Update in Heart Valve Replacement

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Proceedings of the Second European Symposium on the St. Jude Medical Heart Valve

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Solved and Unsolved Problems in Heart Valve Replacement

C. Walton Lillehei

The proceedings published herein were presented at the International Symposium: "Update in Heart Valve Replacement" as part of the IXth European Congress of Cardiology.
These presentations provide a timely analysis of results with virtually all types of heart valves currently being used.
The observations presented in this monograph by the distinguished faculty point out the considerable progress that has been made in the design, fabrication, and application of prosthetic valves. The opportunity is thus provided to evaluate the performance of each type of prosthetic valve under a variety of circumstances.
It is apparent from these proceedings that there have been noteworthy improvements in clinical results obtained at a number of centers with the mechanical prosthesis in the form of the St. Jude Medical bileaflet, all pyrolytic carbon design. However, results with other types of prosthetic valves, including the tissue types, have remained more or less static. In spite of different modifications of preservation and fixation of the biological material it remains questionable whether important improvements have been achieved concerning durability. Answering this question will take many years.
The five-year experience in the St. Jude Medical multicenter study may be considered excellent. There were no prosthetic malfunctions, and the calculated survival and freedom from thromboembolism probabilities appear to be as good as, if not better than, those obtained with other types of valves, although even longer term evaluation will be needed for final comparisons.
These accomplishments have brought us closer to the "ideal valve replacement" than many might realize. The "ideal valve substitute" parameters of lifetime durability, absence of hemolysis, and near normal hemodynamics have been met by one or more of these modern valve substitutes.
Nonetheless, for the fourth parameter of an "ideal valve substitute" namely, a freedom from thromboembolism, problems have not been eliminated, including the need for long-term anticoagulation.
However, a more careful examination of these remaining problems of thromboembolism associated with valvular substitutes does provide some guidelines for further research that may not be fully appreciated at this time even by specialists active in this field.
It is well recognized by all clinicians that in the life history of valvular heart disease certain pathophysiologic changes occur. What is frequently overlooked is the fact that these changes, particularly atrial fibrillation, chamber dilatation and reduced cardiac output may and do cause thromboembolism from other cardiac sites that actually become significantly more important than the diseased valve(s).
Striking confirmation of this clinical observation has been offered by the recent report of Sage and van Uitert (1). These authors reviewed 140 patients with atrial fibrillation due to *nonvalvular* heart disease who had suffered an embolic stroke. They found that 38% of the

patients had died from an initial cerebral infarct. Among 59 survivors who were not anticoagulated, and for whom follow-up data were available, the risk of recurrent stroke was 20% per patient/year for each year of the 9-year study. Patient age and sex were not significant risk factors for recurrent emboli in their data.

The profound significance of this study for clinicians is the demonstration of the very high incidence of thromboemlism in patients with atrial fibrillation and with *normal natural heart valves*.

Thus it becomes very clear that in the patient with valvular heart disease who has progressed to the stage of atrial fibrillation, along with its secondary cardiac effects, even substituting a *normal natural valve* would *not* prevent thromboembolism.

Thus we may conclude that the problem is changing, and that future endeavors to reduce the incidence of thromboembolism in valvular heart patients must lie more with the management of the patient to prevent the onset of atrial fibrillation rather than the often repeated presumption that the "ideal valvular prosthesis" can solve all of these remaining problems.

Reference

1. Sage JI, van Uitert RL (1983) Risk of recurrent stroke in patients with atrial fibrillation and non-valvular heart disease. Stroke 14: 537

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The St. Jude Medical Prosthetic Heart Valve: Results from a Five-Year Multicenter Experience

C. Walton Lillehei

During the past quarter-century, hundreds of new and novel designs for prosthetic heart valves have been described. The majority of these have been introduced into clinical usage with great enthusiasm. A few, perhaps ten or less, have withstood the test of time, and in looking back, can be judged as milestones in the development of valve replacement therapy. The great majority of designs that failed were unable to pass the test of time which exposed substantial or even fatal flaws.

Thus, this first intermediate-term multicenter study showing the detailed clinical results in 584 patients who received their St. Jude Medical® (SJM) prosthesis from 4½ to 6½ years earlier under a variety of clinical and environmental conditions, has particular significance in evaluating the early promise of this prosthesis which has been reported upon by many investigators (1–13).

The St. Jude Medical cardiac prosthesis

The design of a rigid bileaflet prosthesis was first described, tested in vitro, in animals, and reported in a series of publications beginning in the mid '60s by Kalke and Lillehei (14–17). The most striking findings from these earlier studies concerned the hemodynamics. They were superior to all other prostheses available at that time.

In 1976 this design was modified and refined for manufacture entirely from pyrolytic carbon (18) which replaced the titanium of the earlier design.

Although there were a plethora of mechanical and tissue valves available at that time, the hemodynamics in most were significantly inferior to those measured for the SJM prosthesis in vitro. Thus, surgeons and cardiologists began to explore the use of this prosthesis particularly in their problem patients such as those with unusually small anuli and advanced myocardial impairment. It was these reasons together with the attractiveness of the all-pyrolytic carbon design that was responsible for the rather rapid clinical acceptance of this new cardiac prosthesis.

On October 3, 1977, at the University of Minnesota Hospitals, this new design was used clinically for the first time in a 67-year-old woman incapacitated by calcific aortic stenosis (19). She had an immediate and dramatic clinical improvement which still persists (New York Heart Association Class I).

Today, 7½ years later, more than 90,000 St. Jude Medical prosthetic valves have been implanted in patients worldwide. The original bileaflet, central opening to 85°, all-pyrolytic carbon valve design has remained unchanged throughout this entire clinical experience (Figure 1).

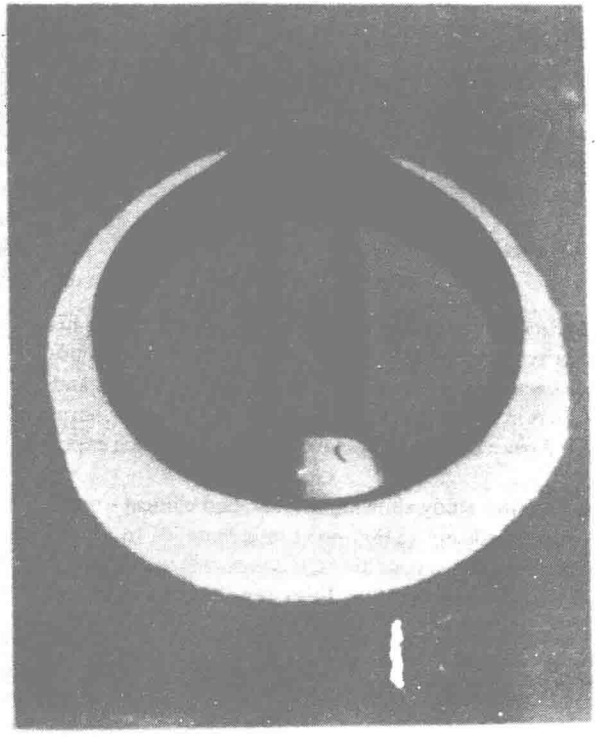

Fig. 1. The St. Jude Medical bileaflet, all-pyrolytic carbon aortic prosthesis is seen from the inflow side in the fully opened (to 85°) mode.

Design of the St. Jude Medical intermediate-term multicenter study

All centers which were early and continuing implanters of the SJM prosthesis with relatively large series of patients and good follow-up procedures were invited to participate in this intermediate-term study of patients operated on for isolated mitral or aortic valve replacement prior to April 30, 1979, (international centers) and prior to December 31, 1979 (U.S.A. hospitals). Agreement to participate was determined entirely by the invited institutions based upon their interest, personnel and facilities. Nearly all eligible centers were able to participate (Table 1). There was no patient selection in this study except for these factors. The principal investigator responsible for the data gathering at each center was determined locally, and was either a cardiac surgeon or cardiologist. Four of the U.S.A. centers listed in Table 1 were also the primary investigative centers for the U.S.A. FDA clinical approval process (approval was granted December 20, 1982).

The surgical techniques were those routine for the particular centers. No special valve orientations were recommended. Permanent warfarin anticoagulation postoperatively was recommended for all patients.

This group of 584 patients comprised 330 isolated aortic valve replacements (AVR) and 254 isolated mitral valve replacements (MVR). The distribution of the SJM valve sizes implanted is portrayed in Figure 2. Double valve implants were excluded from this analysis,

Table 1. Centers participating in the St. Jude Medical Multicenter Intermediate-term Study

International	Principal Investigators
Kantonsspital Basel – Basel, Switzerland	J. Hasse, M.D.
Hôpital Cardiologique – Bordeaux, France	E. M. Baudet, M.D.
Erasme Hospital – Brussels, Belgium	J. LeClerc, M.D.
Medizinische und Chirurgische Universitätsklinik B – Düsseldorf, West Germany	D. Horstkotte, M.D.
Universität Giessen – Giessen, West Germany	F. W. Hehrlein, M.D.
Universität Göttingen – Göttingen, West Germany	E. R. deVivie, M.D.
Universitäts-Krankenhaus Eppendorf – Hamburg, West Germany	P. Kalmar, M.D.
Medizinische Hochschule Hannover – Hannover, West Germany	H. Oelert, M.D.
Universitätskliniken Köln – Köln, West Germany	H. Dalichau, M.D.
Ospedale S. Camillo De Lellis – Rome, Italy	L. D'Alessandro, M.D.
United States	
Hamot Medical Center – Erie, Pennsylvania*	G. D'Angelo, M.D.
St. Luke's Hospital – Fargo, North Dakota*	C. S. Hamilton, Jr., M.D.
Cedars-Sinai Medical Center – Los Angelos, California*	R. Gray, M.D.
Abbott-Northwestern Hospital – Minneapolis, Minnesota	D. Nicoloff, M.D.
Providence Medical Center – Seattle, Washington*	L. Sauvage, M.D.
United Hospital – St. Paul, Minnesota	D. Nicoloff, M.D.
Tucson Medical Center – Tucson, Arizona	C. Maloney, M.D.

* Also primary investigative centers for the U.S.A. FDA clinical approval process

but all patients with major cardiovascular procedures at the time of valve replacement are included. About 33% of these patients had such major additional procedures at the time of their valve replacement. The most common of these was coronary artery bypass grafting (CABG). Other procedures included in this analysis were aneurysm surgery, carotid endarterectomies and various congenital cardiac reparative procedures.

The opening date of this study was October 3, 1977, and the closing dates for the patients' operations have been listed above. The closing date for the patient follow-up for this report was May 31, 1984. All the followed patients in the study were contacted by one or more of the following: office visit, telephone to the patient or family physician, and by questionnaire.

The total patient follow-up was 2,304 patient years broken down to: AVR-1,344 patient years (pt.yrs.) and for MVR-960 pt.yrs. The minimum implant time was 54 months and the maximum was 78 months. The mean follow-up was 49 months and includes all patients who expired or were lost to follow-up prior to the 54th postoperative month.

The probability of patients' survival or freedom from specific complications for five years was calculated by the actuarial life-table method (20), and is given as mean plus the 95% confidence interval. Linearized rates of complications (%/pt.yr.) utilized the methods described by Grunkemeier (20).

In estimating the rate of thromboembolic complications (TE) we have utilized the Stanford criteria (21). That is, TE complications include all new transient or permanent focal neurologic defects (unless they were proven to be due to causes other than the valve), and all non-cerebral arterial emboli. Other pertinent data describing this patient cohort are contained in Table 2.

Table 2. St. Jude Medical Multicenter Intermediate-term Study

Total Patient Cohort	584	
Lost to Follow-up	25 (4.3%)	
Number Followed	559 (95.7%)	
AVR	330	
MVR	254	
Mean age at operation:	54.5 yrs.	
Youngest	1 yr.	
Oldest	79 yrs.	
Total Patient Follow-up: 2304 patient years (pt. yrs.)		
AVR	1344 pt. yrs.	
MVR	960 pt. yrs.	
Implant Time:		
Shortest	4.5 yrs.	
		Mean 4.1 yrs.
Longest	6.5 yrs.	

74.5% of all patients were followed 4.5 years or more

Valve durability

There was no structural failure of a prosthesis or its components reported for the entire study period.

Clinical assessment

Improvement in the New York Heart Association (NYHA) Classification provides a subjective measure of a prosthetic valve's hemodynamic performance postoperatively. Objective hemodynamic studies performed upon the SJM prosthesis have been reported from many of these same centers (6,7–8, 11, 22–24, 26) and others (4, 9, 12, 25). These hemodynamic observations, while not a part of this study, have confirmed objectively the consistent and significant clinical improvements seen in the patients' NYHA Classes (Figure 3).

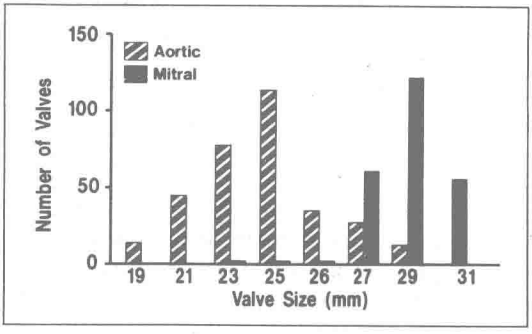

Fig. 2. Valve distribution by size

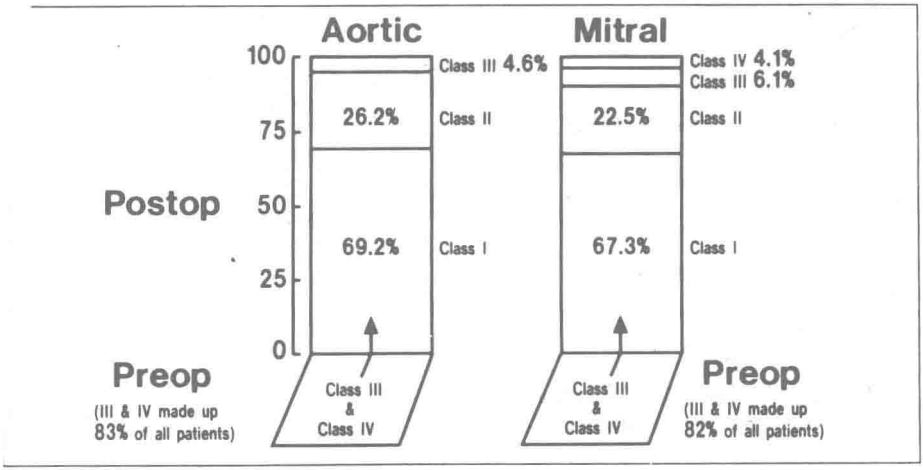

Fig. 3. New York Heart Association Classification

Anticoagulation status and hemorrhagic complications

As part of this intermediate-term follow-up, a survey of the patients' anticoagulation therapy was made, and these results are portrayed in Figure 4. As may be noted, 94.3% of all patients were on either warfarin alone (90.7%) or warfarin in combination with antiplatelet aggregates (3.6%). With the SJM all-pyrolytic carbon prosthesis it was recommended to physicians that the prothrombin reduction could be maintained at 1.5 to 2 times the control level (in seconds) as opposed to earlier goals of 2 to 2.5 times the control (in seconds).

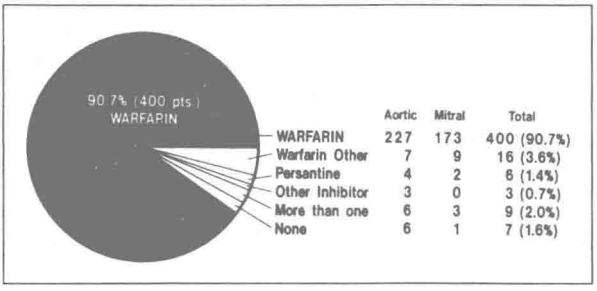

Fig. 4. Current coagulation status

The number and percentages of patients free of complications due to anticoagulation therapy are shown in Figure 5. In the AVR and MVR patients 89.1% and 95.2%, respectively, had been free of any such complications after 5 years.
The number of fatal complications due to anticoagulation was one patient definitely and two possibly (see below "Patient mortality and patient survival").

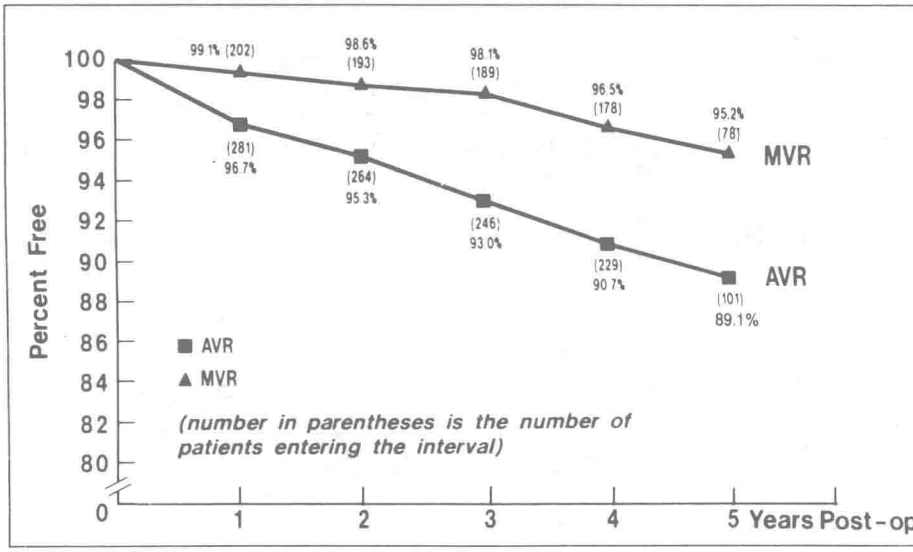

Fig. 5. Patients free of hemorrhagic complications

Thrombogenicity

The percentages of SJM patients who were free of thromboembolic events have been expressed actuarially (Figure 6) and in percent/patient year at 5 years (Table 3). The latter rates were 0.97%/pt.yr. for AVR, and 1.98%/pt.yr. for MVR.

Actuarially the rates at 5 years for SJM patients free of any TE complications were 89.4% for MVR and 95.9% for AVR. The number of fatal TE events has been described below under "Patient mortality and patient survival".

For the MVR patients, there was complete freedom from the dire complication of valve thrombosis during this study period. For AVR, 97% of all patients were free of valve thrombosis up to five years (Figure 7).

Table 3. Overview of results. St. Jude Medical Multicenter, Long-term Study

Implant Site	Total No. Patients	Mortality Early (No. Pts.)	Late (No. Pts.)	Linearized T.E. Rate
Isolated AVR	330	(12) 3.6%	(47) 14.8%	0.97%/pt. yr.
Isolated MVR	254	(24) 9.5%	(33) 14.3%	1.98%/pt. yr.
Totals	584	(36) 6.2%	(80) 13.7%	

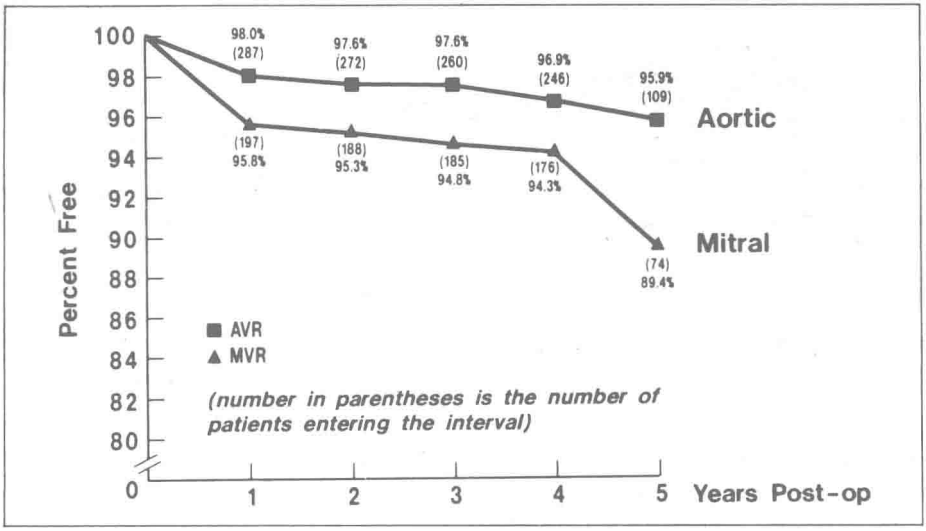

Fig. 6. Patients free of thromboembolism

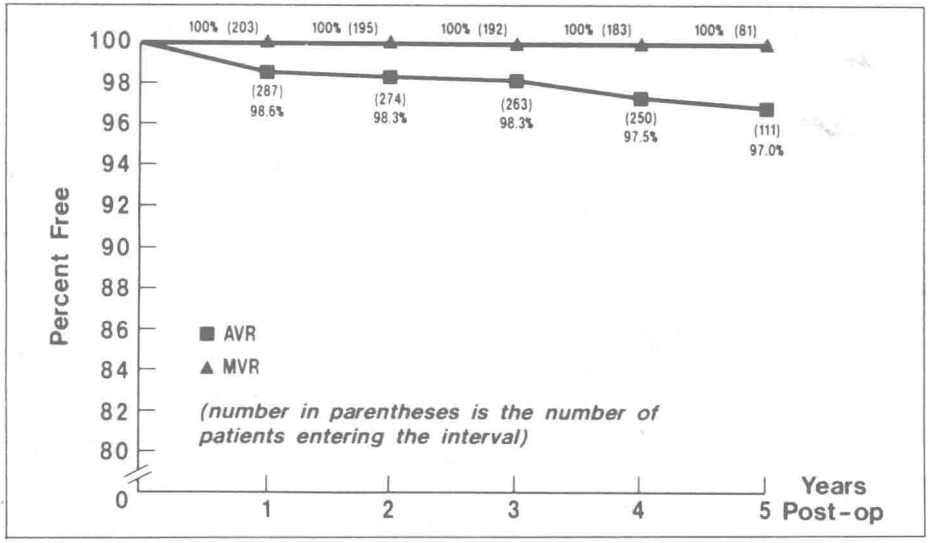

Fig. 7. Patients free of thrombus

Patients free of complications

In this study valve-related complications were considered to be: TE, valve thrombosis, anemia (due to hemolysis), hemorrhagic complications, endocarditis (not pre-existing), and all reoperations or explants. Paravalvular leaks were included when they resulted in reoperations. The actuarial freedom from all complications related to the prostheses at 5 years was 83.0% for MVR and 81.9% for AVR (Figure 8).

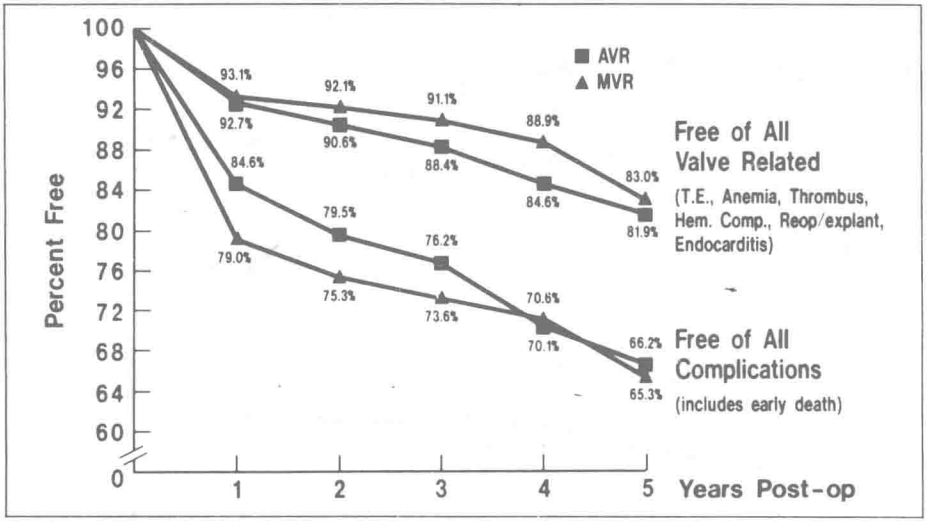

Fig. 8. Percent of patients free of complications

It is of considerable interest that two-thirds of all patients having either an AVR or MVR with a SJM prosthesis remained free of any medical complication whatsoever after five years, including early death (Figure 8) even though over 80% were in NYHA Class III or IV preoperatively.

Patient mortality and patient survival

There were 116 deaths overall (Table 3). Thirty-six were early (first 30 days) postoperatively with an AVR early mortality of 3.6% (12 patients). The MVR early mortality was

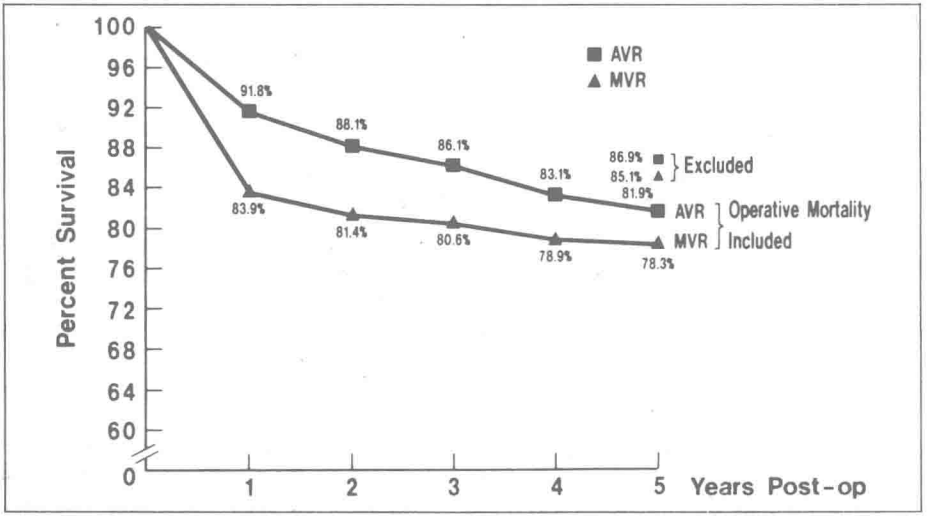

Fig. 9. Overall survival following St. Jude Medical valve replacement

9.5% (24 patients). None of the early deaths in either the AVR or MVR patients was valve-related.

The actuarial probabilities of survival after implantation of the SJM mitral and aortic prostheses, up to 5 years post implantation, are depicted in Figure 9.

The probabilities of 5-year survival for AVR and MVR with the early mortality included are 81.9±4.4% and 78.3±5.4%, respectively. If the early mortality (first 30 days) which is usually not prothesis-related is excluded, the 5-year survival rates are for AVR 85.1% and for MVR 86.9%.

Figure 10 shows cumulative percentages of patient mortality due to cardiac causes that were not valve-related. The valve-related mortality is also shown, and was only 1.0% for MVR and 2.1% for AVR at 5 years.

There were only 9 valve-related deaths during this entire study period, and all were in the late follow-up interval. These deaths were 7 in number after AVR, and 2 after MVR. The two MVR deaths were both cerebral in nature; one was thought to be a TE, and the other was diagnosed as cerebral hemorrhage due to warfarin. Of the 7 AVR deaths, 6 were cerebral in nature, and 1 was due to valve thrombosis in a patient who had stopped taking anticoagulants. Three of the 6 cerebral deaths were believed to be due to thromboembolisms. One of these patients also had stopped anticoagulation. Another cerebral TE death was in a patient with uncontrollable endocarditis.

The two remaining deaths were in patients on warfarin, and appeared to be due to hemorrhage (one had an emergency craniotomy). Whether or not these deaths were definitely attributable to warfarin is not known in the absence of autopsies. Both patients had factors predisposing to hemorrhage (long history of hypertension and advanced age).

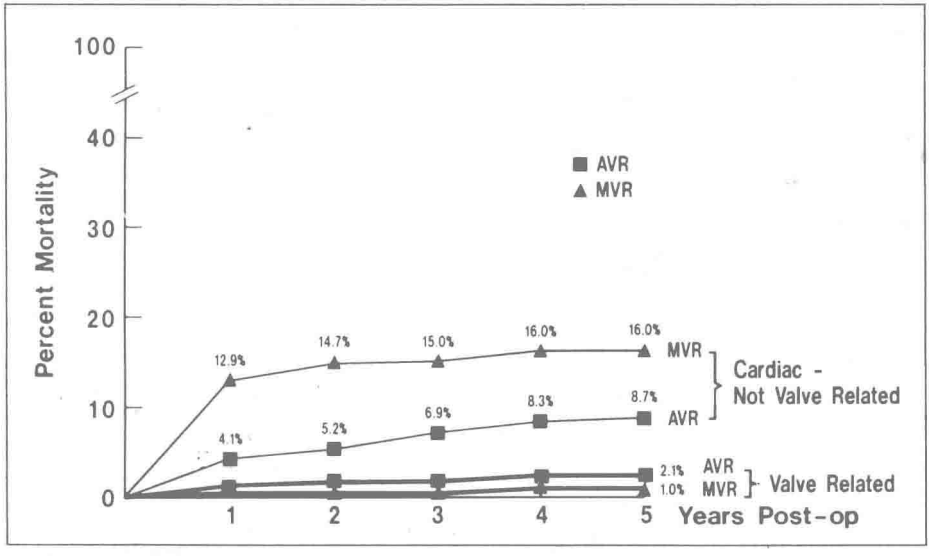

Fig. 10. Causes of patient mortality after St. Jude Medical implantations

St. Jude Medical heart valve – improvement in performance

It is well recognized that complications following prosthetic valve replacement may arise from sources other than the prosthesis itself. However, there is also much evidence from clinical studies over the years which has correlated a better prosthesis with improved survival, fewer complications and a better quality of life (29). Thus, it was of interest and significance to compare the results in this present study with similar long-term studies of the results with other currently used prostheses, both mechanical and biological.

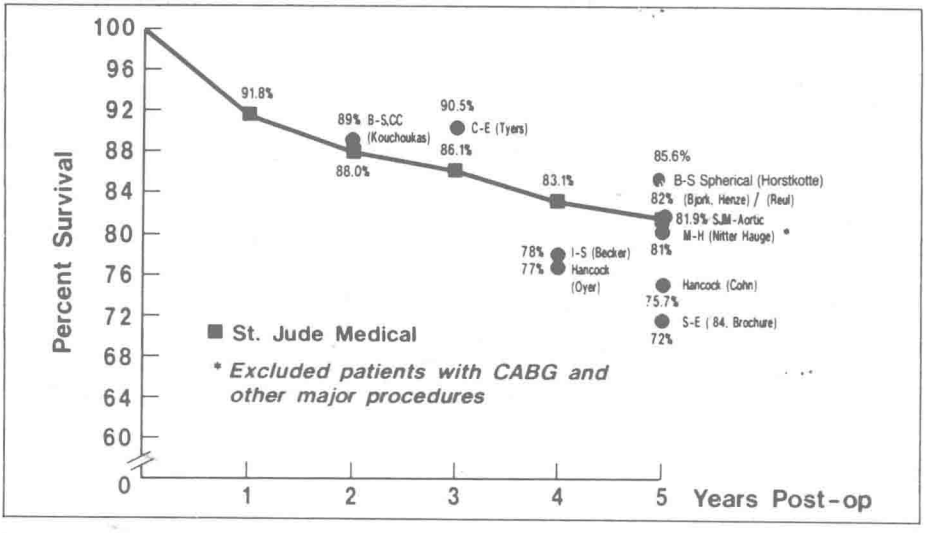

Fig. 11. Survival following aortic valve replacement (St. Jude Medical vs. other valves)

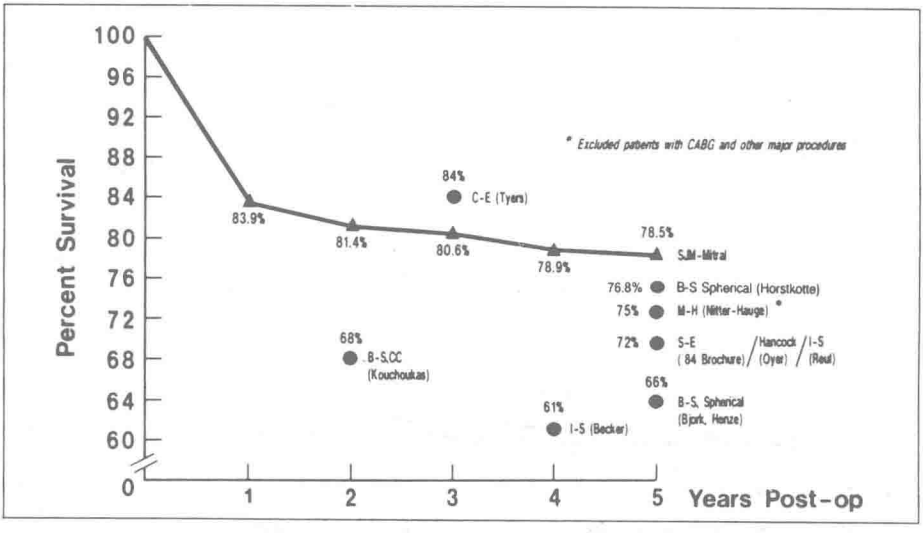

Fig. 12. Survival following mitral valve replacement (St. Jude Medical vs. other valves)