Predictors of Outcome in Patients with Prosthetic Valve Dysfunction

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Background and aim of the study: **The study aim, based on the authors' experience in patients with prosthetic valve dysfunction, was to investigate risk factors for mortality and morbidity by analyzing preoperative, intraoperative and postoperative variables with respect to early and long-term survival.**

Methods: **A retrospective analysis was carried out of 132 patients (47 men, 85 women; mean age 46.8 ± 12.4 years) who presented for treatment of prosthetic valve dysfunction between December 1992 and February 2003. Two patients received thrombolytic therapy and were excluded from the statistical analysis, which comprised only operatively treated patients; four patients underwent successful surgical repair of mitral mechanical prostheses; all other patients (except two who died perioperatively) underwent prosthetic valve re-replacement (n = 124).**

Results: **Overall mortality and hospital mortality rates were 15.2% and 10.6%, respectively. Postoperatively, 54 complications were seen in 42 patients (32.3%). Preoperative left ventricular end-systolic diameter (LVESD) ≥45 mm and cardiopulmonary bypass (CPB) time >140 min were independent risk factors for overall and in-hospital mortality. Female gender, age >60 years and prolonged CPB time were predictors of postoperative complications. The actuarial survival rate was 87.5 ± 0.3% at five years, and 81.7 ± 0.4% at 10 years. A reduced left ventricular ejection fraction (LVEF) was the only independent predictor of late death and long-term survival.**

Conclusion: **Preoperative LVESD ≥45 mm and lower LVEF were found to be independent predictors of postoperative mortality and late survival, respectively. It is possible to obtain a substantial improvement in outcome and long-term survival if a valvular reoperation can be performed with shorter CPB time and before left ventricular dysfunction has developed.**

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Because none of the currently available prosthetic valves can be considered as an ideal valve, certain valve-related complications may develop, whereupon patients may need to be reoperated on or managed with thrombolytic therapy (1). Some factors, such as the increased life expectancy of the population, the reduced overall mortality associated with valvular surgery, endocarditis, insufficient anticoagulation for mechanical prostheses, and the limited durability of bioprostheses due to structural dysfunction, are all responsible for the increased frequency of reoperations required on cardiac valves during recent years (2-4). The improved surgical experience and advanced myocardial protection techniques have enabled cardiac valve re-replacement to be performed with acceptable mortality and morbidity, in addition to better postoperative survival rates. Besides valve re-replacement, repair can also be used in the treatment of certain prosthetic valve dysfunctions caused by excessive tissue ingrowth or paravalvular leak (5). Although surgical thrombectomy and valve replacement have been used routinely for thrombotic prosthetic valve occlusion that has been reported to occur in between 0.5% and 8% of left-sided mechanical prosthetic valves and in up to 20% of tricuspid prostheses, intravenous thrombolytic treatment has been proposed as an alternative to surgery (6-10). Further improvements in the treatment of prosthetic valve dysfunction necessitates the investigation and identification of the risk factors that affect postoperative mortality and morbidity, in addition to survival analyses (1,2). Hence, the present study was designed to describe the authors' experi-

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ence in patients with prosthetic valve dysfunction, and to investigate risk factors for mortality and morbidity by analyzing preoperative, intraoperative and postoperative variables with respect to early and long-term survival.

Clinical material and methods

Patient population and data collection

A total of 132 consecutive patients (47 men, 85 women; mean age 46.8 ± 12.4 years) who were submitted for treatment of prosthetic valve dysfunction between December 1992 and February 2003, were studied retrospectively. Those patients who underwent primary valve replacement due to congenital abnormalities were excluded from the study. The last two patients (1.5%) with prosthetic mitral valve thrombosis who did not show any evidence of severe valve obstruction were treated with intravenous recombinant streptokinase (250,000 IU given over 30 min, followed by infusion of 100,000 IU per hour). Streptokinase was administered with clinical monitoring, and Doppler echocardiography was repeated at 24, 48 and 72 h after starting thrombolysis. Four patients (3.1%) underwent successful surgical repair of mitral mechanical prostheses by replacement of sutures between the annulus and prosthesis which had become detached and caused paravalvular leakage. All other patients, except for two (1.5%) who died perioperatively, underwent prosthetic valve re-replacement (n = 124). All procedures were performed as the first reoperation or intervention. In all patients, transthoracic echocardiography (TTE) evaluations were performed using a Hewlett-Packard Sonos ultrasound imaging system (Hewlett-Packard Co., Palo Alto, CA, USA) with a 2/2.75 MHz phased-array transducer. All measurements were performed as M-mode and two-dimensional (2D), based on standard calculations established by the American Society of Echocardiography. Transvalvular flow velocity was measured using continuous-wave Doppler echocardiography. Transesophageal echocardiography (TEE) was performed in 12 patients (9.1%) in whom TTE evaluations provided suboptimal data. Cardiac catheterization was performed in eight patients (6.1%) who were at risk for coronary artery disease (CAD) (Table I).

The etiology of the primary valve lesion was rheumatic fever in 114 patients (86.4%), degenerative disease in 16 (12.1%) and endocarditis in two (1.5%). Overall, a total of 132 prosthetic valves was implanted in 130 patients (including double valve replacements). The dysfunctioned prostheses included 92 mechanical valves and 38 bioprostheses. Indications for reoperation performed in 130 patients were endocarditis in 14 (10.8%), mechanical valve thrombosis in 50 (38.5%), paravalvular leak in 20 (15.4%), structural valve deterioration in 34 (26.2%) (17 Carpentier-Edwards mitral bioprostheses; Baxter Healthcare Corp., Chicago, IL, USA; and 17 Hancock II mitral bioprostheses; Medtronic Inc., Minneapolis, MN, USA), and tissue ingrowth in 12 (9.2%). Mechanical valve thrombosis due to inadequate anticoagulation was encountered in 18 patients with Edwards-Tekna mitral prostheses (Baxter Healthcare Corp., Edwards Division, Santa Ana, CA, USA), in 10 with Medtronic mitral prostheses (Medtronic Inc.), in 10 with Sorin mitral prostheses (Sorin Biomedica Cardio S.p.a, Via Crescento, Italy), in eight with CarboMedics mitral prostheses (Sulzer Carbomedics Inc., Austin, Texas, USA), and in four

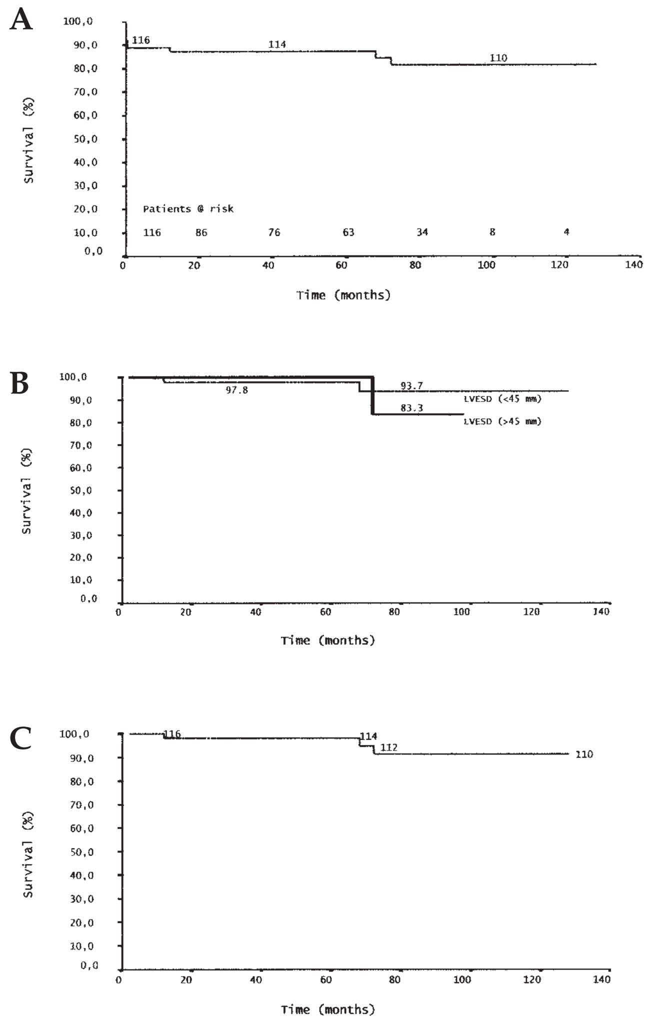

Figure 1: Kaplan-Meier estimated survival in patients with prosthetic valve dysfunction. A) Actuarial survival for all patients. B) Comparative actuarial survival for patients with preoperative left ventricular end-systolic dimension (LVESD) ≥45 mm and <45 mm. C) Cardiac event-free actuarial survival for all patients.

with St. Jude mitral prostheses (St. Jude Medical Inc., St. Paul, MN, USA).

In total, there were 88 (67.7%) cases of mitral valve replacement (MVR), 24 (18.5%) of aortic valve replacement (AVR), 10 (7.7%) of aortic and mitral valve replacement, and two (1.5%) of mitral, aortic and tricuspid valve replacement. Coronary artery bypass grafting (CABG) and peripheral vascular operations were performed as concomitant procedures in four (3.1%) and 12 patients (9.1%), respectively (Table II). All operations were performed urgently (within 72 h of diagnosis of dysfunction) or as an emergency (within 6-12 h of diagnosis). There were 80 (61.5%) and 50 patients (38.5%) in the emergency and urgent groups, respectively. There were no patients with a dysfunctional bioprosthetic valve in the emergency group.

Data acquisition

Data were collected by trained chart reviewers by using standard data forms. As variables that might affect the mortality and morbidity, age >60 years, gender, NYHA functional class, emergency of operation, chronic obstructive pulmonary disease (COPD), diabetes, hypertension, renal failure, peripheral vascular disease, cardiac rhythm, rheumatic fever in etiology, prosthetic procedure, type of prosthesis, cause of prosthetic failure, concomitant CABG or non-cardiac procedure, number of procedures (repair or re-replacement) on prostheses, aortic cross-clamp time, cardiopulmonary bypass (CPB) time, interval from operation, left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), left atrial diameter (LAD), pulmonary artery pressure, aortic

Table I: Preoperative demographic, symptomatic and cardiac variables for all patients.

Patient characteristic	n (min-max)	%
Age (years)	21-70	46.8 ± 12.3*
Age ≥60 years	24	18.5
Male	47	36.2
Female	83	63.8
Congestive heart failure	36	27.7
Hypertension	14	10.8
Diabetes	2	1.5
Renal failure	10	7.7
COPD	10	7.7
Coronary artery disease	4	3.1
Rheumatic disease	112	86.2
Double valve replacement	2	1.5
Aortic mechanical valve	28	21.2 (28/132)
Aortic bioprosthetic valve (homograft)	4	3 (4/132)
Mitral mechanical valve	66	50 (66/132)
Mitral bioprosthetic valve (xenograft)	34	25.8 (34/132)
Patients with mechanical valve	92	70.8
Patients with bioprosthesis	38	29.2
Endocarditis	14	10.8
Inadequate anticoagulation	50	38.5
Acute pulmonary embolism	22	16.9
Stenosis-occlusion	40	30.8
Regurgitation-leakage	90	69.2
Atrial fibrillation	72	55.4
Time without dysfunction (months)	0.3-256	50.6 ± 36.9*
LV end-diastolic dimension (mm)	26-69	49 ± 9.3*
LV end-systolic dimension (mm)	20-57	34.5 ± 8.4*
Left atrial dimension (mm)	35-88	54.6 ± 10.9*
Pulmonary artery pressure (mmHg)	25-138	51 ± 19.1*
LVEF (%)	15-70	58.3 ± 11.7*
NYHA class		
I-II	30	22.7
III-IV	102	77.3

*Values are mean ± SD.
COPD: Chronic obstructive pulmonary disease; Diabetes: Insulin dependent or not; LV: Left ventricular; LVEF: Left ventricular ejection fraction; Renal failure: Serum creatinine >1.5 mg/dl.

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Table II: Perioperative variables.

Variable	n (min-max)	Mean %
Repair	4	3.1
Re-replacement	124	93.9
Perioperative mortality (during operation)	2	1.5
Triple valve replacement	2	1.5
Double valve replacement	10	7.7
Aortic mechanical valve replacement	28	21.5
Aortic homograft valve replacement	4	3.1
Aortic xenograft valve replacement	4	3.1
Mitral mechanical valve replacement	96	73.8
Mitral xenograft valve replacement	4	3.1
Tricuspid mechanical valve replacement	2	1.5
Associated CABG	4	3.1
Associated non-cardiac operation	12	9.1
CPB time (min)	60-300	138.5 ± 57.4*
Cross-clamp time (min)	35-254	105.8 ± 47.3*

*Values are mean ± SD.
CABG: Coronary artery bypass grafting; CPB: Cardiopulmonary bypass.

valve area (AVA), mitral valve area (MVA), aortic root diameter, and gradients across to prosthetic valves were analyzed (Table I; see also Table IV). NYHA classification was used to determine the functional status of patients. A preoperative angiographic finding of coronary artery stenosis ≥50% was considered significant for revascularization.

Surgical technique

All operations were performed via a median sternotomy. The sternum was opened with an oscillating saw and, following its complete division, the two halves were separated from any underlying adhesions to enable a wider mobilization. Thereafter, the dissection was continued until adequate exposure of the aorta and right atrium was obtained for cannulation. The femoral artery and vein were cannulated in four emergency patients with unstable hemodynamic conditions. In all other patients, CPB was performed by cannulating the ascending aorta and both vena cavae through the right atrium. Myocardial cardioplegic protection was carried out using mild hypothermia at 28°C and anterograde cold blood cardioplegic solution. Whenever possible, after the institution of CPB

Table III: Postoperative results.

Outcome	n	Mean %
Overall mortality	20	15.4
Hospital mortality	14	10.8
Overall morbidity	42	32.3
Renal failure	6	4.6
Respiratory failure	2	1.5
Heart failure	8	6.2
Stroke	4	3.1
Ventricular tachyarrhythmias	22	16.9
Hemorrhage and re-exploration	8	6.2
Infection	4	3.1
Atrial fibrillation+	56	43.1
LVEF	23-70	64.8 ± 10.95*
Survival at 10 years	110	81.7 ± 0.1*
Cardiac event-free survival in 10 years	110	91.5 ± 0.1*
Follow-up (months)	0-128	50.6 ± 37.2*

*Values are mean ± SD.
+Also present preoperatively.
LVEF: Left ventricular ejection fraction.

Table IV: Preoperative and perioperative univariate predictors of postoperative complications and mortality.

		Mortality		Hospital mortality		Overall morbidity		Arrhythmia (VTs+SVTs)		Respiratory failure		Renal failure		Heart failure	
		No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
Age															
	≤60	20	4	20	4	10	14	18	6	22	2	20	4	22	2
	> 60	90	16	96	10	78	28	90	16	106	0	104	2	100	6
	p-value	0.529		0.242		0.003		0.190		0.033		0.011		0.454	
Sex															
	Male	38	8	42	4	38	8	44	2	46	0	44	2	44	2
	Female	72	12	74	10	50	34	64	20	82	2	80	4	78	6
	p-value	0.409		0.403		0.007		0.005		0.416		0.641		0.414	
Pr. CHF															
	No	80	14	84	10	72	22	84	10	94	0	94	0	86	8
	Yes	30	6	32	4	16	20	24	12	34	2	30	6	36	0
	p-value	0.802		0.579		<0.001		0.002		0.075		<0.001		0.069	
Pr. Renal F.															
	No	104	16	110	10	84	36	102	18	118	2	120	0	112	8
	Yes	6	4	6	4	4	6	6	4	10	0	4	6	10	0
	p-value	0.047		0.012		0.059		0.065		0.852		<0.001		0.517	
NYHA III-IV															
	No	28	2	30	0	30	0	30	0	30	0	30	0	30	0
	Yes	82	18	86	14	58	42	78	22	98	2	94	6	92	8
	p-value	0.107		0.020		<0.001		0.005		0.590		0.200		0.115	
Endocarditis															
	No	98	18	104	12	84	32	102	14	116	0	110	6	108	8
	Yes	12	2	12	2	4	10	6	8	12	2	4	0	14	0
	p-value	0.632		0.462		0.002		<0.001		0.011		0.498		0.391	
VR															
	No	32	8	38	2	34	6	38	2	40	0	40	0	38	2
	Yes	78	12	78	12	54	36	70	20	88	2	84	6	84	6
	p-value	0.331		0.132		0.005		0.016		0.478		0.104		0.531	
LVEF															
	<50%	26	12	30	8	22	16	28	10	38	0	32	6	34	4
	≥50%	84	8	86	6	66	26	80	12	90	2	92	0	88	4
	p-value	0.001		0.020		0.125		0.066		0.499		<0.001		0.174	
LVESD															
	<45 mm	100	12	104	8	78	34	92	20	110	2	106	6	110	2
	≥45 mm	10	8	12	6	10	8	16	2	18	0	18	0	12	6
	p-value	0.001		0.005		0.236		0.376		0.741		0.401		<0.001	
CPB															
	<140 min	76	6	80	2	64	18	68	14	82	0	78	4	82	0
	≥140 min	34	12	36	10	24	22	38	8	44	2	46	0	38	8
	p-value	0.004		0.001		0.003		0.988		0.131		0.158		<0.001	

CPB: Cardiopulmonary bypass; LVEF: Left ventricular ejection fraction; LVESD: Left ventricular end-systolic dimension; Pr. CHF: Preoperative congestive heart failure; Pr. Renal F: Preoperative renal failure; SVTs: Supraventricular tachyarrhythmias; VR: Valvular regurgitation; VTs: Ventricular tachyarrhythmias.

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Table V: Preoperative and perioperative predictors of mortality by univariate and multivariate analyses.

Variable	Univariate p-value	Odds ratio	95% Confidence limits	Multivariate p-value
Renal failure	0.047	3.887	0.448-33.692	0.218
CPB ≥140 min	0.004	7.592	2.062-27.961	0.002
LVESD ≥45 mm	0.001	10.519	2.323-47.643	0.002
LVEF <50%	0.001	2.206	0.581-8.380	0.245

CPB: Cardiopulmonary bypass; LVEF: Left ventricular ejection fraction; LVESD: Left ventricular end-systolic dimension.

the entire heart was isolated and mobilized carefully in patients requiring MVR. Prostheses were removed using an annular preserving technique, and new prostheses inserted via horizontal mattress sutures after the native annulus had been debrided of fibrous pannus, previous sutures, pledgets, sewing ring and thrombus.

Definitions

Diabetes was defined as the patient receiving antidiabetic medication or insulin for control of blood glucose level. Hypertension was defined as either systolic arterial pressure >140 mmHg or diastolic pressure >90 mmHg, or usage of at least one antihypertensive medication. Inadequate anticoagulation was defined as an International Normalized Ratio (INR) <2. Renal failure was defined as a serum creatinine level >1.5 mg/dl. Ventricular arrhythmia was defined as premature ventricular contractions, ventricular tachycardia or ventricular fibrillation. Respiratory failure was defined as mechanical ventilatory support beyond three days, occurrence of adult respiratory distress syndrome (ARDS), and the need for tracheostomy. Neurological complication referred to a new transient ischemic attack (TIA) or stroke persisting for more than 24 h. The terms 'early-hospital mortality' and 'late mortality' were used to refer to deaths which occurred within 30 days postoperatively and thereafter, respectively. Overall morbidity referred to the total number of patients who presented with at least one complication. The mean follow up period in all patients was 50.6 ± 37.2 months.

Statistical analysis

Statistical analyses were carried out using the SPSS/PC+ (version 10.0) program. Two patients treated with thrombolytic therapy were excluded from the analyses to provide a uniform group that comprised only operatively treated patients. A p-value <0.05 was considered statistically significant. Frequency and % values of categoric variables, and mean, average and SD values of continuous variables were determined. Patient characteristics and hospital outcomes were compared univariately by using *t*-tests for continuous variables and chi-square or Fisher exact tests for categoric variables. Patients were separated as having a particular variable, or not. Therefore, patients with combined symptoms (e.g. respiratory and heart failure) appeared in the analysis of both variables. Differences between preoperative and postoperative symptom status were compared via linear trend analysis. Survival, mortality and morbidity were evaluated using Kaplan-Meier analysis. Correlates of survival, and risk factors affecting mortality and morbidity, were analyzed by using Cox proportional hazards model and multivariate stepwise logistic regression analyses.

Results

Clinical outcome, in-hospital events and follow up

Rates of overall mortality and hospital mortality were 15.2% (n = 20) and 10.6% (n = 14), respectively. If patients treated with thrombolytic therapy were

Table VI: Preoperative and perioperative predictors of in-hospital mortality by univariate and multivariate analyses.

Variable	Univariate p-value	Odds ratio	95% Confidence limits	Multivariate p-value
Renal failure	0.012	4.788	0.540-42.467	0.160
NYHA class III-IV	0.020	1664.59	0.000-31026	0.786
CPB ≥140 min	0.001	16.348	2.471-108.172	0.004
LVESD ≥45 mm	0.005	19.629	2.812-137.028	0.003
LVEF <50%	0.020	1.470	0.274-7.905	0.653

CPB: Cardiopulmonary bypass; LVEF: Left ventricular ejection fraction; LVESD: Left ventricular end-systolic dimension.

Table VII: Postoperative predictors of mortality by univariate and multivariate analyses.

Variable	Univariate p-value	Odds ratio	95% Confidence limits	Multivariate p-value
Heart failure	<0.001	176918	0.000-1.7E+35	0.732
Hemorrhage and Re-exploration	0.019	10.008	1.712-58.508	0.011
renal failure	0.005	20.870	2.863-152.115	0.003

excluded, the mortality and hospital mortality rates were 15.4% and 10.8%, respectively (Table III). In eight of 14 patients (57%) who died during the in-hospital period, low cardiac output was the main cause of death. Other causes of death included renal failure in four patients (29%) and hemorrhage due to coagulation disturbance in two (14%). There were six late deaths (two sudden deaths, four deaths of cardiac origin). Two mortalities of sudden death with unknown origin were also included in valve-related cardiac mortality in statistical analyses. The mean length of stay in the intensive care unit and in hospital were 2.1 ± 1.3 and 7.5 ± 3.8 days, respectively.

Postoperatively, 54 complications were observed among 42 patients (32.3%) (Table III). The most frequent event was ventricular tachyarrhythmia, which was seen in 22 patients (16.9%). Long-term oral amiodarone was given to patients who developed malignant ventricular arrhythmias. All patients with postoperative congestive heart failure (CHF) died during the postoperative early period.

Predictors of mortality

By univariate analyses, preoperative renal failure, severe NYHA functional class (III-IV), low LVEF (<50%), LVESD ≥45 mm and CPB time >140 min were found to be statistically significant predictors of in-hospital mortality. All of these factors except severe NYHA class were also univariate predictors of overall mortality (Table IV). Variables that were determined to have significant influence by univariate analysis were further subjected to multivariate stepwise logistic regression analysis. Preoperative LVESD ≥45 mm and CPB time >140 min appeared as independent risk factors for overall and in-hospital mortality in multivariate analysis (Tables V and VI). Univariate analysis also revealed that postoperative CHF, excessive hemorrhage and re-exploration, and renal failure were significant postoperative risk factors of in-hospital and overall mortality. While excessive hemorrhage and renal failure were found to be significant risk factors of overall mortality (Table VII), no variable was found to be an independent postoperative predictor of in-hospital mortality in multivariate analysis (Table VIII).

Predictors of morbidity

Analysis of factors influencing overall morbidity showed that age >60 years, female gender, CHF, severe NYHA class (III-IV), endocarditis, valvular regurgitation and CPB time >140 min were significant determinants of overall postoperative complications. Factors associated with increased risk for each organ system were also investigated thoroughly. The risk factors of postoperative arrhythmias included female gender, CHF, severe NYHA class (III-IV), endocarditis and valvular regurgitation. Predictors of postoperative renal failure were age, CHF, preoperative renal failure and low LVEF (<50%). Predictors of postoperative CHF were preoperative LVESD ≥45 mm and CPB time >140 min. Age and endocarditis were associated with increased postoperative respiratory failure. No factor was significantly associated with the emergence of stroke (Table IV). These univariate determinants of morbidity were also further subjected to multivariate stepwise logistic regression analysis (Table IX). Prolonged CPB, female gender and age were independent predictors of overall morbidity (Table VIII). Female gender ($p = 0.043$) and endocarditis ($p = 0.041$)

Table VIII: Postoperative predictors of in-hospital mortality by univariate and multivariate analyses.

Variable	Univariate p-value	Odds ratio	95% Confidence limits	Multivariate p-value
Heart failure	<0.001	25268.2	0.000-4.1E+35	0.922
Hemorrhage and re-exploration	0.005	10.525	0.863-128.421	0.857
renal failure	0.001	21.909	1.314-365.429	0.849

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Table IX: Predictors of postoperative complications by univariate and multivariate analyses.

Variable	Univariate p-value	Odds ratio	95% Confidence limits	Multivariate p-value
Age >60 years	0.003	0.288	0.087-0.946	0.040
Female sex	0.007	5.013	1.473-17.057	0.010
NYHA class III-IV	<0.001	13661.5	0.000-1.4E+28	0.736
Preoperative CHF	<0.001	1.142	0.398-3.280	0.805
CPB ≥140 min	0.003	2.944	1.103-7.857	0.031
Endocarditis	0.002	1.848	0.407-8.394	0.427
Valvular regurgitation	0.005	0.317	0.093-1.075	0.065

CHF: Congestive heart failure; CPB: Cardiopulmonary bypass.

were predictors of postoperative arrhythmias. No variable was found to be an independent predictor of postoperative renal failure, postoperative CHF and postoperative respiratory failure.

Long-term survival and changes in functional capacity

The Kaplan-Meier estimated survival curves showed a five-year cumulative survival of 87.5 ± 0.3% and a 10-year cumulative survival of 81.7 ± 0.4% (Fig. 1A). Although LVESD ≥45 mm and prolonged CPB time appeared as risk factors for mortality, they had no significant effect on long-term survival in multivariate analyses (Fig. 1B). There were no cardiac events among the 110 patients still surviving, but four late deaths due to cardiac causes were recorded. In multivariate analysis, a lower LVEF was the only independent predictor of late death and long-term survival (p = 0.040; relative risk = 6.305; confidence interval = 1.092-36.409). The type of prosthesis implanted at reoperation was not a significant risk factor for late postoperative events. Cardiac event-free survival at 10 years was 91.5 ± 0.1% (Fig. 1C). During the preoperative period, 100 patients (77%) were in NYHA class III or IV (mean 3.2 ± 0.8). All of the 110 surviving were in NYHA class I or II (mean 1.1 ± 0.3) at follow up, and this improvement was significant (p <0.001) (Table X).

Discussion

Although advances in surgical experience and myocardial protection techniques have provided significant improvements in surgical outcome, the mortality and morbidity rates of valve reoperations remain higher than those of initial operations. It is therefore important to determine which risk variables might forecast unfavorable outcomes and postoperative survival as well as functional outcome in this group of patients. Once important risk factors were defined, a guideline for the general management of these patient including selection criteria for the best treatment choice (reoperation or thrombolytic therapy) could be established more objectively. To the best of the present authors' knowledge, most of the former studies have focused on early hospital results or only risk factors affecting mortality (2,11,12). There have been few previous reports evaluating the effects of preoperative echocardiographic parameters on mortality and morbidity (2,13). In the present study, a detailed analysis was performed of risk factors including preoperative echocardiographic measurements for mortality and morbidity as well as postoperative survival in patients who underwent valve reoperation.

In similar former studies, operative mortality was decreased from 41% during the period from 1966 to 1977, to 12% between 1977 and 1983, and to 8% between 1984 and 1992 (14). Current studies have

Table X: Comparison of preoperative and postoperative anginal and functional symptoms of patients.

NYHA class	Preoperative (n = 130)		Postoperative (n = 116)	
	n	%	n	%
I	2	1.5	104	89.7
II	28	21.5	12	10.3
III	54	41.5	0	0
IV	46	35.5	0	0

reported mortality rates changing between 7% and 21%, and preoperative conditions of patients appeared to be the most significant predictors of mortality (1,2,14-18). Advanced NYHA class, gender, lower LVEF, preoperative renal failure, longer CPB time, urgency of operation, endocarditis and valve thrombosis were the most frequently encountered predictors of increased mortality and morbidity in many studies (1,2,14-18). The overall mortality rate of 15.4% and hospital mortality rate of 10.8% in the present study were compatible with those of former studies. The present experience also confirmed the higher mortality risk in patients with prolonged CPB times. As indicated by de Almeida Brandao and colleagues (2), prolonged CPB times were associated with other factors, such as longer operations, associated procedures, mutivalvular operations, or unstable patients who needed longer circulatory support. Although advanced NYHA class, lower LVEF and preoperative renal failure were also found to be univariate predictors of mortality, none of these factors (even if NHYA class IV was analyzed separately) gained a significance in multivariate analysis. Some studies reported that lower LVEF, even if a univariate factor, was not associated with increased mortality (2,19). However, in the series of Bortolotti et al. (14), LVEF significantly induced the mortality. In the present study, pulmonary artery pressures did not influence mortality as in former reports (2,20). Carabello et al. (21) indicated the systolic volume index as the only independent echocardiographic predictor of poor prognosis. Furthermore, preoperative LVESD ≥45 mm emerged as an independent predictor of mortality, and probably the most distinguishing result of the present study. In some former studies, LVEDD and LVESD did not influence hospital mortality (2,13). Guidelines of the American College of Cardiology/American Heart Association indicated formerly that, because the end-systolic dimension is a less load-dependent parameter than ejection fraction, it should be <45 mm before mitral valve surgery to ensure normal postoperative LV function (4). The results of the present study also confirmed this recommendation, and therefore this 'gold standard' parameter of mitral valve surgery also appeared to be a limiting factor beyond which mortality rate increased significantly in valve reoperations. Some reports have shown that emergency reoperation was associated with a higher mortality than the elective procedure (14,17,18). Since all of the present operations were performed either urgently or as emergencies, it was not possible to obtain such a comparative conclusion.

Patient gender and age did not significantly affect mortality rates in the present study. De Almeida Brandao et al. (2) and Cohn and colleagues (22) also reported similar results. In contrast, in some other studies female sex, male sex and older age have been described as independent predictors of mortality (14,23). With regard to the indication for reoperation, the type of dysfunctioned prosthesis, the number of valves, valve position, diabetes and other associated comorbidities, the present results were similar to those reported by de Almeida Brandao et al. (2), with no apparent affect of these factors on hospital mortality. While Bortolotti et al. (14) identified the type of prosthesis as a risk factor, McGrath and colleagues found no association between prosthesis type and mortality (24). Although endocarditis was found to be an independent predictor of high mortality in previous studies (14,15,25), it appeared only as a univariate predictor of high morbidity in the present study.

Although preoperative LVESD ≥45 mm and CPB time >140 min affected mortality, these factors were generally considered as contributors to a greater operative risk. Hence, they led to a higher in-hospital mortality with depressed subsequent survival, and it is wise to exclude hospital deaths to determine correct predictors of late deaths and survival. Lower LVEF was the only independent predictor of late deaths and survival, excluding hospital deaths. This important risk factor has also been described by Morishita et al. (1). Being an indicator of left ventricular dysfunction, lower LVEF probably affected negatively postoperative survival. In the present study, the five- and 10-year survival rates of 87% and 81% were better than those of former studies (1,11,16,17), and these better results could be attributed to preserved LV function (LVEF >50%) in the majority of patients (71%).

In the present study, the overall morbidity rate was 32.3% (42/130 patients), and the most frequent complication was postoperative arrhythmia (ventricular tachyarrhythmias with/without supraventricular tachyarrhythmias). Other important complications were CHF and renal failure. The analysis of risk factors of postoperative complications revealed that overall morbidity was influenced by prolonged cross-clamp time (>140 min), female gender, and age >60 years, while postoperative arrhythmias were influenced by female gender and endocarditis. Moreover, no variable was found to be an independent risk factor for other complications and increased length of stay in the intensive care unit. Female gender, which was found not to be an independent risk factor for mortality, appeared as a common denominator of higher morbidity. The present result was similar to that reported by Lytle et al. (23). In contrast, Morishita et al. (1) and Duarte and colleagues (26) found men to be at an increased risk of poor outcome.

Besides valve re-replacement, prosthetic valve repair was also performed in four patients whose valve dysfunction was associated only with paravalvular leak.

Sakata et al. (5) also reported two cases of malfunctioning Starr-Edwards cloth-covered mitral valve prostheses which were repaired successfully at 21 years after valve replacement. The causes were a disturbance of the poppet during the opening movement due to excessive tissue ingrowth, and a paravalvular leak (5). These promising examples suggest that repair can also be used in the treatment of certain prosthetic valve dysfunctions caused by paravalvular leak or tissue ingrowth.

Prosthetic valve thrombosis was detected as the primary cause of valve dysfunction in 50 patients (38.5%) in the present study. Although valve thrombosis was associated with inadequate anticoagulation in all of these patients, the need to investigate any associated coagulation disturbance leading to thrombosis is clear. Some series have identified valve thrombosis as an independent predictor of mortality associated with valvular reoperations (14,16). Although, traditionally, surgery has been the treatment of choice for left-sided prosthetic valve thrombosis, intravenous thrombolysis has been proposed as an alternative to surgical intervention because of the significant risks associated with re-do surgery (6,7). Thrombolysis has a success rate in excess of 80%, but is associated with a 10% risk of systemic embolism and a 7% mortality rate (7). The criteria for using thrombolysis have been identified as recent onset of symptoms, transesophageal echocardiographic evidence of clots on the valve or cardiac chambers, and preserved disc excursions (9,10). In the present study, thrombolyis was also used in two patients who matched these criteria, though it was clear that the success in both thrombolytic therapy and valve repair was closely associated with a careful echocardiographic evaluation.

In conclusion, the results of the present study showed that preoperative LVESD ≥45 mm and lower LVEF were the most important predictors of postoperative mortality and late survival, respectively. It is possible to improve outcome substantially, with excellent long-term survival, if a valvular reoperation can be performed with a shorter CPB time and before the condition of the patient worsens beyond these parameters. Surgical valve repair and thrombolytic therapy are promising alternatives in the management of carefully selected patients with prosthetic valve dysfunction.

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