

STATE-OF-THE-ART PAPER

Choice of Prosthetic Heart Valve for Adult Patients

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This review summarizes the major long-term (≥ 10 to 15 years) patient outcomes after insertion of many Food and Drug Administration approved prosthetic heart valves (PHV). Mechanical PHV was associated with a better survival ($p < 0.02$) at 15 years after aortic valve replacement (AVR) than with a bioprosthesis in the Department of Veterans Affairs (DVA) trial. In both the DVA and the Edinburgh Heart Valve trials, bioprosthesis were associated with structural valve deterioration (SVD) (mitral valve replacement [MVR] $>$ AVR) and, therefore, for replacement of the PHV. Thromboembolism and bleeding rate were higher with mechanical PHV. Mortality after AVR and MVR is high at 10 to 15 years because of the associated comorbid conditions and older age of patients. Outcomes with "new" good valves are similar to that with "older" good valves. Complication rates of thromboembolism, bleeding, endocarditis, and leak vary widely; the rates of these complications are not different among different mechanical PHV and among different bioprosthetic PHV. Structural valve deterioration is rare with mechanical PHV. Structural valve deterioration of bioprosthesis after MVR is higher than after AVR; after AVR, homografts and bioprosthesis have similar rates of SVD. The exact rate of SVD of the pulmonary autograft is uncertain. Valve prosthesis-patient mismatch is clinically important when it is severe and in selected patients when it is moderate. Bioprosthesis have a low rate of SVD in the older patient and, thus, are the PHV of choice for AVR in patients ≥ 60 to 65 years of age and for MVR in patients ≥ 65 to 70 years of age; in younger patients mechanical valves are the PHV of choice. In individual patients there may be exceptions to these general rules. (J Am Coll Cardiol 2003;41: 893-904) © 2003 by the American College of Cardiology Foundation

"You believe that easily, which you hope for earnestly."

Terence (1) c. 190 to 159 B.C.

"What ardently we wish, we soon believe."

Young (2) 1683 to 1765

HAS MUCH CHANGED SINCE THEN?

The results of valve surgery with regard to survival, complications, valve function, cardiac function, and functional class are dependent on patient-related factors, type of surgery, type of prosthesis, and health care-related factors (3). In 1974, McGoon (4) pleaded for a more systematized process of evaluation of patients after valve replacement. In 1975, it was suggested that one way to evaluate differences in patient outcomes between different valves was by a prospective randomized trial (5), which led to the planning and performance of the Department of Veterans Affairs (DVA) randomized trial between a mechanical and bioprosthetic valve (6). Bioprosthesis applies to nonviable tissue of biological origin such as porcine or bovine pericardium (heterograft or xenograft valves) (7). This report summarizes the major long-term (≥ 10 to 15 years) patient outcomes of many Food and Drug Administration (FDA)-approved prosthetic

heart valves (PHV) in the last 27 years in order to develop suggestions for choice of a PHV in individual patients.

RANDOMIZED TRIALS

Two large randomized trials have compared patient outcomes with use of a mechanical valve (spherical tilting disk Bjork-Shiley) and a porcine valve (Hancock or Carpentier-Edwards).

Edinburgh heart valve trial. A total of 541 men and women were randomized between 1975 to 1979; 211 had aortic valve replacement (AVR), 261 had mitral valve replacement (MVR), and 61 had AVR plus MVR (8) (Fig. 1). The average follow-up was 12 years. The major findings were: 1) there was a trend toward an improved survival with the Bjork-Shiley valve ($p = 0.08$); 2) reoperation rates were low and nonsignificant at 5 years; at 12 years there was a higher reoperation rate with the porcine valve versus mechanical valve (AVR, $22.6 \pm 5.7\%$ vs. $4.2 \pm 2.1\%$, $p < 0.01$; MVR, $43.1 \pm 6.0\%$ vs. $9.9 \pm 3.2\%$, $p < 0.001$); younger patients were more likely to require reoperation, with "relative risk of reoperation increasing 55% for each 10 years, continuously over the whole range of ages studied"; 3) the incidence of thromboembolism and of endocarditis were not statistically significantly different; and 4) the bleeding rate was higher with the mechanical valve versus porcine valve after AVR ($32.6 \pm 6.1\%$ vs. $9.7 \pm 4.7\%$, $p < 0.001$) but not after MVR (24.5% vs. 24.5%).

DVA trial. A total of 575 men were randomized between 1997 to 1982; 394 had AVR, and 181 had MVR (6).

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Abbreviations and Acronyms

AVR	= aortic valve replacement
CABG	= coronary artery bypass graft surgery
CAD	= coronary artery disease
DVA	= Department of Veterans Affairs
FDA	= Food and Drug Administration
INR	= international normalized ratio
NYHA	= New York Heart Association
LVEF	= left ventricular ejection fraction
MO	= modified orifice
MVR	= mitral valve replacement
OPC	= optimal performance characteristics
PHV	= prosthetic heart valve
SVD	= structural valve deterioration
VP-PM	= valve prosthesis-patient mismatch

Follow-up was up to 18 years; average follow-up was 15 years. The principal long-term findings were: 1) after AVR, use of mechanical valve resulted in a lower mortality ($66 \pm 3\%$ vs. $79 \pm 3\%$; $p = 0.02$) (Fig. 1) and a lower reoperation rate ($10 \pm 3\%$ vs. $29 \pm 5\%$, $p = 0.004$). The difference became apparent after 10 years, indicating the need for follow-up of ≥ 15 years. The mortality after MVR was similar (81% vs. 79%); 3) after AVR, about 40% of the mortality was related to the PHV; after MVR, 44% of the mortality with mechanical valve and 57% of the mortality with bioprosthesis were related to the PHV; 4) there was no structural valve deterioration (SVD) with the mechanical valve; 5) primary valve failure occurred mainly in patients < 65 years; it began at 5 to 6 years after MVR and at 7 to 8 years after AVR; its incidence was higher after MVR ($44 \pm 8\%$ vs. $23 \pm 5\%$); 6) more than 10 years of follow-up was needed to determine the incidence and deleterious effects of SVD with use of porcine valve; 7) the primary valve failure rate between bioprosthesis and mechanical valve was not significantly different in those ≥ 65 years after AVR; 8) use

of a bioprosthesis resulted in a lower bleeding rate; and 9) there were no significant differences between the two valve types with regard to other valve-related complications, including thromboembolism and all complications.

Major differences between the two trials. The bleeding rate in the Edinburgh Heart Valve trial was 2% to 2.5%/year with the mechanical valve and 0.9% to 2%/year with the porcine valve (3,8). The patients were less heavily anticoagulated and minor bleeding was not recorded for the first five years of follow-up. After MVR, the bleeding rates with a mechanical and porcine valve were not different, probably because many patients with porcine valves needed anticoagulation for other reasons, most likely atrial fibrillation. The exact reasons for the high bleeding rate in the DVA trial are not clear (6). In the DVA trial, it was recommended that prothrombin time should be maintained at 2.0 to $2.5 \times$ control (3), which is excessive anticoagulation. Also, some patients with porcine valves were anticoagulated, and all bleeding episodes were included because it is not possible to separate bleeding due to anticoagulation from that due to other causes.

NUMBER OF PATIENTS. The DVA trial had 87% more patients undergoing isolated AVR and 31% fewer patients undergoing isolated MVR than the Edinburgh Heart Valve trial. These differences may account for differences in outcomes, especially with regard to mortality.

NONRANDOMIZED STUDIES

Mortality. The 10- and 15-year mortality rates after AVR (Table 1) and MVR are high (9–21). The range is large, even with the use of the same brand of PHV, indicating the importance of factors other than the type of PHV. Risk factors for late mortality have included decade of age, left ventricular dysfunction, heart failure, New York Heart Association (NYHA) functional classes III and IV, coronary

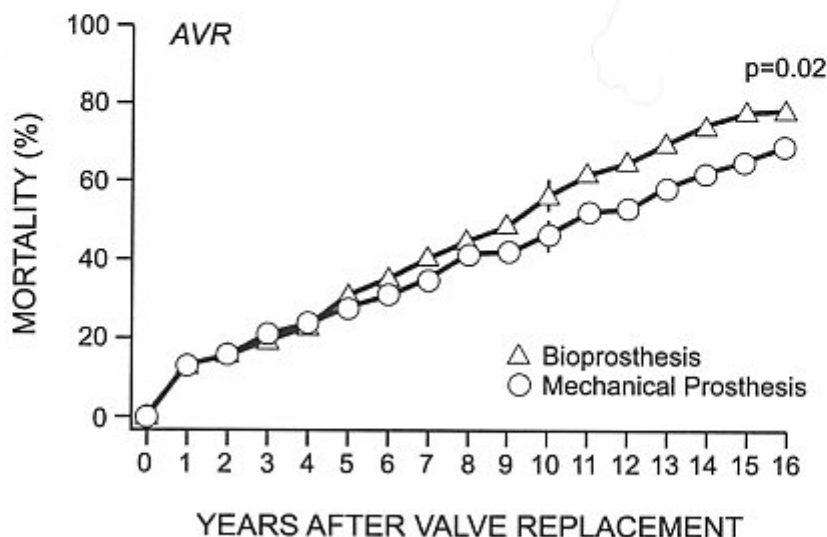


Figure 1. Mortality after aortic valve replacement (AVR) with the Bjork-Shiley and porcine valves from the Department of Veterans Affairs trial. From reference 6.

Table 1. Long-Term Mortality After AVR

Author (Ref. No.)	Type of PHV	No. of Patients	Mortality	
			at Yr	%
Orszulak et al. (9)	Starr-Edwards	1,100	10	40.4
			15	55.1
			20	68.8
Lindblom et al. (10)	Bjork-Shiley	1,753	10	30*
			15	46*
Lund et al. (11)	St. Jude	694	10	42 ± 5
Butchart et al. (12)	Medtronic Hall	736	10	36
			15	55
Peterseim et al. (13)	St. Jude	412	10	50 ± 6
			10	46 ± 3
Yun et al. (14)	Hancock porcine	652	12	49 ± 2
			12	58 ± 3
			12	56 ± 7
Jamieson et al. (15)	C-E supra-annular porcine	1,335	10	40.6 ± 2.1
			12	45.8 ± 2.8
Cohn et al. (16)	Hancock MO porcine	843	10	48 ± 2*
			15	72 ± 3*
Khan et al. (17)	Hancock porcine/ Hancock MO porcine	243	10	45*
			15	64*
Frater et al. (18)	C-E pericardial	267	14	60.7 ± 3.1*
David et al. (19)	Hancock II porcine	670	10	39 ± 2
			15	53 ± 3

*Excluding operative mortality.

AVR = aortic valve replacement; C-E = Carpentier-Edwards; MO = modified orifice; PHV = prosthetic heart valve.

artery disease (CAD), coronary artery bypass grafting (CABG), valve regurgitation, arrhythmias, male gender, pulmonary hypertension, and comorbid conditions such as renal failure, lung disease, hypertension, and diabetes (12,13,16). For example, of 843 patients undergoing AVR with the Hancock modified orifice (MO) porcine valve (16), the 10-year late mortality (i.e., excluding 5% operative mortality) was 48 ± 2%; however, the 10-year mortality in those with associated CABG was 55 ± 6% versus 39 ± 3% ($p \leq 0.0005$) in those without CABG.

The older the patient at the time of PHV implantation, the lower the 10- to 20-year survival (Fig. 2) (22). Older patients are more likely to have clinically significant associated comorbid conditions that are known to adversely affect survival after PHV (see the preceding text). This study provided virtually no information on the patients condition at baseline; thus, it is not possible to know whether the lower long-term survival (22) was the result of older age and/or associated cardiac and noncardiac comorbid conditions. It may be trite, but obviously needs repeating that, the

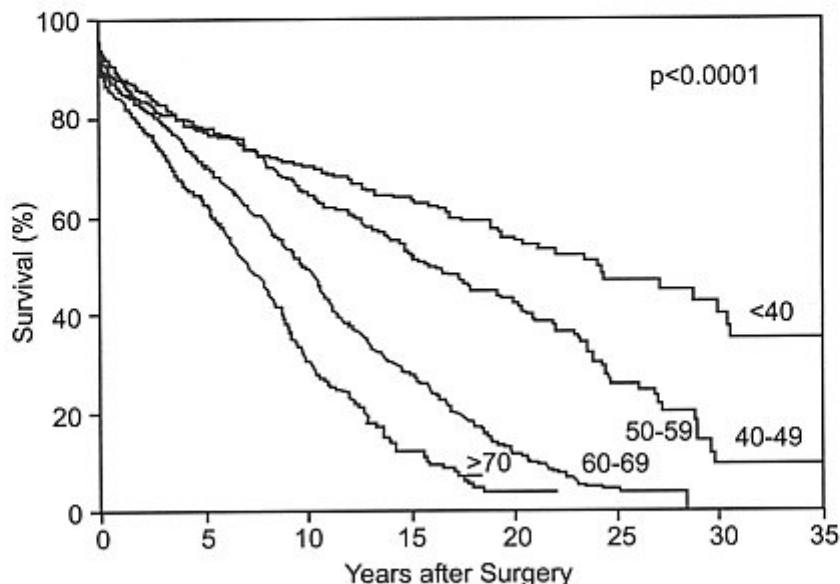


Figure 2. Survival up to 30 years after prosthetic heart valve (PHV) replacement by the patient's age at time of PHV implantation. From reference 22. For limitations of this study, see text.

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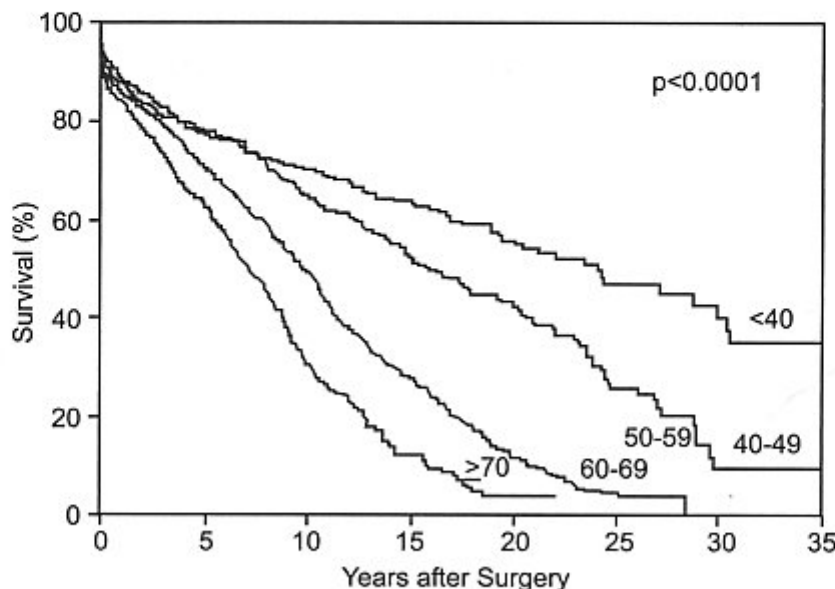


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older one gets, the closer one is to death (an old Asian saying).

Of note, a study of 841 patients undergoing AVR (13) showed that subgroups with lower survival at 10 years were those with renal disease at any age (survival, $27 \pm 8\%$), lung disease in patients older than 60 years (survival, $30 \pm 6\%$), left ventricular ejection fraction (LVEF) <0.40 ($35 \pm 6\%$), CAD any age (survival, $35 \pm 5\%$), and age >65 years (survival, $41 \pm 4\%$).

These data indicate that patient characteristics at baseline are a major determinant of late mortality after PHV replacement.

"Older" valves versus "newer" valves. In the 1960s and 1970s, patients with severe aortic stenosis in NYHA functional classes III and IV and clinical heart failure had AVR with use of the #1260 Starr-Edwards valve (23). After AVR, LVEF increased from $0.34 \pm 0.03\%$ to $0.63 \pm 0.05\%$, heart failure was relieved, 91% of the patients were in NYHA functional classes I and II; the 7-year survival was $67 \pm 11\%$ and, in operative survivors, was $84 \pm 10\%$. This is better than the known $\geq 90\%$ mortality at one to two years in medically treated patients with severe aortic stenosis and heart failure (24).

Data from the Mayo Clinic (9) showed that, with use of the Starr-Edwards model #1260 valve, the 10- and 20-year survival after AVR was 60% and 35% (Table 1); the incidence of thromboembolism was 1.4% per year. Albert Starr's data of event rates with Starr-Edwards valves #1260 and #6120 up to 30 years after AVR and MVR are good (25). Preliminary data (five years) from a prospective randomized trial from London, UK, showed no statistically significant difference in patient outcomes between the St. Jude and Starr-Edwards valves (26). Mortality and complication rates in patients with use of various PHVs with follow-up longer than 10 years are described in detail (vide supra and infra) and indicate there were no major differences in patient outcomes with use of the various PHVs among mechanical PHV and among bioprosthesis. In the DVA trial, there was not a single instance of SVD with the "old" Bjork-Shiley valve to 18 years of follow-up (6). In summary, there is no good evidence that, in patients with similar or "identical" characteristics at baseline, patient outcomes are better with "newer good" PHVs than with "older good" PHVs.

Complications of PHVs. To approve a PHV, the FDA (27,28) requires studies with ≥ 800 valve years of follow-up. The incidence of complications should be ≤ 2 optimal performance characteristics (OPC) determined by the FDA, which were calculated to allow an alpha error of 5% ($p < 0.05$) and beta error of 20% (power of 80%).

A review (29) of mechanical valves comprising 95 published series, 37,253 valves, and 187,220 valve-years of follow-up and of biological valves (porcine, pericardial, and homograft) comprising 70 published series, 24,202 valves, and 132,519 valve years of follow-up shows: 1) there is no significant difference among the various mechanical valves

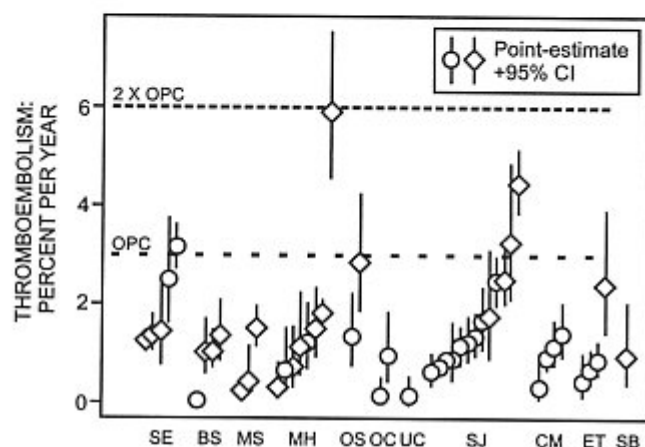


Figure 3. Thromboembolism rates for mechanical aortic valves. The vertical axis is the linearized rate in percentage per year. Each symbol represents one series. Circles indicate that only late events were used to calculate the rates; diamonds indicate that both early and late events were used. BS = Bjork Shiley; CM = Carbomedics; ET = Edwards Tekoa or Duromedics; MH = Medtronic Hall; MS = Monostrut; OC = Omniscience; OS = Omniscience; SB = Sorbin Bicarbon; SE = Starr Edwards; SJ = St. Jude; UC = Ultracor. From reference 29.

for thromboembolism (Fig. 3), and also among the various bioprosthesis; this is also true for rates of thrombosis, bleeding, endocarditis, and leak; they are also within the $2 + OPC$ s; 2) the incidence of thromboembolism is higher in patients with mitral PHV than in those with aortic PHV; 3) bioprosthesis are not free of thromboembolic risk, but the risk is lower than with use of a mechanical valve; 4) complication rates with use of the same brand of PHV varies widely; and 5) the risk of SVD with all currently used mechanical valves is "negligible" (29) (i.e., very small). These findings reconfirm that, with the use of FDA-approved PHV, these complications are largely related to factors other than the type of PHV.

Patients undergoing PHV implantation with a mechanical valve who are at the lowest risk of thromboembolism are those in sinus rhythm; have normal left ventricular function; have not had previous thromboembolism; do not smoke; do not have thrombus in left ventricle and/or left atrium, coronary or carotid disease, diabetes or hypertension; are seronegative for *Chlamydia pneumoniae*; have adequate and low anticoagulation variability; and do not have clotting disorder(s) (3,30-32).

Bleeding. The bleeding rates associated with use of a variety of mechanical aortic valves and with a variety of mechanical mitral valves are similar (29). The data on bleeding in the two trials are discussed in the preceding text. In the randomized trials of anticoagulation in atrial fibrillation, patients average age ranged from 67 to 75 years, the incidence of major bleeding in the placebo group ranged from 0% to 4.6% per year, and the incidence of minor bleeding was up to 10.5% per year, and there were some deaths from bleeding (33-38). The bleeding rates were obtained with follow-up times of about two years; thus, bleeding rates might be higher if obtained over longer

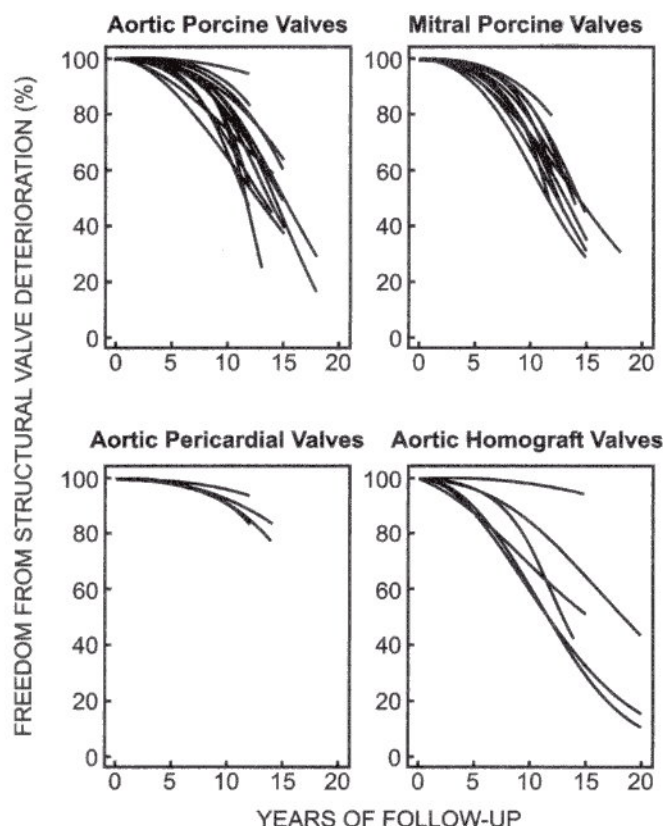


Figure 4. Freedom from structural valve degeneration with four types of biological valves with the superimposed Weibull distribution fits. Modified and adapted from reference 29.

follow-up times. Indeed, in patients with mechanical valves and the same level of anticoagulation, at 7 years, patients >60 years of age had up to seven times the bleeding rate than that of patients <60 years of age (39). In the Stroke Prevention in Atrial Fibrillation III (40) trial with international normalized ratio (INR) of 2.0 to 3.0, the incidence of bleeding was 1.5%/year, which is what one would expect with AVR in sinus rhythm according to current practice. With MVR, it will be somewhat higher because the INR after MVR is maintained at a higher level (6).

SVD. The rate of SVD of bioprostheses is importantly related to: 1) the site of PHV implantation (SVD in MVR > in AVR); (6,8,29), and 2) to the age of the patient at time of PHV implantation (29). In patients age 16 to 39 years, at 10 years, SVD after AVR is 60% and at 16 years is $\geq 90\%$, whereas in patients ≥ 70 years, it is $\leq 15\%$ at 15 years (14). The rate of SVD at 12 years in patients followed for more than 10 years is high with aortic and mitral porcine valves and with aortic homografts (Fig. 4) (29). It is lowest with Carpentier-Edwards pericardial valve for AVR (Fig. 4), which may partly be accounted for by the older age of the patient at the time of PHV implantation (29). In *in vitro* studies, the pericardial aortic valve has lower gradient and larger PHV area when compared with several other PHV (41) and also a larger estimated aortic PHV area in patients in valve sizes 19 to 29 (42) (Fig. 5). These data indicate that

the pericardial aortic valve may be the bioprosthesis of choice in "older" people (≥ 60 to 65 years of age). Patients ≥ 65 to 70 years also have a lower rate of SVD after MVR (30). The rate of SVD is not significantly different for the standard Hancock, Hancock MO, and Carpentier-Edwards porcine valves (43). The rate of SVD of newer porcine valves (Hancock MO and the stentless porcine valve) (16,44) at nine years is within the expected range of SVD of earlier stented porcine valves (43) (Fig. 6), indicating that, at present, all porcine valves have similar rates of SVD.

PHV size. Is it clinically important? Yes and no. The original 1978 report on valve prosthesis-patient mismatch (VP-PM) (45) stated that VP-PM "can be considered to be present when the effective prosthetic valve area, after insertion into the patient, is less than that of a normal human valve. The reduced prosthetic valve area is usually mild to moderate in severity and often of no immediate clinical significance. However, occasionally it can be a severe problem because the patient may be hemodynamically and symptomatically worse after valve replacement," which was subsequently documented (45-47).

Pibarot and Dumesnil's (48) extensive review of VP-PM showed that, depending on its severity, VP-PM may result in higher valve gradients at rest and on exercise, less reduction of left ventricular mass, greater physical limitation, and higher morbidity and mortality.

The present review emphasizes a few features of VP-PM: 1) in patients with severe aortic stenosis, mean aortic valve gradient <30 mm Hg, heart failure, and LVEF <0.35; the only predictor of an operative mortality of 21% was a small prosthesis size (47% for PHV ≤ 21 mm vs. 15% for PHV ≥ 23 mm, $p = 0.03$) (49). In another study, only small body size was identified in the early hazard phase for mortality (50). Thus, an appropriate-sized prosthesis may be more important in the early hazard phase in critically ill patients. A clue to appropriate size may be determined preoperatively (48); 2) Hé et al. (51) have shown that, in patients with small aortic root who received PHV sizes ≤ 21 mm, the only independent predictor of poorer 10-year survival was patient size. In patients with body surface area ≥ 1.7 m² vs. those <1.7 m², the survival was approximately 10% versus 50% ($p = 0.014$). Thus, VP-PM is dependent not only on the small annulus/root but also on the size of the patient. For example, 19-mm valves produced only mild VP-PM in two studies from Asia (52,53), but, in the study from North America, almost half of the patients had moderate or severe VP-PM, the improvement in NYHA functional class was less, and, at five years, the incidence of clinical heart failure was significantly greater ($15 \pm 3\%$ vs. $7 \pm 2\%$, $p = 0.05$) (54). People in some countries are smaller than in others, and in each country women are, on an average, smaller than men. In the study from Pisa, Italy (55), 28% of patients with the 19-mm St. Jude valve had severe VP-PM versus 5% of those with the 21-mm valve ($p = 0.004$). Thus, 82% of patients who received 19-mm PHV did not have severe VP-PM; 89% of patients who received the 19-mm valve

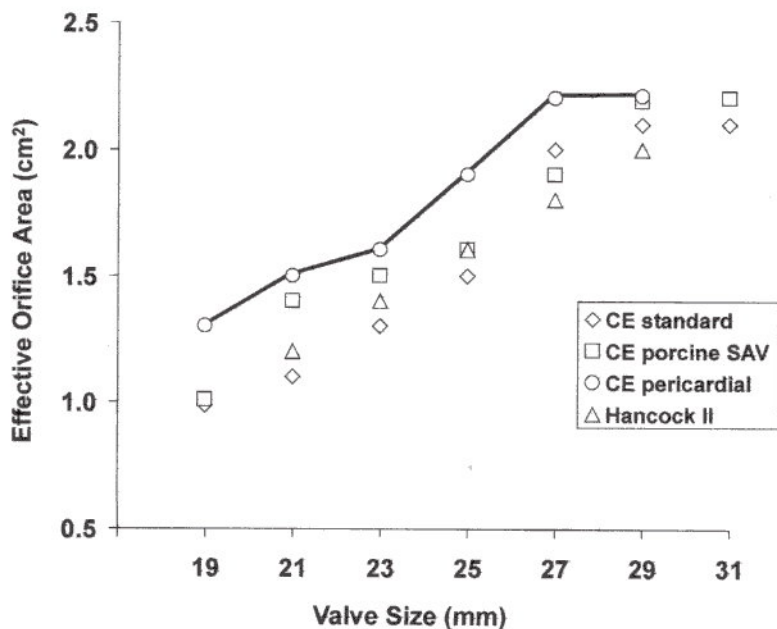


Figure 5. Estimated effective orifice area (prosthetic heart valve [PHV] area) of four different bioprostheses based on manufacturer's specifications for each valve size. Figure constructed from data in Table 1 in reference 42. Carpentier-Edwards (C-E) pericardial valve (line) has the largest PHV area in valve sizes 19 to 29 mm. Although the actual PHV areas after PHV insertion will be lower, starting with a larger valve area is an advantage that could be important. SAV = supra-annular valve.

were women, indicating that smaller patients who receive a small PHV may not have severe VP-PM; 3) associated CABG was an independent predictor of mortality in the He et al. (51) study; the 10-year survival of those who had associated CABG versus those who did not was approximately 35% versus 60%, $p = 0.0002$ (51). In the Connolly et al. study (49), the 3- and 5-year survival of those with CAD was 58% and 28% (49), and, in those without CAD, was 71% and 71% (49); 4) on the other hand, another study (50) stated that, after AVR patients who received ≤ 19 mm, PHV had a similar long-term survival as those who had

received larger PHV and concluded that moderate VP-PM appears not to adversely affect survival. This suggestion is not new (45). The study is problematic because: 1) patients undergoing simultaneous CABG were excluded; 2) smaller patients had received a smaller size PHV; thus, PHV area corrected for body size needs to be calculated. The PHV area was calculated on the manufacturer's stated in vitro size of the inserted PHV and not on the PHV area weeks and months after insertion into the patient. The manufacturers stated in vitro valve size does not necessarily mean all valves of any one size, even of the same brand, have exactly the

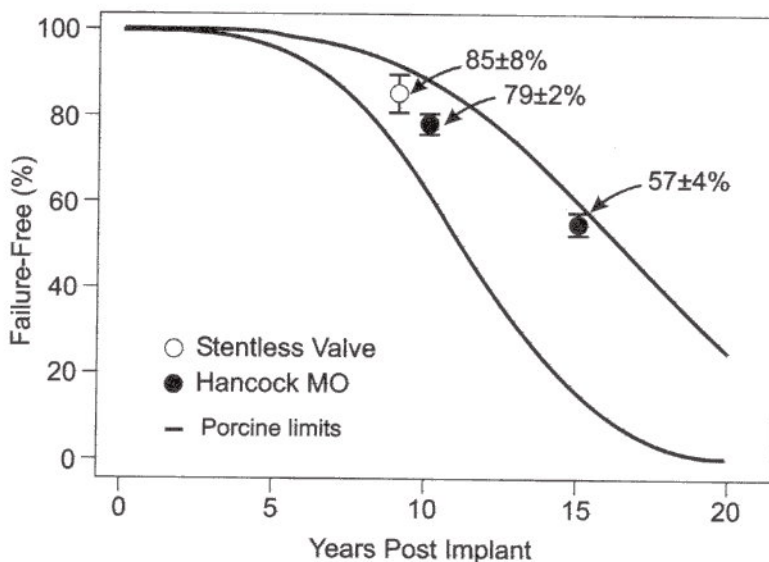
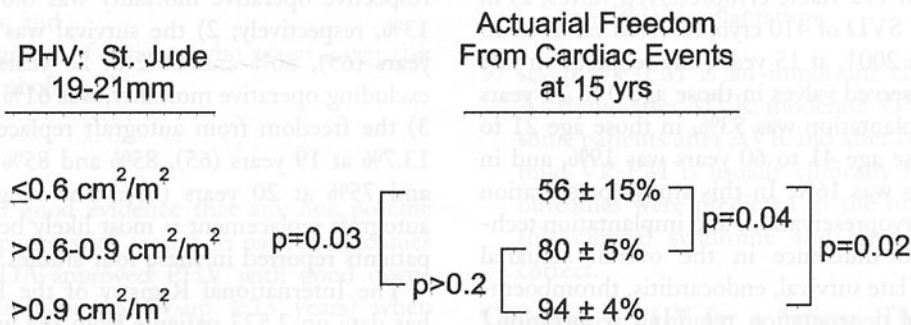
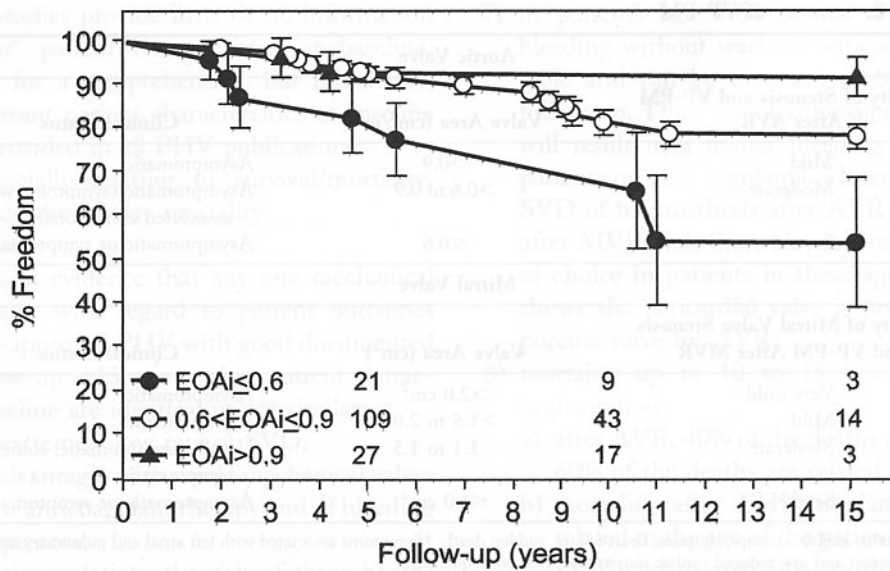


Figure 6. Failure-free rate of the Hancock modified orifice (MO) valve (from reference 16) and the stentless valve (from reference 44). "Porcine limits" are the limits of failure of stented bioprostheses failure rates (from reference 43).



Milano AD et al. *Ann Thorac Surg* 2002;73:37-43

Figure 7. Percentage actuarial freedom from cardiac events up to 15 years of the St. Jude 19- to 21-mm valves by the prosthetic heart valve (PHV) effective orifice area index (EOAi) (calculated from the echocardiographic/Doppler valve area obtained at time of hospital discharge after PHV insertion). Adapted from reference 55.

same PHV area (48). Moreover, after PHV insertion, tissue in-growth and endothelialization occur the extent of which varies from patient to patient. Both of these factors result in a range of PHV areas for any given valve size (56). Furthermore, multiple, complex statistical analyses were used to determine PHV areas (50); 3) data were not provided on the causes of late deaths. It is possible that most patients with PHV < 19 mm might have died of causes related to PHV, whereas, in those with larger PHV, most patients might have died of causes not related to the PHV. Note that, in the DVA trial, after AVR, only 40% of late deaths were prosthesis-related; and 4) there was no information about the patients functional class, symptomatic status, cardiac function, and complications, such as heart failure; 5) the study of Milano et al. from Pisa, Italy (55), showed that, at 15 years, patients who received a 19-mm St. Jude valve when compared with those who received the 21-mm St. Jude valve had a poorer NYHA functional class; less left ventricular mass reduction; and had a higher

incidence of severe VP-PM (18% vs. 5%, p = 0.004); congestive heart failure (7.5 ± 0.8 vs. 0.5 ± 0.2%, p = 0.002); valve-related death, including sudden death (16 ± 6% vs. 10 ± 5%, p = 0.02); and cardiac events (43 ± 13% vs. 14 ± 4%, p = 0.008). Valve prosthesis-patient mismatch was calculated on basis of PHV area obtained by echocardiography/Doppler at time of hospital discharge after PHV implantation, and those with severe VP-PM had higher cardiac event rates (Fig. 7).

For long-term outcomes, the issue is not PHV size before valve replacement but the effective prosthetic valve area month(s) (? 6 months [56]; ? 12 months [48]) after insertion into the patient and on the patient's body size. The outcome of the patient depends on patient-related and other factors and also on whether PHV produces mild, moderate, or severe VP-PM (Table 2).

Homografts (allografts). Homografts for AVR have a similar rate of SVD as bioprosthesis (Fig. 4) (29). O'Brien et al. (57-59) reported: 1) in 1987, a 0% incidence of SVD

Table 2. Severity of VP-PM

Aortic Valve		
Severity of Stenosis and VP-PM After AVR	Valve Area (cm ² /m ²)	Clinical Status
Mild	>0.9	Asymptomatic
Moderate	>0.6 to 0.9	Asymptomatic (symptoms with associated conditions)
Severe	≤0.6	Asymptomatic or symptomatic*
Mitral Valve		
Severity of Mitral Valve Stenosis and VP-PM After MVR	Valve Area (cm ²)	Clinical Status
Very mild	>2.0 cm ²	Asymptomatic
Mild	>1.5 to 2.0	Asymptomatic
Moderate	1.1 to 1.5	Usually asymptomatic, some symptomatic
Severe	≤1.0 cm ²	Asymptomatic or symptomatic†

*Symptoms: angina, syncope, dyspnea, heart failure, sudden death; †Symptoms associated with left atrial and pulmonary arterial hypertension and low reduced cardiac output and their consequences.

AVR = aortic valve replacement; MVR = mitral valve replacement; VP-PM = valve prosthesis-patient mismatch.

at 10 and 15 years in 192 viable cryopreserved valves; 2) in 1991, the "assumed" SVD of 410 cryopreserved valves at 15 years was 15%; 3) in 2001, at 15 years, the reoperation rate for SVD off cryopreserved valves in those age 0 to 20 years at time of PHV implantation was 53%, in those age 21 to 40 was 15%, in those age 41 to 60 years was 19%, and in those age >60 years was 16%. In this study "preservation techniques (4°C or cryopreservation) and implantation techniques displayed no difference in the overall actuarial 20-year incidence of late survival, endocarditis, thromboembolism, or structural degeneration requiring reoperation," and 4) in 2002, of 570 patients (age: 48 ± 16 years) with cryopreserved homografts undergoing echocardiographic/Doppler study at 6.8 ± 4.1 years after AVR, 72.1% patients had signs of homograft dysfunction (i.e., SVD) on echocardiography (60). By American College of Cardiology/American Heart Association guidelines criteria for aortic stenosis, severe stenosis was present in 2.5% and moderate stenosis in 10%; moderate to severe regurgitation was present in 15.4%. It needs to be emphasized that reoperation rates for SVD may not account for all SVD.

The pulmonary autograft for AVR (Ross principle) (61).

The Ross principle is a more complex and more difficult procedure, but has at least some very major advantages, namely, when inserted in children, the valve "grows" (increases in size) as the child grows, and pregnancy may not result in SVD (61,62). The incidence of thromboemboli was 0% to 1.2% per year; of infective endocarditis, was 0% to 1.2% per year; the rate of reoperation within the first six months was 0%, 1.5%, and 3.8% in three different studies, and in one small study was 10%, and late reoperation rates ranged from 0.4% to 1.5% per year (29). Those with rheumatic heart valve disease (63,64) may develop rheumatic valvulitis in the autograft.

The only studies with follow-up greater than 10 years are four from Ross's group (65-68). In these four studies: 1) the

respective operative mortality was 6.6%, 7.4%, 7.4%, and 13%, respectively; 2) the survival was 57.3 ± 9.6% at 19 years (65), 80% and 80% at 20 years (66,67), and, after excluding operative mortality, was 61% at 20 years (68); and 3) the freedom from autograft replacement was 48.5% ± 13.7% at 19 years (65), 85% and 85% at 20 years (66,67), and 75% at 20 years (68). The range of freedom from autograft replacement is most likely because of selection of patients reported in these four studies.

The International Registry of the Ross Procedure (69) has data on 2,523 patients from the world. There are very major concerns about the information in this database: 1) data entry is voluntary; the Registry has no information whether all patients from any one center are reported to the Registry, 2) follow-up data are available in only 70%, and 3) there is no information about the extent and completeness of the available follow-up data. They report the incidence of reoperation was 10.1% and of ≥2+ aortic regurgitation was 14% (69).

Conclusions. From the data cited, the following general conclusions are possible:

- 1) since the introduction of mechanical PHV in 1960 and of homograft valves in 1962 to 1964, advances in PHV have occurred in comparatively small increments except for the introduction of bioprosthesis and of the autograft;
- 2) the results of valve surgery with regard to survival, complications, cardiac function, and functional class are importantly dependent on patient-related factors and also on type of surgery, type of prosthesis, and healthcare-delivery related factors. Thus, one should not compare, or at least be extremely cautious about comparing, outcomes with use of different PHV or even the same brand of PHV from different studies unless the baseline characteristics of the patients is identical or at least very similar;

- 3) most published studies provide little or no information about "important" patient characteristics at baseline. There is a need for a comprehensive, but reasonable, number of important patient characteristics at baseline that should be provided in all PHV publications;
 - 4) late results, especially relating to survival/mortality, should not exclude the 30-day mortality.
 - 5) mechanical valves:
 - a) there is no good evidence that any one mechanical valve is superior with regard to patient outcomes (among FDA-approved PHV with good documented results at follow-up ≥ 15 years) when patient characteristics at baseline are identical or are similar;
 - b) they have an extremely low rate of SVD;
 - c) the major disadvantages with use of mechanical valves are the need for anticoagulant therapy and of bleeding and its consequences;
 - d) with good anticoagulation, the risk of thromboembolism with use of a mechanical PHV valve is similar to that with use of bioprosthetic PHV without anticoagulants; and
 - e) there is a subgroup of patients who are at lower risk for thromboembolism.
 - 6) biological valves:
 - a) bioprostheses:
 - 1) there is no good evidence that any one porcine valve is superior with regard to patient outcomes (among FDA-approved PHV with good documented results at follow-up ≥ 15 years) when patient characteristics at baseline are identical or are similar;
 - 2) SVD begins at year 5 after MVR and year 8 after AVR;
 - 3) SVD is greater after MVR than after AVR;
 - 4) a minimum follow-up of ≥ 15 years is necessary to evaluate the incidence of SVD of FDA-approved PHV;
 - 5) the younger the patient at time of PHV implantation, the higher the rate of SVD;
 - 6) the major disadvantages with use of bioprosthesis are the incidence of SVD and of reoperation and their consequences including mortality;
 - 7) if patients with biological valves need anticoagulation, bleeding rates will be similar to that with use of mechanical valves;
 - 8) the SVD of a stentless porcine valve is similar to that of a stented porcine valve;
 - 9) data on patient outcomes ≥ 10 to 15 years after PHV using stentless porcine valves are needed;
 - b) there is no proven benefit in patient outcomes and of SVD with use of a homograft when compared with a bioprosthesis; and
 - c) more good studies with follow-up of ≥ 15 years are needed in adults with use of pulmonary autografts;
 - 7) in patients age ≥ 60 to 65 years, the incidence of bleeding without warfarin anticoagulation is not negligible and can be expected to be greater with longer follow-up. Thus, use of anticoagulants in this age group will result in a higher bleeding rate than in younger patients on anticoagulants. Moreover, in this age group, SVD of bioprosthesis after AVR is very low and is low after MVR and, thus, bioprosthesis would be the PHV of choice in patients in these age groups; current data shows the pericardial valve is probably superior to the porcine valve for AVR;
 - 8) mortality up to 10 to 15 years is high after PHV implantation:
 - a) after AVR, 40% of the deaths and after MVR 40% to 60% of the deaths are related to the PHV;
 - b) mortality after PHV implantation is importantly related to the age of the patient at time of insertion of PHV and to associated cardiac and noncardiac comorbid conditions; and
 - c) subgroups of patients have a low survival at 10 years after PHV implantation;
 - 9) severe VP-PM is an important clinical problem after AVR and after MVR; moderate VP-PM is a problem in some patients after AVR and after MVR; uncomplicated mild VP-PM is usually clinically not important; these outcomes were predicted in the original description of this clinical syndrome and have been shown to be correct.
- Choosing a PHV for a patient.** The following factors/issues have to be considered in choosing a PHV for an individual patient: 1) known long-term results of PHV from randomized trials and databases; 2) patient characteristics: age, associated cardiovascular lesions, and comorbid conditions; 3) expected survival of the patient based on age and gender of patients, associated cardiovascular and other comorbid conditions and known outcomes described above; 4) unique patient needs; 5) complete and accurate discussion and information of all of the above with the patient; and 6) joint decision by patient, cardiologist, and cardiac surgeon.
- A suggested algorithm for choice of PHV for AVR for those age ≥ 60 to 65 years and age < 60 years is shown in Figure 8. For MVR, the algorithm is the same except the split by age is ≥ 65 to 70 years and age < 65 years. There are exceptions. At least three issues need to be emphasized:
- 1) bioprosthetic SVD after AVR is not reduced suddenly at age 65 years or after MVR at age 70; in other words, the major reduced rate of SVD begins a few years (5 to 10 years) earlier. Thus, if the patient is willing to accept a "small" increased risk of SVD if PHV were to be implanted five years earlier for the benefit of not needing anticoagulant treatment with use of mechanical PHV, then the decision to insert a bioprosthetic PHV at that age may be reasonable;

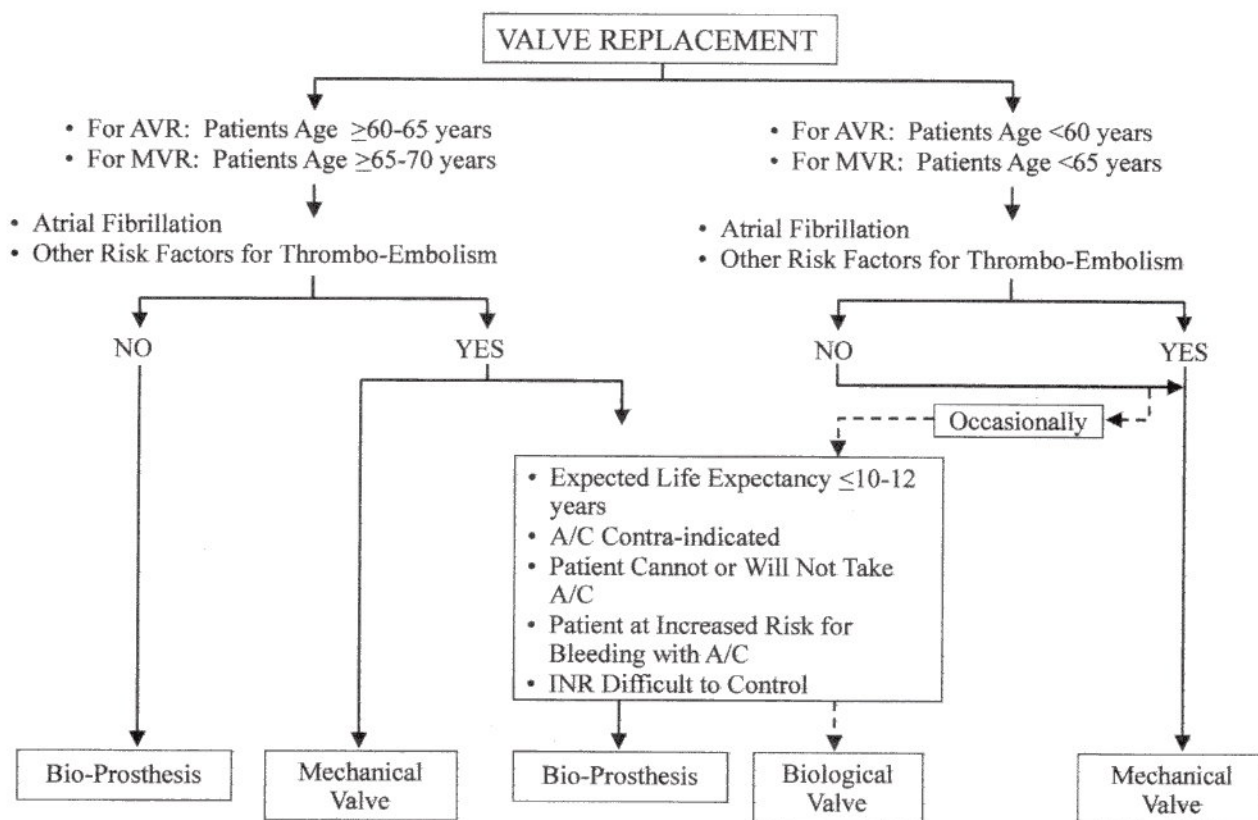


Figure 8. An algorithm for choice of prosthetic heart valve. A/C = anticoagulation; AVR = aortic valve replacement; INR = international normalized ratio; MVR = mitral valve replacement.

- 2) in certain circumstances, even though the patient needs anticoagulant therapy for other indications such as atrial fibrillation, it might still be preferable to insert a bio-prosthetic valve. For example, a patient age 60 to 70 years who has atrial fibrillation is at an increased risk of thromboemboli but is also at an increased risk of bleeding with anticoagulant therapy. If bleeding requires discontinuing warfarin therapy for an extended period of time, then this puts the mechanical valve at risk of thrombosis; therefore, one could consider insertion of a bioprosthetic PHV; and
- 3) reoperating on older patients for SVD must be kept in perspective. For example, in a patient age 65 years who needs MVR and does not need anticoagulation for another reason, the need of reoperating on this patient at age 80 years for SVD may be small. The probability of being alive 15 years after MVR may be 20%, and, if the probability of SVD at this age is, say, 25%, then, if initially 100 patients had MVR with a bioprosthetic valve, only 4 of the initial 100 patients will need reoperation.

It needs to be reemphasized that: 1) the patient is taking the risks of complications from a choice of PHV and not the physicians; 2) the cardiologist is the physician taking care of the patient before PHV implantation and on follow-up; 3) the surgeon is implanting the PHV and its replacement; 4) therefore, the choice of PHV must be a joint decision by the

patient, cardiologist, and cardiac surgeon after a full and complete discussion of the risks and benefits, described in the preceding text, with the patient; and 5) both the cardiologist and cardiac surgeon who are in the decision-making process of choice of PHV should be very knowledgeable about all the known patient outcomes with use of various PHVs.

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