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Loss in Life Expectancy After Surgical Aortic Valve Replacement

SWEDEHEART Study

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ABSTRACT

BACKGROUND Contemporary data on loss in life expectancy after aortic valve replacement (AVR) are scarce, particularly in younger patients.

OBJECTIVES The purpose of this national, observational cohort study was to analyze long-term relative survival and estimated loss in life expectancy after AVR.

METHODS The study included 23,528 patients who underwent primary surgical AVR with or without concomitant coronary artery bypass grafting in Sweden between 1995 and 2013 from the SWEDEHEART (Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies) register. Individual level linking with other national health-data registers was performed to obtain baseline characteristics and vital status. The expected survival from the general Swedish population matched by age, sex, and year of surgery was obtained from the Human Mortality Database. The relative survival was used as an estimate of cause-specific mortality. Flexible parametric models based on relative survival were used to estimate the loss in life expectancy.

RESULTS The mean follow-up was 6.8 years. The 19-year observed, expected, and relative survival was 21%, 34%, and 63% (95% confidence interval [CI]: 59% to 67%), respectively. The loss in life expectancy was 1.9 years (95% CI: 1.2 to 2.6 years) in the total study population. The estimated loss in life expectancy increased with younger age: 0.4 years (95% CI: 0.3 to 0.5 years) versus 4.4 years (95% CI: 1.5 to 7.2 years) in patients ≥80 and <50 years of age, respectively. There was no difference in loss in life expectancy between men and women.

CONCLUSIONS This study found a shorter life expectancy in patients after AVR compared with the general population. The estimated loss in life expectancy was substantial, and increased with younger age. These results provide important information to quantify disease burden after AVR, and are relevant for clinicians counseling patients before and after AVR. (HeAlth-data Register sTudies of Risk and Outcomes in Cardiac Surgery [HARTROCS]; NCT02276950)
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To understand the natural history after aortic valve replacement (AVR), it is important to estimate the mortality specifically associated with or due to AVR. This information can be used to assess prognosis and to better inform patients and physicians before and after surgery. Severe aortic stenosis is present in 3.4% of patients aged older than 75 years (1), and the incidence rate of severe aortic stenosis in patients aged older than 65 years is estimated at 4.4%/year (2). After symptoms develop, the prognosis is poor. Without treatment, the annual mortality is 25%, and the mean survival is 2 to 3 years (3). There is no medical treatment that stops or halts the progression of aortic stenosis. The standard treatment option for severe aortic valve disease is AVR, which can be performed either surgically or through transcatheter aortic valve replacement (TAVR). After AVR, the prognosis is believed to be excellent and similar to that of the general population (4–6), especially in older patients. However, studies providing data regarding prognosis after AVR in relation to the general population are scarce, particularly in younger patients. We hypothesized that patients undergoing AVR have a lower survival than the general population. Therefore, we performed a population-based, nationwide observational cohort study analyzing the long-term relative survival and the estimated loss in life expectancy in patients after AVR with or without concomitant coronary artery bypass grafting (CABG).

SEE PAGE 34

METHODS

STUDY DESIGN. This observational, population-based, nationwide cohort study was approved by the regional Human Research Ethics Committee, Stockholm, Sweden. No informed consent was required. All patients who underwent surgical AVR in Sweden between January 1, 1995, and December 31, 2013, were included from the SWEDEHEART (Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies) register (7,8). The SWEDEHEART register is a nationwide health register covering all cardiac surgeries in Sweden since 1992. Additional baseline characteristics were obtained from the National Patient Register (9), and the longitudinal integration database for health insurance and labor market studies (maintained by Statistics Sweden) (10). Patients with prior cardiac surgery and patients with concomitant procedures other than CABG were excluded, as were patients who underwent emergent surgery and surgery due to endocarditis. The Cause of Death register (11) was used to obtain survival status and cause and date of death. Individual cross-linking between the national registers was performed using the unique personal identity number assigned to all Swedish citizens (12). The national registers have been described previously (13).

STATISTICAL METHODS. The patients' baseline characteristics are presented as frequencies and percentages for categorical variables

ABBREVIATIONS AND ACRONYMS

AVR = aortic valve replacement

CABG = coronary artery bypass grafting

TAVR = transcatheter aortic valve replacement

TABLE 1 Baseline Characteristics in 23,528 Patients Who Underwent Aortic Valve Replacement in Sweden Between 1995 and 2013

Age, yrs	70.7 ± 10.8
Female	9,296 (39.5)
Civil status	
Not married or cohabiting	6,937 (29.5)
Household disposable income, kSEK	213 (145, 310)
Education, yrs	
<10	8,096 (47.6)
10–12	6,107 (35.9)
>12	2,815 (16.5)
Region of birth	
Non-Nordic countries	979 (5.2)
Biological valve prosthesis	15,692 (66.7)
Body mass index, kg/m^2	26.7 ± 4.4
Diabetes mellitus	3,991 (17.0)
Atrial fibrillation	3,328 (14.1)
Hypertension	5,717 (24.3)
Hyperlipidemia	2,230 (9.5)
Stroke	2,240 (9.5)
Peripheral vascular disease	1,466 (6.2)
Chronic pulmonary disease	1,752 (7.4)
Prior myocardial infarction	3,522 (15.0)
Prior PCI	1,929 (8.2)
Prior major bleeding event	1,205 (5.1)
Alcohol dependency	383 (1.6)
Liver disease	206 (0.9)
Cancer	1,762 (7.5)
eGFR, ml/min/1.73 m^2	
>60	13,140 (66.8)
45–60	4,291 (21.8)
30–45	1,724 (8.8)
15–30	317 (1.6)
<15 or dialysis	201 (1.0)
Heart failure	4,494 (19.1)
Left ventricular ejection fraction, %	
>50	10,187 (72.8)
30–49	3,004 (21.5)
<30	799 (5.7)
Isolated AVR	13,727 (58.3)
Year of surgery	
1995–2000	7,403 (31.5)
2001–2006	7,030 (29.9)
2007–2013	9,095 (38.7)

Values are mean ± SD, n (%), or median (quartile 1, quartile 3).

AVR = aortic valve replacement; eGFR = estimated glomerular filtration rate; kSEK = 1,000 Swedish krona; PCI = percutaneous coronary intervention.

TABLE 2 Survival by Age Group, Sex, Surgical Procedure, and Time Period in 23,528 Patients Who Underwent Aortic Valve Replacement in Sweden Between 1995 and 2013

		Survival, %			
	n (%)	5 yrs	10 yrs	15 yrs	19 yrs
Overall	23,258 (100.0)	79.7	54.6	32.2	21.3
Age group, yrs					
<50	1,109 (4.7)	93.0	88.0	82.7	78.8
50-59	2,278 (9.7)	91.0	82.1	70.3	60.8
60-69	5,314 (22.6)	86.8	70.5	49.4	32.1
70-79	10,170 (43.2)	77.0	47.5	19.7	7.1
≥80	4,657 (19.8)	68.5	27.2	4.2	NA
Sex					
Female	9,296 (39.5)	80.7	52.9	28.0	16.4
Male	14,232 (60.5)	79.1	55.7	35.2	24.8
Surgery					
Isolated AVR	13,727 (58.3)	83.5	61.5	41.3	30.0
AVR with concomitant CABG	9,801 (41.7)	74.7	45.7	20.8	10.1
Time period					
1995–2000	7,403 (31.5)	77.8	52.8	31.2	20.6
2001–2006	7,030 (29.9)	79.9	55.1	NA	NA
2007–2013	9,095 (38.7)	81.6	NA	NA	NA

Survival was estimated with the Kaplan-Meier method.
AVR = aortic valve replacement; CABG = coronary artery bypass grafting; NA = not available.

and as means and SDs for continuous variables. The outcome measures were survival in patients who underwent AVR, relative survival, and loss in life expectancy after surgical AVR. The relative survival can be used as an estimate of cause-specific mortality without the need for accurate cause of death information. It is defined as the ratio between the observed survival rates and the expected survival rates in the general population (14). The observed survival was assessed as the Kaplan-Meier estimated survival in the AVR cohort included in this study. Cox proportional hazard regression was used to analyze the association between patient characteristics and all-cause mortality. The expected survival from the general population in Sweden matched by age, sex, and year of surgery was obtained from the Human Mortality Database (15). The Human Mortality Database provides detailed mortality and population data from 40 countries or areas with open and international public access to these data. This database contains 6 data types, including annual counts of live births by sex, death counts, population size, estimates on the number of individuals exposed to the risk of death at a certain time period, death rates, and probabilities of death (life tables). The Human Mortality Database is updated continuously and includes mortality data from Sweden until 2017. The relative survival was estimated using the Ederer II method. All survival curves were constructed with the *strs* Stata command. The loss in life expectancy can be estimated as the difference between the mean observed survival in patients who underwent AVR and the mean expected survival in the general population. We used flexible parametric models based on relative survival according to the methods proposed by Andersson et al. (14) to estimate the loss in expectation of life. Patients contributed person-time from the date of surgery until the date of death or the end of follow-up (March 24, 2014). In addition to the analysis of the overall population, we also investigated relative survival and loss in expectation of life according to age group, sex, type of surgery, and time period. Data management and statistical analyses were performed using Stata 15.1 (Stata Corp LP, College Station, Texas) and included the use of the *strs* (16) and *stpm2* (17) programs.

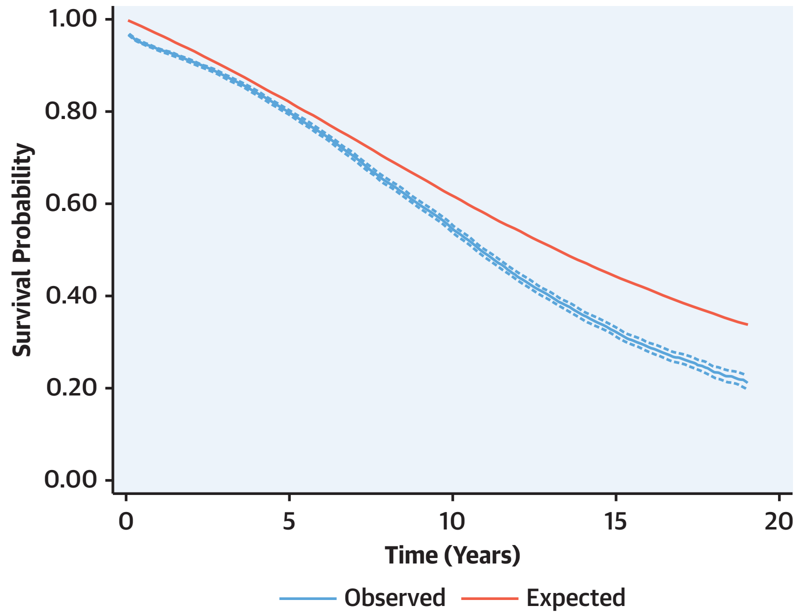
RESULTS

A total of 23,528 patients who underwent primary AVR in Sweden between 1995 and 2013 were included in the study. The baseline characteristics of the patients who underwent AVR are shown in **Table 1**. The mean age was 70.7 years. In the study population, 9,296 (39.5%) were women, 13,727 (58.3%) underwent isolated AVR, and 15,692 (66.7%) received a biological valve prosthesis. The survival rates of these patients were compared with the survival rates of the general population in Sweden matched by age, sex, and year of surgery.

SURVIVAL. During a mean follow-up time of 6.8 years (maximum 19.2 years) and a total follow-up time of 159,394 patient-years, 9,821 (42%) of the patients who underwent AVR died. Of these, 754 (3.2%) died within 30 days after surgery, and 41% died of cardiovascular causes. The 5-, 10-, 15-, and 19-year survival was 80%, 55%, 32%, and 21%, respectively. The survival rates in patients who underwent AVR according to age group, sex, type of surgery, and time period are shown in **Table 2**. The 5-, 10-, 15-, and 19-year expected survival in the comparison group from the general population was 82%, 62%, 44%, and 34%, respectively. The observed and expected survival curves for all patients are shown in **Figure 1**. The observed and expected survival curves for subsets of patients are shown in **Figures 2A and 2B**. The multivariable-adjusted association between patient characteristics and all-cause mortality is shown in Online Table 1.

RELATIVE SURVIVAL. The 5-, 10-, 15-, and 19-year relative survival was 97% (95% confidence interval [CI]: 97% to 98%), 88% (95% CI: 87% to 90%), 73% (95% CI: 71.0% to 75.0%), and 63% (95% CI: 59% to 67%), respectively. In other words, in the hypothetical

FIGURE 1 **Survival After Aortic Valve Replacement**



The observed survival (95% confidence interval) in patients after aortic valve replacement **(blue line)** compared with the expected survival of an age-, sex-, and calendar-year-matched Swedish population **(red line).**

scenario where the only possible cause of death is the one associated with, or due to AVR, the 19-year survival after AVR would be 63% of the expected survival in the general population. Expressed in terms of mortality, at 19 years after AVR, 37% of the patients would have died of causes associated with, or due to, AVR. The clinical interpretation of this hypothetical scenario is that the difference between the relative and the Kaplan-Meier estimated survival at 19 years (63% − 21% = 42%) represents deaths from other causes (e.g., cancer) than those associated with or due to AVR.

LOSS IN LIFE EXPECTANCY. The loss in life expectancy was 1.9 years (95% CI: 1.2 to 2.6 years) for the overall AVR study population. Younger patients had a significantly higher loss in life expectancy compared with older patients: for patients younger than 50 years of age, the loss in life expectancy was 4.4 years (95% CI: 1.5 to 7.2 years), and for patients older than 80 years of age it was 0.4 years (95% CI: 0.3 to 0.5 years). There was no difference in loss in life expectancy between men and women. Also, after stratification for age, there was no difference in loss in life expectancy between patients who received mechanical and biological valve prostheses. The loss in life expectancy was higher in patients operated on earlier compared with the later years of the study period. The loss in life expectancy and the observed and expected survival in the overall study population and in subgroups are shown in Table 3. The loss in life expectancy according to age group and sex is shown in the Central Illustration. All of the analyses were repeated conditional on surviving the first 30 days after AVR; these analyses showed similar results and a similar pattern with a higher loss in life expectancy in younger patients.

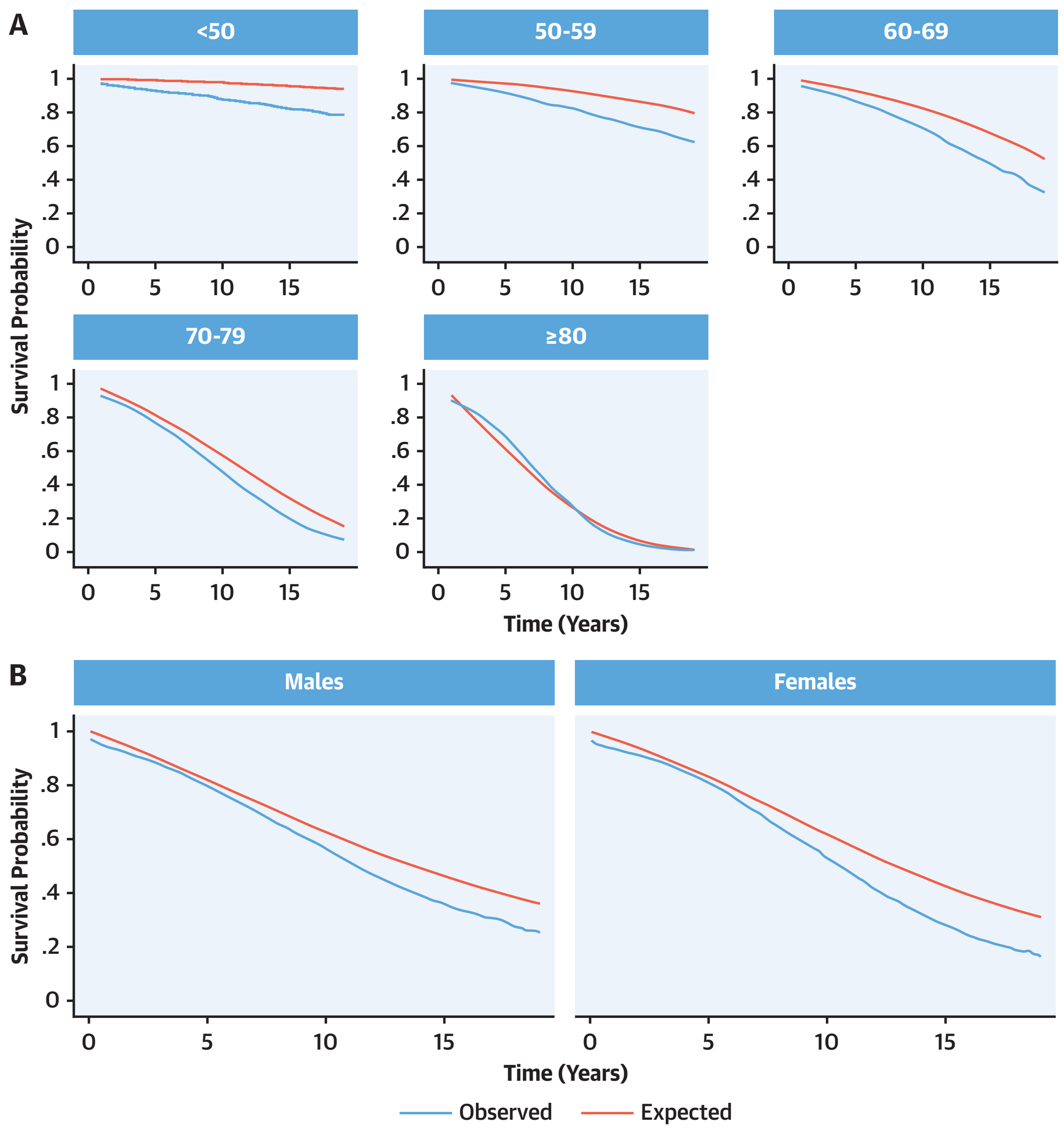
DISCUSSION

Long-term survival in patients who underwent AVR was lower compared with the general population. The estimated loss in life expectancy after AVR was 1.9 years for the overall population and 4.4 years in patients younger than 50 years of age. Younger patients had a significantly increased loss in life expectancy compared with older patients.

Lassnigg et al. (6) analyzed relative and absolute survival in 1,848 patients who underwent AVR at their institution between 1997 and 2008. In 1,709 patients who survived the first year after surgery, they found a survival similar to that of the matched normal population.

We found that survival was lower after AVR than in the general population, and that the difference in survival becomes more pronounced after

FIGURE 2 Survival After Aortic Valve Replacement



The observed survival in patients after aortic valve replacement compared with the expected survival in the general population according to age categories **(A)** and sex **(B).**

approximately 6 years. The differences between the studies can be explained by the large number of patients in our study, and thereby increased precision. Moreover, we included all patients from the date of surgery, not only patients who survived the first year. The patients in the study by Lassnigg et al. (6) were also younger, and they did not exclude patients with emergent surgery, which might have influenced the results. Similar to our study, Lassnigg et al. (6) found that older patients had a survival curve that was close to that of the general population.

Kvidal et al. (5) performed a cohort study including 2.359 patients who underwent primary AVR at their institution between 1980 and 1995. They found excess mortality for patients who underwent AVR compared with an age-, sex-, and calendar period-

TABLE 3 Loss in Expectation of Life and Estimated Observed and Expected Mean Survival Time (Years) by Age Group, Sex, Surgical Procedure, and Time Period in 23,528 Patients Who Underwent Aortic Valve Replacement in Sweden Between 1995 and 2013

	n (%)	Loss in Expectation of Life (95% CI)	Observed Mean Survival (95% CI)	Expected Mean Survival
Overall	23,528 (100.0)	1.9 (1.2-2.6)	13.7 (13.0-14.4)	15.6
Age group, yrs				
<50	1,109 (4.7)	4.4 (1.5-7.2)	37.2 (34.3-40.0)	41.5
50-59	2,278 (9.7)	3.8 (2.3-5.2)	23.8 (22.4-25.2)	27.5
60-69	5,314 (22.6)	2.8 (1.8-3.8)	16.5 (15.5-17.5)	19.3
70-79	10,170 (43.2)	1.5 (1.1-1.9)	10.4 (10.0-10.9)	11.9
≥80	4,657 (19.8)	0.4 (0.3-0.5)	6.9 (6.8-7.0)	7.3
Sex				
Female	9,296 (39.5)	1.8 (1.1-2.5)	12.8 (12.1-13.5)	14.9
Male	14,232 (60.5)	2.1 (1.4-2.8)	14.2 (13.6-14.9)	16.1
Surgery				
Isolated AVR	13,727 (58.3)	2.2 (1.3-3.0)	15.3 (14.5-16.2)	17.5
AVR with concomitant CABG	9,801 (41.7)	1.6 (1.1-2.0)	11.3 (10.9-11.8)	12.9
Valve prosthesis				
Bioprosthesis	15,692 (66.7)	1.3 (0.8-1.8)	11.2 (10.7-11.7)	12.5
Mechanical valve prosthesis	7,836 (33.3)	3.2 (2.2-4.2)	18.6 (17.6-19.6)	21.8
Time period				
1995-2000	7,403 (31.5)	2.8 (2.3-3.3)	13.0 (12.5-13.5)	15.8
2001-2006	7,030 (29.9)	2.0 (1.4-2.7)	13.6 (12.9-14.2)	15.6
2007-2013	9,095 (38.7)	1.1 (0.3-2.0)	14.2 (13.4-15.1)	15.4

CI = confidence interval.

matched general population. However, the early mortality (within 30 days after surgery) was 5.6%, which is substantially higher than the early mortality seen in our study. Even if these patients were excluded in the analysis of long-term mortality, these results suggest possible differences in baseline characteristics. Also, some of the patients included in their study underwent AVR almost 4 decades ago, which limits the generalizability to contemporary patient cohorts. Both the studies by Lassnigg et al. (6) and by Kvidal et al. (5) are limited by being single-center studies and by the relatively small number of patients.

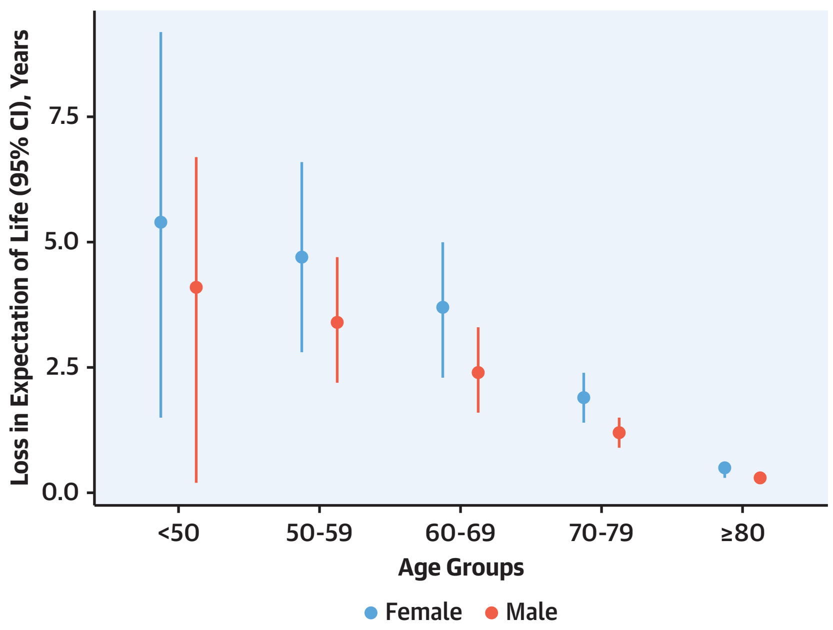
Some previous studies found an excellent prognosis after AVR in elderly patients (18-20). This is in line with our results. A possible explanation for this finding might be that elderly patients accepted for AVR are healthier than the average elderly individual in the general population.

In our study, we found higher loss in life expectancy with decreasing patient age. This pattern has also been seen in other diseases, such as in patients with different cancer diagnoses (21). Bioprostheses are increasingly used in all age groups (13). Therefore, we also analyzed the difference in loss in life expectancy between patients who received mechanical and biological valve prostheses. In the initial analysis, we found that patients who underwent AVR with mechanical valve prostheses had higher loss in life expectancy compared with patients who received bioprostheses. However, after stratification for age, the difference between the 2 types of prostheses was no longer significant. Thus, the initially observed difference in loss in life expectancy between the 2 types of prostheses was merely mirroring the higher loss in life expectancy seen in younger age groups. Additionally, we found a higher survival and a lower loss in life expectancy during the later years of the study period. It is possible that patients with more comorbidities were operated with TAVR instead of surgical AVR, as TAVR was introduced during the last decade. However, before 2014, the majority of patients operated with TAVR were those deemed inoperable. It is also possible that pre-, peri-, and post-operative care has improved with time.

To optimize patient care postoperatively, it is important to understand the cause-specific mortality after AVR with and without concomitant CABG. Our study provides robust numbers on relative survival and loss in life expectancy in a large, nationwide, and contemporary patient cohort with long follow-up. We found a loss in life expectancy of 1.9 years in the overall population and 4.4 years in the youngest age group, which is comparable to findings in patients diagnosed with breast or prostate cancer (21).

There are several explanations for the lower survival after AVR compared with the general

CENTRAL ILLUSTRATION Loss in Life Expectancy After Aortic Valve Replacement



Glaser, N. et al. J Am Coll Cardiol. 2019;74(1):26–33.

The loss in life expectancy (95% confidence interval [CI]) expressed in years according to sex and age categories in 23,528 patients who underwent aortic valve replacement in Sweden between 1995 and 2013.

population: the aortic stenosis itself as well as undergoing open heart surgery and AVR might affect survival. Furthermore, implantation of both biological and mechanical aortic valve prostheses comes with the inevitable risk of short- and long-term complications, such as bleeding, stroke, prosthetic valve endocarditis, and valve degeneration and subsequent reoperation (13,22).

Younger patients have a higher frequency of aortic stenosis imposed on bicuspid aortic valves. This may present a different disease progress compared with acquired calcific changes on a tricuspid aortic valve, which is the most frequent cause of aortic stenosis in older patients. It is possible that the optimal timing for surgical AVR differs between different age groups. Because we did not have information about disease stage or detailed echocardiographic data at time of surgical AVR, further studies are needed to answer this clinically relevant question.

With TAVR being increasingly used as an alternative to surgical AVR, it would also be of interest to know the prognosis after TAVR in relation to the general population. Even though our results cannot be directly extrapolated to TAVR patients, a similar pattern would likely be seen in patients after TAVR.

STUDY STRENGTHS AND LIMITATIONS. The patients who underwent AVR in our study were matched with the general population according to age, sex, and year of surgery. It is possible that other factors, such as comorbidities and socioeconomic status, differed between the AVR-population and the general population, which might have introduced bias to our study. We recognize that other aspects of health following AVR, in addition to survival, are important, such as functional capacity and health-related quality of life. However, these outcome measures were not possible to assess in this study. Particular strengths of this study were the large number of patients and the long and complete follow-up, which was possible because of the high quality national Swedish health-data registers. Also, the population-based design with patient inclusion from all centers providing cardiac surgery in Sweden increased the generalizability of our study.

CONCLUSIONS

We found a shorter life expectancy in patients after AVR with or without concomitant CABG compared with the general population. The estimated loss in life expectancy was substantial and increased with younger age. Our results provide important information to quantify disease burden after AVR in the society, and are relevant for clinicians counseling patients before and after AVR.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Patients who underwent surgical AVR have shorter life expectancy than the general population. The loss in life expectancy increases with younger age at the time of operation.

TRANSLATIONAL OUTLOOK: Additional studies are needed to investigate the reasons for lower life expectancy in patients undergoing AVR and the implications of this observation for the timing of surgery in relation to patient age.

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KEY WORDS aortic valve replacement, cardiac surgery, life expectancy, relative survival

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