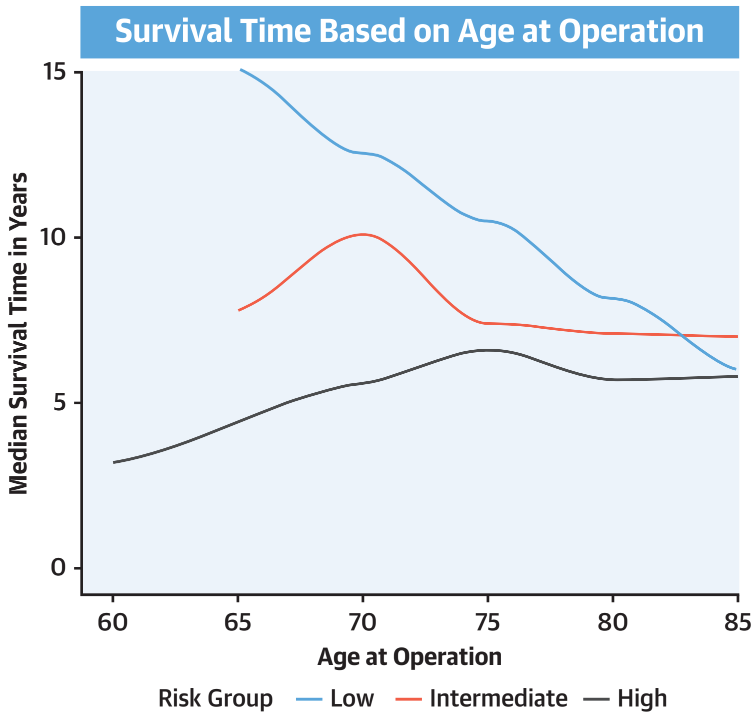
The patients are grouped into high, intermediate, and low risk based on the European System for Cardiac Operative Risk Evaluation (EuroSCORE). Cumulative mortality was estimated using Kaplan-Meier curves. Median survival time was 10.9 years in low-risk, 7.3 years in intermediate-risk, and 5.8 years in high-risk patients.

FIGURE 2 **Smoothed Line Plot of Survival Time Based on Age at Operation**



The median survival time as a function of age for low-, intermediate-, and high-risk patients. As is illustrated, older age had a substantial impact on median survival for patients in the low-risk group but the impact was attenuated for intermediate- and high-risk patients.

(derived from Kaplan-Meier curves), whereas the same group reported a median survival time of approximately 15 years in those aged 50-69 years following a bioprosthetic SAVR procedure with or without concomitant coronary artery bypass surgery (24). None of these studies have specifically reported long-term survival in patients undergoing SAVR in whom TAVI would have been a treatment option (ie, the population selected in the present study). By contrast, Sharabiani et al (25) reported a median survival of 10.9 years in a single-center study assessing 967 isolated SAVR patients >65 years. No distinction was made based on underlying disease (stenosis vs regurgitation) or between different risk and chronological age combinations.

In the present study, 85%, 11%, and 4% of the patients who underwent SAVR were classified as low, intermediate, and high risk, respectively, using the EuroSCORE risk assessment tool. This is a marginally larger proportion of patients with low risk than included in a large study from the STS-database, in which 80%, 14%, and 6%, respectively, of the patients were low-, intermediate- and high-risk candidates for surgery according to the STS-PROM score (26). Whether this reflects an actual lower risk in Swedish patients or whether it relates to a difference between EuroSCORE and STS-PROM calculations remains unclear. Thirty-day mortality in the STS-database study and the present study was comparable, but the STS-database study did not report long-term mortality.

The current study found a higher percentage of patients stratified as intermediate- or high-risk patients in the time span in which the logistic EuroSCORE was used. The most probable explanation is the introduction of TAVI as a complementary intervention during the EuroSCORE II period, mainly used in intermediate- and high-risk patients. In fact, during this later period (2012-2017), >90% of SAVR patients receiving a bioprosthesis were low surgical risk patients.

We divided the patients who underwent SAVR according to surgical risk (low, intermediate, and high) and chronological age categories in the present study. We observed, as expected, that surgical risk had a

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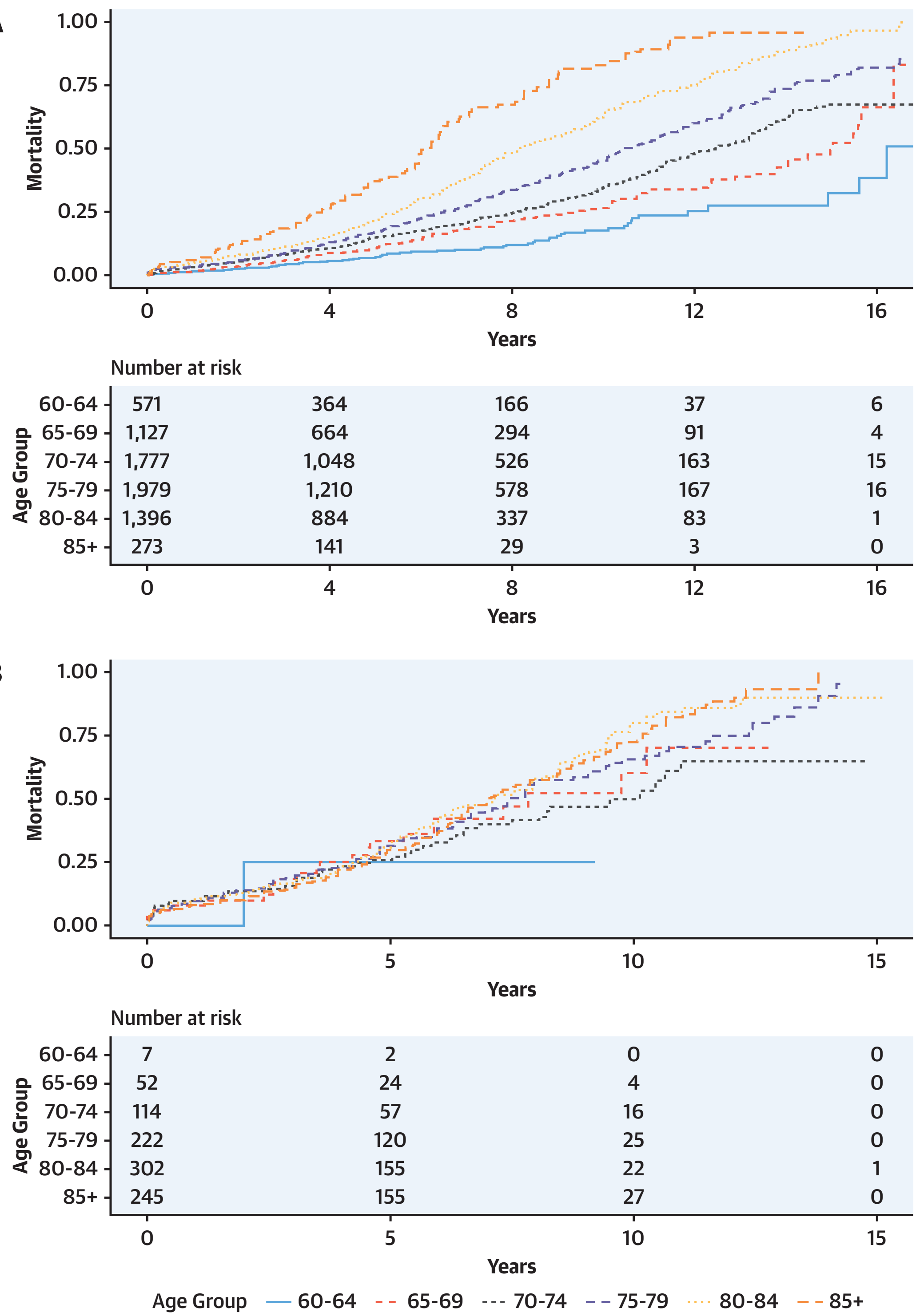
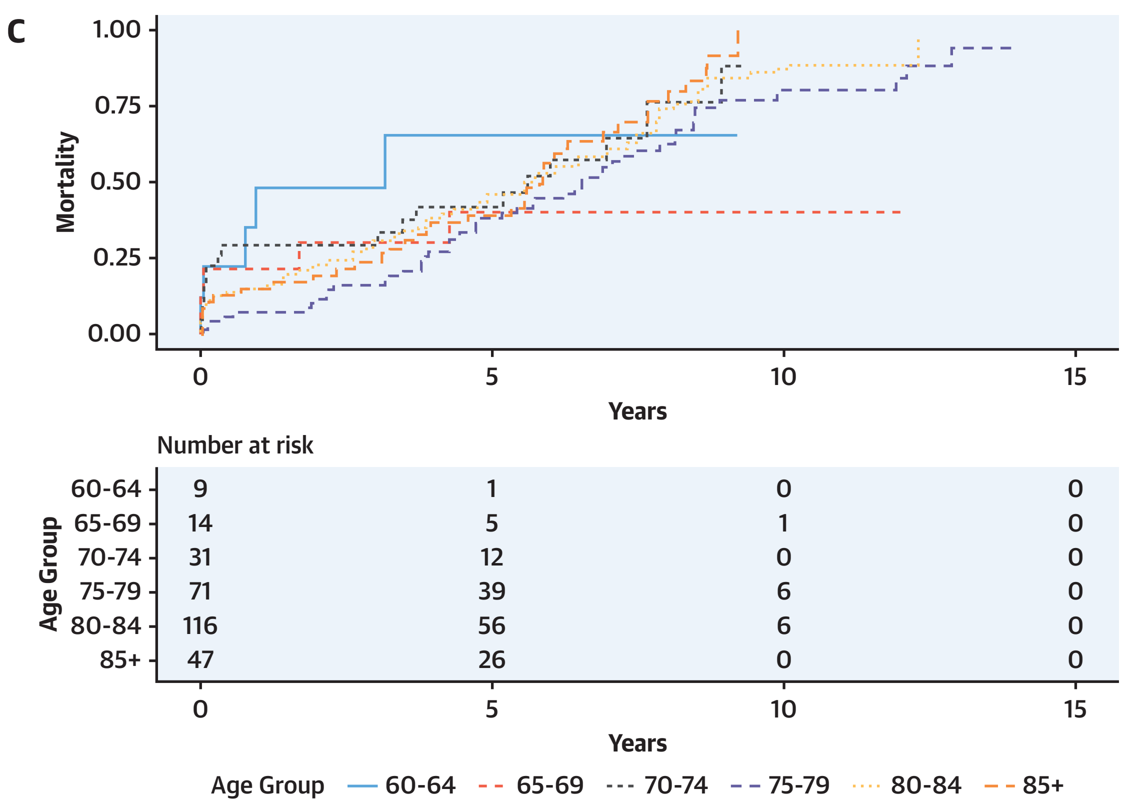
FIGURE 3 Cumulative Mortality in Different Risk and Age Groups



(A) Cumulative mortality in low-risk patients. **(B)** Cumulative mortality in intermediate-risk patients. **(C)** Cumulative mortality in high-risk patients. Patients are stratified into low-, intermediate, and high-risk groups; in addition, the patients are grouped according to age at the time of surgical aortic valve replacement (SAVR). Cumulative mortality was estimated using Kaplan-Meier curves. The survival time decreased stepwise for the older age groups in the low-risk population. In the intermediate- and high-risk groups, there was no clear separation between age groups.

Continued on the next page

FIGURE 3 Continued



marked impact on long-term survival, as illustrated in **Figure 1 and Table 5**. The overall median survival was 10.9 years in low-risk patients and substantially longer in younger low-risk patients, being >15 years in patients aged 60-70 years. The documented long-term durability for TAVI valves overall is still limited to 7-8 years (2,27) and markedly shorter, covering only 2 years, for low-risk patient cohorts (28).

At the time of surgery, chronological age was in the present study significantly associated with 5-year mortality in low-risk patients but not in intermediate-risk and high-risk patients. Hence, the findings support current ESC/EACTS guidelines, which recommend TAVI in high-risk patients irrespective of age, although SAVR may also be a valid option in selected patients (1). Conversely, the results suggest that chronological age remains important in low-risk patients and should be considered during the Heart Team discussion for these patients. The lack of association between age and survival in

TABLE 5 Median Survival Time in Patients Undergoing SAVR With a Biological Prosthesis for Aortic Stenosis

	Low-Risk		Intermediate-Risk		High-Risk	
Age Group, Years	Median Survival Time, Years	5-Year Mortality, %	Median Survival Time, Years	5-Year Mortality, %	Median Survival Time, Years	5-Year Mortality, %
60-64	16.2 (15.6-NA)	6.8 (4.4-9.1)	NA	25.0 (0-57.0)	3.2 (0.8-NA)	65.4 (2.2-87.8)
65-69	15.0 (14.1-NA)	10.7 (8.6-12.8)	7.8 (5.9-NA)	33.3 (17.6-46.0)	NA	40.1 (4.3-62.5)
70-74	12.5 (11.7-13.2)	14.9 (13.0-16.8)	10.1 (7.5-NA)	25.9 (16.7-34.2)	5.6 (3.5-NA)	41.8 (20.1-57.6)
75-79	10.5 (10.1-11.2)	16.9 (15.0-18.8)	7.4 (6.6-8.9)	31.5 (24.7-37.7)	6.6 (5.2-8.2)	38.1 (25.1-48.9)
80-84	8.2 (7.8-8.8)	21.6 (19.0-23.9)	7.1 (6.2-8.1)	32.9 (27.0-38.3)	5.7 (4.7-7.0)	45.9 (35.7-54.5)
≥85	6.1 (5.9-6.6)	37.1 (30.1-43.3)	7.0 (6.5-8.2)	28.8 (22.7-34.3)	5.8 (4.6-7.2)	39.0 (23.1-51.6)

Medial survival time is presented in years, with 95% confidence intervals (CIs). Five-year survival is presented as a proportion of patients with 95% CI. Values are derived from event rates. The patients are grouped into high-, intermediate-, and low-risk patients based on the European System for Cardiac Operative Risk Evaluation (EuroSCORE) and into age groups.

NA = not available because of a low number of patients; SAVR = surgical aortic valve replacement.

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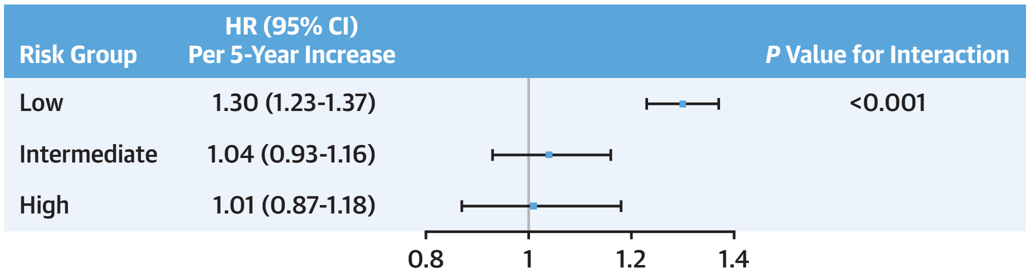
FIGURE 4 Age and HRs of Mortality per 5-Year Increase



A forest plot indicating the HR per 5-year increase patients with low, intermediate, or high surgical risk, in patients undergoing SAVR with a biological prosthesis. The plot illustrates that the risk associated with age was primarily present in low-risk patients and not for patients with intermediate and high risk. CI = confidence interval; HR = hazard ratio; SAVR = surgical aortic valve replacement.

intermediate- and high-risk groups may be caused by a ceiling effect in the higher-risk groups, that is, the mortality risk for these elderly individuals is already increased to the level of risk saturation for age and that other comorbid conditions are relatively more important regarding mortality. Another plausible explanation is that the increased risk due to age is already adequately accounted for in the EuroSCORE in intermediate- and high-risk patients.

STUDY STRENGTHS AND LIMITATIONS. The strengths include the real-world setting, the large nationwide study population with complete follow-up, and the use of validated registers. Limitations include that the study populations in the intermediate- and high-risk group are markedly smaller than in the low-risk group, making the results less robust in these groups than in low-risk patients. Furthermore, patients may also be judged as intermediate and high risk based on procedural, technical, or individual factors other than those captured by the EuroSCORE. Consequently, some patients in the present study's low-risk group may belong to one of the higher-risk groups; however, this would further reduce the long-term mortality risk in the remaining low-risk patients and prolong their life span. The interpretation of the risk associated with increasing age for patients of intermediate and high risk according to EuroSCORE is limited by the inclusion of age in the EuroSCORE. Eleven percent of patients had missing EuroSCORE values; however, imputation of these did not significantly change the survival estimates. The database lacks STS scores, which makes direct comparisons to contemporary trials of SAVR versus TAVI challenging. Finally, there is an inherent risk for selection bias and residual confounding in observational studies.

CONCLUSIONS

In patients with aortic stenosis aged ≥60 years in whom both TAVI and SAVR may be considered, EuroSCORE identifies 85% of patients who underwent SAVR as having low surgical risk. The median survival after SAVR is >15 years in low-risk patients <70 years of age and is substantial also in older patients. Chronological age remains important in low-risk patients. This information needs to be considered by the Heart Team when treatment modality is selected in individual patients.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: While the influence of patient age on survival after SAVR is captured by risk scores for intermediate- and high-risk patients, for low-risk patients life expectancy after SAVR is substantial.

TRANSLATIONAL OUTLOOK: Longer-term follow-up studies of patients after TAVI are needed to better inform decisions about choice of intervention for patients with aortic stenosis in various risk strata.

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KEY WORDS aortic stenosis, aortic valve replacement, epidemiology, valvular heart disease

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