LONG-TERM OUTCOME AFTER BIOLOGIC VERSUS MECHANICAL AORTIC
VALVE REPLACEMENT IN 841 PATIENTS
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James E. Lowe, Walter G. Wolfe and Donald D. Glower

J Thorac Cardiovasc Surg 1999;117:890-897

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Objective: The purpose of this study was to optimize selection criteria of biologic versus mechanical valve prostheses for aortic valve replacement. Methods: Retrospective analysis was performed for 841 patients undergoing isolated, first-time aortic valve replacement with Carpentier-Edwards (n = 429) or St Jude Medical (n = 412) prostheses. Results: Patients with Carpentier-Edwards and St Jude Medical valves had similar characteristics. Ten-year survival was similar in each group (Carpentier-Edwards 54% ± 3% versus St Jude Medical 50% ± 6%; \( P = .4 \)). Independent predictors of worse survival were older age, renal or lung disease, ejection fraction less than 40%, diabetes, and coronary disease. Carpentier-Edwards versus St Jude Medical prostheses did not affect survival (\( P = .4 \)). Independent predictors of aortic valve reoperation were younger age and Carpentier-Edwards prosthesis. The linearized rates of thromboembolism were similar, but the linearized rate of hemorrhage was lower with Carpentier-Edwards prostheses (\( P < .01 \)). Perivalvular leak within 6 months of operation was more likely with St Jude Medical than with Carpentier-Edwards prostheses (\( P = .02 \)). Estimated 10-year survival free from valve-related morbidity was better for the St Jude Medical valve in patients aged less than 65 years and was better for the Carpentier-Edwards valve in patients aged more than 65 years. Patients with renal disease, lung disease (in patients more than age 60 years), ejection fraction less than 40%, or coronary disease had a life expectancy of less than 10 years. Conclusions: For first-time, isolated aortic valve replacement, mechanical prostheses should be considered in patients under age 65 years with a life expectancy of at least 10 years. Bioprostheses should be considered in patients over age 65 years or with lung disease (in patients over age 60 years), renal disease, coronary disease, ejection fraction less than 40%, or a life expectancy less than 10 years. (J Thorac Cardiovasc Surg 1999;117:890-7)
Although many surgeons have agreed that younger and healthier patients should receive mechanical valves and older and sicker patients should receive bioprosthetic valves, a large difference in opinion exists as to the appropriate management of valvular disease in patients between ages 60 and 70 years who often have multiple comorbidities.13 This retrospective analysis from one institution investigates whether the outcomes of patients who underwent aortic valve surgery differ with the use of mechanical versus bioprosthetic valves. An algorithm for prosthesis selection in patients with aortic valvular disease is proposed.

Methods

From 1976 to 1996, 1676 patients underwent aortic valve replacement at Duke University Medical Center. To obtain a more homogeneous population, we excluded patients undergoing a concurrent operation for placement of another valve, patients aged less than 18 years, patients receiving valves sized less than 19 mm, and patients with a previous sternotomy. To further improve population homogeneity and to eliminate prostheses that are now less used, we also excluded 489 patients who by surgeon preference received aortic homografts or prostheses used in small numbers. The resultant study population consisted of all 841 patients undergoing isolated, first-time aortic valve replacement with the Carpentier-Edwards (CE) standard porcine prosthesis (n = 429; model 2625; Baxter Healthcare Corp, Irvine, Calif) or the St Jude Medical (SJ) prosthesis (n = 412; model A102; St Jude Medical, Inc, St Paul, Minn). As of 1996, follow-up was 100% complete, that is, all patients were known to be either dead or alive on January 1, 1996. Data were obtained from chart review (18%), telephone interview (43%), the National Death Index (33%), or autopsy (6%).

All aortic valve operations were performed through a median sternotomy with the use of cardiopulmonary bypass and crystalloid or blood cardioplegic solution. Patients with bioprostheses were generally started on long-term aspirin therapy beginning on the first postoperative day.14 Patients with mechanical prostheses were started on warfarin sodium (Coumadin) therapy on postoperative day 2, either with or without aspirin therapy. Most patients with a mechanical valve were followed up by their local physicians to maintain an international normalized ratio of 2.0 to 3.0.

Outcomes were defined according to the standard definitions.15 Renal disease was identified as a preoperative creatinine level greater than 2.0 mg/dL. Pulmonary disease included any ongoing pulmonary diagnosis requiring treatment. Coronary diameter reduction of 75% or more was considered to be significant. Endocarditis was defined as a clinical diagnosis of endocarditis. Valve-related morbidity was considered to be any hemorrhage, thromboembolism, aortic valve reoperation, or endocarditis. Perivalvular leak was defined as moderate or severe aortic regurgitation not the result of prosthetic dysfunction.

Data were analyzed with SAS software release 6.12 (SAS Institute, Cary, NC). Continuous data were expressed as mean ± SD. Comparisons of the 2 groups were made with the Mann-Whitney U test for continuous data not distributed normally. Cox proportional hazards regression model was used in the survival and valve-related outcome analysis. The assumptions of the proportional hazards model were checked graphically. The variables of age and ejection fraction were stratified or converted to binary form to accommodate a non-linear relationship to risk. Variables were selected for models by a forward and backward stepwise elimination procedure. All univariable factors significant at P < .10 were examined. All the statistical analyses were conducted with α = .05. To obtain estimates of 10-year survival free of valve-related morbidity in selected age groups where several groups contained fewer than 10 patients, log curve fitting was used16.

Table I. Preoperative patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>CE (n = 429)</th>
<th>SJ (n = 412)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>64 ± 12</td>
<td>62 ± 13</td>
<td>NS</td>
</tr>
<tr>
<td>Year of operation</td>
<td>1984 ± 5</td>
<td>1990 ± 3</td>
<td>.001</td>
</tr>
<tr>
<td>Male (%)</td>
<td>307 (72)</td>
<td>243 (59)</td>
<td>.001</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>50 ± 15</td>
<td>51 ± 14</td>
<td>NS</td>
</tr>
<tr>
<td>Atrial fibrillation (%)</td>
<td>67 (16)</td>
<td>55 (13)</td>
<td>NS</td>
</tr>
<tr>
<td>Coronary disease (%)</td>
<td>178 (41)</td>
<td>169 (41)</td>
<td>NS</td>
</tr>
<tr>
<td>Valve size (mm)</td>
<td>24 ± 3</td>
<td>23 ± 3</td>
<td>.001</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>45 (10)</td>
<td>82 (20)</td>
<td>.001</td>
</tr>
<tr>
<td>Heart failure class</td>
<td>2.9 ± 1.0</td>
<td>3.0 ± 1.0</td>
<td>NS</td>
</tr>
<tr>
<td>Angina class</td>
<td>2.1 ± 1.2</td>
<td>2.0 ± 1.2</td>
<td>NS</td>
</tr>
<tr>
<td>Endocarditis (%)</td>
<td>22 (5)</td>
<td>8 (2)</td>
<td>.001</td>
</tr>
<tr>
<td>Lung disease (%)</td>
<td>82 (19)</td>
<td>62 (15)</td>
<td>NS</td>
</tr>
<tr>
<td>Cerebrovascular disease (%)</td>
<td>41 (10)</td>
<td>42 (10)</td>
<td>NS</td>
</tr>
<tr>
<td>Renal disease (%)</td>
<td>28 (7)</td>
<td>13 (3)</td>
<td>.02</td>
</tr>
<tr>
<td>Peptic ulcer disease (%)</td>
<td>47 (11)</td>
<td>44 (11)</td>
<td>NS</td>
</tr>
<tr>
<td>Gastrointestinal bleed (%)</td>
<td>21 (5)</td>
<td>16 (4)</td>
<td>NS</td>
</tr>
</tbody>
</table>
Patients with a CE prosthesis and an SJ prosthesis did not differ significantly in age (Table I). Coronary artery bypass grafting was performed in 152 of 429 patients (35%) with a CE prosthesis and in 175 of 412 patients (42%) with an SJ prosthesis ($P = \text{NS}$). In the SJ prosthesis group, the number of patients undergoing coronary bypass grafting exceeded the number of patients with coronary disease because 6 patients received grafts for vessels with less than 75% diameter reduction. Patients with a CE prosthesis were more likely to be male and to have an earlier year of operation and larger valve size; they were less likely to have diabetes or renal disease, but more likely to have endocarditis. However, there was no significant difference in ejection fraction, coronary disease, angina, or heart failure.

**Thirty-day survival.** The absolute 30-day mortality rate was 35 of 429 patients (8% ± 1%) for patients with a CE prosthesis and 15 of 412 patients (4% ± 1%) for patients with an SJ prosthesis ($P < .01$). By logistic regression, independent predictors of 30-day mortality were earlier year of operation ($\chi^2 = 8.2; P = .004$) and concurrent coronary bypass grafting ($\chi^2 = 6.3; P = .01$). Valve make (CE versus SJ prosthesis) was not an independent predictor of 30-day mortality ($\chi^2 = 2.6; P = .10$). Thus the higher 30-day mortality rate for patients with a CE versus an SJ prosthesis was largely attributable to the earlier year of operation for patients with a CE versus an SJ prosthesis and the improvement in operative mortality rate from 1976 to 1996.

**Late survival.** After aortic valve replacement, there was no significant difference in survival of patients receiving a CE versus an SJ prosthesis (54% ± 3% vs 50% ± 6% at 10 years; $P = .4$; Fig 2). By Cox model analysis, independent multivariable factors predicting worse survival included older age, renal disease, ejection fraction less than 40%, lung disease, coronary artery disease, and diabetes (Table II). A CE versus an SJ make of valve ($P = .4$) and year of operation ($P = .5$) were not significant predictors of late survival by multivariable analysis. Causes of all deaths (early and late) were not significantly different ($P = .8$) between patients with a CE prosthesis and patients with an SJ prosthesis (Table III).

**Valve-related complications.** At discharge, 4 of 377 patients (1%) with a CE prosthesis and 364 of 379 patients (96%) with an SJ prosthesis were receiving warfarin therapy. At last follow-up for living patients, 12 of 171 patients (7%) with a CE prosthesis and 219 of 225 patients (97%) with an SJ prosthesis were receiving warfarin therapy. Discharge medications were unknown.
in 13 of 390 patients (3%) with a CE prosthesis and in 15 of 394 patients (4%) with an SJ prosthesis; medications at last follow-up were unknown in 51 of 222 patients (23%) with a CE prosthesis and in 82 of 307 patients (27%) with an SJ prosthesis. Ten-year freedom from hemorrhage was higher for patients with a CE prosthesis than for patients with an SJ prosthesis (97% ± 1% vs 91% ± 3%; \(P = .01\); Fig 3). By Cox model analysis, the only variable predictive of hemorrhage was SJ valve make (\(P = .003\)); patient age did not significantly affect hemorrhage. The linearized rate of hemorrhage was significantly lower for patients with a CE prosthesis than for patients with an SJ prosthesis (0.3% ± 0.1%/pt-y versus 1.2% ± 0.3%/pt-y; \(P = .001\)). Ten-year freedom from thromboembolism was not significantly different for patients with a CE prosthesis versus patients with an SJ prosthesis (93% ± 2% vs 94% ± 2%; \(P = .9\); Fig 3). By Cox model analysis, no variables including age were identified to be predictive of thromboembolism. The linearized rates of thromboembolism were not significantly different for patients with a CE prosthesis versus patients with an SJ prosthesis (0.7% ± 0.2%/pt-y vs 1.0% ± 0.3%/pt-y; \(P = .3\)).

Perivalvular leak was noted in 21 of 429 patients (5%) with a CE prosthesis and 18 of 412 patients (4%) with an SJ prosthesis (\(P = .7\)). Perivalvular leak was treated...
with reoperation in 12 of 21 patients (57%) with a CE prosthesis versus 6 of 18 patients (33%) with an SJ prosthesis \((P > .1)\). Ten-year freedom from perivalvular leak was not significantly different for patients with a CE prosthesis versus patients with an SJ prosthesis \((92\% \pm 2\% \text{ vs } 91\% \pm 3\%; P = .3)\). Perivalvular leak was significantly more likely to be noted in the first 6 months after operation with an SJ versus a CE prostheses \((8 \text{ of } 412 \text{ patients } [1.9\%] \text{ vs } 1 \text{ of } 429 \text{ patients } [0.2\%]; P = .02)\). The linearized rate of perivalvular leak was \(0.7\% \pm 0.1\%/\text{pt-y}\) for a CE prosthesis versus \(1.0\% \pm 0.2\%/\text{pt-y}\) for an SJ prosthesis \((P = .2)\).

Ten-year freedom from endocarditis was not significantly different between patients with a CE prosthesis and patients with an SJ prosthesis \((96\% \pm 1\% \text{ vs } 97\% \pm 1\%; P = .5; \text{Fig 3})\). By Cox model analysis, the only variable predictive of late endocarditis was preoperative endocarditis \((\beta = 2.3 \pm .5; \chi^2 = 20.5; P = .0001)\), and age did not significantly affect late endocarditis. The linearized rates of endocarditis were \(0.4\% \pm 0.1\%/\text{pt-y}\) for patients with a CE prosthesis and \(0.4\% \pm 0.1\%/\text{pt-y}\) for patients with an SJ prosthesis \((P = .9)\).

Ten-year freedom from aortic valve reoperation was significantly better for patients with an SJ prosthesis \((98\% \pm 1\% \text{ vs } 83\% \pm 3\%; P = .02)\). By Cox model analysis, the only independent variables predictive of aortic valve reoperation were CE valve make \((\beta = -1.0 \pm .4; \chi^2 = 6.6; P = .01)\) and younger patient age \((\beta = -0.044 \pm .009; \chi^2 = 25.2; P = .0001)\). For patients over

65 years old, valve make did not affect aortic valve reoperation \((P = .4; \text{Fig 4})\). For patients aged 65 years and younger, freedom from reoperation was significantly better for an SJ versus a CE prosthesis \((P = .02; \text{Fig 4})\). After reoperation, the 30-day mortality rate was 4 of 63 (6%) for all patients and 1 of 9 (11%) in all patients with coronary bypass grafting with the original aortic valve operation.

**Survival free from valve-related morbidity.** After an examination of all 841 study patients, there was no significant difference in survival free from valve-related morbidity (defined earlier) between patients receiving a CE versus an SJ prostheses \((43\% \pm 3\% \text{ vs } 41\% \pm 5\%; P = .8; \text{Fig 5})\). By Cox model analysis, independent multivariable factors predicting worse survival free from valve-related morbidity were ejection fraction less than 40\% \((\chi^2 = 11.9; P = .0005)\), renal disease \((\chi^2 = 10.1; P = .002)\), diabetes \((\chi^2 = 8.2; P = .004)\), and coronary artery disease \((\chi^2 = 6.5; P = .01)\). For the entire pool of 841 patients, make of valve (CE vs SJ) and year of operation were not significant predictors of survival free from valve-related morbidity.

Because age was a determinant of both survival and reoperation, survival free from valve-related morbidity was examined as a function of patient age. At 10 years after operation, survival free from valve-related morbidity was better with CE valves in patients over 65 years old and was better with SJ valves in patients under 65 years old (Fig 1).

For patients not surviving 10 years, CE bioprostheses would be preferable because of the absence of anticoagulant-related hemorrhage and because of the rarity of reoperation within 10 years in these patients. Several groups of patients with a life expectancy less than 10 years (thus favoring bioprostheses) included patients over 65 years old, patients with lung disease who are under age 60 years, and patients at any age with renal disease, ejection fraction less than 40\%, or coronary

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Actual 10-year freedom from reoperation on survival (%)</th>
<th>CE aortic valve (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal disease, any age</td>
<td>27 \pm 8</td>
<td>100 \pm 0</td>
</tr>
<tr>
<td>Lung disease (patient older than 60 y)</td>
<td>30 \pm 6</td>
<td>96 \pm 2</td>
</tr>
<tr>
<td>Ejection fraction &lt; 40%, any age</td>
<td>35 \pm 6</td>
<td>95 \pm 2</td>
</tr>
<tr>
<td>Coronary artery disease, any age</td>
<td>35 \pm 5</td>
<td>98 \pm 0.8</td>
</tr>
<tr>
<td>Age &gt; 65 y</td>
<td>41 \pm 4</td>
<td>98 \pm 0.7</td>
</tr>
</tbody>
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Fig 5. Survival free from valve-related morbidity after aortic valve replacement with the CE or SJ prostheses.
disease. Even in patients under 55 years old, the presence of coronary disease produced a 10-year survival of 35% ± 13% for patients with a CE prosthesis and patients with an SJ prosthesis combined. For patients in any of these groups who received a CE bioprosthesis, the actual 10-year freedom from aortic valve reoperation \(^{15}\) was at least 95% (Table IV).

**Discussion**

Only a few large studies have compared outcomes between biologic and mechanical valve replacement; the results of the most recent studies are summarized in Table V. The current study confirmed a greater incidence of hemorrhage with mechanical versus biologic valves. \(^{8-11,18}\) The hemorrhage rate with mechanical prostheses in this study (1.2% ± 0.3%/pt-y) was somewhat less than the 2%/pt-y reported in most series. \(^{8-11,18}\) This difference may result from the low-risk population (first-time isolated aortic valve replacement) and the recent time frame in this study where anticoagulation was maintained at lower levels than in earlier years. The thromboembolic rate of this study is comparable with other reports for both biologic and mechanical prostheses. \(^{8-11,18}\) This study confirms the higher incidence of aortic valve reoperation in patients receiving a bioprosthesis and in younger patients. \(^{19}\)

This retrospective analysis of 841 patients differs from previous studies in several respects. No recent study compared the modern CE and SJ prostheses, \(^{20,21}\) and the current study is the third largest study comparing biologic and mechanical aortic valves to date. \(^{13,21}\) In the two larger series, both biologic and mechanical patient groups included several makes of prostheses, which may differ in durability, flow characteristics, or thrombogenicity. \(^{11,21}\) Only the Cleveland Clinic study with multiple valve makes used multivariable analysis to examine the effects of comorbidity on survival after biologic versus mechanical aortic valve replacement. The Cleveland Clinic study confirmed that age and mechanical prostheses impaired event-free survival, but only in patients over age 60 years or not receiving anticoagulation over age 40 years. \(^{21}\)

The current study is the first to provide numeric data supporting guidelines to select biologic versus mechanical devices based on patient comorbidity other than age (Table IV). The current study provides data that support a specific age (65 years) over which survival free from valve-related events is better with biologic valves, \(^{22,23}\) although outcome tended to be better with mechanical valves in younger patients (Table IV; Fig 1). Previous studies not examining comorbidities other than coronary disease have placed the cutoff for biologic versus mechanical prostheses at 65 to 70 years. \(^{22,23}\) Patient selection bias (eg, patients with biologic valves having significantly less coronary disease) may explain why the Cleveland Clinic study showed better event-free survival with bioprostheses in patients over age 40 years. \(^{21}\)

The significantly higher incidence of early perivalvular leak rate in the SJ group has not been previously reported. Explanations for this finding may include differences in sewing ring width and shape between SJ and CE prostheses, along with the tendency to use SJ prostheses in smaller aortic roots where valve seating may be more difficult (Table I). SJ and other valve makes are now available with large sewing rings that were not used in this study.

The nonrandomized, retrospective nature of this study limits the findings. The major bias between the CE and SJ groups was the earlier year of operation and the resultant higher 30-day mortality in patients with a CE prosthesis. One possible effect of overestimating early deaths after CE aortic valve replacement may be to underestimate 10-year survival free from valve-related morbidity in patients with a CE prosthesis. In turn, this bias may mean that the CE and SJ curves in Fig 1 actually should cross at age 65 years instead of age 70 years. These data therefore suggest that the age at

### Table V. Linearized rates of complications

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<tbody>
<tr>
<td></td>
<td>Bio (n = 429)</td>
<td>Mech (n = 412)</td>
<td>Bio (n = 412)</td>
<td>Bio (n = 100)</td>
<td>Bio (n = 100)</td>
</tr>
<tr>
<td></td>
<td>(n = 326)</td>
<td>(n = 250)</td>
<td>(n = 100)</td>
<td>(n = 100)</td>
<td>(n = 100)</td>
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<tr>
<td></td>
<td></td>
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<td></td>
<td>(n = 196)</td>
<td>(n = 102)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>(n = 198)</td>
<td>(n = 109)</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>0.3</td>
<td>1.2</td>
<td>0.94</td>
<td>3.0</td>
<td>0.1</td>
</tr>
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<td></td>
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<tr>
<td>Thromboembolism</td>
<td>0.7</td>
<td>1.0</td>
<td>1.29</td>
<td>3.3</td>
<td>0.6</td>
</tr>
<tr>
<td></td>
<td></td>
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<tr>
<td>Leak (%/pt-y)</td>
<td>0.7</td>
<td>1.0</td>
<td>0.14</td>
<td>0.24</td>
<td>0.18</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Endocarditis (%/pt-y)</td>
<td>0.4</td>
<td>0.4</td>
<td>0.14</td>
<td>0.36</td>
<td>0.6</td>
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which CE valves become advantageous is 65 years in this patient population.

An additional shortcoming of this study is the limited follow-up in the SJ group after 10 years, at which time differences between biologic and mechanical valves may be magnified by increased reoperation for structural deterioration of the bioprostheses. Fifteen-year data await further study; however, the conclusions of this study are based on 10-year results and are unlikely to be changed by data from the small number of patients surviving 15 years or more. Although the current study was limited to first-time isolated aortic valve procedures (with or without coronary bypass grafting), the results could well be different in patients with a previous cardiac operation or multiple valve operations. Although this study is among the largest studies to date, the small patient numbers in some subgroups may have limited the ability to define ages where life expectancy could exceed 10 years and where results might therefore favor mechanical prostheses (eg, young patients with coronary disease; Table IV). In addition, the presence of previous coronary grafts in a young patient undergoing reoperation for a failed bioprosthesis could increase late mortality rates, although the reoperative mortality was a modest 11% for patients of all ages with previous coronary bypass grafts in the current study. The reported mortality rate for aortic valve operation has been 14% after previous aortic valve operation (Fig 1). Specific subsets of patients (eg, young patients with coronary disease; Table IV; Fig 1) would be reasonable candidates for aortic bioprostheses to avoid anticoagulation with an extremely low likelihood of aortic valve reoperation (Table IV).

Results tend to favor mechanical aortic valves in patients under age 65 years with a life expectancy of at least 10 years (Fig 1). Specific subsets of patients undergoing multiple valve operation or repeat cardiac operation merit further investigation.

The current study evaluated a second generation porcine bioprosthesis that has been partly displaced by pericardial bioprostheses (models 2700 and 2800; Baxter Healthcare Corp). Yet, the study is still relevant because pericardial and porcine aortic prostheses have similar durability and performance characteristics. The SJ valve (model A102) used in this study continues to be widely used.

Choice of an aortic bioprosthesis versus mechanical prosthesis should be individualized on the basis of the patient’s ability to take warfarin and the patient’s age and life expectancy. This choice primarily is one of increased likelihood of reoperation with bioprostheses versus increased likelihood of hemorrhage with mechanical prostheses. The relatively low 10-year survival of 50% to 54% and the high frequency of cardiac deaths (Table III) suggest that other factors, such as optimal timing of operation, may be more important to survival than prosthesis selection. The results of this study support the general philosophy that older, sicker patients tend to benefit more from bioprostheses and that younger, healthier patients should receive mechanical prostheses. Otherwise, patients who are unable to reliably take warfarin or who have medical illnesses precluding anticoagulation should receive a bioprosthesis.

The current study provides data that suggest age cutoff points for selecting biologic versus mechanical valves in different patient subgroups (Table IV; Fig 1). Patients with an expected survival of less than 10 years (more than 65 years old, renal disease, lung disease, patients who are more than 60 years old), ejection fraction of less than 40%, or coronary disease (Table IV; Fig 1) would be reasonable candidates for aortic bioprostheses to avoid anticoagulation with an extremely low likelihood of aortic valve reoperation (Table IV). Results tend to favor mechanical aortic valves in patients under age 65 years with a life expectancy of at least 10 years (Fig 1).

REFERENCES

Appendix

Preoperative variables included in Cox proportional hazards models:

- Valve type
- Age older than 65 years
- Sex
- Ejection fraction less than 40%
- Operation year
- New York Heart Association heart failure class IV
- Diabetes
- Renal failure
- Liver disease
- Lung disease
- Atrial fibrillation
- Aortic regurgitation
- Number of diseased coronary vessels
- Peptic ulcer disease
- Previous gastrointestinal hemorrhage
- Endocarditis within 6 months
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