Is Tissue Valve the Preferred Option for Patients Aged 60 Years and Older?

Selection of Aortic Valve Prostheses: Contemporary Reappraisal of Mechanical Versus Biologic Valve Substitutes

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Approximately 200,000 patients worldwide undergo aortic valve replacement (AVR) each year. The selection of an appropriate valve substitute is often a complex decision influenced by both patient and physician preferences. The basic choices available for surgical AVR include mechanical prosthetic valves (largely bileaflet) and biological (porcine or bovine pericardial). Mechanical valves are characterized by excellent structural durability but require lifelong systemic anticoagulation. In contrast, bioprostheses may free patients from valve-related oral anticoagulation, but structural valve failure often necessitates reoperation 10 to 15 years after implantation. Furthermore, degeneration of biological valves occurs more rapidly in younger patients in comparison with those of advanced age. Other valve substitutes, such as aortic valve homografts and pulmonary autografts (Ross procedure), are usually reserved for special circumstances such as aortic root reconstruction following infection (homografts) or young patients who have not achieved full somatic growth (pulmonary autografts) because of technical complexity of implantation and inconstant durability.

Response by Kaneko et al on p 1380

Current guidelines for selection of valve prostheses based on clinical data, including 2 randomized trials, recommend use of bioprosthetic valves in patients aged ≥65 years because (1) the risk of structural valve degeneration is low in elderly patients, and (2) there are advantages in avoiding systemic anticoagulation in frail patients with additional morbidities. Much of these data were derived from clinical practice 2 to 3 decades ago, however surgical techniques, valve design, and anticoagulation strategies have all markedly evolved. Despite interim changes in clinical practice and recent clinical outcomes data, many clinicians continue to cite antiquated studies advocating use of biological valves in younger patients (<65 years). The aim of using bioprostheses in adults aged <65 years is to decrease the risk of anticoagulant-related hemorrhagic events and to spare patients lifestyle-related restrictions related to warfarin use, however implicit in this strategy are 2 presumptions, first that survival of patients after AVR is similar with mechanical and bioprostheses, and second that current third-generation bioprostheses will have greater durability than the limited longevity associated with earlier designs.

Decision-making has become further complicated by the promise of percutaneous valve-in-valve rescue from the inevitable failure of senescent bioprostheses. Indeed, some cardiologists and surgeons now advise young patients to choose a bioprosthesis for initial valve replacement, reassuring them of the future availability of this therapy. The policy of recommending biological aortic valve prostheses in younger patients, however, assumes generally equivalent outcomes as regards patient survival and nonfatal complications. To understand the evolution in outcomes and rationale regarding aortic prosthesis choice in younger adult patients undergoing AVR, we first will review the historical data from earlier generation prosthetic valve substitutes. We will then analyze the outcomes of current generation devices as detailed in randomized trials, registries, and large observational series.
Patient Survival

During preoperative consultation, many cardiologists and surgeons focus on lifestyle-related considerations (including oral anticoagulant use), morbidity (hemorrhage and thromboembolic complications), and quality of life metrics after surgical AVR. Important in the discussion, yet incompletely understood among some medical professionals (and many patients), are possible differences in long-term survival between various heart valve substitutes.

Randomized Trials and Registry Data

There are, unfortunately, few randomized data to guide decision-making in selection of aortic valve prostheses. Indeed, results from 2 earlier randomized trials of first-generation mechanical and biological heart valves provided conflicting results regarding patient survival. Between 1977 and 1982, The Veterans Affairs Cooperative Study enrolled and randomized 575 men between 50 and 70 years of age to receive a Hancock porcine bioprosthesis or a Björk-Shiley mechanical valve for aortic (n=394) or mitral valve replacement (n=181). At 15-year follow-up of patients having AVR, there was a clear survival benefit of mechanical valves (mortality rate 66% versus 79% for bioprostheses, \( P = 0.02 \)). Primary valve failure accounted for 8 of 63 valve-related deaths in the bioprosthetic AVR group and none in the mechanical valve group.

During the same era, the Edinburgh randomized trial compared the durability and the incidence of valve-related complications of the Björk-Shiley mechanical prosthesis with the Hancock and the Carpentier-Edwards porcine valves. Average age of the 533 patients was 54 years, and 56% were women. A total of 211 had AVR, and both aortic and mitral valves were replaced in 61. The authors noted a trend toward improved actuarial survival after 12 years with the Bjork-Shiley mechanical prosthesis, but this did not continue when the follow-up was extended over 20 years, and there was no significant survival difference between prostheses in the subgroups of patients undergoing AVR, mitral valve replacement, or combined AVR and mitral valve replacement. Interpretations of these trials have been thoroughly discussed and debated, but the results stand despite the fact that the prosthetic designs used in the trial are no longer available. Integrating these results into contemporary practice is confounded further because results were not stratified by age groups, and perioperative mortality was higher than current standards.

Because of the continued uncertainty regarding selection of aortic valve prostheses for patients ages 55 to 70 years, Stassano and colleagues randomized 310 patients to receive either a bioprosthesis (93 Carpentier-Edwards SAV and 62 Carpentier-Edwards Pericardial, Edwards Lifesciences, Irvine, CA) or a mechanical valve (107 St. Jude bileaflet, St. Jude Medical, Inc., St. Paul, MN) and 48 CarboMedics (Sorin SpA, Milan, Italy). The study was conducted between January 1995 and June 2003, and at last follow-up, which averaged 8.8 years, the investigators reported no significant difference in overall survival. On close inspection of the survival curves detailing cardiac-related death, the authors demonstrated a clear trend toward improved survival among patients with a mechanical aortic valve (Figure 1).

Additional recent information suggests that late survival with a mechanical valve may be superior to that seen in patients with bioprostheses. A report of a registry from the Society of Cardiothoracic Surgery in Great Britain and Ireland detailed outcomes of 41227 patients undergoing conventional AVR with or without coronary artery bypass surgery from 2004–2009. The investigators highlighted the increase in volume of procedures in the recent era, the advancing age of patients having AVR, as well as improvement in early postsurgical mortality. They further noted the increased use of biological valves, 65% in 2004 to 2005 versus 78% in 2008 to 2009. Despite relatively short follow-up, the implantation of a mechanical valve was a strong and independent predictor of improved late survival compared to use of a biological device (hazard ratio, 1.46; 95% confidence interval, 1.35–1.57).

Figure 1. Cardiac-related survival of patients who received either MP or BP valves. BP indicates biological prosthesis; and MP, mechanical prosthesis. Adapted from Stassano et al. Authorization for this adaptation has been obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.
Observational Studies

Recruitment of patients to randomized comparisons of aortic valve substitutes is difficult because of strong preferences of cardiologists and surgeons as well as perceptions generated from unfiltered information that patients may obtain from online resources. Single-center observational studies are useful but may also reflect institutional bias regarding selection of valve prostheses. Lund and Bland\textsuperscript{13} summarized the late outcomes of AVR with mechanical and biological devices in a meta-analysis of studies published between 1989 and 2004 using only those series with a maximum follow-up of $\geq 10$ years. In an analysis of 17,439 patients with 101,819 patient-years follow-up, the authors found substantial differences in clinical characteristics of patients receiving mechanical and biological prostheses. Compared with bioprostheses patients, those who had a mechanical aortic valve were generally younger (mean age 58 versus 69 years), and less likely to have coronary artery disease as reflected by less frequent associated coronary artery bypass grafting (16% versus 34%), but more likely to have preoperative endocarditis (7% versus 2%). The overall death rate was lower in patients with mechanical aortic prostheses (3.99 versus 6.33%/patient-year), but the investigators suggested that this difference might be attributable to patient-related variables and concluded that corrected death rate was similar for mechanical and biological prostheses irrespective of age. Again, results of this meta-analysis reflect the outcomes of prior generation valve devices, and direct comparison with contemporary valve substitutes is difficult.

Several recent observational studies have examined late survival after AVR using contemporary biological and mechanical valve prostheses in relatively large cohorts of patients.\textsuperscript{11,16,17} Although these studies differ in several ways, including use of more recent models of biological and mechanical valves, some important trends emerge. A recent series by Weber et al\textsuperscript{17} included patients aged $<60$ years who underwent AVR with or without concomitant procedures. The authors found that propensity-matched patients receiving mechanical valves (bileaflet design, either St Jude Medical, Minneapolis, MN, or ATS Medical, Plymouth, MN) had improved survival 6 years postoperatively (98.0 versus 90.3%, $P=0.038$) compared with those undergoing bioprosthetic AVR with a stented Carpentier-Edwards pericardial tissue valve (model 3000TFX and 3300TFX, Edwards Lifesciences, Irvine, CA). They concluded that because use of a biological valve increased the adjusted mortality risk, there remains insufficient evidence to recommend bioprosthetic valves for AVR in most younger ($<60$ years) patients.

Similar results have been observed in studies of other bileaflet mechanical prostheses. Badhwar et al\textsuperscript{18} performed a propensity-matched analysis of 469 aortic and mitral valve operations in which the Carpentier-Edwards Perimount bovine pericardial prosthesis (Edwards Lifesciences, Irvine, CA), Medtronic Mosaic porcine device (Medtronic, Minneapolis, MN), or On-X bileaflet mechanical (On-X Life Technologies, Austin, TX) valves were used. Five years postoperatively, the authors reported that there was a trend toward lower mortality among patients with mechanical valves ($P<0.30$). Similarly, in patients aged $<65$ years who had AVR, survival at 7.5 years was significantly improved ($P=0.04$) in patients with mechanical valves (Figure 2).

A report from Brown et al\textsuperscript{11} examined the late results of AVR (including those undergoing concomitant coronary artery bypass grafting) using either St Jude bileaflet valves (St Jude Medical Inc, Minneapolis, MN) or a Carpentier-Edwards bioprosthetic valve (model numbers 2625, 2700, and 2800; Edwards Lifesciences LLC, Irvine, CA) in patients aged between 50 and 70 years. Four hundred forty patient pairs were matched for age, sex, associated coronary artery bypass grafting, and valve size. The 5- and 10-year survivals of the matched pairs were 87% and 68% for patients having mechanical valves and 72% and 50% for patients receiving bioprosthetic valves ($P<0.01$). After further adjustment for unmatched variables that significantly impacted prognosis, patients with mechanical AVR had substantially lower independent likelihood of late death (hazard ratio, 0.46; $P<0.01$) compared to patients with bioprostheses. It is important to note that these findings in individuals aged 50 to 70 years contrast with our experience in elderly ($\geq 70$ years) patients where survival after AVR was related to comorbidities and not to valve type alone.\textsuperscript{19}

Additional information regarding the influence of valve type on survival comes from Jamieson et al.,\textsuperscript{16} who reviewed 3343 patients undergoing AVR to determine the impact of patient-prosthesis mismatch. Although mismatch did not influence late survival, independent predictors of overall mortality included older age, New York Heart Association (NYHA) III/IV functional class, and use of a biological device in the aortic position (relative risk, 1.2; $P=0.018$).
To gain further insight into influence of valve selection on survival after AVR, we analyzed the outcome of patients age <70 years and excluded those with confounding prognostic variables such as significant coronary disease, associated aortic disease, or mitral, tricuspid, or pulmonary valve surgery. Patients with aortic homografts or pulmonary autografts were also not included in this analysis. Patient characteristics were prospectively recorded, and this analysis was approved by the Mayo Clinic Institutional Review Board.

**Patient Characteristics and Operative Details**

Between 1993 and 2009, a total of 2066 patients underwent isolated AVR and met all inclusion criteria; 741 (35.9%) were women, and the mean (SD) age was 64 (13) years (median, 68 years). A total of 1156 patients received an aortic bioprosthesis, and 910 had a mechanical valve. Mean follow-up was 5.2 (4.5) years. In unadjusted comparisons, the groups differed in several respects; patients who had a biological valve were less likely to be men (61.5% versus 67.5%, \( P = 0.005 \)), were older (mean [SD] age, 70.2 [9.3] versus 56.7 [12.1] y; \( P < 0.001 \)), had a greater likelihood of NYHA functional class III or IV status (58.4% versus 53.9%; \( P = 0.04 \)), were more likely to have smoked previously (56.5% versus 51.7%; \( P = 0.03 \)), had a higher Charlson comorbidity index (mean [SD], 3.0 [3.3] versus 2.3 [2.8]; \( P < 0.001 \)), but were less likely to have undergone prior cardiac surgery (17.2% versus 23.4%; \( P < 0.001 \); Table 1).

From the cohort of 2066 patients, 820 patients (410 mechanical valves, 410 bioprosthetic valves) were matched one-to-one according to propensity score. Baseline characteristics were similar after matching (Table 1) except that patients with mechanical AVR were more likely to have had prior heart surgery (27.8% versus 14.1%, \( P < 0.001 \)).

**Survival of AVR Patients With Mechanical and Bioprosthetic Valves**

Overall late survival was significantly better among patients in the mechanical valve group than in patients with bioprostheses (\( P < 0.001 \); Figure 3). After propensity matching, 5-year (81.3% versus 78.1%), 10-year (57.7% versus 50.7%), and 15-year (32.9% versus 17.8%) survivals were all still superior in patients receiving a mechanical valve in the aortic position (\( P = 0.03 \); Figure 4 and Table 2).

**Predictors of Overall Mortality**

Univariate and multivariate predictors of mortality were obtained using regression analysis and are shown in Table 3.
Use of a bioprosthetic aortic valve (hazard ratio, 1.27; \( P = 0.03 \)) was an independent predictor of lower late survival. Further, an exploratory multivariate model demonstrated that the interaction between valve type and age was not significant \( (P=0.13) \), suggesting that there was a protective effect of mechanical valves on late survival in all age categories of patients who were aged <70 years at implantation.

**Late Complications Related to Aortic Valve Prostheses: Thrombosis, Thromboembolism, Hemorrhage, and Reoperations**

Nonfatal complications of prosthetic valves are often considered and reported as combined end points, such as “valve-related morbidity”\(^2\) and, more recently, as “clinical efficacy” or “time-related valve safety.”\(^2\) Some late complications of aortic valve prostheses, such as bland paravalvular leakage and pannus ingrowth, are related to healing of sewing rings and occur infrequently but at generally similar rates with bioprostheses and mechanical valves. Similarly, because there is no evidence that the risk of early or late endocarditis varies between biological and mechanical devices, any differences in late complications relate mainly to thromboembolism, bleeding, and reoperation.

**Randomized Trial Data**

The Veterans Affairs Randomized Trial reported no differences in overall valve-related complications comparing mechanical valves and bioprostheses 15 years postoperatively.\(^5\) There was a greater incidence of bleeding after mechanical AVR, 51\% versus 30\% \( (P=0.0001) \), but the risk of primary valve failure was higher in patients with bioprostheses 23\% versus 0\%, \( (P=0.001) \). Important and consistent findings in this and all other comparative studies of valve types are the similar late risks of thromboembolism and endocarditis among patients having mechanical valves (using systemic Warfarin anticoagulation) and those with bioprostheses.

The Edinburgh Trial also demonstrated equivalent late risks of embolic complications comparing Bjork-Shiley-valve group and porcine-valves.\(^4\)\(^,\)\(^7\) Further, at 20 years postoperatively, major bleeding episodes were recorded in 37.8\% of AVR patients with mechanical valves compared with 32\% of those with bioprostheses. Although this difference reached statistical significance \( (P=0.021) \), the high risk of bleeding in AVR patients receiving bioprosthetic valves is notable. A likely explanation for this is the frequent use of Warfarin in patients randomized to receive a bioprosthesis. Five years after AVR 15\% of those with a bioprosthesis were receiving Warfarin, and by 15 years this proportion had risen to 33\%.

In the more current randomized trial of Stassano et al,\(^1\) there were also no differences in late risks of thromboembolism or endocarditis comparing mechanical valves and bioprostheses. Interesting is the fact that the authors concluded that the yearly risk of bleeding was similar for mechanical [1.47\% (0.81–2.13)] versus biological [0.72\% (0.25–0.19)] aortic valves \( (P=0.08) \).

**Figure 4.** Overall survival for matched patients. Kaplan–Meier curves estimating overall survival according to valve type \( (n=410; \) mechanical [solid line] vs bioprosthetic \( [n=410; \) dashed line]) in matched patients undergoing isolated aortic valve replacement.

**Table 2. Survival After Mechanical Versus Bioprosthetic Aortic Valve Replacement by Age Category**

<table>
<thead>
<tr>
<th>Age Category</th>
<th>Mechanical Valve</th>
<th>Bioprosthetic Valve</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Deaths</td>
<td>Survival*</td>
</tr>
<tr>
<td></td>
<td>20–39 y ( (n=96) )</td>
<td>P=0.97 †</td>
</tr>
<tr>
<td></td>
<td>43–59 y ( (n=382) )</td>
<td>P=0.053 †</td>
</tr>
<tr>
<td></td>
<td>≥60 y ( (n=432) )</td>
<td>P=0.001 †</td>
</tr>
<tr>
<td>1-y</td>
<td>97.2%</td>
<td>(93.3%–100.0%)</td>
</tr>
<tr>
<td></td>
<td>97.5%</td>
<td>(95.7%–99.2%)</td>
</tr>
<tr>
<td></td>
<td>95.7%</td>
<td>(93.7%–97.7%)</td>
</tr>
<tr>
<td>5-y</td>
<td>95.2%</td>
<td>(89.8%–100.0%)</td>
</tr>
<tr>
<td></td>
<td>91.2%</td>
<td>(87.9%–94.7%)</td>
</tr>
<tr>
<td></td>
<td>82.1%</td>
<td>(78.2%–86.2%)</td>
</tr>
<tr>
<td>10-y</td>
<td>95.2%</td>
<td>(89.8%–100.0%)</td>
</tr>
<tr>
<td></td>
<td>79.7%</td>
<td>(74.2%–85.6%)</td>
</tr>
<tr>
<td></td>
<td>62.0%</td>
<td>(56.6%–67.9%)</td>
</tr>
<tr>
<td>15-y</td>
<td>89.2%</td>
<td>(77.6%–100.0%)</td>
</tr>
<tr>
<td></td>
<td>63.3%</td>
<td>(54.8%–73.3%)</td>
</tr>
<tr>
<td></td>
<td>36.7%</td>
<td>(29.9%–45.1%)</td>
</tr>
</tbody>
</table>

*Values are survival percentage (95\% CI).
†Comparison of survival vs bioprosthetic valve recipients in the same age category.
Table 3. Univariate and Multivariate Risk Factor Analysis for Mortality in Patients Undergoing Aortic Valve Replacement

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Univariate</th>
<th></th>
<th></th>
<th>Multivariate</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR</td>
<td>P Value</td>
<td>HR</td>
<td>P Value</td>
<td>HR</td>
<td>P Value</td>
</tr>
<tr>
<td>Age, per 1-y increase</td>
<td>1.06</td>
<td>&lt;0.001</td>
<td>1.05</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI, per 1-point increase</td>
<td>1.02</td>
<td>.01</td>
<td>…</td>
<td>…</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF (per 10% decrease)</td>
<td>1.02</td>
<td>&lt;0.001</td>
<td>1.01</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NYHA class III or IV</td>
<td>2.48</td>
<td>&lt;0.001</td>
<td>1.81</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking history</td>
<td>1.37</td>
<td>&lt;0.001</td>
<td>1.32</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Charlson index ≥2</td>
<td>1.87</td>
<td>&lt;0.001</td>
<td>1.46</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bioprosthesis</td>
<td>2.41</td>
<td>&lt;0.001</td>
<td>1.27</td>
<td>.03</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BMI indicates body mass index; HR, hazard ratio; LVEF, left ventricular ejection fraction; and NYHA, New York Heart Association.

Observational Studies

The recent publication by Weber et al17 as well as the investigation of Brown and associates of patients 50 to 70 years of age11 reported similar rates of late stroke or other embolic events (and endocarditis) among patients with mechanical prostheses in comparison to those having bioprosthetic valves. Noteworthy again was the fact that 19% of patients with bioprosthetic valves were maintained on Warfarin at last follow-up.11 In the most recent study from our Clinic of patients aged <70 years undergoing AVR (described above), 158 matched pairs with complete follow-up, also had equivalent freedom from late complications at 5, 10, and 15 years (P=0.55; Figure 5).

In the very recent study of Badhwar et al.18 late risks of thromboembolism and bleeding were strikingly low and, again, similar in patients receiving a bioprosthesis or the On-X mechanical valve. The authors carefully managed anticoagulation in patients with home international normalized ratio (INR) monitoring using a target INR of 2.0. Using this protocol, there were no bleeding complications in patients with mechanical valves. Importantly, at a median follow-up of 4 years, risk of thromboembolism was only 0.77% per patient-year among patients with mechanical valve compared with 0.78% per patient-year for patients with bioprostheses.

These impressively low risks of bleeding and thromboembolism after mechanical aortic valve replacement are not unique to one prosthesis or locale. Recently, Nishida et al21a presented current follow-up of 763 patients who received CarboMedics bileaflet mechanical heart valves (Carbomedics, Inc, Austin, TX). Among the 220 patients who had primary aortic valve replacement, rates of bleeding and thromboembolism over a mean follow-up of 12 years were 0.65 and 0.8%/pt-year, respectively. There were no instances of thrombosis of the Carbomedics aortic prosthesis.21a

The concern regarding the difficulty of anticoagulation may be overemphasized, especially in elderly patients. Two recent studies from Italy assessed quality of life in elderly patients having mechanical or bioprosthetic aortic valve replacement. Both Vichio et al22 and de Vincentiis et al23 demonstrated excellent quality of life scores in octogenarians after AVR overall, and there was no difference in scores between patients having mechanical or bioprosthetic valves. Interestingly, in both of these series, survival rates were higher in patients with mechanical prostheses. The potential impact of prosthesis “noise” upon quality of life is difficult to quantify and perhaps consequently, has received less attention in decision-making algorithms to date.

Standardized anticoagulation protocols and patient self-testing have enhanced the feasibility and safety of oral anticoagulant therapy. Self-testing of INR and self-management of warfarin minimize lifestyle disturbance, and these options should be accurately presented to patients during discussion of the risks and benefits of prosthesis choice in contemporary heart valve practice.24-26

Biological Devices in Younger Patients?

Ruel and colleagues27 examined outcomes after bioprosthetic or mechanical valve implantation in those younger than 60 years and reported no significant prosthesis- or age-related differences in late survival. The study population, however, included those having aortic and mitral valve replacements along with other concomitant surgical procedures that might be expected to influence prognosis. Also, van Geldorp et al.,28 using a computer-generated model of outcome after AVR (including those undergoing concomitant coronary artery bypass grafting surgery), suggested that event-free survival may theoretically be higher (mathematically simulated) after valve replacement with a prior generation bioprosthesis. It is difficult to generalize the conclusions of these data to the current era, particularly in light of the possible survival advantage seen after isolated AVR with mechanical valves in the large, more recent studies.

Permanence of the aortic valve substitutes becomes an important consideration in patients aged <65 years, and
many reports have documented an age-related decrease in durability of bioprostheses, both porcine heterografts and bovine pericardial prostheses.29–31 Chan et al32 reported that median interval to reoperation in patients undergoing AVR with current generation stented aortic bioprostheses was 7.7 years in patients aged <40 years, and 12.9 years in patients between 40 and 60 years of age. The trend of decreasing age for biological AVR candidacy may thus have important adverse consequences from both the perspective of diminished survival and increased need for reoperation.

Explaining the Survival Advantage of Mechanical Heart Valves

Which biological or methodological factor(s) might explain the finding of better patient survival with mechanical valves used for aortic valve replacement? Some question whether mechanical valves tend to be implanted preferentially in patients with longer life expectancy, and that bioprostheses, when selected for younger patients, are chosen because survival is thought to be limited. This reasoning goes on to suggest that some favorable (and unfavorable) clinical characteristics obvious on clinical evaluation are not captured in clinical databases and, therefore, cannot be adjusted for in comparative analyses of nonrandomized cohorts. This may be true to a certain extent, but in our experience, the occasional young patient with limited life expectancy needing AVR is encountered much less frequently than the relatively common clinical situation of a young patient, often male, who, on hearing the options for aortic prostheses, chooses a bioprosthesis believing he is too healthy and active to take warfarin because it would interfere with his lifestyle.

Other possible explanations for difference in survival between the 2 valve types have to do with intrinsic performance of the prosthesis or some benefit of chronic anticoagulation. Hemodynamic performance of currently available mechanical valves (St. Jude, Sorin, Medtronic, On-X) and bioprosthetic valves (porcine and pericardial) are generally similar, and it seems unlikely that any small difference in function of normal prostheses would translate into a significant survival benefit. Moreover, despite the early promise of enhanced physiological performance of stentless, valves, a clear hemodynamic or survival advantage over their stented counterparts remains unproven.33 A more plausible explanation for improved survival of patients with mechanical valves is, by contrast, the cumulative hemodynamic consequence of living with a degenerating bioprosthesis in place. Although primary tissue failure of bioprostheses may progress rapidly, some patients endure months or years of exposure to hemodynamically significant valvular regurgitation, stenosis, or both before critical prosthetic failure is identified and replacement is advised. It is likely that that a simple examination of rates and risks of reoperation underestimates the impact of valve failure on mortality.32

Caution Regarding the Discontinuation of Anticoagulation After Biological Aortic Valve Replacement

The debate regarding ideal aortic valve prosthesis choice in adults has been largely focused around the assumption that anticoagulant use is obviated by the implantation of a bioprosthetic valve. Prior series have demonstrated this not to be the case; many aging patients require treatment with vitamin-K antagonists or direct thrombin inhibitors for nonvalve related reasons, even after bioprosthetic implantation. Previous evidence suggests also that anticoagulation with Warfarin early after biological valve implantation may improve survival.26 An analysis of the Danish National Patient Registry evaluated the association of Warfarin treatment with the risk of thromboembolic complications, bleeding, and cardiovascular death after bioprosthetic implantation in the aortic position. Among 4075 patients having AVR with a bioprosthesis, 3186 received Warfarin and, compared with patients without anticoagulation, risk of stroke was 2.69 versus 7.00, risk of thromboembolic events was 3.97 versus 13.07, and risk of cardiovascular death (30–89 days postoperatively) was 3.83 versus 31.74. Analysis of the number of patients needed to treat/number needed to harm within 90 to 180 days after surgery revealed that for every 23 (95% confidence interval, 14–54) patients not being treated with Warfarin, 1 patient died from cardiovascular cause, and for every 74 (95% confidence interval, 27–95) patients being treated with Warfarin, 1 patient experienced bleeding complications requiring hospital admission. The authors concluded that Warfarin treatment for ≥6 months after biological AVR surgery was beneficial and associated with decreased risk of cardiovascular death. Further long-term analyses will be necessary to gain a better understanding of the liabilities associated with discontinuation of Warfarin after biological AVR.

Second Versus Third Generation Biological Valve Substitutes

Some assert that latest generation biological aortic valve substitutes have improved durability (freedom from structural valve deterioration) despite the paucity of long-term clinical follow-up.34 Indeed, there are few data indicating that a substantial difference exists between either (1) current model porcine and bovine pericardial prostheses or (2) second- versus third-generation porcine and pericardial valves in the aortic position. A study from Mayo Clinic35 analyzed the outcomes of 2979 patients aged ≥65 years having AVR with pericardial (most frequently Carpentier-Edwards Perimount or Mitroflow, n=1976) or porcine (most commonly Medtronic Mosaic, Carpentier-Edwards, Hancock modified orifice, and St. Jude Biocor, n=1003) devices between January 1993 and December 2007. Survival at 5, 10, and 12 years was 68%, 30%, and 16% for patients with pericardial valves, versus 69%, 38%, and 27% for porcine bioprostheses (P=NS). Moreover, biological valve type was not predictive of late survival in a multivariate model. Freedom from reoperation was 96%, 92%, and 90% at 5, 10, and 12 years, and freedom from any reoperation
was similar with different valve types ($P=0.72$). In a review of 1134 patients with the Hancock II porcine bioprostheses (Medtronic, Minneapolis, MN), David and colleagues concluded that the Hancock II bioprosthesis (and by inference, not the third generation Mosaic device) is “durable in patients 60 years and older and is probably the gold standard of bioprosthetic valve durability in this patient population.”

The clinical relevance of novel anticalcification formulae tested in animal models remains unclear. It is thus difficult to substantiate the assertion that durability of either current third generation (versus second generation) or pericardial (versus porcine) bioprosthesis durability is significantly different from prior generation devices. A recent randomized report from Mayo Clinic demonstrates that the early hemodynamic differences between current generation porcine and pericardial devices are minimal. Long-term morbidity, survival, and durability profiles will be informative as follow-up is accrued.36

Conclusion

Long-term survival after AVR may be better in patients receiving the latest-generation mechanical valves compared with biological prostheses (pericardial or porcine) across a broad range of age groups up to 65 to 70 years. The possible survival advantage of mechanical aortic valve prostheses and the low rate of valve-related adverse events (thromboembolism and hemorrhage) among all current-generation devices should be thoroughly discussed during preoperative consultation. Biological aortic valve substitutes are suitable for elderly patients, those with multiple comorbidities that limit life expectancy, and young women who anticipate pregnancy and choose the inevitable need for reoperation to avoid risk of Warfarin embryopathy. Some otherwise healthy young patients may choose a bioprosthesis to avoid anticoagulation with Warfarin, but this decision should be made with the full understanding that the choice may increase late mortality, that oral anticoagulation may be necessary in the future, and that subsequent management of prosthetic failure with transcatheter valve-in-valve insertion is an attractive but unproven long-term strategy.

Acknowledgments

We thank Dr Simon Maltais for assistance in data-gathering and Zhuo Li for expert assistance with statistical analysis.

Disclosures

Dr Suri is a Principle Investigator for the FDA IDE Trial of the Perceval Valve (Sorin, bovine pericardial), Sire Principle Investigator for the PARTNER II Trial (Edwards, bovine pericardial), Principle Investigator Randomized Bioprosthetic AVR Trial (St. Jude, Sorin, Edwards). Dr Schaff is a Principle Investigator FDA IDE Trial Trifecta Valve (St. Jude, bovine pericardial), Co-Investigator Edwards PARTNER II Trial (bovine pericardial).

References


Response to Suri and Schaff
Tsuyoshi Kaneko, MD; Lawrence H. Cohn, MD; Sary F. Aranki, MD

The data presented by Drs Suri and Schaff in favor of long-term survival of mechanical valves in the aortic position are based on an anecdotal, observational, single-center study and are not corroborated by large randomized studies. What is more striking, in our opinion, is that despite their strong belief in the superiority of mechanical valves, the trend in their center favors the use of bioprosthesis. In patients aged <70 years, a bioprosthesis was used in 56% of their patients over a period of 16 years starting in 1993. They do not provide the trend in the recent years of the study, which we believe is similar to other large centers that also mirror the national trend (STS Database), where there was a massive surge in favor of bioprosthesis at any age. Therefore, we cannot ignore the strong emerging trend toward use of bioprosthesis. In our institution, reviewing 5759 patients who underwent aortic valve replacement from 1994 to 2012, use of bioprosthesis has increased from 48% in 1994 to 85.4% in 2011. For patients aged 60 to 65 years, the use of bioprosthesis increased from 14.3% to 82.2% and for patients aged <55 years from 14.7% to 46.9% during the same period. This trend appears to have occurred before the introduction of transcatheter aortic valve-in-valve procedure. We think this is related to increased patient knowledge and discussions with referring physicians before surgical consultations. After all, one cannot ignore solid numbers documenting this emerging trend in use of bioprosthesis regardless of the published data for survival and valve-related morbidity.
Selection of Aortic Valve Prostheses: Contemporary Reappraisal of Mechanical Versus Biologic Valve Substitutes
Rakesh M. Suri and Hartzell V. Schaff

Circulation. 2013;128:1372-1380
doi: 10.1161/CIRCULATIONAHA.113.001681
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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