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Comparison of survival after mitral valve replacement with biologic and mechanical valves in 1139 patients

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Objective: We sought to compare 10-year survival in patients after mitral valve replacement with biologic or mechanical valve prostheses.

Methods: Retrospective survival analysis was performed on data from 1139 consecutive patients older than 18 years of age undergoing mitral valve replacement with Carpentier-Edwards (n = 495; Baxter Healthcare Corp, Irvine, Calif) or St Jude Medical (n = 644; St Jude Medical, Inc, St Paul, Minn) prostheses.

Results: The 10-year survival was not statistically different between the patients receiving Carpentier-Edwards valves and those receiving St Jude Medical valves (P = .16). Adjusted survival estimates at 2, 5, and 10 years were 82% ± 2% (95% confidence intervals, 79%-85%), 69% ± 2% (95% confidence intervals, 64%-73%), and 42% ± 3% (95% confidence intervals, 37%-48%), respectively, for the Carpentier-Edwards group and 83% ± 2% (95% confidence intervals, 80%-86%), 72% ± 2% (95% confidence intervals, 69%-76%), and 51% ± 3% (95% confidence intervals, 45%-58%), respectively, for the St Jude Medical group. Predictors of worse survival after mitral valve replacement are older age, lower ejection fraction, presence of class IV congestive heart failure, coronary artery disease, renal disease, smoking history, hypertension, concurrent other valve surgery, and redo heart surgery.

Conclusion: Choice of biologic or mechanical prosthesis does not significantly affect long-term patient survival after mitral valve replacement.

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The advantages and disadvantages of mechanical valve prostheses and bioprostheses have been known to us since the beginning of the first successful implantation of a valve prosthesis. Mechanical valve prostheses were first implanted in 1960, 6 years before the first bioprostheses were routinely used.[1,2] Because of the risk of thromboembolism and the hazards of continuous anticoagulation associated with mechanical valve prostheses, tissue valves were widely used for mitral valve replacement from the 1970s until the early 1980s.[3] However, one disadvantage of the bioprostheses was predictable structural failure, often leading to reoper-

TABLE 1. Distribution of demographic and medical history variables by valve type (all patients)

	CE (n = 495)	SJ (n = 644)	*P* value
Age (y)*	62 (52-69)	61 (50-69)	.327
Male sex	42%	33%	.001
Ejection fraction*	50 (44-59)	54 (46-61)	.001
Atrial fibrillation	53%	56%	.242
Coronary disease	31%	29%	.352
Liver disease	4%	2%	.097
Lung disease	14%	18%	.080
Renal disease	6%	4%	.311
NYHA class IV	40%	54%	.001
Diabetes	10%	14%	.063
Hypertension	36%	45%	.001
Smoking history	43%	41%	.654
Redo heart surgery	17%	27%	.001
Mitral stenosis	42%	49%	.01
Regurgitation grades 3 and 4	79%	74%	.073
Year of operation*	1982 (1979-1986)	1990 (1988-1993)	.0001

NYHA, New York Heart Association.
*Median (interquartile range).

TABLE 2. Distribution of valve cause by valve type

Cause	CE (n = 495)	SJ (n = 644)	*P* value
Ischemic	10%	7%	.147
Prolapse	23%	15%	.001
Rheumatic	36%	41%	.087
Perivalvular leak/ prosthetic dysfunction	7%	17%	.001
Calcific	7%	3%	.001
Congenital	1%	1%	.675
IHSS	1%	1%	.184
Infectious	4%	4%	.841
Other*	5%	7%	.098
Missing	6%	4%	.141

IHSS, Idiopathic hypertrophic subaortic stenosis.
*Degenerative and other category.

ation, whereas mechanical valves provided durability. As a result, an increased preference for mechanical valve prostheses was observed after 1983. Currently, the use of bioprostheses has decreased to less than one third of the total.[4]

The above information indicates that many physicians and patients after 1983 prefer mechanical valve prostheses. The 2 randomized clinical trials[5,6] on comparison of mechanical valve prostheses and bioprostheses conducted in the 1970s and early 1980s support the acceptability of either valve type, with comparable 10-year mortality and valve-related complications between the 2 valve groups. However, the valve models tested in these 2 randomized trials are seldom used now, and no subsequent large-scale randomized trials have compared biologic and mechanical prostheses.

A number of recent articles have supported the use of bioprostheses. For example, Myken and associates[7] reported that bleeding was more hazardous than reoperation. Fradet and colleagues[8] suggested that bioprostheses reduced the overall rate of postoperative valve-related complications. Cobanoglu and coworkers[9] stated that successful reoperations should not be considered as treatment failure, and Holper and associates[10] argued that reoperation on bioprostheses seemed not to be a significant risk for patients 65 years or older.

Although we can debate whether reoperation is more hazardous than having increased risks of strokes and hemorrhage, long-term mortality should be an important criterion for comparison of the 2 valve types, if not the most important one. The objective of this article is to compare long-term survival in patients who undergo mitral valve replacement in a more recent time frame. The present study examines the 2 most current and widely used stent-mounted porcine xenografts and bileaflet mechanical prostheses in regard to long-term survival. Valve-related complications will be addressed in a future study because of constraints on the length of this article.

Methods

This study is based on data from 1139 consecutive patients greater than 18 years of age undergoing mitral valve replacement with 1 of 2 prostheses between 1976 and 1995 at Duke University Medical Center. The patient population contains 495 patients with the Carpentier-Edwards (CE) standard porcine prosthesis (model 6625; Baxter Healthcare Corp, Irvine, Calif) and 644 patients with the St Jude Medical (SJ) prosthesis (model M101; St Jude Medical, Inc, St Paul, Minn). Patients receiving other prostheses were excluded from analysis.

Patient Population

Selection of a mechanical SJ or a porcine CE prosthesis is determined by patient preference and by surgeon judgment on the basis of patient age and comorbidities, including illness predisposing to bleeding, and patient lifestyle, including history of compliance with anticoagulant therapy.[11] Because the advantage of mechanical valves is extended durability, patients with a long life expectancy after the operation are usually given a mechanical valve. As Czer and coworkers[12] mention, "The selection process has resulted in mechanical and bioprosthetic valve recipients who form two distinctly different patient populations."

At our center, the CE biologic valve prosthesis was implanted starting in 1976, whereas the SJ mechanical valve prosthesis was first implanted in 1983. As a result, there are different follow-up times for the recipients of the 2 types of prostheses. For example, the median follow-up time is 12 years for the CE group and 6 years for the SJ group; the maximum follow-up time is 21 years for the CE group and 15 years for the SJ group. Data analysis therefore has to address potential selection biases, including differing years of operation and follow-up times and changes in operative techniques and medical care practice.

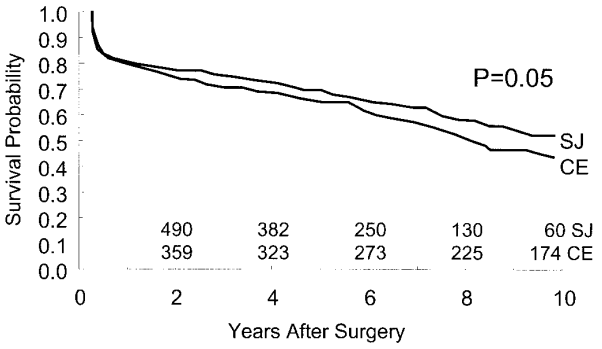

Figure 1. Unadjusted 10-year survival curves of the SJ group and the CE group, with patient numbers remaining at risk given at 2, 4, 6, 8, and 10 years after the operation. The data set was all patients.

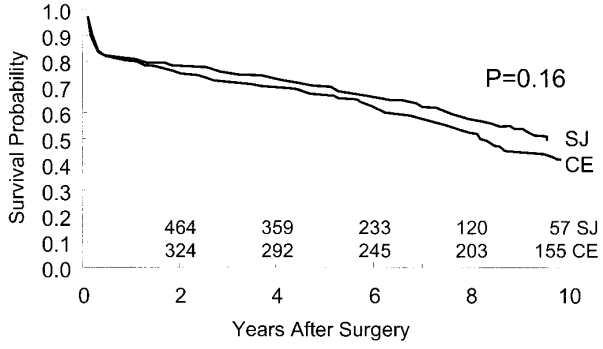

Figure 2. Adjusted 10-year survival curves of the SJ group and the CE group, with patient numbers remaining at risk given at 2, 4, 6, 8, and 10 years after the operation. The data set was all patients.

Statistical Methods

Demographics, clinical characteristics, and surgical procedure information on patients undergoing valve replacement at Duke University Medical Center were retrospectively extracted from the prospectively collected Duke patient medical records and the computerized Duke patient database. The predictor variables collected for this analysis include 2 types of variables. The continuous numeric variables include age, ejection fraction, and date of operation. The categoric variables indicating presence of disease include atrial fibrillation, coronary artery disease, diabetes, liver disease, lung disease, renal disease, hypertension, smoking history, redo heart surgery, concomitant valve surgery, acute presentation at the time of the operation, mitral stenosis, and mitral insufficiency. Other categoric variables of nominal or ordinal characteristics are causes of the mitral valve disease and congestive heart failure class.

Prognostic variables are defined as clinical diagnoses (Table 1). *Renal disease* was defined as a serum creatinine level of 2.0 mg/dL or greater. *Redo heart surgery* is defined in this article as any prior cardiac operation, including aortic, mitral, or tricuspid replacement or repair or coronary artery bypass grafts. *Concomitant valve surgery* is defined in this article as concomitant aortic valve replacement or tricuspid valve repair or replacement along with the present mitral valve replacement. All disease variables are coded as 1, representing the presence of the disease, and 0, representing the absence of the disease.

Medical history variables and baseline characteristics of this patient population were extracted from medical records into a database, and follow-up telephone interviews were conducted on a yearly basis. Patient follow-up information regarding survival status was obtained by use of telephone interview (65%), medical records (28%), and the National Death Index (7%). As of March 1999, the survival status of 96% of the patients was known. Survival time was calculated from the date of patient valve replacement to the date of patient death, loss to follow-up, or last follow-up. Patients lost to follow-up or still alive as of March 1999 were censored at the date last seen.

The distributions of continuous predictor variables within valve type are described with medians and interquartile ranges. Dichotomous predictor variables are described with proportions. Statistical comparisons of the 2 patient groups on these predictors are performed with the use of the Mann-Whitney *U* test for continuous variables and the Pearson χ^2 test for dichotomous variables.

In the analysis of our observational data, one potential problem is that differences in long-term survival demonstrated by the unadjusted raw survival estimates may be due to assignment of valve type on the basis of prognostic factors. Multivariate regression modeling in the Cox survival model with propensity score used as a covariate is performed to assess the effect of valve type on the probability of survival after mitral valve replacement. The incorporation of a propensity score balances the weight of covariates between the 2 valve types on each patient level so that comparisons of these 2 groups of patients are more meaningful.[13,14]

The assumption of proportional hazards is checked for all prognostic variables listed in Table 1 with the use of diagnostics on the basis of weighted residuals.[15] Univariate survival analysis is carried out for each of the predictor variables in Table 1. Stepwise regression analysis with the forward selection and backward elimination technique is used to select significant variables for inclusion in a final model from the list of predictor variables in Table 1. Hazard ratios and 95% confidence intervals (CI) are provided. The Kaplan-Meier method is used to generate unadjusted raw survival curves for the 2 valve groups. The log-rank statistic is reported for the comparison of the unadjusted survival curves. The α level for univariate and multivariable comparisons is set at .05. SAS software, version 6.12 (SAS Institute, Inc, Cary, NC), was used to perform all statistical analyses and graphics.

Survival according to valve type is compared in all patients with CE or SJ prostheses, including all operation years between 1976 and 1995. We refer to these data later as the *all-patients* data set. To address the issue of different distributions of date of operation in the CE and SJ groups, we performed a second analysis in a subset of patients with years of operation after 1983 when both CE and SJ prostheses were used. This is the data set that we refer to later as the *patients-after-1983* data set. The same list of prognostic variables provided in Table 1 is used for generating final survival models for both the all-patients and patients-after-1983 data sets.

To check whether one valve type is associated with sicker patients, we compared operative mortality or 30-day mortality percentages for

TABLE 3. Results of univariate testing (all patients)*

Variable	*P* value	Hazard ratio	Lower	Upper
Age (10-y increment)	<.0001	1.37	1.27	1.47
Male sex	.009	1.24	1.06	1.46
Ejection fraction (10% lower)	<.0001	1.20	1.11	1.30
Atrial fibrillation	.665	1.04	0.88	1.22
Coronary artery disease	<.0001	2.12	1.79	2.51
Liver disease	.017	1.61	1.09	2.39
Lung disease	.002	1.39	1.13	1.70
Renal disease	<.0001	2.98	2.20	4.05
Congestive heart failure, class IV	<.0001	1.70	1.44	2.00
Diabetes	.0002	1.55	1.23	1.95
Hypertension	<.0001	1.50	1.27	1.76
Smoking history	.093	1.15	0.98	1.35
Redo heart surgery	<.0001	1.52	1.26	1.83
Concomitant valve surgery	.003	1.3	1.10	1.57
Acute presentation	<.0001	1.62	1.32	2.00
Valve cause (9 degrees of freedom)†	.05			
Mitral stenosis	.035	0.84	0.72	0.99
Mitral insufficiency grade 3 and 4	.41	1.09	0.89	1.34
Valve prosthesis	.006	0.79	0.66	0.93
Year of operation	.85	1.00	1.00	1.00

*Results from univariate testing are the unadjusted raw results not taking into consideration possible confounding effects of other parameters.
†Valve cause with 9 degrees of freedom was not tested for hazard ratio and 95% CI.

TABLE 4. Variables in the final survival model using propensity score (all patients)

Variable	*P* value	Hazard ratio	Lower	Upper
Valve type (1 = SJ, 0 = CE)	.155	0.83	0.64	1.07
Score*	.156	0.77	0.53	1.11
Age (10-y increment)	.0001	1.31	1.21	1.42
Ejection fraction (10% lower)	.001	1.14	1.05	1.23
Coronary artery disease†	.0001	1.65	1.37	1.99
Concomitant valve surgery†	.001	1.37	1.14	1.66
Redo heart surgery†	.0001	1.69	1.38	2.08
Renal disease†	.0001	2.21	1.59	3.08
Lung disease†	.022	1.28	1.04	1.6
Congestive heart failure, class IV†	.0001	1.57	1.32	1.87
Hypertension†	.009	1.27	1.06	1.51

*Propensity score that reflects the probability of being assigned to the mechanical valve group.
†1 = yes, 0 = no.

the 2 patient groups. Logistic regression is used to test for predictors of 30-day survival. To cover for the possibility that the operating room techniques could have improved since 1990, we use date of operation as a dichotomous variable (before 1990 vs after 1990) to test the effect of valve type on operative or 30-day mortality.

Younger and Older Patients

To explore the common assumption that younger patients should receive mechanical prostheses and older patients should receive biologic prostheses, we tested the interaction between age group (<60 years vs ≥60 years) and valve model. Separate survival analyses were also carried out in the younger patient population (age <60 years) and in the older patient population (age ≥60 years) by using the statistical methods described above. The year of age cutoff (60 years) is based on clinical relevance with consideration of comparable number of patients in each subgroup. To answer possible questions regarding elderly patients, we also compare survival of the 2 valve groups in patients 70 years or older at the time of operation.

Results

All Patients

The CE and SJ recipient groups are not statistically different in terms of age, coronary disease, atrial fibrillation, liver disease, lung disease, renal disease, diabetes, smoking his-

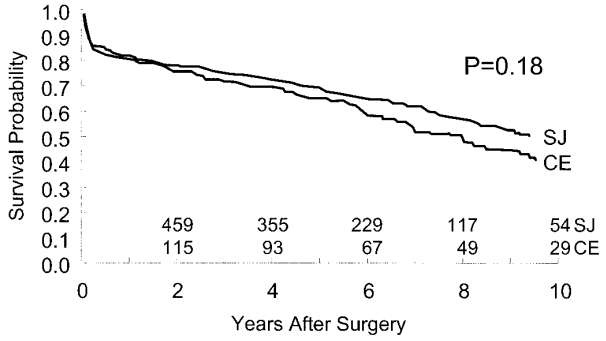

Figure 3. Adjusted 10-year survival curves of the SJ group and the CE group, with patient numbers remaining at risk given at 2, 4, 6, 8, and 10 years after the operation. The data set was patients after 1983.

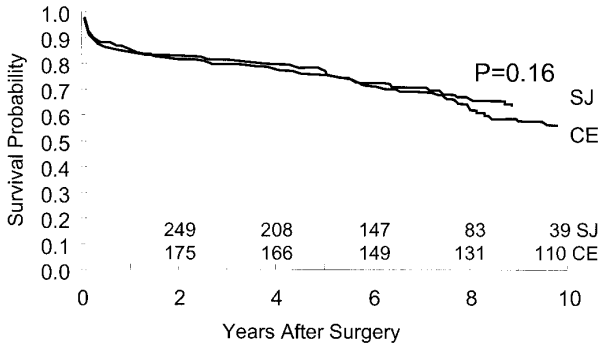

Figure 4. Adjusted 10-year survival curves of the SJ group and the CE group in all patients less than 60 years of age, with patient numbers remaining at risk given at 2, 4, 6, 8, and 10 years after the operation. The data set was all patients.

tory, or mitral regurgitation (Table 1). However, the CE group has worse ejection fraction, higher percentage of acute presentation at the time of the operation, and earlier year of operation. The SJ group has a higher proportion of hypertension, mitral stenosis, and redo heart surgery.

Valve cause (Table 2) is predominantly rheumatic, and it is equally distributed in the 2 patient groups. There is a higher percentage of paravalvular leak/prosthetic dysfunction in the SJ group (17%) than in the CE group (7%), whereas a higher percentage of mitral prolapse is observed in the CE group (23%) than in the SJ group (15%).

All variables from Table 3 were checked for the assumption of proportional hazards by using the weighted residual technique.[15] A global test of proportional hazards on all these variables was nonsignificant ($P = .16$). Individual tests on each variable showed that valve type meets the proportionality assumption ($P = .56$), as do the other variables, except for age, which showed a minor deviation from proportional hazards ($P = .02$). Allowing age to reflect its nonproportionality by dichotomizing it did not affect the survival result.

Univariately, significant predictors of worse survival are CE valve type, older age, male sex, lower ejection fraction, presence of coronary artery disease, lung disease, liver disease, renal disease, congestive heart failure class IV, diabetes, hypertension, redo heart surgery, concomitant other valve surgery, acute presentation, and mitral stenosis (Table 3). Unadjusted raw survival curves comparing the 2 valve types are presented in Figure 1.

Absolute 30-day mortality is not different between the 2 valve types: 12.5% (62/495) for CE recipients and 10.4% (67/644) for SJ recipients ($P = .3$). Independent predictors of increased 30-day mortality are age ($P < .0001$), redo heart surgery ($P = .001$), renal disease ($P < .0001$), absence of mitral prolapse ($P = .006$), and whether the year of operation was before 1990 ($P = .001$). Valve type (CE vs SJ) is not an independent predictor of 30-day mortality in the cohort of all patients ($P = .9$).

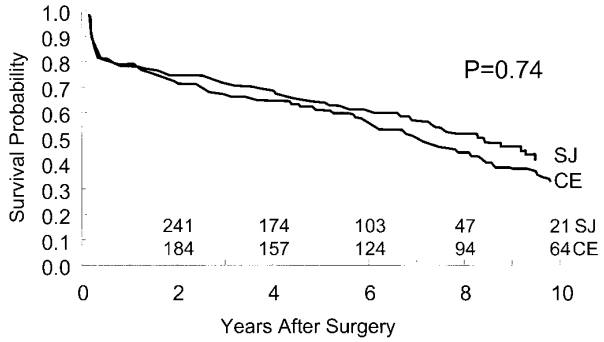

Figure 5. Adjusted 10-year survival curves of the SJ group and the CE group in all patients age 60 years or older, with patient numbers remaining at risk given at 2, 4, 6, 8, and 10 years after the operation. The data set was all patients.

By means of the logistic model, important variables that predict the assignment of valve type are age ($P < .0001$), concomitant other valve surgery ($P = .0008$), atrial fibrillation ($P = .013$), mitral stenosis ($P < .0001$), class IV congestive heart failure ($P = .012$), hypertension ($P = .049$), and date of operation ($P < .0001$). The propensity score (0-1) generated from the logistic model is the probability of being assigned to the mechanical valve group.

The prognostic variables from Table 1 that enter the final model are listed in Table 4. Controlling for these covariates, valve type does not predict survival ($P = .16$). Significant predictors of worse survival are older age, lower ejection fraction, presence of coronary artery dis-

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TABLE 5. Distribution of demographic and medical history variables by valve type (patients after 1983)

	CE (n = 225)	SJ (n = 644)	*P* value
Age (y)*	68 (60-73)	61 (50-69)	.0001
Male sex	40%	33%	.037
Ejection fraction*	51 (42-61)	54 (46-61)	.0012
Atrial fibrillation	46%	56%	.006
Coronary disease	42%	29%	.001
Liver disease	4%	2%	.246
Lung disease	18%	18%	.965
Renal disease	7%	4%	.107
NYHA class IV	42%	54%	.004
Diabetes	13%	14%	.797
Hypertension	43%	45%	.517
Smoking history	42%	41%	.940
Redo heart surgery	19%	27%	.024
Mitral stenosis	31%	49%	.001
Regurgitation grade 3 and 4	74%	56%	.001
Year of operation*	1986 (1984-1990)	1990 (1988-1993)	.0001

NYHA, New York Heart Association.
*Median (Q1, Q3).

TABLE 6. Variables in the final survival model using propensity score (patients after 1983)

Variable	*P* value	Hazard ratio	Lower	Upper
Valve type	.187	0.84	0.64	1.09
Score*	.014	0.42	0.21	0.84
Age (10-y increment)	.0001	1.26	1.12	1.42
Ejection fraction (10% lower)	.0001	1.2	1.1	1.32
Coronary artery disease	.0004	1.52	1.21	1.92
Concomitant valve surgery	.0008	1.53	1.19	1.97
Redo heart surgery	.0001	1.7	1.33	2.16
Renal disease	.0001	2.61	1.73	3.96
Congestive heart failure, class IV	.0001	1.64	1.3	2.08

*Propensity score that reflects the probability of being assigned to the mechanical valve group.

ease, lung disease, renal disease, class IV congestive heart failure, hypertension, redo heart surgery, and concomitant other valve surgery (Table 4). Adjusted survival estimates at 2, 5, and 10 years are 82% ± 2% (95% CI, 79%-85%), 69% ± 2% (95% CI, 64%-73%), and 42% ± 3% (95% CI, 37%-48%), respectively, for CE recipients and 83% ± 2% (95% CI, 80%-86%), 72% ± 2% (95% CI, 69%-76%), and 51% ± 3% (95% CI, 45%-58%), respectively, for SJ recipients. Figure 2 shows the adjusted survival curves of the 2 valve groups.

Patients After 1983

In this cohort of patients (n = 869), the 2 patient groups are statistically different in terms of several variables (Table 5). The SJ recipients (n = 644) statistically differ from the CE recipients (n = 225) in age, male percentage, ejection fraction, class IV congestive heart failure, atrial fibrillation, coronary disease, liver disease, redo heart surgery, mitral stenosis, mitral insufficiency grade 3 and 4, and date of operation.

By means of the logistic model, younger age ($P < .0001$), concomitant other valve surgery ($P = .0008$), atrial fibrillation ($P < .0001$), class IV congestive heart failure ($P = .015$), and later date of operation ($P < .0001$) are associated with the assignment of SJ valve type. The prognostic variables from Table 1 that enter the final survival model are listed in Table 6. Controlling for those covariates, valve type does not predict survival ($P = .18$) in this subset of patients (Table 4). The result confirms our earlier results from all patient data sets. Figure 3 shows the survival curves of the 2 valve groups in patients after 1983.

Younger and Older Patients

There is no significant interaction between patient age category (<60 vs ≥60 years) and valve type (CE vs SJ). However, for clinical insights, we compared the 10-year survival of the CE and the SJ recipients in a younger patient population and in an older patient population by using the data set of all patients.

For younger patients, age less than 60 years (n = 527), the CE recipients (n = 222) statistically differ from the SJ recipients (n = 305) in terms of greater percentage of male subjects, lower ejection fraction, less class IV congestive heart failure, less mitral stenosis, and earlier date of operation (Table 7). Significant predictors in patients age less than 60 years are class IV congestive heart failure ($P < .0001$), hypertension ($P < .0001$), coronary artery disease ($P < .0001$), redo heart surgery ($P = .001$), and renal disease ($P = .0007$). Adjusting for the significant prognostic variables, valve prosthesis is not a significant predictor of survival in the younger patients ($P = .16$, Figure 4).

For older patients, age greater than 60 years (n = 612), the CE recipients (n = 273) are not statistically different from the SJ recipients (n = 339) in terms of age, male percentage, ejection fraction, atrial fibrillation, coronary disease, liver disease, lung disease, renal disease, diabetes, smoking history, and mitral insufficiency. CE recipients differ from SJ recipients in terms of less class IV congestive heart failure, less hypertension, less redo heart surgery, and earlier year of operation (Table 8). Significant predictors in patients age 60 years or greater are class IV congestive heart failure ($P < .0001$), coronary artery disease ($P = .012$), redo heart surgery ($P < .0001$), diabetes ($P = .048$), and history of smoking ($P = .008$). Controlling for the significant prognostic variables, valve prosthesis is not a significant predictor of survival in patients age 60 years or older ($P = .74$, Figure 5).

TABLE 7. Distribution of demographic and medical history variables by valve type (age <60 years)

	CE (n = 222)	SJ (n = 305)	*P* value
Age (y)*	51 (43-56)	49 (41-55)	.234
Male sex	45%	29%	.001
Ejection fraction*	50 (43-56)	54 (47-61)	.0005
Atrial fibrillation	50%	51%	.773
Coronary disease	20%	17%	.361
Liver disease	5%	2%	.032
Lung disease	13%	15%	.512
Renal disease	4%	5%	.576
NYHA class IV	37%	49%	.01
Diabetes	8%	11%	.221
Hypertension	29%	33%	.278
Smoking history	54%	48%	.22
Redo heart surgery	23%	26%	.33
Mitral stenosis	47%	58%	.03
Regurgitation grade 3 and 4	76%	68%	.104
Year of operation*	1980 (1979-1982)	1990 (1988-1992)	.0001

NYHA, New York Heart Association.
*Median (interquartile range).

TABLE 8. Distribution of demographic and medical history variables by valve type (age ≥ 60 years)

	CE (n = 273)	SJ (n = 339)	*P* value
Age (y)*	68 (64-73)	68 (64-73)	.763
Male sex	39%	36%	.46
Ejection fraction*	50 (44-61)	54 (45-62)	.154
Atrial fibrillation	55%	61%	.151
Coronary disease	40%	39%	.79
Liver disease	3%	3%	.806
Lung disease	15%	21%	.072
Renal disease	7%	4%	.086
NYHA class IV	41%	58%	.001
Diabetes	12%	16%	.137
Hypertension	40%	54%	.001
Smoking history	34%	35%	.716
Redo heart surgery	12%	28%	.001
Mitral stenosis	38%	43%	.206
Regurgitation grade 3 and 4	81%	78%	.395
Year of operation*	1984 (1981-1988)	1991 (1989-1993)	.0001

NYHA, New York Heart Association.
*Median (interquartile range).

Discussion

In this article we have used multivariable modeling with the incorporation of propensity scores to minimize the biases in this observational study and have demonstrated that the choice of biologic or mechanical valve prosthesis does not significantly affect patient long-term survival up to 10 years.

A few recent studies specifically examined the CE or SJ prosthesis individually. Fradet and associates[8] reported a 52.3% survival at 10 years with CE in the mitral position. Ibrahim and coworkers[16] reported a 58.8% survival with SJ in the mitral position at 10 years, whereas Khan and colleagues[17] reported a 42% survival with SJ in the mitral position at 10 years. These reports compare well with the 10-year survival of 52% with SJ and 42% with CE in our current series.

Several other recent retrospective studies have directly compared biologic and mechanical valve prostheses. Fradet and colleagues[8] provided a comprehensive comparison between bioprostheses and mechanical prostheses in both aortic and mitral positions and reported significantly better 10-year survival with porcine valves in the mitral position. Fradet and colleagues had a large number of mitral patients (n = 2030), with an approximate 10-year follow-up time for bioprosthesis recipients and an 8-year follow-up time for mechanical prosthesis recipients. However, their mechanical series comprised 4 models, 2 of which are seldom used today, and their biologic series comprised 2 models, CE supra-annular and CE standard porcine bioprostheses. Czer and colleagues[12] reported no difference in survival between the porcine and SJ valve recipients with follow-up times limited to 5 years.

A few other articles have compared valve-related complications. Myken and colleagues[7] compared long-term valve-related complications in patients with mechanical versus biologic valve prostheses and reported significantly less 10-year valve-related mortality with porcine valves. However, Myken and colleagues had a small sample size (n = 200) and did not distinguish patients with valve replacement in aortic or mitral positions. Cobanoglu and coworkers[9] compared tissue and mechanical valves using a patient-oriented definition of treatment failure that included valve-related death or permanent patient disability. The results demonstrate an advantage of porcine valves over mechanical valves at 7 years. The contributions of their study were using treatment failure as a measurement criterion and being the first to suggest that successful reoperation should not be considered treatment failure.

We think it is important to examine valve-related complications, as well as long-term survival, when we compare the CE and SJ recipients. However, because of complicated statistical methods and subsequent lengthy explanations relating to competing risk issues when we examine valve-related complications, we have decided to focus on comparison of long-term survival in the current study and will address the issues of valve-related complications and quality of life of these patients in future studies.

A few articles have examined the role of age in selection of valve prostheses. Holper and colleagues[10] examined patients 65 years or older who underwent isolated aortic, mitral, or combined aortic and mitral valve replacement. Their findings were that valve type does not affect survival up to 15 years in the older patient population. Grossi and

coworkers[18] examined choice of mitral prostheses in patients age 70 years or older. Their findings were that valve type does not influence 10-year freedom from noncardiac death. These findings support our conclusion that valve type does not influence survival in younger or older patients.

Previous studies have examined determinants of survival after mitral valve replacement. Teoh and colleagues[19] reported age and left ventricular function as independent predictors of postoperative survival after mitral valve replacement, with a mean follow-up time of 2.7 years. Teply and coworkers[20] examined valve replacement procedures in aortic (52%), mitral (34%) and double-valve (2%) and triple-valve (2%) positions, with a mean follow-up time of approximately 6 years. They reported recent year of operation, younger age, and female sex to be predictors of late survival. Lee and Bay[21] reported that risk factors change with time. For long-term mortality, predictors were older age, surgeon, mitral insufficiency, and earlier year of operation. Adbelnoor and colleagues[22] reported that, among patients with mechanical prostheses, male sex, greater New York Heart Association class, mitral regurgitation, and relative heart volume were predictors of worse survival.

Our findings from our all patient data sets show older age, lower ejection fraction, concomitant other valve surgery, redo heart surgery, presence of coronary artery disease, renal disease, lung disease, class IV congestive heart failure, and hypertension predict long-term mortality. Our results suggest that valve type does not predict survival. The result from our all patient data sets is confirmed by the subset analysis in patients after 1983 only. Survival comparisons in the younger (age <60 years) and older (age ≥60 years) populations fail to suggest a difference in survival in younger or older populations because of valve prosthesis type.

The current study is the largest to compare the CE biologic and the SJ mechanical valve prostheses with a 10-year long-term follow-up time. Our study does not include multiple biologic or multiple mechanical valve models and therefore provides a pure comparison of 2 of the most widely used prostheses at the present time. Our survival analyses use the technique of propensity score in the multivariable Cox proportional hazards model and examine a large number of explanatory variables (Table 3) that could affect the outcome of survival. Our findings on long-term survival comparison confirm the results from the 2 randomized trials. Our exploratory survival analyses in the younger and older patient populations suggest that prosthesis selection does not affect long-term survival in younger or older patients.

Our study is limited by its retrospective nature and by the shorter median follow-up time in the SJ group. A difference in survival may be observed with a longer follow-up duration in the SJ group. At this point, the effect of prosthesis type on long-term survival in the mitral position at 10 years and beyond remains unclear. A comparison 5 years from now should shed light on the subsequent effect of prostheses on long-term 15-year survival.

Although our study is limited by its retrospective nature, our statistical methods attempt to control for most of the bias in the assignment of valve type. Randomized trials themselves are limited because randomization requires stratification on many prognostic variables and thus often leads to a selection of very specific groups of patients with results that lack generalizability. In addition, randomization is based on a few variables that the investigators consider the most significant predictors of the outcome. In contrast, propensity score analysis provides a balance of the 2 compared groups with weighted effects of the covariates on the treatment variable and thus is able to minimize the bias relating to imbalances in the assignment of treatment type.

This study suggests that choice of biologic or mechanical prostheses in the mitral position has little effect on survival up to 10 years. At the present time, choice of biologic or mechanical prostheses in the mitral position should be based on the patient ability to take anticoagulation, patient preference, and the likelihood of reoperation. Future studies should examine whether reoperation on bioprostheses between 10 and 15 years after the original operation adversely affects 15-year survival. Future studies should also compare morbidity, quality of life, and long-term care costs for patients undergoing mitral valve replacement with mechanical or biologic prostheses.

References

1. Harken DE, Soroff HS, Taylor WJ, Lefemine AA, Gupta SK, Lunzer S. Partial and complete prostheses in aortic insufficiency. *J Thorac Cardiovasc Surg.* 1960;40:744-62.
2. Starr A, Edwards ML. Mitral valve replacement: clinical experience with a ball-valve prosthesis. *Ann Surg.* 1961;154:726-40.
3. McGoon DC. Prosthetic reconstruction of the aortic valve. *Mayo Clin Proc.* 1961;36:88-96.
4. Turina J, Hess OM, Turina M, Krayenbuehl HP. Cardiac bioprostheses in the 1990s. *Circulation.* 1993;88:775-81.
5. Bloomfield P, Kitchin AH, Wheatley DJ, Walbaum PR, Lutz W, Miller HC. A prospective evaluation of the Björk-Shiley, Hancock, and Carpentier-Edwards heart valve prostheses. *Circulation.* 1986;73:1213-22.
6. Hammermeister KE, Sethi GK, Henderson WG, Oprian C, Kim T, Rahimtoola S. A comparison of outcomes in men 11 years after heart-valve replacement with a mechanical valve or bioprosthesis. *N Engl J Med.* 1993;328:1289-96.
7. Myken PS, Caidahl K, Larsson P, Larsson S, Wallentin I, Berggren HE. Mechanical versus biological valve prosthesis: a ten-year comparison regarding function and quality of life. *Ann Thorac Surg.* 1995;60:S447-52.
8. Fradet GJ, Jamieson WR, Abel JG, Lichtenstein SV, Miyagishima RT, Ling H, et al. Clinical performance of biological and mechanical prostheses. *Ann Thorac Surg.* 1995;60:S453-8.
9. Cobanoglu A, Jamieson WR, Miller DC, McKinley C, Grunkemeier GL, Floten HS, et al. A tri-institutional comparison of tissue and mechanical values using a patient-oriented definition of "treatment failure." *Ann Thorac Surg.* 1987;43:245-53.
10. Holper K, Wottke M, Lewe T, Baumer L, Meisner H, Paek S-U, et al. Bioprosthetic and mechanical valves in the elderly: benefits and risks. *Ann Thorac Surg.* 1995;60:S443-6.
11. Peterseim DS, Cen YY, Cheruvu S, Landolfo K, Bashore TM, Lowe JE, et al. Long-term outcome after biologic versus mechanical aortic

ACD

valve replacement in 841 patients. *J Thorac Cardiovasc Surg.* 1999;117:890-7.
12. Czer LS, Matloff JM, Chaux A, DeRobertis MA, Gray RJ. Porcine bioprosthetic and St. Jude valve replacement. *Chest.* 1987;91:503-14.
13. Graf E. The propensity score in the analysis of therapeutic studies. *Biometrical J.* 1997;39:297-307.
14. Rosenbaum PR. The central role of the propensity score in observational studies for causal effects. *Biometrika* 1983;70:41-55.
15. Grambsch P, Therneau T. Proportional hazards tests and diagnostics based on weighted residuals. *Biometrika.* 1994;81:515-26.
16. Ibrahim M, O'Kane H, Cleland J, Gladstone D, Sarsam M, Patterson C. The St. Jude Medical prosthesis: a thirteen-year experience. *J Thorac Cardiovasc Surg.* 1994;108:221-30.
17. Khan S, Chaux A, Matloff J, Blanche C, DeRobertis M, Kass R, et al. The St. Jude Medical valve: experience with 1,000 cases. *J Thorac Cardiovasc Surg.* 1994;108:1010-9.
18. Grossi EA, Galloway AC, Zakow PK, Miller JS, Buttenheim PM, Baumann FG, et al. Choice of mitral prosthesis in the elderly: an analysis of actual outcome. *Circulation.* 1998;98:116-9.
19. Teoh KH, Ivanov J, Weisel RD. Determinants of survival and valve failure after mitral valve replacement. *Ann Thorac Surg.* 1990;49:643-8.
20. Teply JF, Grunkemeier GL, Sutherland HD, Lambert LE, Johnson VA, Starr A. The ultimate prognosis after valve replacement: an assessment at twenty years. *Ann Thorac Surg.* 1981;32:111-9.
21. Lee JK, Bay K. Mortality risk factors associated with mitral valve replacement: a survival analysis of 10 year follow-up data. *Can J Cardiol.* 1991;7:11-8.
22. Abdelnoor M, Fjeld NB, Vaage K, Svennevig JL, Klingen G, Wickstrom E, et al. Risk factors for morbidity and mortality in mitral valve replacement. *Eur J Cardiothorac Surg.* 1990;4:425-30.

Comparison of survival after mitral valve replacement with biologic and mechanical valves in 1139 patients

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