Prognosis After Aortic Valve Replacement With a Bioprosthesis : Predictions Based on Meta-Analysis and Microsimulation

J. P. A. Puvimanasinghe, E. W. Steyerberg, J. J. M. Takkenberg, M. J. C. Eijkemans, L. A van Herwerden, A. J. J. C. Bogers and J. D. F. Habbema

Circulation 2001;103;1535-1541
Circulation is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 72514
 Print ISSN: 0009-7322. Online ISSN: 1524-4539

Prognosis After Aortic Valve Replacement With a Bioprosthesis

Predictions Based on Meta-Analysis and Microsimulation

J.P.A. Puvimanasinghe, MBBS, MSc, MD; E.W. Steyerberg, PhD; J.J.M. Takkenberg, MD; M.J.C. Eijkemans, MSc; L.A van Herwerden, MD, PhD; A.J.J.C. Bogers, MD, PhD; J.D.F. Habbema, PhD

Background—Bioprostheses are widely used as an aortic valve substitute, but knowledge about prognosis is still incomplete. The purpose of this study was to provide insight into the age-related life expectancy and actual risks of reoperation and valve-related events of patients after aortic valve replacement with a porcine bioprosthesis.

Methods and Results—We conducted a meta-analysis of 9 selected reports on stented porcine bioprostheses, including 5837 patients with a total follow-up of 31 874 patient-years. The annual rates of valve thrombosis, thromboembolism, hemorrhage, and nonstructural dysfunction were 0.03%, 0.87%, 0.38%, and 0.38%, respectively. The annual rate of endocarditis was estimated at 0.68% for >6 months of implantation and was 5 times as high during the first 6 months. Structural valve deterioration was described with a Weibull model that incorporated lower risks for older patients. These estimates were used to parameterize, calibrate, and validate a mathematical microsimulation model. The model was used to predict life expectancy and actual risks of reoperation and valve-related events after implantation for patients of different ages. For a 65-year-old male, these figures were 11.3 years, 28%, and 47%, respectively.

Conclusions—The combination of meta-analysis with microsimulation enabled a detailed insight into the prognosis after aortic valve replacement with a bioprosthesis for patients of different ages. This information will be useful for patient counseling and clinical decision making. It also could serve as a baseline for the evaluation of newer valve types. **(*Circulation*. 2001;103:1535-1541.)**

Key Words: heart diseases ■ surgery ■ valves ■ meta-analysis ■ prognosis ■ survival

Nearly 40 years after the pioneering efforts of Starr and Edwards in heart valve replacement, a wide variety of mechanical, bioprosthetic, and human tissue prostheses are now available for clinical use. Mechanical valves have a greater durability and consequently lower reoperation rates than other valve types. However, they are associated with a greater risk of thromboembolism, which necessitates regular anticoagulation with the concomitant risk of hemorrhage. In contrast, bioprostheses have a low thrombogeneity, which in most patients obviates the need for regular anticoagulation and consequently reduces hemorrhagic accidents. However, the main factor limiting their use is the propensity to undergo tissue degeneration, often necessitating reoperation. Human tissue valves have a relatively low rate of thromboembolism and endocarditis. However, the long-term incidence of structural valve deterioration (SVD) of these valves is uncertain, and human valves are scarce.[1–3]

With the aging of the general population, the number of elderly patients requiring aortic valve replacement has increased rapidly during recent years. Hence, the choice and long-term performance of a valve prosthesis becomes of paramount importance. Currently, bioprostheses are recommended for elderly patients who do not have risk factors for thromboembolism. These valves may also be used in younger patients presenting with a contraindication to long-term anticoagulation.[3]

Because of the limited life expectancy (LE) of elderly patients, the benefits of avoiding anticoagulation may outweigh the disadvantages of a possible reoperation, ie, the valve will probably outlive the patient. However, in younger patients, reoperations will be frequent, and reoperation-free LE and event-free LE are important considerations in making decisions about implantation.

The purpose of this study was to provide insight into the prognosis of patients of different ages after implantation with a stented porcine bioprosthesis. We incorporated data from various smaller clinical studies in a mathematical microsimulation model.

Received August 11, 2000; revision received November 21, 2000; accepted November 29, 2000.

From the Center for Clinical Decision Sciences, Department of Public Health (J.P.A.P., E.W.S., M.J.C.E., J.D.F.H.), and the Department of Cardio-thoracic Surgery (J.J.M.T., L.A.v.H., A.J.J.C.B.), Erasmus University Medical Center, Rotterdam, The Netherlands.

Correspondence to Dr E.W. Steyerberg, Department of Public Health, Ee2091, Erasmus University Medical Center Rotterdam, PO Box 1738, 3000 DR Rotterdam, Netherlands. E-mail steyerberg@mgz.fgg.eur.nl

Circulation **is available at http://www.circulationaha.org**

Methods

Meta-Analysis

Literature Search

We conducted a literature search of the PubMed and Medline databases for the period January 1990 to December 1999. The terms used for the search were both MeSH terms and the text words "heart valve prostheses," "aortic valve," or "bioprostheses" in combination with "porcine," "stented," "Hancock," "Carpentier-Edwards," or "modified orifice." The search was limited to "human" and to the English language. We then screened the titles and abstracts of the remaining studies to select those that examined the valve-related events, outcomes, or survival of patients after aortic valve replacement with a bioprosthetic valve. Reports that considered stentless and pericardial valves were excluded during this process. The references in the reports were cross-checked for other potentially relevant studies. This resulted in 53 published reports.

We stipulated 5 criteria to obtain a group of similar studies: (1) studies that described 1 or more of the following stented porcine bioprostheses: Carpentier-Edwards standard and Carpentier-Edwards supra-annular valves (Baxter Healthcare Corp) or Hancock standard, Hancock modified orifice, and Hancock II valves (Medtronic Inc); (2) isolated valve implantation in the aortic position; (3) valves $\geq$19 mm in size implanted in patients $>$15 years of age; (4) valve-related events defined according to the standard definitions published in 1988[4] and 1996[5] (valve-related events included valve thrombosis, thromboembolism, hemorrhage, endocarditis, nonstructural dysfunction, and SVD; for this analysis, we only included studies that contained data on at least 1 of these valve-related events); and (5) no duplicate publication or overlapping patient population. When these criteria were used, 44 studies were excluded, leaving 9 studies for the present analysis.[6–14]

Data Extraction and Analysis

We reviewed the 9 reports to obtain the input data required for the microsimulation model. The annual hazards of valve thrombosis, thromboembolism, hemorrhage, and nonstructural dysfunction were assumed to be constant over time. Hence, combined estimates of the linearized occurrence rates for these events were calculated as the ratio of the sums of the number of events and patient-years of follow-up in the individual reports. The combined mortality and reoperation rates after an event were similarly calculated.

Pooling of time-to-event curves was performed for survival, freedom from endocarditis, and SVD. Published curves were scanned and enlarged in a graphical computer package. The heights of these curves were measured at each year, and corresponding survival probabilities were calculated with their complementary log-log transformations. These transformed probabilities were pooled with weighting according to the estimated number of patients at risk at each year and transformed back to obtain a summary curve.[15] Homogeneity of the curves was assessed graphically and judged satisfactory.

The risk of endocarditis was assumed to take 2 phases of constant hazard, with a hazard during the first 6 months greater than the subsequent period. Therefore, we fitted a 2-period exponential model on the pooled freedom-from-endocarditis curve, which was based on 3 reports.[7,10,13]

The risk of SVD depended on the time elapsed since valve replacement and the age of the patient at implantation. This relationship was described by a Weibull model.[16,17] This model is a generalization of the exponential distribution to accommodate a changing risk over time. The shape parameter of the Weibull model was estimated from the average freedom-from-SVD curve, which was pooled from 4 reports.[7,8,12,13] The age effect was incorporated in the scale parameter of the Weibull model, based on 1 study.[12]

Microsimulation Model

Parameters in the Model

We used the estimates from the meta-analysis to parameterize a previously developed microsimulation model (Figure 1).[18] The model incorporates SVD (age dependent), other valve-related events (valve thrombosis, thromboembolism, hemorrhage, endocarditis, and nonstructural dysfunction), and the background mortality of aortic valve recipients (non–valve-related deaths). The simulation model calculates patient survival rates by superimposing the mortality associated with valve-related events on a background mortality. The background mortality may well exceed that of the general population owing to the aortic valve disease as such, cardiomyopathy, and the valve replacement procedure.[19–21] Therefore, hazard ratios were applied to the age-specific survival rates of the Dutch population to calibrate the model outputs with the age-specific survival curves obtained from the literature.[12] Operative mortality was estimated as 1.5% for a 40-year-old man, increasing with odds ratios of 1.022 for age (per year) and 1.7 for every reoperation.[18,21]

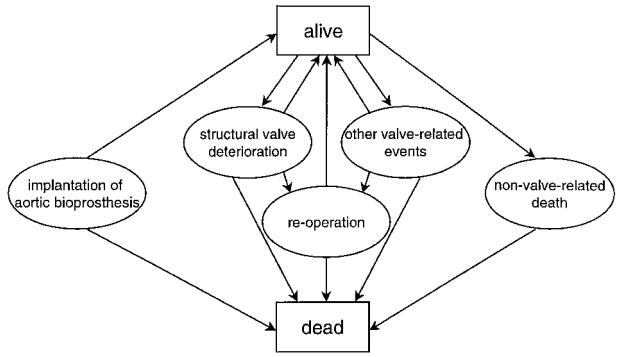


Figure 1. Structure of microsimulation model. After implantation of bioprosthesis, valve-related events can occur, which can lead to reoperation and mortality. Non–valve-related death indicates background mortality.

Evaluation and Validation

Microsimulation is a type of Monte Carlo simulation.[17] For our evaluations, 10 000 virtual life histories were randomly drawn. Age at death and occurrence of events and reoperation were registered for each simulated patient. This enabled us to calculate the LE, event-free LE, and reoperation-free LE, as well as actual risks of valve-related events and reoperation, for a patient of a given age and sex. The model output was validated against the pooled survival curve, as obtained from 3 reports.[8,10,12]

Sensitivity Analyses

We performed 1-way sensitivity analyses to investigate the effect of uncertainty in the parameter estimates. When we varied the estimates of valve-related events according to their 95% CIs, we found only very small variations in event-free LE. We therefore defined larger ranges for the valve-related events, ie, from half to double the baseline parameter values. The mortality hazard ratio was assumed to exceed 1, ie, mortality was at least at the level of the general population.

Results

Literature Search

The 9 selected reports contained data on 5837 bioprosthetic valve recipients with a total follow-up of 31 874 patient-years (Table 1).[6–14] The majority of patients were male, and the mean age of the population was 64.6 years, although differences between the component studies were noted. Most patients were in New York Heart Association class III or IV (on average 71%), and a coronary artery bypass graft was present in approximately one third (on average 36%).

Data Extraction and Analysis

A summary of the meta-analysis is given in Table 2. Adequate data on valve thrombosis were available in only 4

TABLE 1. Characteristics of 9 Studies Selected for Meta-Analysis of Prognosis After Implantation of a Stented Porcine Bioprosthesis in the Aortic Position

Study No. (Reference No.)	Patients, n	Males, n (%)	Mean Age (SD), y	Age Range, y	Follow-Up, pt-years	Preop NYHA Class III and IV, n (%)	CABG, n (%)
1 (12)	1108	546 (49)	74 (8)	24–91	4 735	749 (68)	*
2 (13)	429	309 (72)	64 (12)	≥18	3 000	*	152 (35)
3 (6)	843	490 (58)	69 (*)	16–91	5 093	704 (84)	365 (43)
4 (14)	1594	1124 (71)	60 (15)	16–94	10 212	908 (57)	545 (34)
5 (9)	536	391 (73)	64 (12)	18–86	2 276	393 (73)	213 (40)
6 (15)	165	116 (70)	67 (9)	27–87	551	127 (77)	32 (19)
7 (16)	571	*	59 (*)	15–85	3375	531 (93)	*
8 (17)	196	163 (83)	48 (12)	17–70	1 368	167 (85)	*
9 (8)	395	245 (62)	65	22–84	1 264	*	122 (31)
Total	5837	3384 (64)	64.6	15–94	31 874	3579 (71)	1429 (36)

pt-years indicates patient-years; preop, preoperative; and NYHA, New York Heart Association.
*Data not available.

reports,[7,9,11,13] which yielded 3 events from 9925 patient-years of follow-up. Two of these patients died, giving a death rate of 67% for this rare event. Assuming a constant hazard, a linearized occurrence rate was calculated for each of 4 types of valve complications, of which thromboembolism was the highest with 0.87% per patient-year. The incidence of endocarditis was estimated as 0.68% per patient-year beyond the first 6 months after valve replacement and 3.4% per patient-year before that (ie, 5 times as high).

The average incidence of SVD was estimated by a Weibull model, as shown in Figure 2. The formula for freedom from SVD was $S(t) = e^{-(t/\sigma)^{\wedge}\beta}$, where S(t) indicates the probability of being free from SVD at time t, and σ and β indicate the scale and shape parameters in the Weibull model, respectively. The value of σ depended on age: $\sigma = e^{2.11+0.0112\times age}$, and the value of β was 3.49. With these parameters, the median time until SVD was 17.1 years for a 65-year-old patient.

Model Calibration

The simulation model was calibrated by comparing survival curves produced by the model (for both males and females of varying ages) with empirical survival curves of the corresponding age ranges.[12] Hazard ratios of 8.0, 3.6, 1.5, 1.1, and 1.0 were found adequate for the background mortality in men aged 35, 45, 55, 65, and 75 years, respectively.

Model Validation

An overall impression of the validity of the model was obtained by comparison of expected and observed overall survival. The observed survival was obtained by pooling the curves from 3 reports in which the mean age was 61.5 years.[8,10,12] The expected survival was calculated with the model for male and female patients aged 62 years. These curves closely approximated the pooled survival curve (Figure 3, top).

Age-Specific Results

Survival curves were estimated for men of different ages at implantation of the valve (Figure 3, bottom). The area under each survival curve equals the LE. The LE decreases with advancing age, ie, from 17.1 to 7.2 years for men aged 35 to 75 years. The reoperation-free LE and event-free LE show a remarkable pattern: an increase to age 55 years, followed by a decrease (Figure 4). The increase is caused by the age dependency of the SVD risk (decreasing with age), whereas the eventual decrease is caused by the dominating effect of

TABLE 2. Summary of Meta-Analysis of Prognosis After Implantation of Stented Porcine Bioprosthesis in the Aortic Position

Valve-Related Events	Events, n	LOR (per 100 pt-years)	Outcome		Freedom From Event, %	
			Death Rate	Reop Rate	At 5 Years	At 10 Years
Valve thrombosis	3	0.030	0.67	0.33	99.8	99.7
Thromboembolism	277	0.869	0.19	0	95.7	91.6
Hemorrhage	113	0.382	0.21	0	98.1	96.2
Endocarditis	167	3.4/0.68*	0.34	0.55	96.0‡	92.4‡
NSD	94	0.384	0.05	0.52	98.1	96.2
SVD	352	†	0.10	0.84	99.4‡	85.2‡

LOR indicates linearized occurrence rate (or hazard); pt-years, patient-years; Reop, reoperation; and NSD, nonstructural dysfunction.
*A 2-period exponential model was constructed for risk during and after the first 6 months after implantation.
†A Weibull model was constructed incorporating age dependency.
‡Percentages from summary survival curves.

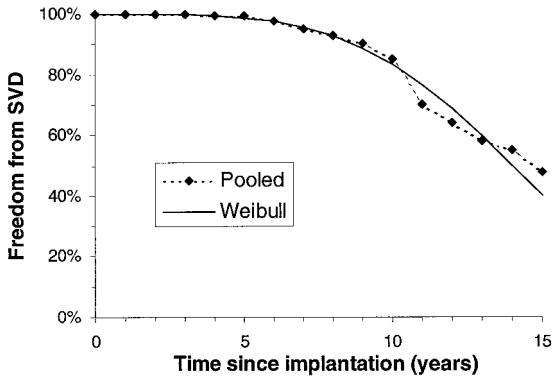


Figure 2. Average freedom from SVD as estimated from literature (pooled) and with Weibull model.

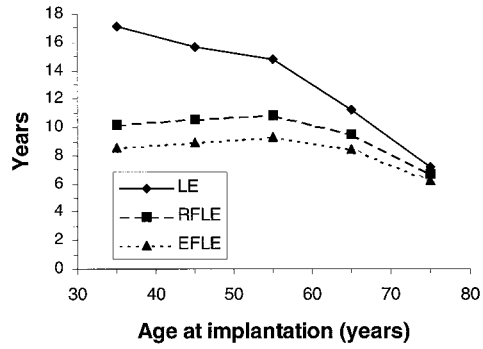
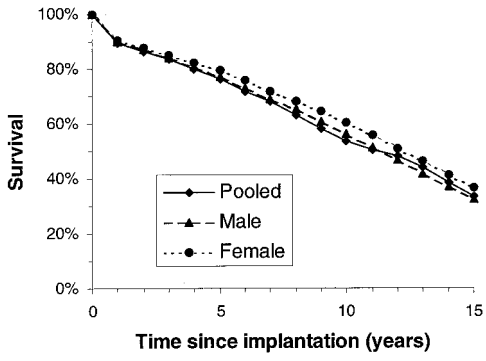


Figure 4. LE, reoperation-free LE (RFLE), and event-free LE (EFLE) for men of different ages.

background mortality at older age. For a 65-year-old man, the LE, reoperation-free LE, and event-free LE were 11.3, 9.5, and 8.4 years, respectively.

We further calculated the actual lifetime risk of a reoperation or a valve-related event after aortic valve replacement. The lower these risks, the better the prognosis. As shown in Figure 5, the probability of ever undergoing a reoperation or experiencing a valve-related event rapidly decreased with age at implantation, from 63% and 83% at 35 years to 11% and 24%, respectively, at 75 years.

Furthermore, we compared the LE of male bioprosthesis recipients with the LE of men in the general Dutch population. The relative LE increased with the age of valve replacement (Figure 6). We also estimated the relative LE of a hypothetical valve recipient, were he immune to valve-related events. The relevant parameters in the model were set to zero. This enabled us to quantify the impact of the increased background mortality. This impact was large for young patients (eg, 46% for 35-year-old men) and decreased to 0% for 75-year-old men, corresponding to the decrease in hazard ratio to 1. The difference between the curves in Figure 6 represents the loss in LE due to the occurrence of valve-related events. This relative difference was ≈12% for all ages. On an absolute scale, the difference decreases with age.



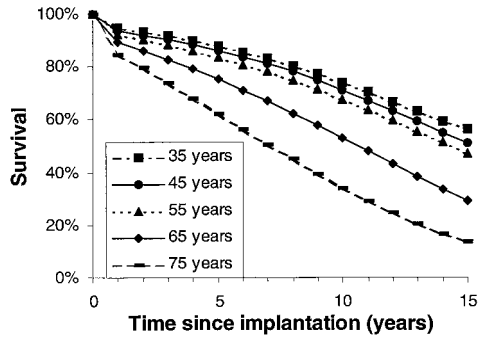


Figure 3. Survival after implantation of stented porcine bioprosthesis. Top, Pooled estimate from literature (pooled) and predicted survival for 62-year-old men and women according to model. Bottom, Predicted survival for men of different ages.

Sensitivity Analyses

The event-free LE of a 65-year-old male patient is shown in Table 3 for extreme values of the valve-related events while other parameters are kept at baseline values. Changes in SVD risk had the largest influence. A doubling of the median failure time would increase the event-free LE by 1.5 years (from 8.4 to 9.9 years) and a halving would reduce the event-free LE by 2.8 years (from 8.4 to 5.6 years). Furthermore, increasing the hazard ratio associated with the background mortality from 1.1 to 1.5 resulted in an event-free LE of 7.6 instead of 8.4 years.

Discussion

We used a meta-analysis of empirical data and a mathematical microsimulation model to predict the LE and actual

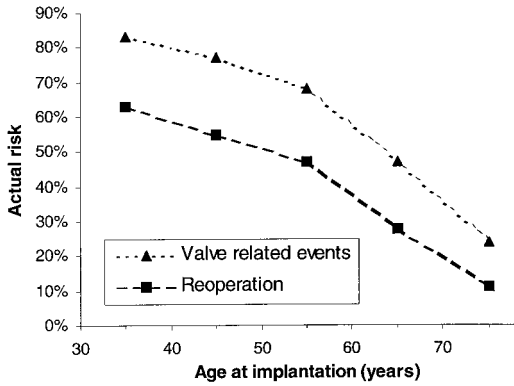


Figure 5. Actual risks of reoperation and of valve-related events for men of different ages.

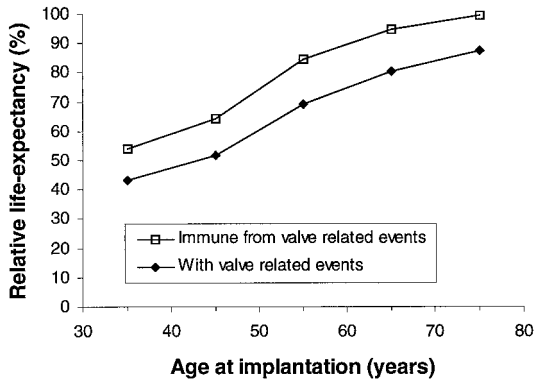


Figure 6. LE of men with aortic valve disease relative to that of men in the general population for different ages.

lifetime risk of reoperation and valve-related events for patients after implantation with a stented porcine bioprosthesis. The microsimulation model generates the life histories of a large number of virtual patients. Compared with standard statistical methods, the added value of modeling is that it provides detailed insights into the occurrence of valve-related and non–valve-related events. For a 65-year-old man, for example, the model predicted an LE of 11.3 years and a lifetime risk of reoperation and a valve-related event of 28% and 47%, respectively, after implantation with a bioprosthesis. Such information will be useful for patient counseling and for the surgeon and patient in making decisions. We envision being able to present a user-friendly version of the model on the Internet in the near future that could serve as a bedside tool to the surgeon. The model results may also serve as a baseline for the evaluation of newer valve types.

We chose 5 types of stented porcine bioprostheses, both first and second generation, which were not markedly different from one another. The Hancock standard prosthesis and the Carpentier-Edwards standard prosthesis, 2 of the initial stented porcine valves, were introduced in the early 1970s.[2,22] The composite Hancock modified orifice prosthesis was designed to improve hemodynamic performance by substituting the septal leaflet with a nonseptal leaflet from a second porcine valve.[6,23] In contrast to the above, the second-generation Carpentier-Edwards supra-annular bioprosthesis and the Hancock II bioprosthesis were introduced in the 1980s and incorporated several considered improvements, including a supra-annular configuration, to maximize the effective orifice of the prosthesis.[7,8]

Similarities in the performance of these valve types have been documented in the literature. A randomized prospective comparison of the Hancock standard and the Carpentier-Edwards standard valves showed no clear difference in durability or other valve-related complications after 10 years.[22] Also, no important differences were found in durability or other valve-related complications between the Hancock modified orifice valve and the 2 standard valve types.[23] The second-generation porcine bioprostheses (Carpentier-Edwards supra-annular, Hancock II) were designed to improve clinical performance by reducing the incidence of SVD. However, Jamieson and others[24] failed to demonstrate clinically relevant differences with regard to freedom from SVD between the Carpentier-Edwards standard and Carpentier-Edwards supra-annular valves, except for the 21- to 40-year-old age group. The risk of valve-related complications with the Hancock II prosthesis has been reported to be similar to the previously mentioned valve types.[25,26] However, the limited improvement in durability of the second-generation valves could be related to enhanced surveillance and early intervention.

Ideally, for the application of simulation methodology, a sufficiently comprehensive "super data set" should be analyzed.[19] Such a data set should contain detailed information on patients who underwent aortic valve replacement, have complete and long-term follow-up for all patients, and consider all relevant valve-related events. However, no such databases are available as yet, although reports on larger series with long-term follow-up have become more frequent.[27,28] We pooled the results of selected reports that satisfied strict criteria and calculated quantitative estimates for the parameters of interest (Table 2). An advantage of pooling was that the estimates represented the experience of many institutions with possibly slightly varying patient populations. Single-center results may be less generalizable because of typical patient populations and unique surgical practices.

TABLE 3. Summary of Sensitivity Analyses

		Plausible Range†		Event-Free LE, y	
Parameter	Baseline Estimate*	Favorable	Unfavorable	Favorable	Unfavorable
Valve thrombosis	0.030	0.015	0.06	8.45	8.43
Thromboembolism	0.869	0.43	1.74	8.67	8.02
Hemorrhage	0.382	0.19	0.76	8.54	8.24
Endocarditis	0.680	0.34	1.36	8.66	8.05
NSD	0.384	0.19	0.77	8.53	8.25
SVD	17.1‡	34.2‡	8.5‡	9.89	5.57
Hazard ratio	1.1	1	1.5	8.66	7.66

NSD indicates nonstructural dysfunction.

*The event-free LE was 8.44 years in the baseline analysis.

†The plausible range was defined by a halving or doubling of the baseline estimate.

‡Median time until SVD according to the Weibull model.

Standard actuarial statistical techniques (eg, Kaplan-Meier) have been used in many studies to assess the survival of patients and the performance of valve prostheses, while "actual" analysis has recently gained interest.[29] For survival, the actuarial and actual methods provide identical estimates. However, when the actuarial method is applied to nonfatal complications, such as SVD, the risk described is that which patients would experience provided they were immortal. Patients with valve disease have relatively high annual risks of death. Hence, a more relevant estimate of valve failure is the actual percentage of patients who will experience an event before they die.[27,29,30] The simulation model provides estimates of the actual risk of reoperation and of valve-related events according to age (Figure 5). This information is more meaningful than actuarial risks or actual risks for "average" patients. The estimates by Grunkemeier and colleagues[29] for the actual risk of ever experiencing an SVD (20% for the age group 70 to 73 years and 40% for the 59- to 63-year-old age group) were rather similar to our model estimates (18% for 71-year-old and 42% for 61-year-old males, respectively).

The microsimulation model calculates patient survival rates by superimposing the mortality associated with valve-related events on a background mortality rate. The background mortality is the non–valve-related mortality of the valve recipients. It was previously assumed that in the absence of morbid valve events, patients would follow the trajectory of the general population.[18] This assumption may not be tenable, because valve disease, cardiomyopathy, and the valve replacement procedure per se may cause higher non–valve-related mortality than noted in the general population.[19–21] By applying age-specific hazard ratios to the age-specific survival curves of the general population, we aimed to obtain a more accurate prediction of patient prognosis. For young patients, the increase in background mortality was substantial compared with the general population (eg, a 36% lower LE for a 45-year-old man).

Limitations of our microsimulation model included that certain structural assumptions had to be made. For example, a constant hazard was assumed for valve thrombosis, thromboembolism, hemorrhage, and nonstructural dysfunction, where in fact, these hazards may be time and age dependent. Furthermore, endocarditis risk was assumed to be piecewise constant before and after 6 months of follow-up, and SVD risk was described with a Weibull model. Additional studies need to address these assumptions. Furthermore, survival after aortic valve replacement will not only depend on age and sex but also on many risk factors, including preoperative New York Heart Association class and the presence of coronary heart disease.

In addition to structural assumptions, uncertainty existed in parameter values owing to small or moderate numbers of events. The time to SVD was the most important factor for event-free LE. This is of interest in assessing the value of newer bioprostheses, eg, stentless types.[31,32] When more data become available on such valves, these can easily be included in our model to quantify the impact on patient prognosis. Furthermore, a change in background mortality resulted in a marked variation in the LE. This illustrates the need for incorporation of more detailed information on the clinical characteristics of the patients into the model. Also, updating of the model with the growing experience with bioprostheses is essential to provide valid estimates of prognosis in the future.

Acknowledgment

This study was supported in part by grant 99141 from the Dutch Board of Health Care Insurance.

References

1. Akins CW, Buckley MJ, Daggett WM, et al. Risk of reoperative valve replacement for failed mitral and aortic bioprostheses. *Ann Thorac Surg*. 1998;65:1545–1551.
2. Jamieson WR, Munro AI, Miyagishima RT, et al. Carpentier-Edwards standard porcine bioprosthesis: clinical performance to seventeen years. *Ann Thorac Surg*. 1995;60:999–1006.
3. Bonow RO, Carabello B, de Leon AC, et al. ACC/AHA guidelines for the management of patients with valvular heart disease: executive summary. *J Heart Valve Dis*. 1998;7:672–707.
4. Edmunds LH Jr, Cohn LH, Weisel RD. Guidelines for reporting morbidity and mortality after cardiac valvular operations. *J Thorac Cardiovasc Surg*. 1988;96:351–353.
5. Edmunds LH Jr, Clark RE, Cohn LH, et al. Guidelines for reporting morbidity and mortality after cardiac valvular operations. *Ann Thorac Surg*. 1996;62:932–935.
6. Cohn LH, Collins JJ Jr, Rizzo RJ, et al. Twenty-year follow-up of the Hancock modified orifice porcine aortic valve. *Ann Thorac Surg*. 1998; 66:S30–S34.
7. Wilson ES, Jamieson MP. Carpentier-Edwards supra-annular bioprosthesis in the aortic position: has altered design affected performance? *J Heart Valve Dis*. 1996;5:40–44.
8. David TE, Armstrong S, Sun Z. The Hancock II bioprosthesis at ten years. *Ann Thorac Surg*. 1995;60:S229–S234.
9. Logeais Y, Langanay T, Leguerrier A, et al. Aortic Carpentier-Edwards supraannular porcine bioprosthesis: a 12-year experience. *Ann Thorac Surg*. 1999;68:421–425.
10. Peterseim DS, Cen YY, Cheruvu S, et al. Long-term outcome after biologic versus mechanical aortic valve replacement in 841 patients. *J Thorac Cardiovasc Surg*. 1999;117:890–897.
11. Hurle A, Meseguer J, Llamas P, et al. Clinical experience with the Carpentier-Edwards supra-annular porcine bioprosthesis implanted in the aortic position. *J Heart Valve Dis*. 1998;7:331–335.
12. Fann JI, Miller DC, Moore KA, et al. Twenty-year clinical experience with porcine bioprostheses. *Ann Thorac Surg*. 1996;62:1301–1311.
13. Jamieson WR, Allen P, Miyagishima RT, et al. The Carpentier-Edwards standard porcine bioprosthesis: a first- generation tissue valve with excellent long-term clinical performance. *J Thorac Cardiovasc Surg*. 1990;99:543–561.
14. Bortolotti U, Milano A, Mazzucco A, et al. Extended follow-up of the standard Hancock porcine bioprosthesis. *J Card Surg*. 1991;6:544–549.
15. Earle CC, Pham B, Wells GA. An assessment of methods to combine published survival curves. *Med Decis Making*. 2000;20:104–111.
16. Thomam DR, Bain LJ, Antle CE. Inferences on the parameters of the Weibull distribution. *Technometrics*. 1969;11:445–460.
17. Law AM, Kelton WD. *Simulation Modeling and Analysis*. New York, NY: McGraw-Hill; 1991. McGraw-Hill Series in Industrial Engineering and Management Science.
18. de Kruyk AR, van der Meulen JH, van Herwerden LA, et al. Use of Markov series and Monte Carlo simulation in predicting replacement valve performances. *J Heart Valve Dis*. 1998;7:4–12.
19. Blackstone EH. The choice of a prosthetic heart valve: how shall patient-specific recommendations be made? *J Heart Valve Dis*. 1998;7:1–3.
20. Sand ME, Naftel DC, Blackstone EH, et al. A comparison of repair and replacement for mitral valve incompetence. *J Thorac Cardiovasc Surg*. 1987;94:208–219.
21. Steyerberg EW, Kallewaard M, van der Graaf Y, et al. Decision analyses for prophylactic replacement of the Bjork-Shiley convexo-concave heart valve: an evaluation of assumptions and estimates. *Med Decis Making*. 2000;20:20–32.
22. Sarris GE, Robbins RC, Miller DC, et al. Randomized, prospective assessment of bioprosthetic valve durability: Hancock versus Carpentier-Edwards valves. *Circulation*. 1993;88(suppl II):II-55–II-64.

23. Yun KL, Miller DC, Moore KA, et al. Durability of the Hancock MO bioprosthesis compared with standard aortic valve bioprostheses. *Ann Thorac Surg*. 1995;60:S221–S228.
24. Jamieson WR, Burr LH, Tyers GF, et al. Carpentier-Edwards standard and supra-annular porcine bioprostheses: 10 year comparison of structural valve deterioration. *J Heart Valve Dis*. 1994;3:59–65.
25. David TE, Armstrong S, Sun Z. The Hancock II bioprosthesis at 12 years. *Ann Thorac Surg*. 1998;66:S95–S98.
26. Legarra JJ, Llorens R, Catalan M, et al. Eighteen-year follow up after Hancock II bioprosthesis insertion. *J Heart Valve Dis*. 1999;8:16–24.
27. Grunkemeier GL, Li HH, Starr A. Heart valve replacement: a statistical review of 35 years' results. *J Heart Valve Dis*. 1999;8:466–470.
28. Hokken RB, Steyerberg EW, Verbaan N, et al. 25 years of aortic valve replacement using mechanical valves: risk factors for early and late mortality. *Eur Heart J*. 1997;18:1157–1165.
29. Grunkemeier GL, Jamieson WR, Miller DC, et al. Actuarial versus actual risk of porcine structural valve deterioration. *J Thorac Cardiovasc Surg*. 1994;108:709–718.
30. Mahoney CB, Miller DC, Khan SS, et al. Twenty-year, three-institution evaluation of the Hancock Modified Orifice aortic valve durability: comparison of actual and actuarial estimates. *Circulation*. 1998;98(suppl II):II-88–II-93.
31. Goldman B, Christakis G, David T, et al. Will stentless valves be durable? The Toronto valve (TSPV) at 5 to 6 years. *Semin Thorac Cardiovasc Surg*. 1999;11:42–49.
32. Melina G, Rubens MB, Birks EJ, et al. A quantitative study of calcium deposition in the aortic wall following Medtronic Freestyle compared with homograft aortic root replacement: a prospective randomized trial. *J Heart Valve Dis*. 2000;9:97–103.