The St. Jude Medical Cardiac Valve Prosthesis:

A 25-Year Experience with Single Valve Replacement

Running title: St. Jude Medical Valve 25-Year Experience

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Abstract

BACKGROUND: From 10/77 – 10/02, 4480 patients (range 17-94 years, average 64 ± 13) underwent single valve replacement with the St. Jude Medical (SJM) heart valve. Of 2982 aortic (AVR) and 1498 mitral valve replacements (MVR), concomitant coronary bypass was performed on 42% and 33% respectively.

METHODS: Cardiac Surgical Associates has maintained an independent database of patients having valve replacement with the SJM prosthesis since the world's first implant. Patients were contacted by questionnaire and/or phone from 11/02 through 6/03. Hospital course and valve-related events were verified by patient chart review and/or physician contact.

RESULTS: Follow-up was 95% complete. Operative mortality was 4% AVR and 9% MVR. Total follow-up was 32,190 patient years (range 1 month to 24.8 years, average 7 ± 5 years). Over the study period, patient freedom from late mortality was 61% (AVR 61%, MVR 63%), and from valve-related mortality 92% (AVR 93%, MVR 91%). Freedom from thromboembolic events was: 85% (86% AVR, 81% MVR), from bleeding events: 81% (81% AVR, 81% MVR), from reoperation: 98% (99% AVR and 97% MVR), from endocarditis: 98% (99% AVR and 98% MVR), and from valve thrombosis: 99% (99% AVR and 98% MVR). There was 1 MVR structural failure (.06%).

CONCLUSION: The SJM valve has proven to be an effective and durable valve prosthesis with a low event rate over the long term.

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Introduction

On October 3, 1977, the first St. Jude Medical (SJM) Valve was implanted by Dr. Demetre M. Nicoloff. This prosthesis represented a significant advance in clinically available mechanical valve prostheses. In vitro and in vivo data indicated excellent hemodynamics, resistance to wear, and flow patterns predictive of a low incidence of valve related events (VRE) [1, 2]. Two long-term reports have demonstrated continued attributes [3, 4] of this prosthesis recording over 1,300,000 implants. Of the more than 70 mechanical valves that have been introduced clinically, the SJM has been the most successful [5].

To continue documentation of the results over the long term, this report represents an analysis of patient outcomes after single valve implantation with the SJM prosthesis in the aortic (AVR) and the mitral (MVR) position over a 25-year experience.

During this time three models of the SJM valve have been utilized in the aortic position and the single model of the mitral has remained unchanged since introduction. The aortic valve modifications include a change in the sewing ring from the original design *renamed* the SJM HP where the bulk of the sewing ring was reduced. A larger effective orifice area by approximately one size could be implanted.

The latest modification, the Regent® valve, involved a change of the valve housing in which a half millimeter was removed in order to allow implantation of an even larger device, approximately 1½ sizes larger than the original design, resulting in excellent hemodynamics [6].

Methods

Pertinent demographic data on patients over 17 years of age having SJM valve implantation by Cardiac Surgical Associates surgeons were maintained in an independent database in Cardiac Surgical Associates Research Foundation (CSRF). This database has been continuously updated from the first implant in October 1977 through October 2002 for all patients having valve implantation with the SJM valve and interim reports issued [7-12].

Clinical charts were reviewed to assure postoperative events and complications through the original operative period were captured. To assure that the SJM valve itself was evaluated, patients maintained in our database that had other model valves in addition to the SJM prosthesis, and all patients with composite graft replacements were eliminated from this study. The primary objective was to document patient survival and valve related events in up to a 25-year experience.

Follow up was conducted by questionnaire and telephone contact with the patient, and if warranted or valve related complications occurred, the primary physician and/or the patient's hospital records were accessed. Due to the extended time frame of the study to assure that all events were captured, clinical study documents obtained in prior studies were crosschecked [10, 12]. Causes of patient deaths were determined from hospital records and government authorized death certification. All sudden or unknown causes of death were considered valve-related [13].

Operative data was entered into a database upgraded from the STS model to meet CSRF requirements. For consistency with earlier recorded VREs, data was collected in accordance with standards subscribed by Edmunds et al. [13] and the FDA document: *Replacement of Heart Valve Guidance, 1996* [16].

The surgical techniques were consistent over the 25 years of this study and have been previously reported [8] with only changes in individual techniques of myocardial preservation.

Anticoagulation

Chronic Coumadin anticoagulation has been recommended in all patients with the exception of some pediatric patients who are not included in the current review [14]. In the first 15 years of this study, prothrombin time was used to monitor anticoagulation (target range equals 1½ times control), between years 15 and 20 a transition from prothrombin time to international normalized ratio (INR), and in the last 5 years INR has been recommended exclusively for anticoagulation follow up. The target INR is 1.8 to 2.5 for AVR, 2.0 to 3.0 for MVR, and if atrial fibrillation is present the target INR is 2.5 to 3.5. Low dose aspirin was also added in the latter portion of the study [15].

Statistical Analysis

Continuous variables were reported as mean plus or minus standard deviation. Actuarial rates were calculated using nonparametric actuarial Kaplan-Meier calculations. Linearized event rates were expressed in percentage per patient year (%/pt-yr). This analyses as well as statistical parameters were contracted independently outside of CSRF. Actuarial analysis offer a different estimate of the non-fatal endpoints, therefore "actual" curves are included in the graphs for most common VREs (reoperation, anticoagulation related hemorrhage and thromboembolism) to be consistent with other reports [4, 17]. In graphic representations, the number of patients at risk for each time interval is shown at the base of the graph.

Results

From October 3, 1977 through October 3, 2002, 6,470 SJM prostheses were implanted; of these, 2 were triple valve replacement, 343 were double valve replacement, 3 were pulmonary valve replacement, and 10 were tricuspid valve replacement. These patients were eliminated. Due to the additional exclusion criteria mentioned previously this study includes 4,480 patients with a total of 4,508 valves.

The patient population consists of 2,982 single aortic (AVR) and 1,498 mitral (MVR) valve replacements; of these 28 had repeat single AVR or MVR. Distribution of valve type and size is shown in Table 1. The mean age was 64 ± 13 years (range 17-94 years) and the mean follow-up was 7 ± 5 years. The longest patient follow up was 24.8 years and the oldest patient, 102 years of age, had the SJM valve for nearly 8 years. Follow up was 95 % complete and the total follow up was 32,190 patient years. Patient demographics and operative procedures are shown in Table 2.

Patient Survival

The total operative mortality was 6% (n=256) and 19 of these (7.4% of deaths; 0.4% of patient population) were determined valve related deaths. Over the 25-year follow up, an additional 1,650 (37%) patients died and of these 341 (21% of deaths, 7.6% of patient population) were valve related. Valve related causes of mortality are shown in Table 3. Actuarial freedom from death and from valve related death for AVR and MVR are shown in Figures 1 and 2 respectively.

Valve Related Events (VRE)

Valve related events are discussed in the following subsections. The data for 5-year time frames including cumulative incidence and 95% confidence limits are shown in Table 4 and 5 for aortic and mitral valves respectively. Note that confidence limits are not shown in the graphic representatives as the incidence over time was low enough not to be clearly visible.

Reoperation

Over 25 years, 71 (1.6%) patients required reoperative replacement or repair of their SJM valve. Causes included: valve thrombosis (incidence =0.2% AVR; incidence = 0.5% MVR), prosthetic valve

endocarditis (incidence = 0.4% AVR; incidence = 0.2% MVR), paravalvular leak (incidence = 0.4% AVR, incidence = 1.0% MVR), and entrapment/pannus formation (incidence = 0.1% AVR, incidence = 0% MVR). The cause of one reoperation is unknown. There was one structural failure early in our experience due to embolization of one leaflet. Patient mortality for reoperation was 10%. The cumulative freedom from reoperation at 10 and 20 years from AVR was 98 ± 0.15% and 97 ± 0.35% and for MVR was 97 ± 0.25% and 96 ± 0.5%. Freedom from reoperation is shown in Figure 3.

Anticoagulant Related Hemorrhage (ARH)

Anticoagulant related hemorrhage was the most common event, occurring in 589 AVR and 285 MVR. In patients having AVR, 4% (n=122) had a major bleeding event prior to hospital discharge and 16% (n=467) in subsequent follow-up. Mortality related to bleeding events was 2.5% (n=3) and 13.0% (n=60) of patient deaths respectively. In the MVR group, 5% (n=74) had events prior to discharge and 16% (n=211) in follow up. Mortality related to these events was 1.4% (n=1) and 9.8% (n=20) of patient deaths respectively. The overall incidence of events was 2.7%/pt. year for AVR and 2.7%/pt. year for MVR. Freedom from ARH is shown in Figure 4.

Thromboembolic Events (TE)

A total of 421 TE events occurred in the AVR and 293 events in the MVR group. AVR pre-discharge TIA occurred in 42, permanent strokes in 42 and peripheral events in 15, a total of 3% of patients. Post discharge 153 TIAs, 139 permanent strokes and 30 peripheral events occurred in the follow-up period for a total of 11% incidence. Mortality related to these events (n=421) was 0.7% (n=3) early and 14 % (n=58) late. The incidence of TE post AVR was 1.9 %/pt.year.

With MVR, 23 patients had TIA, 30 permanent stroke and 9 peripheral events pre-discharge. Post-discharge 116 TIAs, 92 permanent strokes and 23 peripheral events occurred (15% incidence). Mortality related to these events (n=293) was 0.7% (n=2) early and 15% (n=43) late. The incidence of TE post MVR was 2.8% per/pt year. Freedom from TE over the 25-year follow-up period is shown in Figure 6.

Prosthetic Valve Endocarditis (PVE)

A total of 71 patients had PVE events. Eleven of these were in the operative period (5 AVR: 0.2% and 6 MVR: 0.4%). Post-discharge 60 cases of PVE developed, 39 AVR (1%) and 21 MVR (2%). Fifteen of these patients required reoperation. Overall mortality related to PVE was 0.5%. The overall incidence of PVE was 0.2%/pt year for AVR and 0.3%/pt year for MVR.

Valve Thrombosis

Thrombosis of the prosthetic valve occurred in 34 patients, 15 AVR (0.5%) and 19 MVR (2.0%). Reoperation was reported in 13 patients. The incidence of valve thrombosis is 0.06%/pt year AVR and 0.18%/pt year MVR. Patient mortality related to valve thrombosis was 0.07% AVR and 0.3% MVR.

Structural Failure

One patient had early structural failure. Embolization of one leaflet was due to a manufacturing flaw, not to prosthetic material wear. Reoperation was required. Overall freedom from structural failure was 100% AVR and 99.9% MVR.

Comment

This retrospective study represents the longest, largest and most complete report on a bileaflet prosthetic valve. Grunkemeier et al. reported on a 35-year experience with aortic and mitral replacement, however, multiple valve models were reported. As opposed to their results, over the current study period, AVR mortality remained consistent in spite of a prospectively older patient population while MVR mortality decreased likely related to change in replacement techniques (preservation of the posterior leaflet chord) and improved myocardial protection [18].

Excellent hemodynamic performance was the initial benefits of the SJM valve compared to the other clinically available mechanical valve prostheses. There were still, however, hemodynamic gradients in the smaller sizes [19, 20]. This led to the change in the sewing ring configuration (SJM HP) and ultimately to the valve housing itself (SJM Regent®) further improving hemodynamics and becoming the first mechanical valve to demonstrate improved LV mass regression [6].

Due to the long time frame, enough stress cannot be placed on the efforts made to capture VREs. All living patients who reported events were further contacted. Hospital records of deceased and living patients were reviewed and their primary attending physicians contacted. Official causes of death were ascertained from hospital record or by contact with the county or state clerk of records in ten states. Only 44/1906 patient deaths (7%) did not have a cause of death identified. The role of valve related mortality which is quite low over the long time frame is overstated, as sudden unexplained patient death was the most common cause of valve related mortality. In this study 28% of patients followed up were over 80 years of age. This cohort of patients had their prosthetic valve for 5±3 years. As in other studies, the long-term patient mortality in this series is due much more commonly to patient related factors than the presence of a prosthetic valve [4, 21].

The need for reoperation due to structural valve failure was nearly non-existent (1/4480). There were no valve failures due to prosthetic material wear. Reoperation for other reasons was also rare encompassing 1.9% of the entire study.

Patients having valve replacement surgery do not survive in parallel to the normal population [4]. This has been attributed to patient related factors rather than the prostheses itself. The longevity of the prostheses is its most notable component.

Chronic anticoagulation remains the major cause of VREs in patients with mechanical prostheses. Butchart et al. [22] suggested that patient related factors may be more important than the presence of a prosthetic valve per se. We concur. In young patients with limited risk factors, it was demonstrated that VRE events were exceedingly low [23]. With this information, we have revised our recommendations for target INR based on patient risk, comparable to that of Butchart et al. [22]

Consistent management of INR minimizes VRE over the long term. Koertke et al. recently reported that early INR home-management enables patients to lower target anticoagulation levels [24]. Home monitoring was not utilized on our patients. Patients are at greatest risk for events the more time spent out of the target INR range [25]. Horstkotte et al. noted that VREs occurred during fluctuation in anticoagulant levels later reflected in the findings of Koertke [24, 26]. Unfortunately, we were unable to verify this as anticoagulant levels were not available at the actual time of events in the majority of patients.

Consistent with Ikonomidis et al., we found ARH most commonly occurred early with nearly half of all events occurring in the first year (Figure 4). We agree with recommendations to slowly bring the patient to therapeutic anticoagulant range in the early post-operative period as the risk of ARH is greater than TE. After five years there were very few bleeding events in the AVR population while in the MVR population

ARH occurs on a more consistent basis (Figure 5). This is likely related to the higher recommended target INR. The INR is a more precise measurement of anticoagulation than the less reliable prothrombin time. Importantly, alternative thrombin inhibitors are being researched, and their application will change the landscape for mechanical valve therapy [27].

Thromboembolism, on the other hand, appears to occur more commonly after the operative period and remains a continued risk throughout the patient's life. This is somewhat counter-intuitive as one would expect increased TE risk early in the face of a new implanted valve sewing ring. As patients age, risk factors for TE increase and the patients may be at risk to have an increasing number of events [22]. While TE events between AVR and MVR groups are equal for the first 10 years, the incidence separates at 10 years, likely due to the increased incidence of atrial fibrillation in MVR patients (Figure 6). The TE rates of biologic valves without anticoagulation are equivalent to those of mechanical prostheses on anticoagulants, underlining the importance of patient risk factors [3]. The TE rate reported is similar to Khan et al and Ikonomides et al [3, 4].

Analogous to the recent experience of Ikonomidis et al. [4], our use of biologic prostheses has increased due to the greater number of elderly patients and the increased life expectancy of modern biologic valves. Yet in making this decision, one has to take into account that reoperation is not without risk, 10% mortality in this study, while the re-reoperative mortality rate is even higher. Up to one-third of patients with biologic valves are placed on chronic anticoagulation over the long term, negating the advantage [28]. As the incidence of ARH does not differ between patients over or under 65 years of age, in and of itself, is not a contraindication to mechanical valve replacement [29, 30, 31]. Mechanical valves are optimal for patients who already require chronic anticoagulation and those at risk for future anticoagulant therapy. The need for chronic anticoagulation can be predicted by using a table of patient risk factors and should be considered in discussions with patients [22]. Patients are living longer after valve replacement due to the availability of more reliable prosthetic valves, and more accurate anticoagulant management.

This likely accounts for the fact that over one-quarter of our follow-up patients were over 80 years, most having valve replacement prior to age 75.

Current recommendations to our patients include the use of a mechanical valve in the aortic position if the patient is less than 70 years of age, and in the mitral if less than 75. In the more elderly and those that are already taking or are at high risk for being placed on anticoagulation, a mechanical valve is recommended. Because there is risk of bioprosthetic valve loss as early as 6 to 8 years post implant, mean time to biologic re-replacement may be short. Thus, we recommend mechanical valve replacement for reoperative patients, regardless of the reason for reoperation [3, 28].

Finally, mention should be made regarding the Silzone® sewing ring. Forty-three patients had AVR with this modified sewing ring and 17 in the MVR group. There were no reoperations for PVE or for perivalvular leak. This differs from the multicenter AVERT trial [32]. The number is small, but may reflect our group's effort at extensive annular decalcification at the time of surgery and the use of closely placed pledgeted mattress sutures.

In summary, this extensive experience demonstrates excellent function of the SJM valve in the mitral or aortic position. Valve related events were low, most commonly due to patient related factors as opposed to the presence of a prosthetic valve. Valve related mortality was low and there have been no reoperations due to valve wear. The SJM valve can be recommended to patients as a prosthesis that will last their life time.

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Doctor Joyce has nothing to disclose.

Doctor Nicoloff has nothing to disclose.

Christopher C. Krogh has nothing to disclose.

Ann M. Emery has nothing to disclose.

Kathy Benyo-Albrecht has nothing to disclose

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FIGURE LEGENDS

Figure 1 Freedom from late morality in patients having valve replacement with the SJM valve prosthesis over 25 years.

Figure 2 Freedom from valve-related morality in patients having valve replacement with the SJM valve prosthesis over 25 years.

Figure 3 Freedom from reoperation in patients having valve replacement with the SJM valve prosthesis over 25 years.

Figure 4 Freedom from anticoagulant related hemorrhage in patients having valve replacement with the SJM valve prosthesis over 25 years.

Figure 5 Freedom from thromboembolism in patients having valve replacement with the SJM valve prosthesis over 25 years.

APPENDIX – Abbreviations used

ARH	Anticoagulation related hemorrhage
AVR	Aortic valve replacement
CSRF	Cardiac Surgical Research Foundation
INR	Interventional normalization ratio
MVR	Mitral valve replacement
PVE	Prosthetic valve endocarditis
TE	Thromboembolism
TIA	Transient ischemic attack
SJM	St. Jude Medical
SJM HP	St. Jude Medical high performance
VRE	Valve related events

Table 1 *Distribution of valve types implanted for patients having aortic or mitral valve replacement with the St. Jude Medical cardiac valve prosthesis over 25 years.*

Valve size (mm)	Aortic			Mitral
	Standard	HP	Regent	Standard
17	0	15	0	0
19	129	140	3	0
21	395	303	9	2
23	645	182	11	7
25	678	92	8	76
26	5	0	0	0
27	321	1	3	348
29	55	0	0	631
31	0	0	0	319
33	0	0	0	128
Total	**2228**	**733**	**34**	**1511**

Table 2 *Demographics and operative procedures for patients having aortic or mitral valve replacement with the St. Jude Medical cardiac valve prosthesis over 25 years.*

Parameter	AVR	AVR + CAB	AVR + Other	AVR + CAB + Other	MVR	MVR + CAB	MVR + Other	MVR + CAB + Other	Total
Patients (%)	1696 (38)	1201 (27)	60 (1)	38 (1)	961 (21)	466 (10)	57 (1)	27 (1)	4506 (100)*
Age (years)*	62 ± 14.1	70 ± 9.3	59 ± 15.4	71±9.1	60 ± 12.8	66 ± 9.0	69 ± 12.0	68±9.7	64 ± 12.8
Gender (%)									
Male	990 (58)	826 (69)	33 (55)	28 (74)	383 (40)	264 (57)	29 (51)	15 (56)	2568 (56)
Female	706 (42)	375 (31)	27 (45)	10 (26)	578 (60)	202 (43)	28 (49)	12 (44)	1938 (44)
Follow up (years)									
Total	13244	7773	553	171	7198	2837	309	105	32190
Average per patient	7.8	6.5	9.2	4.5	7.5	6.1	5.4	3.9	7.2
Mortality (%)									
Operative	52 (3)	66 (5)	4 (7)	6 (16)	60 (6)	59 (13)	7 (12)	4 (15)	248 (6)
Late	540 (32)	533 (44)	17 (28)	14 (37)	329 (34)	211 (45)	9 (16)	7 (26)	1639 (36)
Valve-related	131 (8)	97 (8)	0 (0)	2 (5)	88 (9)	39 (8)	2 (4)	1 (4)	360 (8)

*Total number differs from study population due to reoperative procedures

Table 3 *Causes of valve related mortality for patients having aortic or mitral valve replacement with the St. Jude Medical cardiac valve prosthesis over 25 years.*

Valvular Cause of Death	AVR	MVR
Bleeding Event-Neuro	43	12
Bleeding Event-Other	20	9
Embolic-Neuro	59	43
Embolic-Peripheral	2	2
Non-structural Dysfunction	1	0
Prosthetic Valve Endocarditis	17	4
Reoperation of Prosthetic Valve	6	1
Sudden Unexplained, Unknown	79	54
Valve Thrombosis	2	4

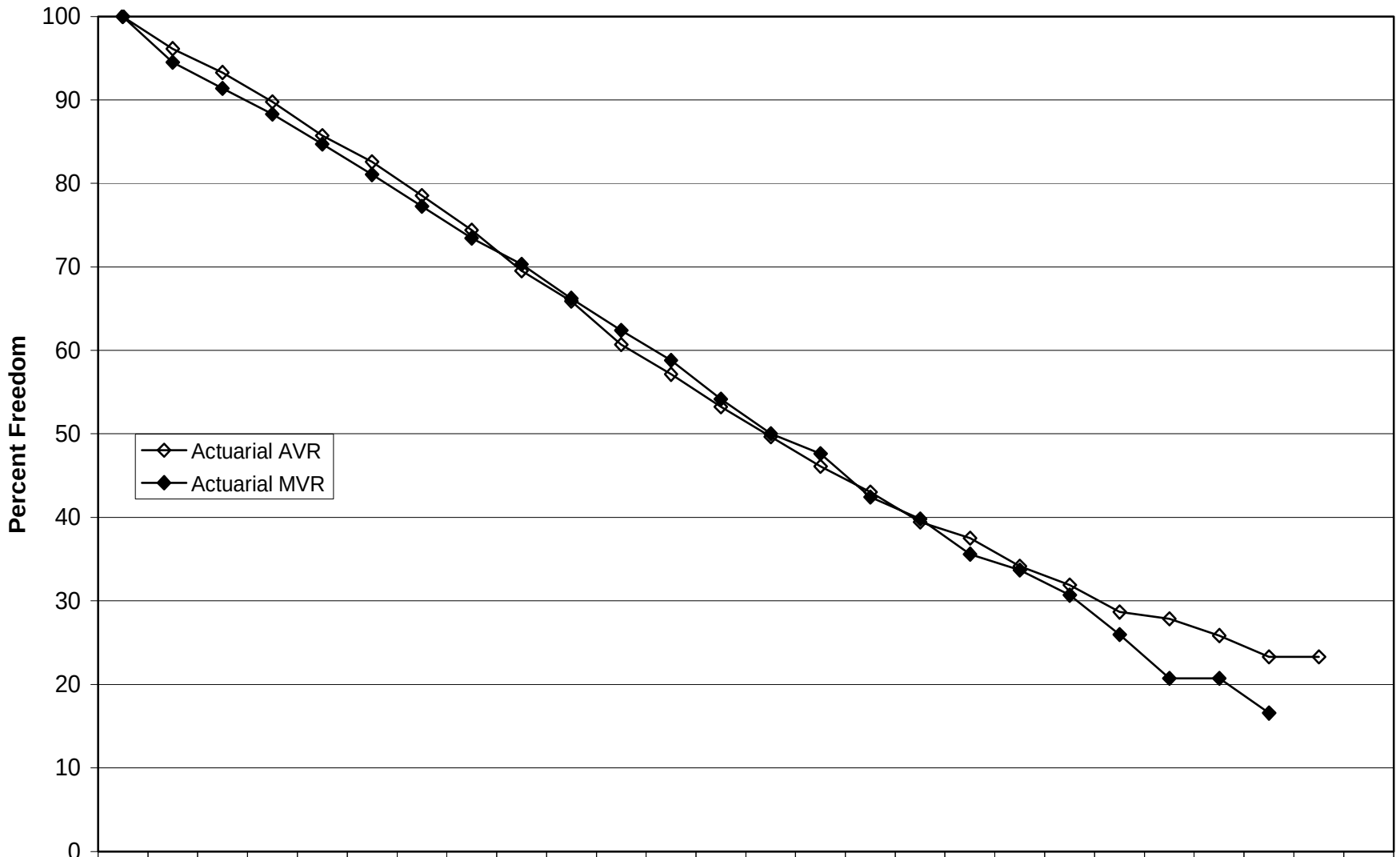
Table 4 *Cumulative incidence estimates for patients having aortic valve replacement with the St. Jude Medical cardiac valve prosthesis over 25 years.*

Event	YR	Cum Inc(%)	SE(Cum Inc)	95 % CI	# Left
TE	5	7.2	.5	(6.2, 8.2)	1761
	10	11.3	.6	(10.0, 12.6)	784
	15	14.7	.8	(13.1, 16.3)	311
	20	16.6	1.0	(14.7, 18.5)	116
Bleeding	5	12.4	.6	(11.2, 13.6)	1693
	10	17.5	.8	(16.0, 19.0)	789
	15	20.7	.9	(18.9, 22.4)	336
	20	22.5	1.0	(20.6, 24.5)	144
Thrombosis	5	.1	.1	(0, .3)	1853
	10	.5	.2	(.2, .8)	841
	15	.8	.2	(.4, 1.3)	329
	20	1.0	.3	(.4, 1.6)	90
Endocarditis	5	1.2	.2	(.8, 1.6)	1845
	10	1.7	.3	(1.1, 2.2)	838
	15	2.0	.3	(1.4, 2.6)	327
	20	2.0	.3	(1.4, 2.6)	91
Re-operation	5	1.0	.2	(.6, 1.4)	1844
	10	1.4	.2	(.9, 1.8)	838
	15	1.6	.3	(1.1, 2.2)	328
	20	1.9	.3	(1.2, 2.6)	89

Table 5 *Cumulative incidence estimates for patients having mitral valve replacement with the St. Jude Medical cardiac valve prosthesis over 25 years.*

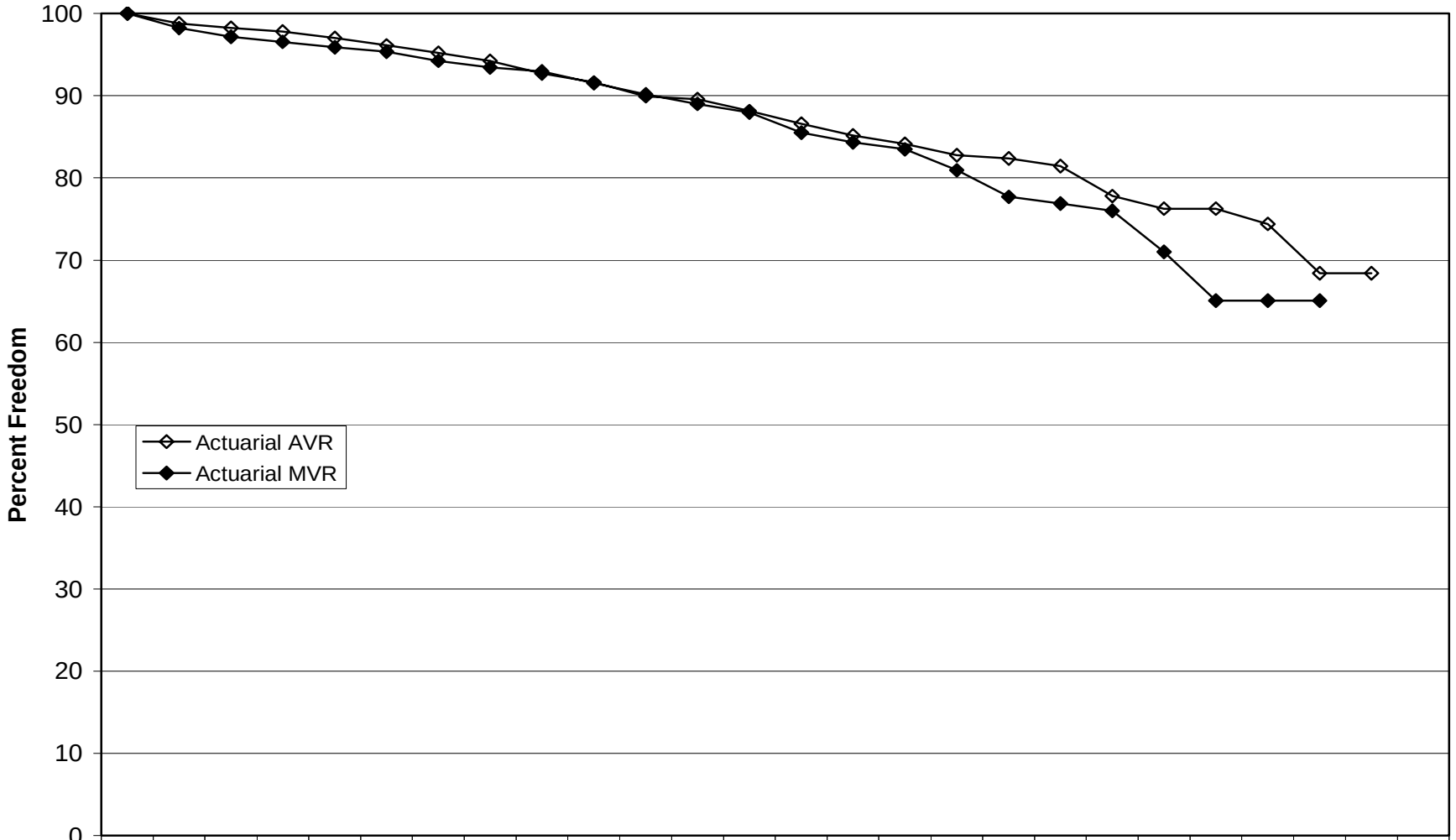
Event	YR	Cum Inc (%)	SE(Cum Inc)	95 % CI	# Left
TE	5	8.6	.8	(7.2, 10.1)	834
	10	14.6	1.0	(12.6, 16.7)	439
	15	20.3	1.3	(17.7, 22.8)	208
	20	21.8	1.4	(19.1, 24.6)	116
Bleeding	5	13.0	.9	(11.2, 14.7)	803
	10	17.6	1.1	(15.5, 19.7)	413
	15	20.4	1.2	(18.0, 22.7)	210
	20	22.1	1.3	(19.5, 24.6)	106
Thrombosis	5	.9	.3	(.4, 1.4)	884
	10	1.2	.3	(.6, 1.8)	471
	15	1.8	.4	(1.0, 2.7)	217
	20	1.8	.4	(1.0, 2.7)	98
Endocarditis	5	1.7	.3	(1.0, 2.4)	876
	10	1.8	.4	(1.1, 2.5)	465
	15	2.0	.4	(1.2, 2.8)	220
	20	2.2	.5	(1.3, 3.2)	97
Re-operation	5	1.7	.3	(1.0, 2.4)	878
	10	2.1	.4	(1.3, 2.9)	464
	15	2.2	.4	(1.4, 3.1)	214
	20	2.7	.5	(1.7, 3.8)	95

Figure 1 *Freedom from late morality in patients having valve replacement with the SJM valve prosthesis over 25 years.*



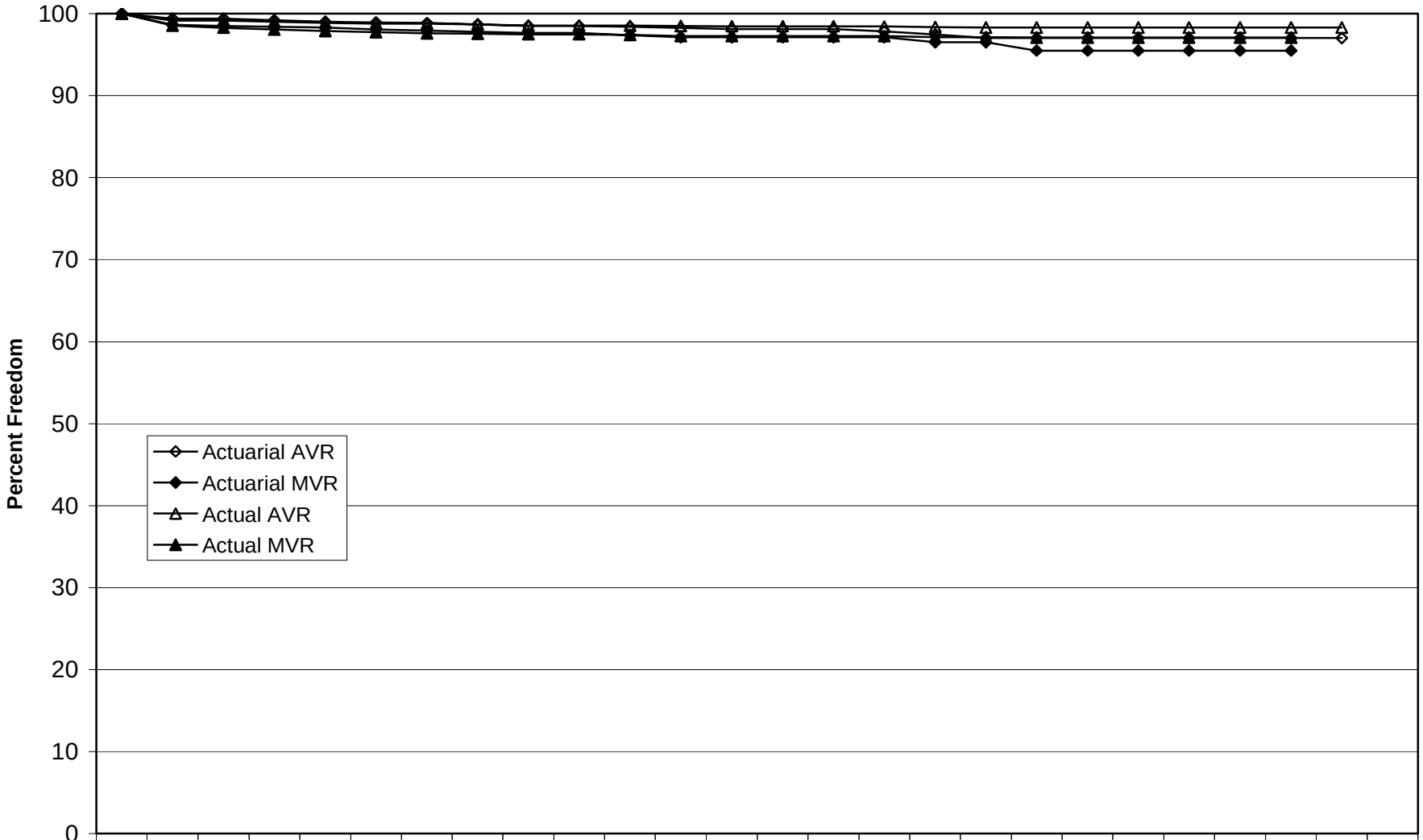
Year	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
AVR	2856	2664	2484	2254	2018	1827	1631	1418	1207	1021	820	675	547	456	376	313	250	195	144	119	73	54	35	15	6	0
MVR	1369	1244	1158	1059	942	833	741	642	552	486	416	355	300	246	210	169	143	101	82	62	44	26	17	3	0	0

Figure 2 *Freedom from valve-related morality in patients having valve replacement with the SJM valve prosthesis over 25 years.*



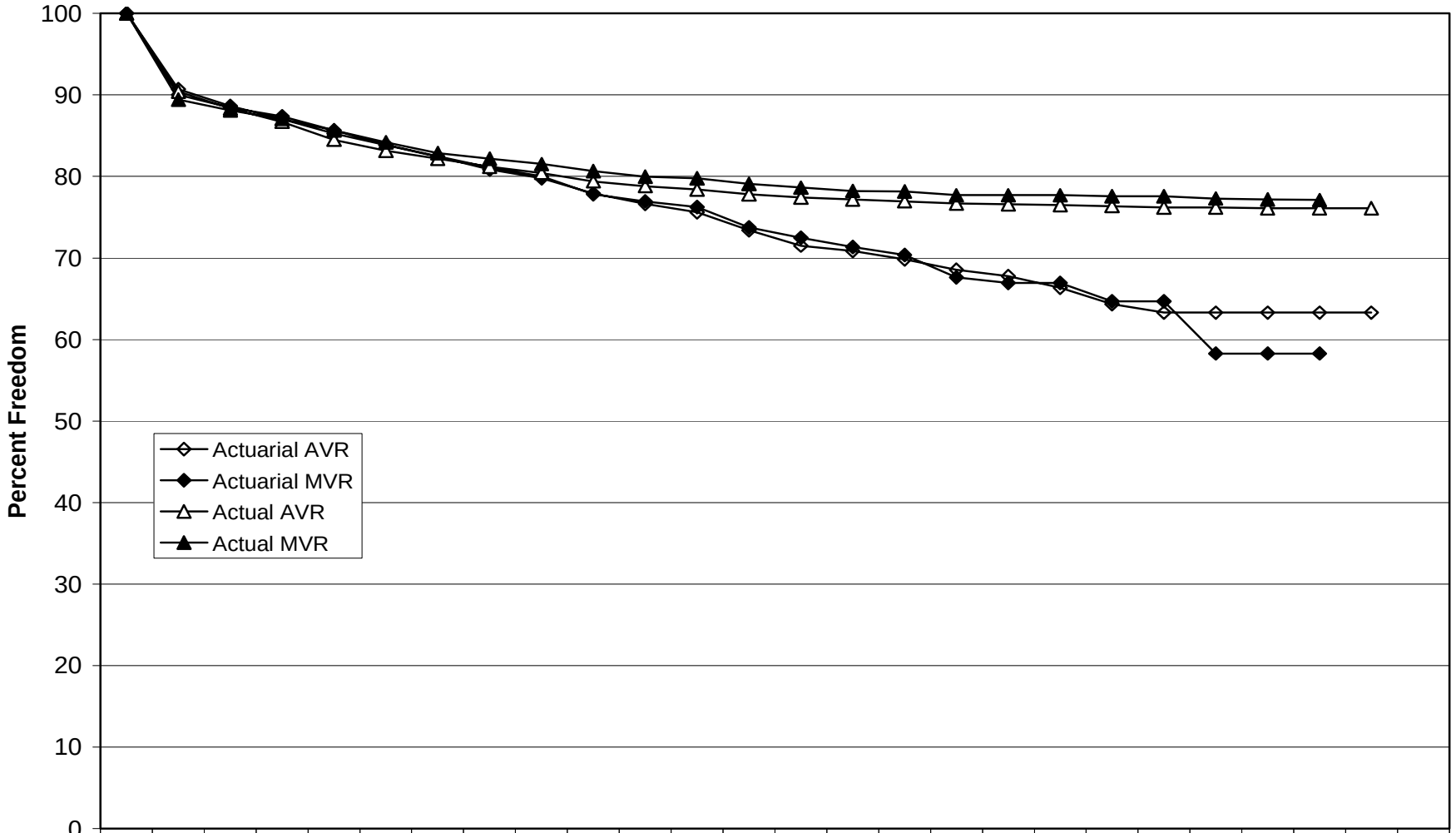
Year	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
AVR	2982	2664	2484	2254	2018	1827	1631	1418	1207	1021	820	675	547	456	376	313	250	195	144	119	73	54	35	15	6	0
MVR	1498	1244	1158	1059	942	833	741	642	552	486	416	355	300	246	210	169	143	101	82	63	44	26	18	3	0	0

Figure 3 *Freedom from reoperation in patients having valve replacement with the SJM valve prosthesis over 25 years.*



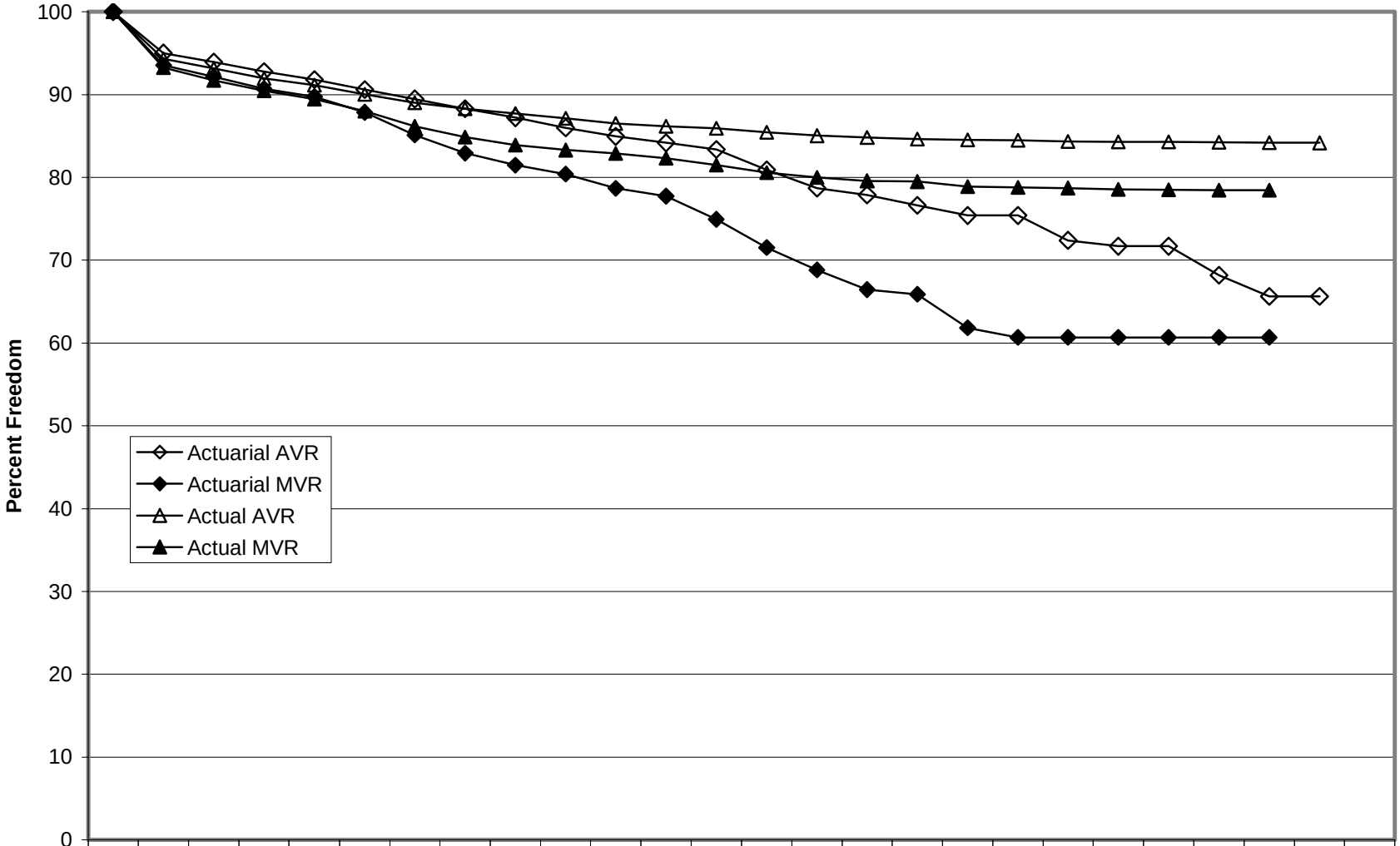
Year	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
AVR	2982	2652	2472	2240	2004	1814	1619	1404	1194	1010	811	668	542	452	373	309	246	193	142	118	71	52	33	14	6	0
MVR	1498	1231	1145	1047	932	822	729	631	541	476	405	345	291	237	201	160	136	94	75	57	40	23	15	1	0	0

Figure 4 *Freedom from anticoagulant related hemorrhage in patients having valve replacement with the SJM valve prosthesis over 25 years.*



Year	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
AVR	2982	2443	2242	2010	1779	1592	1412	1210	1024	861	691	560	441	354	293	245	195	150	112	91	54	42	24	12	4	0
MVR	1498	1137	1040	943	834	727	643	548	466	399	338	295	246	200	168	137	114	80	67	49	33	19	14	3	0	0

Figure 5 *Freedom from thromboembolism in patients having valve replacement with the SJM valve prosthesis over 25 years.*



Year	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
AVR	2982	2542	2348	2115	1887	1692	1494	1285	1087	910	721	585	474	385	313	255	203	155	117	100	61	44	28	12	6	0
MVR	1498	1172	1079	979	865	750	654	552	474	416	353	297	245	196	164	127	106	75	58	47	34	22	15	3	0	0