

The Influence of Coronary Artery Disease on Quality of Life after Mechanical Valve Replacement

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Background and aim of the study: Coronary artery disease (CAD) is known to impact negatively on long-term survival following valve replacement (VR). However, its influence on quality of life (QOL) remains undefined in patients with mechanical VR.

Methods: A total of 318 consecutive patients undergoing VR with the St. Jude Medical (SJM) mechanical valve were matched for age and gender with 318 patients who had VR (SJM valve) and coronary artery bypass grafting (VR+CABG). The VR group comprised 197 men and 121 women; the VR+CABG group also comprised 197 men and 121 women. The mean age of all patients was 66.0 ± 8.0 years (range: 40-87 years). The Short Form-36 (SF-36) health survey was administered to all survivors at follow up examination.

Results: Operative mortality was comparable between groups (4.7% for VR, 7.5% for VR+CABG; $p = 0.186$). Hospital complications were also similar, except for reoperation for bleeding ($p = 0.049$). The mean follow up was 6.0 years for VR patients and 4.7 years for VR+CABG patients. Actuarial survival was

significantly better in VR patients than VR+CABG patients ($79.4 \pm 2.4\%$ versus $75.0 \pm 2.7\%$ at five years; $58.6 \pm 4.3\%$ versus $47.5 \pm 4.5\%$ at 10 years; $p = 0.018$). The equality of survival distribution was significantly different ($p = 0.008$). Multivariate analysis identified CABG as a predictor of late mortality ($p = 0.003$) but not of late QOL. QOL was similar on the eight health scales and physical health (44.5 ± 10.3 versus 45.5 ± 10.7) and mental health (52.4 ± 9.8 versus 52.5 ± 10.1) summary components, respectively. Age ($p = 0.004$), time from surgery to SF-36 administration ($p = 0.007$) and gender ($p = 0.029$), but not CABG, were significantly associated with QOL as assessed by the SF-36.

Conclusion: CAD is a predictor of late mortality after mechanical VR. However, provided CABG is performed concomitantly with VR, the patient's long-term QOL appears to return to that expected for the general population.

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Coronary artery disease (CAD) has been shown to adversely affect the outcomes of valvular heart surgery (1). This negative impact has been documented to decrease both perioperative and long-term survival (2,3), as well as to increase the risk of postoperative complications (4,5). Similar findings have been reported in both the mitral (6) and aortic (7) positions, and with both mechanical (8) and bioprosthetic (9) valves. However, one point which has not been systematically evaluated is the impact of CAD on the patient-assessed quality of life (QOL) following valve replacement surgery.

Traditionally, the patient's QOL has been assessed by

the physician, without the benefit of any validated or standardized evaluation instrument. As a result, clinical bias may have influenced the evaluation of various interventions on the patient's health status and sense of well-being. With the advent of a validated and reliable instrument to assess the patient's perception of his or her health status, a more definitive and quantifiable measurement of the patient's QOL can now be achieved (10).

Since the majority of patients undergoing heart valve replacement currently receive a mechanical valve, and since the St. Jude Medical (SJM) mechanical heart valve is the most widely used mechanical prosthesis, the aim of the present study was to evaluate the impact of CAD on early and late survival in patients undergoing valve replacement with the SJM prosthesis, and its subsequent influence on long-term, patient-assessed QOL.

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Clinical material and methods

Patient population

A population of 1,130 consecutive patients who underwent valve replacement (VR) with a SJM mechanical valve between April 1983 and December 1998 was reviewed. A subset of these patients (n = 636) was further divided into two groups - those who underwent VR only (n = 318), and those with VR and coronary artery bypass grafting (VR+CABG) (n = 318). The VR+CABG patients were matched by age and gender to the VR group.

CAD in the VR+CABG group requiring surgical intervention in the present study was defined as an estimated reduction in luminal diameter $\geq 50\%$. Those patients who did not meet the established criteria and did not undergo CABG were considered as not having CAD.

The VR and VR+CABG groups each comprised 197 men and 121 women. Overall, the mean patient age was 66.0 ± 8.0 years (range: 40 to 87 years). The clinical characteristics of the two patient groups are listed in Table I.

Surgery was performed electively in 244 patients (76.7%) in the VR group, and in 235 (73.9%) in the VR+CABG group. Surgery was performed urgently in 69 patients (21.7%) in the VR group and in 70 (22.0%) in the VR+CABG group, and as an emergency in five patients (1.6%) in the VR group and 13 (4.1%) in the VR+CABG group. The current procedure represented

a reoperation in 97 patients (30.5%) of the VR group, and in 70 patients (22.0%) of the VR+CABG group (p = 0.019).

Definitions

Preoperative variables

Hypertension was defined as blood pressure ≥ 140 mmHg systolic or ≥ 90 mmHg diastolic on two occasions, or currently on antihypertensive medication. Hypercholesterolemia was defined as a serum cholesterol level > 200 mg/dl on admission to hospital. Renal insufficiency was defined as a documented history of renal failure with a serum creatinine level ≥ 2.0 mg/dl on dialysis.

Elective surgery was defined as an operation, which could be deferred without increased risk of compromised cardiac outcome. Urgent surgery was defined as being required within 48 h in an effort to prevent further clinical deterioration. Emergency surgery was defined as those instances when the patient had intractable angina or heart failure that did not respond to aggressive clinical measures or had impending infarction, or when decompensation occurred in the cardiac catheterization laboratory and measures such as defibrillation, extended cardiac massage, balloon counterpulsation, or inotropic support were required.

Postoperative variables

Respiratory insufficiency was defined as patients requiring ventilatory support for more than 48 h, or

Table I: Comparison of preoperative clinical variables by patient group.

Variable	VR	VR+CABG	p-value
No. of patients	318	318	
Preoperative			
Family history of CAD	74 (23.2)	75 (23.6)	0.474
Hypertension	125 (39.3)	168 (52.8)	0.001
Hyperlipidemia	48 (15.1)	91 (28.6)	0.001
Smoking history	153 (48.1)	143 (45.0)	0.474
Diabetes mellitus	35 (11.0)	87 (27.4)	0.001
Renal insufficiency	32 (10.1)	22 (6.9)	0.200
CVD	36 (11.3)	32 (10.1)	0.700
PVD	39 (12.3)	43 (13.5)	0.723
Prior MI	45 (14.2)	122 (38.4)	0.001
History of CHF	200 (62.9)	168 (52.8)	0.013
Arrhythmia	117 (36.8)	83 (26.1)	0.005
Angina (unstable)	101 (31.8)	208 (65.4)	0.001
NYHA class IV	90 (28.3)	135 (42.5)	0.001
Ejection fraction (< 0.50)	168 (52.8)	185 (58.2)	0.308
Prior PCI	12 (3.8)	49 (15.4)	0.001

Numbers in parentheses are percentages.

CABG: Coronary artery bypass grafting; CAD: Coronary artery disease; CHF: Congestive heart failure; CVD: Cerebrovascular disease; MI: Myocardial infarction; PCI: percutaneous coronary intervention; PVD: Peripheral vascular disease; VR: Valve replacement.

tracheostomy (or both). Cerebrovascular accident (CVA) was defined as a neurological deficit that remained unresolved and presented for more than 24 h. Perioperative myocardial infarction (MI) was defined as a new onset of Q waves with or without elevation of myocardial enzymes, or a substantial elevation of myocardial enzymes alone. Low cardiac output syndrome was defined as clinical evidence of hypotension, oliguria, and peripheral vascular constriction with normal or supranormal left ventricular filling pressure or a measured cardiac index <2 l/min/m², necessitating the administration of catecholamines or use of the intra-aortic balloon pump, or both. Deep sternal infection was defined as instability of the sternum with positive wound cultures necessitating an additional surgical procedure, such as incision and drainage, debridement, or secondary closure.

Hospital mortality was defined as death occurring during the operation or the hospitalization in which the procedure was performed, or death occurring after discharge from the hospital but within 30 days of the surgical procedure, unless the cause was clearly unrelated to the operation.

Operative technique

All operations were performed via a median sternotomy using similar cardiopulmonary bypass (CPB) and myocardial protection techniques (intermittent antegrade or combined antegrade/retrograde cold sanguinous hyperkalemic cardioplegia). Reversed saphenous vein and internal mammary artery grafts were used in all patients in the VR+CABG group. Single aortic cross-clamping was used for valve replacement and for the construction of distal anastomosis in coronary grafts. A valve suture technique was performed with interrupted pledget-reinforced 2.0 mattress sutures. Mitral and tricuspid reconstruction for regurgitation was performed by annuloplasty and

reinforced with the use of an appropriately sized valve ring.

Operative data

A total of 362 valves was implanted in the VR group. Among these valves, 215 (59.4%) were implanted in the aortic position, 144 (39.8%) in the mitral position, and three (0.8%) in the tricuspid position. Forty-four patients (13.8%) in the VR group underwent multiple valve replacement.

A total of 333 valves was implanted in the VR+CABG group, including 191 (57.7%) in the aortic position and 142 (42.6%) in the mitral position. Fifteen patients (4.7%) in the VR+CABG group received multiple valve replacements. A total of 689 coronary artery grafts was performed in the VR+CABG group (mean 2.17 per patient; range: 1 to 5 grafts).

QOL assessment

QOL assessment was conducted with the SF-36 developed by Ware (10) and associates. The SF-36 is a standardized instrument which comprises 36 items designed to measure eight dimensions of overall health. These include: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health. For each dimension, item scores are computed, totaled and converted into a scale, which ranges from 0 for worst health to 100 representing best health.

Two summary components - a physical and mental health score - are also computed. A high score in the Physical Health Summary component indicates no physical limitations, disabilities, decrements in well-being and/or high energy levels. A low score indicates substantial limitations in self-care, physical, social and role activities, severe bodily pain, or persistent tiredness.

In the Mental Health Summary component, a high

Table II: Comparison of hospital complications by patient group.

Complication	VR	VR+CABG	p-value
No. of patients	318	318	
Reoperation for bleeding	13 (4.1)	4 (1.3)	0.049
Respiratory insufficiency	35 (11.0)	48 (15.1)	0.158
CVA	8 (2.5)	15 (4.7)	0.203
Postoperative MI	3 (0.9)	6 (1.9)	0.502
Renal insufficiency	34 (10.7)	31 (9.7)	0.793
Low cardiac output	47 (14.8)	64 (20.1)	0.095
Cardiac arrest	17 (5.3)	25 (7.9)	0.264
Deep sternal infection	6 (1.9)	8 (2.5)	0.787

Numbers in parentheses are percentages.

CABG: Coronary artery bypass grafting; CVA: Cerebrovascular accident; MI: Myocardial infarction; VR: Valve replacement.

score demonstrates recurring positive affect, absence of psychological distress and a sense of emotional well-being. A low score is indicative of the presence of psychological disturbance and substantial social and role dysfunction due to emotional instability. The physical and mental health summary scores are scaled to have a mean of 50 and a standard deviation of 10 in the general population (11). The instrument has been used in a number of public health studies. It is generally completed in approximately 10-15 min, and may be administered in person, by telephone or by mail.

Data collection and management

Perioperative data were obtained by prospective review of the patient's hospital record, catheterization reports, cineangiograms and echocardiography applying a standardized methodology and definition of terms. A 'Patient Registration Form' was completed for each patient in the study at the time of operation. Data were entered into a 'Cardiac Surgery Clinical Database' and subsequently retrieved for analysis. Follow up information was obtained between March 1999 and April 2001 through comprehensive questionnaires and by telephone interview with surviving patients, family members, or the patient's personal physician, and a 'Patient Follow Up Form' was completed.

The use of these data collection instruments provided for standardized reporting of each patient's clinical status before and after the operation. Follow up was 97.5% complete in the VR group, with eight patients being lost after discharge from hospital. In the VR+CABG group, follow up was 98.1% complete, with six patients lost after discharge.

Statistical analysis

Data were presented as frequency distributions and simple percentages. Values of continuous variables were expressed as mean \pm SD. Analysis of discrete variables was accomplished by χ^2 test, the continuity-adjusted χ^2 analysis, or a two-tailed Fisher's exact test. Spearman's rank correlation coefficient was used to

discern the relationship between selected parameters. Comparison of means for continuous variables was conducted by an unpaired Student's *t*-test. A Cox proportional hazards regression model was developed to identify preoperative and intraoperative factors associated with late death (12). A stepwise multivariate linear regression model was used to determine independent predictors of physical summary score on the SF-36.

Patient survival was expressed by actuarial analysis according to the method of Kaplan and Meier (13), using time zero as the date of operation and late death as the end point (with variability expressed as the SEM). The equality of survival distribution for the two patient groups was computed using the Log Rank algorithm (14). Data collected were subjected to both quantitative and qualitative analysis using the biostatistical capabilities of the Patient Analysis and Tracking System (PATS; Axis Clinical Software, Inc., Portland, OR, USA) and the Number Cruncher Statistical Systems (NCSS; Kaysville, UT, USA).

A statistically significant difference between measurements was defined as $p \leq 0.05$.

Results

Hospital mortality

The hospital mortality rate for VR patients was 4.7% (15/318) and 7.5% (24/318) for VR+CABG patients (not significant).

The mortality rate for aortic valve replacement in the VR group was 4.2% (7/167) and 5.7% (10/174) in the VR+CABG group, and for mitral valve replacement in the VR group was 4.2% (4/96) and 9.7% (12/124) in the VR+CABG group. The mortality rate for multiple valve replacement was 9.1% (4/44) in the VR group and 0.0% (0/15) in the VR+CABG group. Comparison of mortality rates by valve position and for multiple valve replacement achieved no significant difference between the groups.

Table III: Variables influencing late mortality as evidenced by Cox regression analysis in St. Jude Medical valve patients undergoing mechanical valve replacement.

Variable	Regression coefficient	SE	Relative hazard	p-value*
Age	0.0399	0.0099	1.0407	0.001
CABG	0.5418	0.1486	1.7191	0.003
CHF	0.8742	0.1771	2.3970	0.001
CVD	0.6162	0.2016	1.8518	0.002
RI	0.7795	0.2140	2.1803	0.003

*Only significant variables ($p < 0.05$) listed.

CABG: Coronary artery bypass grafting; CHF: Congestive heart failure; CVD: Cerebrovascular disease; RI: Renal insufficiency

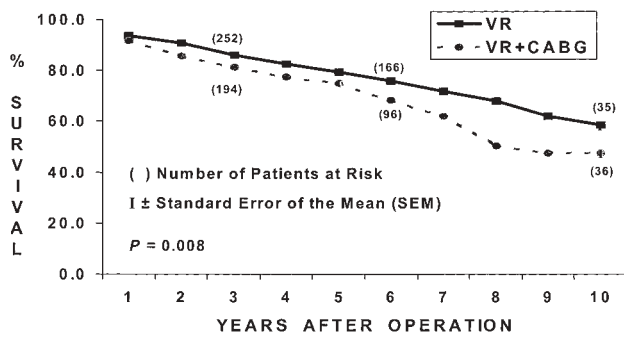


Figure 1: Comparison of actuarial survival of valve replacement (VR) and VR+ coronary artery bypass grafting (VR+CABG) patients.

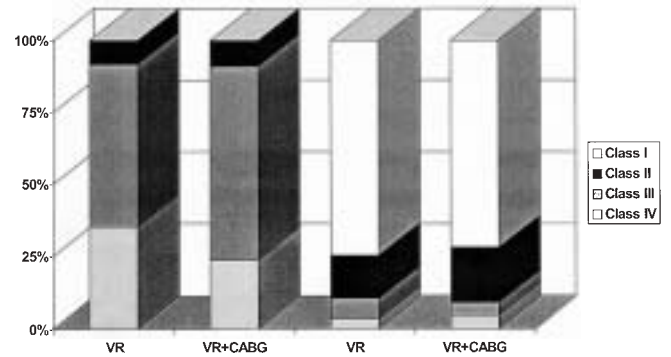


Figure 2: Preoperative and postoperative NYHA functional classification of current survivors for valve replacement (VR) and VR+ coronary artery bypass grafting (VR+CABG) patients.

Hospital morbidity

A series of hospital complications was documented for both groups which included: reoperation for bleeding, respiratory insufficiency, CVA, perioperative MI,

renal insufficiency, low cardiac output, cardiac arrest and deep sternal infection. The hospital complication rates for the two groups are listed in Table II. Only reoperation for bleeding achieved statistical signifi-

Table IV: Comparison of preoperative clinical variables for patients completing the SF-36 Quality of Life assessment at follow up by patient group.

Variable	VR	VR+CABG	p-value
No. of patients	199	181	
Gender			
Male	128 (64.3)	121 (66.9)	0.604
Female	71 (35.7)	90 (33.1)	
Age (years)			
Mean	64.8 ± 7.8	65.0 ± 7.7	0.819
Range	41 to 87	40 to 81	
Preoperative			
Family history of CAD	45 (22.6)	36 (19.9)	0.517
Hypertension	73 (36.7)	100 (55.2)	0.001
Hyperlipidemia	39 (19.6)	67 (37.0)	0.001
Smoking history	103 (51.8)	79 (43.6)	0.114
Diabetes mellitus	17 (8.5)	44 (24.3)	0.001
Renal insufficiency	16 (8.0)	6 (3.3)	0.049
CVD	19 (9.5)	13 (7.2)	0.407
PVD	19 (9.5)	22 (12.2)	0.413
Prior MI	24 (12.1)	66 (33.1)	0.001
History of CHF	110 (55.3)	73 (40.3)	0.004
Arrhythmia	66 (33.2)	44 (24.3)	0.057
Angina (unstable)	96 (48.2)	135 (74.6)	0.001
NYHA class IV	44 (23.6)	64 (35.4)	0.012
Ejection fraction (<0.50)	105 (52.8)	106 (58.6)	0.256
Prior PCI	8 (4.0)	30 (16.6)	0.001

Numbers in parentheses are percentages.

CABG: Coronary artery bypass grafting; CAD: Coronary artery disease; CHF: Congestive heart failure; CVD: Cerebrovascular disease; MI: Myocardial infarction; PCI: percutaneous coronary intervention; PVD: Peripheral vascular disease; VR: Valve replacement.

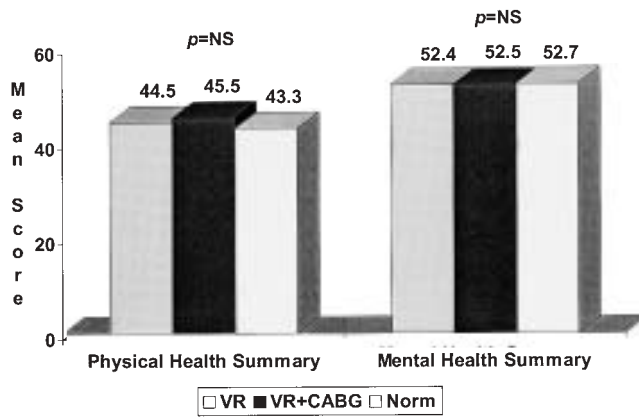


Figure 3: Comparison of SF-36 Physical and Mental Health Summary scores for valve replacement (VR) and VR+ coronary artery bypass grafting (VR+CABG) patients with age-adjusted norms.

cance between the groups ($p = 0.049$). The overall incidence of postoperative morbidity was lower in the VR+CABG group ($n = 90$; 28.3%) than in the VR group ($n = 106$; 33.3%), but this difference did not achieve statistical significance.

Long-term follow up

Follow up data were collected for 303 VR patients and 294 VR+CABG patients discharged from hospital. The mean follow up for VR patients was 6.0 years (range: 1 month to 15.0 years), and for VR+CABG patients was 4.7 years (range: 1 month to 15.0 years). The cumulative follow up was 1,817.3 patient-years (pt-yr) for VR patients, and 1,383.4 pt-yr for VR+CABG patients.

In order to discern the predictors of late mortality, 25 preoperative and intraoperative variables (see Appendix I) were entered into a Cox proportional hazards regression model to explore their relationship to late death (>30-day mortality). Cox regression analysis showed the independent influence of five covariates: age ($p < 0.001$), CABG ($p < 0.003$), congestive heart failure (CHF) ($p < 0.001$), cerebrovascular disease (CVD) ($p < 0.002$) and renal insufficiency ($p < 0.003$). The complete results of this analysis are shown in Table III.

On completion of the current follow up, 204 (67.3%) of the 303 VR hospital survivors, and 186 (63.3%) of the 294 VR+CABG hospital survivors, were alive. There were 91 (35.7%) late deaths in the VR group, and 102 (9.9%) in the VR+CABG group. Eight patients (2.6%) in the VR group and six (2.4%) in the VR+CABG group were lost to follow up.

The actuarial survival data for the VR and VR+CABG patients are displayed in Figure 1. At five years, mean (\pm SEM) survival was $79.4 \pm 2.4\%$ for VR

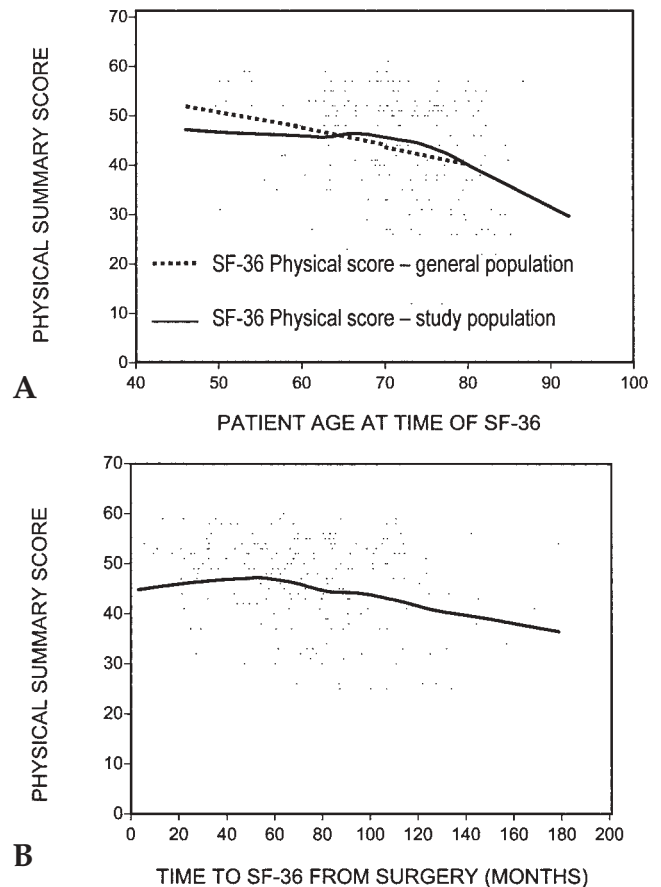


Figure 4: A) Relationship of SF-36 Physical Summary Score to patient age at survey administration compared to norms. B) Relationship of SF-36 Physical Summary Score for time from surgery (months) to survey administration.

patients, and $75.0 \pm 2.7\%$ for VR+CABG patients. At 10 years, survival was $58.6 \pm 4.3\%$ for VR patients, and $47.5 \pm 4.5\%$ for VR+CABG patients. The equality of survival distribution for the two groups was tested, and a significant difference was noted ($p = 0.008$).

On completion of follow up, many current survivors were clinically and functionally improved, with an enhanced QOL, and with 91.2% of VR patients ($p = 0.001$) and 89.8% of VR+CABG patients ($p = 0.001$) in NYHA class I or II. The preoperative and postoperative NYHA functional class for current survivors in both groups is shown in Figure 2.

The number and rate of major adverse cardiac events (MACE) in VR survivors were as follows: non-fatal MI, two events (1.0%); CVA, 10 events (4.9%); hemorrhage requiring hospitalization, five events (2.5%); and reoperation, one event (0.5%). In the VR+CABG patients, the number and occurrence rate of MACE were as follows: non-fatal MI, four events (2.2%); CVA, four events (2.2%); hemorrhage requiring hospitalization, four events (2.2%); and reoperation, two events (1.1%).

Table V: Health Status scale scores for isolated valve replacement (VR) and valve replacement plus coronary artery bypass grafting (VR+CABG) patients at follow up.

Scale score	VR (n = 199)	VR+CABG (n = 181)	p-value
Physical Functioning	62.91 ± 28.16	65.9 ± 28.1	0.150
Role-Physical	71.11 ± 40.75	74.2 ± 39.6	0.226
Bodily Pain	79.29 ± 24.96	78.8 ± 27.0	0.426
General Health	66.74 ± 24.77	68.8 ± 22.4	0.193
Vitality (Energy/Fatigue)	57.56 ± 20.53	59.0 ± 21.5	0.259
Social Functioning	83.26 ± 26.01	84.8 ± 25.4	0.285
Role-Emotional	77.73 ± 37.78	80.9 ± 34.5	0.194
Mental Health	78.09 ± 18.63	76.9 ± 19.4	0.270
Physical Health Summary	44.5 ± 10.3	45.5 ± 10.7	0.177
Mental Health Summary	52.4 ± 9.8	52.5 ± 10.1	0.461

Values are mean ± SD.

Comparison of the occurrence of MACE between the two patient groups demonstrated no significant difference.

QOL assessment at follow up

At the time of patient follow up, QOL assessment with the SF-36 was conducted for survivors in the VR group (97.5%; 199/204) and in the VR+CABG group (97.3%; 181/186). A description of the preoperative clinical variables for the two patient groups completing the SF-36 is provided in Table IV. No differences were noted in the distribution of gender or in patient age - the two variables on which the two study cohorts were originally matched. In fact, even though the two groups differed significantly in several of the variables, the distribution of these differences mirrored the initial cohorts undergoing surgery (see Table I), except with regard to renal insufficiency. This variable was not significantly different between the preoperative groups; however, among those patients who underwent follow up evaluation and completed the SF-36, renal insufficiency was more prevalent in the VR group (8.0%; 16/199) than in the VR+CABG group (3.3%; 6/181) ($p = 0.049$).

The means and standard deviations for each of the eight Health Status Scale scores and the Physical and

Mental Health Summary score for the two groups are listed in Table V. Between-group comparisons on the eight Health Status Scale scores and the two summary components achieved no statistically significant differences.

In order to identify the covariates associated with the physical summary score of the SF-36, 26 pre-, intra- and postoperative variables were entered into a stepwise multivariate linear regression model (Appendix II). Significant predictor variables in the model are shown in Table VI.

A comparison of the Physical and Mental Health Summary scores of VR patients with age-adjusted norms also demonstrated no significant difference. A similar comparison of the Physical and Mental Health Summary scores for VR+CABG patients with age-adjusted norms also achieved no significant difference (Fig. 3). An analysis of the relationship between age and Physical Health Summary score demonstrated an inverse relationship ($r = -0.207$; $p = 0.001$), which was linear and progressive in nature and may infer that the older the patients at the time the SF-36 is administered, the lower the score (Fig. 4A). However, the relationship between the SF-36 Physical Summary score and the length of time between surgery and survey administration revealed a progressive improvement in score

Table VI: Independent predictors of SF-36 Physical Summary score by stepwise multivariate linear regression analysis.

Predictor	Regression coefficient	SE	t-value	p-value*	R2
Age	-0.2133	0.0733	-2.910	0.0038	0.0292
Months to SF-36 administration	-0.0490	0.0181	-2.711	0.0070	0.0608
Female gender	2.7339	1.2498	2.187	0.0294	0.0760

*Only significant variables ($p < 0.05$) listed.

until approximately 40 months, following which time there was an overall decline in the score (Fig. 4B). Moreover, an analysis of the relationship between the patient's NYHA class at follow up and the SF-36 Physical Summary score achieved a moderate negative relationship ($r = -0.421$; $p = 0.001$). These findings demonstrated that VR and VR+CABG patients have comparable QOL, similar to that of the general population.

Discussion

During the past three decades, unprecedented strides have been taken in the design, development and manufacture of prosthetic heart valves. Moreover, improvements in operative technique, myocardial preservation, anesthesia and perioperative care have made heart valve replacement surgery a safer and more successful procedure (15).

Numerous reviews have documented favorable outcomes and long-term clinical results in patients undergoing heart valve replacement (16,17), and this trend has encouraged surgeons to operate on an older and sicker population. The patient's QOL has become an ever-increasingly important consideration in clinical decision-making and in the arena of public policy and its attendant concern for the most appropriate allocation of precious healthcare resources.

Patient QOL is a complex and multidimensional concept with many social, psychological and physical ramifications (18). These issues may be related to general health concerns, specific disease state, operative and technical considerations as well as individual-specific parameters (19). With the advent of the SF-36 (10), the patient's subjective perceptions and expectations of these varied elements can be transformed into an objective assessment of perceived QOL.

Validation in multiple healthcare settings have demonstrated the reliability and sensitivity of the SF-36 in various cohorts of patients, while permitting comparisons with age- and gender-matched controls from the general population. The SF-36 has documented significant improvement in patient self-assessed QOL following heart valve surgery (20,21).

As a result, this approach was applied to an evaluation of the impact of concurrent CAD on QOL following valvular heart surgery. Although patient groups in the present study were well matched for age and gender as well as the distribution of valvular operations, there were significant differences in the patient's clinical characteristics, as might be expected. These differences tend to highlight the impact of CAD, while focusing on a homogeneous sample of SJM mechanical valve patients. This would tend to minimize the impact of confounding variables related to valve selec-

tion and performance. Since a majority of patients undergoing valvular surgery in the USA currently receive a mechanical valve, and the SJM prosthesis is the most widely used and one of the most well-studied of these, the selection of this group of patients affords the widest applicability with the fewest unknown clinical parameters.

In order to provide the proper forum for the evaluation of QOL, it is critical to assess the clinical status of the patients according to well-established conventions. As may have been anticipated, the operative mortality was higher in the VR+CABG group than in the VR group, though this difference was not statistically significant. This may have been due to the limited sample size or to the presence of other more compelling risk factors in this study population - namely, that 91.5% (291/318) of VR patients and 92.7% (298/318) of VR+CABG patients were in NYHA classes III or IV preoperatively. Further, the majority of patients in the two groups - 52.8% (168/318) and 58.2% (185/318) respectively - had impaired left ventricular function.

There were no significant differences among postoperative complications documented between groups, with the exception of a higher rate of reoperation for bleeding in the VR group (4.1%; 13/318) than in the VR+CABG group (1.3%; 3/318). The higher bleeding rate in the VR group may have been related to the increased occurrence rate of preoperative atrial fibrillation, with its attendant need for chronic anticoagulation and relative depletion of coagulation factors at the time of operation. Although the incidence of other complications may have been too low to achieve statistical significance, the overall incidence of postoperative morbidity was also found not to differ between groups.

Long-term follow up in the present study revealed an improved actuarial survival for VR patients compared with the VR+CABG patients. This finding was consistent with that reported elsewhere (1-3,6-9). Using Cox proportional hazards regression analysis, CABG was determined to be a powerful predictor of late mortality. Of note, surgical site - viz., the aortic or mitral position - was found not to be a predictor of late mortality, while both CHF and CVD were.

These results may imply that the reasons for the generally observed worse prognosis in mitral valve patients may be more related to the underlying condition of the ventricle rather than to the anatomic site of valve implantation. Even though it has been suggested that coronary patients may be more vulnerable to coagulation-related complications of valvular surgery (4), this phenomenon was not observed in the present study.

The measured outcomes herein demonstrated an excellent patient-perceived QOL, as assessed by the

SF-36. In fact, it was comparable with that of an age-matched population. This favorable self-assessment of QOL likely reflects the relatively low rate of late adverse cardiac events in the two groups. Moreover, these excellent results corroborate marked improvements in the patients' clinical status as assessed by the NYHA classification, which showed 89.8% (167/186) of VR and 91.2% (186/204) of VR+CABG patients to be in NYHA class I or II at follow up. The present data document a positive correlation between low NYHA class and higher score on the SF-36 Physical Summary score. This finding is consistent with studies of coronary patients (22) and those with porcine bioprostheses (23), documenting a relationship between physical functioning scores on the SF-36 and NYHA class.

Although late follow up in patients with SJM valves using the SF-36 has likewise documented a similar QOL to age-matched controls (8), some studies in elderly patients have even shown an improved survival following valve surgery compared with age-matched controls (23). This latter phenomenon may in fact be influenced by the occurrence of a greater degree of morbidity and other comorbid health-related issues in the elderly population.

The overall outcomes on the SF-36 were similar between groups, and the pattern of improvement was also comparable. No difference was observed between VR and VR+CABG patients on any of the eight Health Status domains surveyed through the SF-36. This raises an obvious question - if CAD was found to be a powerful predictor of late mortality, why does it not similarly impact on QOL in late survivors?

The suggested reasons may be multidimensional. First, the mean duration of follow up for the VR patients was 6.0 years, but only 4.7 years for the VR+CABG patients. Moreover, there is evidence to suggest that the patient-assessed QOL degrades after the first 12 months postoperatively, as valve-related complications and progression of underlying disease factors become more prevalent (24). The present findings document a similar pattern of initial improvement, followed by decline, but date the beginning of that decline to approximately 42 months rather than 12 months. This difference between the studies may be due to differences in patient population (Kwok's study had only 26% valve patients), methodology (scheduled follow up rather than cross-sectional analysis) and duration of follow up (24 months versus up to 15 years). Nevertheless, the implication is that, after surgery, there is an initial period of improvement in the patients' perception of QOL, which subsequently begins to decline over time. This decline could, in theory, be disease-specific. However, in an elderly cohort of patients as in the present group it is more likely due to the multiple contributing factors, which cause such

a pattern of decline in SF-36 scores with increasing age in the general population. This latter explanation is strongly supported by congruence of the present scores with those seen in the general population, both on average (Fig. 3) and with increasing age (Fig. 4A).

Since the VR patients were followed for an average of 6.0 years and the VR+CABG patients for an average of 4.7 years, it might be anticipated that the VR+CABG patients, who were closer to the early 'peak' in SF-36 scores than the VR patients, should have a higher mean summary score. The fact that they did not might therefore imply that, relatively speaking, the QOL in the VR+CABG patients was lower than anticipated, suggesting a negative influence of CABG on QOL. In fact, this hypothesis was tested directly, and there was no significant difference between SF-36 scores between groups for any time period during follow up. Therefore, the findings can be viewed as truly comparable.

Second, the definition of CAD in this cohort included only patients with bypassable vessels with angiographically demonstrable reduction of luminal diameter >50%. Due to the limitations of angiography in the assessment of perhaps more clinically relevant phenomena such as coronary flow reserve and the inevitable existence of 'non-bypassable' lesions, there may well have been a certain level of CAD in the VR group which was not bypassed at the time of operation. This possibility is reflected in the presence of risk factors and angina in the VR group. The presence of non-bypassed CAD clearly increases late mortality in valvular heart surgery patients (1,25,26). Perhaps, the small increment of unrecognized or unbypassed CAD in the VR group was sufficient to reverse any improvements in QOL which otherwise would have been anticipated from the VR group relative to the VR+CABG group.

More likely than either of these explanations, however, is the fact that all demonstrable CAD was bypassed. Given the excellent long-term results of CABG, as well as multiple advances in recent years in the medical management of these patients, it is very likely that the VR+CABG patients were, by virtue of their operation, restored to a clinical status approaching that of VR-only patients. Therefore, the patients' perceived health status was not negatively impacted by the preoperative presence of CAD. In fact, the occurrence of increased preoperative coronary symptoms, once alleviated in the postoperative period, may have resulted in even greater relative symptomatic improvement. This, in turn, may have influenced an even greater improvement in self-assessed health status. However, as there was no preoperative QOL assessment in this cohort of patients, this issue cannot be clearly addressed.

Lastly, it should be considered that the reason for an absence of any demonstrable difference between groups is that the results of the self-perceived SF-36 health assessment may be less sensitive to differences that may occur between operations or their underlying pathophysiologies than they are to other parameters of psychological functioning. Stoll and colleagues (27) showed that patients who underwent CABG and aortic valve replacement described enhanced life satisfaction summary scores when compared with healthy control groups. However, patients with evidence of post-traumatic stress disorder reported the lowest SF-36 Mental Health Summary scores, regardless of the type of operation performed. These findings demonstrate the importance of competing variables in the complex set of factors which generate these scores. In the present study, despite the high degree of statistical significance achieved by the factors identified by linear regression analysis (p-values), their relatively small impact on the overall scores (R^2 -values) suggests that these variables had little overall predictive power. More simply, this analysis suggests that once patients have undergone successful valvular surgery, they return to the QOL of the general population. The present results showing scores consistent with age-matched controls from the general population confirm this finding. Specific disease or surgical factors, such as the presence or absence of CAD may impact on long-term survival, but appear to have little effect on the long-term QOL of survivors.

Study limitations

Despite the contributions offered by this investigation, as with any retrospective study there are several limitations that must be considered. As this was a cross-sectional study, patient QOL was assessed at different points during the postoperative course. This, as noted above, may have introduced a source of variability in the results. Further, as noted above, there was no preoperative assessment, and therefore a baseline measurement does not exist with which to compare preoperative status. Although the use of age-matched norms does furnish an alternative to standardize the results, it would have been of value to discern the perceived preoperative health status of the two groups. It should be noted that their clinical status is clearly different in certain regards, and their self-assessed QOL may also have been quite different in certain areas. Lastly, even though it is the most widely studied instrument in heart valve patients, the SF-36 has not been defined as the 'gold standard' to assess QOL in valvular heart surgery patients.

In conclusion, the present study clearly demonstrated that surgical treatment of valvular heart disease with

the SJM mechanical valve in patients with and without concomitant CABG can be accomplished with acceptable hospital mortality and morbidity. In these patients, even though CAD is known to adversely impact long-term survival, it does not appear to diminish the excellent long-term QOL experienced by patients undergoing valvular heart surgery if the myocardial revascularization is performed concomitantly with valve replacement.

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Appendix I: Covariates used to predict late mortality.

Preoperative variables

- 1 Female gender
- 2 Age
- 3 Date of surgery
- 4 Family history of coronary artery disease
- 5 Hypertension (diastolic pressure >90 mmHg)
- 6 Hypercholesterolemia (cholesterol >200 mg/dl)
- 7 Smoking history
- 8 Diabetes mellitus
- 9 Renal insufficiency
- 10 Cerebral vascular disease
- 11 Peripheral vascular disease
- 12 History of congestive heart failure
- 13 Arrhythmia
- 14 Unstable angina
- 15 NYHA class III/IV
- 16 Prior percutaneous coronary intervention
- 17 Ejection fraction
- 18 Surgical urgency (urgent/emergent)
- 19 Surgical history
- 20 Intra-aortic balloon pump inserted

Intraoperative variables

- 21 Perfusion time (min)
 - 22 Cross-clamp time (min)
 - 23 Aortic valve replacement
 - 24 Mitral valve replacement
 - 25 Coronary artery bypass grafting
-

*Appendix II: Covariates used to predict the SF-36 Physical
Summary score.*

Preoperative variables

- 1 Female gender
- 2 Age
- 3 Family history of coronary artery disease
- 4 Hypertension (diastolic pressure >90 mmHg)
- 5 Hypercholesterolemia (cholesterol >200 mg/dl)
- 6 Smoking history
- 7 Diabetes mellitus
- 8 Renal insufficiency
- 9 Cerebral vascular disease
- 10 Peripheral vascular disease
- 11 History of congestive heart failure
- 12 Arrhythmia
- 13 Unstable angina
- 14 New York Heart Association class III/IV
- 15 Prior percutaneous coronary intervention
- 16 Ejection fraction
- 17 Surgical urgency (urgent/emergent)
- 18 Surgical history
- 19 Intra-aortic balloon pump inserted

Intraoperative variables

- 20 Perfusion time (min)
- 21 Cross-clamp time (min)
- 22 Aortic valve replacement
- 23 Mitral valve replacement
- 24 Coronary artery bypass grafting

Postoperative variables

- 25 Presence of hospital complications
 - 26 Time (months) from surgery to SF-36 administration
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