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Original Research Paper

Outcome After Aortic Valve Replacement in Patients with Severe Aortic Stenosis with Left Ventriclular Dysfunction

Medical Science

KEYWORDS : Aortic stenosis, left ventricular dysfunction, aortic valve replacement, survival

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ABSTRACT

Severe Aortic Stenosis (AS) With Left Ventricular Dysfunction Has A Poor Prognosis. The Average Life Expectancy Being Of Less Than 2 Years Without Surgical Correction.: The Aim Of This Study Was To Assess The Effects Of Aortic Valve Replacement (AVR) On The Recovery Of Left Ventricular Function And The Predictors Of Five Year Survival In Patients Suffering From Isolated Severe Aortic Stenosis (AS) With A Significant Left Ventricular Dysfunction (LVD).In This Retrospective Study Which Was Conducted On 92 Patients With Isolated Severe AS And LVD (Left Ventricular Ejection Fraction (LVEF) ≤ 40%)Who Underwent AVR In Our Hospital Between January 2006 And January2011 ,Different Variables Were Analyzed And Result Shows That Preoperative NYHA Functional Class ≥3 Was Found To Be Predictive Of Early Mortality. A Positive Change Was Observed In The LVEF And Mean LVEF Increased Significantly. Hazards Regression Analysis Demonstrated Diabetes Mellitus And Intraaortic Balloon Pump Use As Significant Predictors For Late Mortality.

1. INTRODUCTION

Severe aortic stenosis (AS) with left ventricular dysfunction has a poor prognosis. The average life expectancy being of less than 2 years without surgical correction (1,2). Patients with severe AS and good left ventricular function will benefit from aortic valve replacement (AVR) with an acceptable operative mortality, an improved long-term survival and an increase in the left ventricular ejection fraction (LVEF), while those with left ventricular dysfunction (LVD) benefit less from surgery (3-5). Symptomatic AS has poor prognosis compared to asymptomatic AS, so AVR should be considered even in asymptomatic patients before LVD develops (4). Although AVR is the only effective treatment modality in patients with AS and LVD, perioperative risk and worse late outcomes are observed more often (6, 7). The objective of this study was to assess the predictors of early and five year survival, and the effect of surgery on the recovery of left ventricular function.

2. MATERIALS & METHODS

2.1 PATIENT CHARACTERISTICS

A total of 92 consecutive patients with isolated severe AS and LVD (LVEF ≤40%) underwent AVR in LTMG hospital January 2006 and January2011 . The study was conducted in a retrospective manner and all data were collected from hospital records.. All patients with coronary artery disease ,with more than moderate aortic regurgitation (>2), with previous valve replacement or repair and with other valve pathologies,patient requiring concomitant procedure on aorta were excluded from the study. Cardiac catheterization and coronary angiography was performed in 80 patients (86.9%) preoperatively.

Preoperative patient characteristics are listed in Table 1.
Table 1

Age, years	54.02±◎12.8.3 (18-74)
Gender (male/female),	74/18
Body surface area, m2	1.69◎±0.19 (1.35-2.3)
Etiology, Congenital Rheumatic Degenerative	 6 48 38
Comorbidities, Systemic hypertension Diabetes mellitus	 12 6
Preoperative symptoms, Dyspnea Angina Syncope	 70 40 20
New York Heart Association functional class, II III IV	 14 58 20
Rhythm Sinus rhythm Atrial fibrillation	 80 12

2.2 ECHOCARDIOGRAPHIC MEASUREMENTS

Pre-operative transthoracic echocardiographic measurements were performed in all patients. Measurements of left ventricular dimensions were made from 2- dimensional echocardiographic images in the parasternal long-axis view and M-mode. Echocardiographic left ventricular volumes and LVEF were calculated by modification of Simpson's method with two apical views. Mean and peak aortic gradients were determined by Doppler measurements, and native aortic valve orifice area was calculated by the continuity equation. Left ventricular mass was calculated using Devereux-modified American Society of Echocardiography (ASE)equation considering the diastolic measurements of left ventricular internal diameter, interventricular septal thickness and posterior wall thickness (8). Left ventricular mass index (LVMI) was calculated by dividing left ventricular mass by body surface area. Stress echocardiography with dobutamine in presence of low transvalvular gradients was performed in 28 patients to distinguish severe LV dysfunction and real low transvalvular gradients.

2.3 SURGICAL DATA

An aortic valve replacement using a mechanical prosthesis was performed under moderate hypothermia and cold blood antegrade cardioplegia The mean cardiopulmonary bypass (CPB) time was 96.6±◎34.4 minutes (ranged from 60 to 210 min) and the mean cross-clamp time was 75.4±18.9 minutes (ranged from 38 to 147 min).

2.4 FOLLOW-UP

All cases were retrospectively assessed. Total 76 patients were examined during a follow-up period of 70.2± 39.5 months (range 7-154 months). The data records of eight patients who died during hospital stay were retrospectively reviewed. The eight patients who died during follow-up were telephonically confirmed by relatives. Follow-up including an echocardiographic control was completed for all survivors.

2.5 STATISTICAL ANALYSIS

Statistical analysis was performed using the statistical software SPSS 12.0 for Windows. Data are expressed as mean ± standard deviation for continuous variables and as numbers with percentages for categorical variables. Logistic regression analysis was used to assess the predictors for early mortality, and Cox proportional hazard regression analysis was used to study survival after AVR. All multivariate analyses were performed with p <0.05 as the limit on univariate analysis for entering or removing variables. Wilcoxonrank-sum test was used as appropriate for comparison of continuous variables (between preoperative and post operative stages). Survival curve was plotted using the Kaplan-Meier method. A p value <0.05 was considered statistically significant.

3. RESULTS

3.1 EARLY MORTALITY

Early mortality was 8.6% with eight patients. All those eight patients required high dose inotropic support in postoperative period and they died due to low cardiac output syndrome:one on postoperative day one, four patients on postoperative second day, two on postoperative third day and one on postoperative tenth day.

3.2 PREDICTORS OF EARLY MORTALITY

Predictors of early mortality were analyzed using logistic regression analysis. The following variables were analyzed: etiology, age , sex, preoperative New York Heart Association (NYHA) functional class, chronic obstructive pulmonary disease, hypertension, diabetes, peripheral arterial disease, chronic renal insufficiency, CPB time , aortic cross-clamp (ACC) time , intraaortic balloon pump (IABP)support, inotropic support. As the result of univariate logistic regression analysis, preoperative NYHA functional class ≥3 was found to be predictive of early mortality. Patients with NYHA class≥3 had 12.4 times (OR: 12.4; 95%CI: 1.2-131.3; p=0.034) higher probability of early mortality than those with a lower NYHA class. However, multivariate logistic regression analysis failed to identify any independent predictor of early mortality. Advanced age, presence of comorbidities such as diabetes and hypertension, prolonged CPB and ACC times were not found to be predictors of early mortality (p>0.05).

3.3 POSTOPERATIVE OUTCOMES

During the postoperative period, 48 patients required inotropic support, and six of them required IABP. Univariate analysis revealed that the ACC time ≥90 minutes (p=0.006) andCPB time ≥120 minutes (p<0.001) were associated with the increased requirement of inotropic use. Mechanical ventilation longer than 24 hours was necessary in twelve patients (13%), but eight of them died during the early postoperative period. Two patients required a permanent pacemaker implantation. The mean duration of stay in the intensive care unit was 5.15 ±2.11 days (ranged from 3 to 35 days) and in the hospital was 15.02±7.46 days(ranged from 7 to 112 days).

3.4 LATE OUTCOMES

Late mortality(Five year mortality)

There were eight (8.6%) late deaths. The late deaths were cardiac in six patients and non-cardiac in two patient,four of them required IABP support during the early postoperative period.

Survival

Kaplan-Meier survival analysis revealed that the overall 5-year survival rate was 82.1%±6.1

Determinants of 5 year survival

Cox proportional hazards regression analysis demonstrated diabetes mellitus (HR: 6.4; 95% CI: 1.19-36.9, p=0.030) and intraaortic balloon pump use (HR: 10.5; 95% CI: 2.8-39.7, p<0.001)to be significant predictors for late mortality.

Echocardiographic recovery

Echocardiographic evaluation was obtained in all surviving patients after 6-month follow-up (Table 2).

A positive change in LVEF was observed in 77.3% of patients and LVEF significantly improved from 36.5±.3.9% preoperatively to 45.7%±10.4% afterAVR (p < 0.001). NYHA functional class Significant improvement was observed in most of patients.

Table -2

Echocardiographic variables	Preoperative (n=92)	Postoperative (n=76)	p*
Left ventricular ejection fraction, %	36.5±.3.9%(25-40)	45.7%±10.4%(25-65)	0.005
Aortic valve area, cm2	0.74±0.09 (0.5-0.92)	1.66±0.48(1.2-3)	0.001
Mean trans-valvular gradient, mmHg	58.2±11.8 (28-82)	29.68±8.38 (12-44)	<0.001
Left ventricular end-systolic diameter, cm	5.12±0.86 (3.8-7.2)	4.54±0.86 (3.4-6.2)	0.1
End-diastolic diameter, cm	6.42±0.98 (5-9.5)	5.96±0.86 (4.8-7.6)	0.5
Septal diastolic wall thickness, cm	1.28±0.18 (1-1.9)	1.22±0.26 (0.8-1.8)	0.7
Posterior wall thickness, cm	1.2±0.18 (1-1.7)	1.18±0.16 (1-1.6)	0.7
Mass index, gr/m2	236.79±78.78 (116.68-504.61)	188.02±42.46 (110.12-293.45)	0.002

Data are expressed as mean ± standard deviation (range) for continuous variables and n (%) for categorical variables. *p values of Wilcoxon rank-sum test; statistical significance is expressed as p<0.05.

4. DISCUSSION

LV dysfunction is a major prognostic indicator of the outcome in patients undergoing aortic valve replacement for aortic stenosis (9). This group of patients constitutes the most controversial and clinically challenging patients with AS. This study conducted on patients suffering from isolated severe AS with significant LVD,aortic valve replacement was found to be beneficial. A positive change was observed in the LVEF in 77.3% of survivors and the mean LVEF increased from 36.5% to 45.7% (p<0.001). Operative mortality was 8.6% and late mortality(Five year) was 8.6

%. Multivariate logistic regression analysis failed to demonstrate any predictor for early mortality, where Cox proportional hazards regression analysis demonstrated diabetes mellitus (p=0.030) and IABP use(p<0.001) as significant predictors for late mortality.

In our study, gender, advanced age, presence of atrial fibrillation and concomitant diseases such as diabetes mellitus and hypertension, prolonged CPB and ACC times, were not found to be predictive of early mortality.Only preoperative NYHA functional class ≥3 was identified as a predictor of early mortality on univariate logistic regression analysis (p=0.034); whereas multivariate analysis failed to identify any independent predictor of early mortality. Patients with NYHA class≥3 had 12.4 times (OR: 12.4; 95%CI: 1.2-131.3; p=0.034) higher probability of early mortality than those with a lower NYHA class. It can be suggested that these patients would better be referred for assessment of surgical treatment before severe LVD with symptoms (NYHA functional capacity ≥3) develop. Although current guidelines for treating severe AS identify the onset of symptoms as the critical point, some studied (4) has showed recently that relying on symptoms alone in therapeutic decision making is inadequate and higher NYHA functional class is one of the most significant risk factors for late death. That means that AVR should be performed before severe LVD develops.

Operative mortality rate is higher in certain patient groups such as those undergoing concomitant coronary artery bypass grafting (10). Therefore, it is suggested that patients with severe AS and accompanying LVD should have coronary angiography and early AVR in the earliest phase of LVD even if they are asymptomatic (10). Unlike most other studies in the literature which included patients with CAD, we excluded those patients with CAD to evaluate the isolated effect of AVR on ventricular function, mortality and morbidity in isolated AS. Left ventricular dysfunction may occur due to afterload mismatch in patients with severe AS, and AVR results in an improvement of LVEF in these patients. Development of fibrosis leads to irreversible myocardial dysfunction and reduces potential benefits of AVR in patients with aortic stenosis. However, in patients with concomitant CAD, previous myocardial infarctions and the presence of hibernation may cause LVD and these patients should be evaluated carefully before operation. It is difficult to interpret the effect of AVR on the recovery of LVD in the presence of preoperative myocardial hibernation. Therefore, in order to prevent such confusion and assess the effect of surgery on the recovery of the left ventricular function in patients with isolated severe AS and LVD, we excluded patients with CAD.

The overall 5-year survival rate was 82.60.%±5.9%. Five-year survival rate is in line with the rates (range 49%-75%) reported in other studies (4, 11). These findings signify the importance of AVR for the improvement of late survival of this patient group and support the suggestion that severe AS rarely has clinical contraindications to surgery for cardiac reasons. We also observed that 50% of the late deaths showed no improvement of LVEF after the operation. This can be explained by the fixed myocardial damage instead of afterload mismatch, which results in the same mortality rate seen in non-operated patients. The proper use of dobutamine stress stest may help to differentiate these patients who would benefit from surgery (7). Diabetes mellitus was found to be a significant risk factor for late death in our study like others (2, 6).Different from the other studies we found that IABP support was a

significant risk factor for late death. We can explain that preoperatively severe LVD may cause low cardiac output syndrome after surgery and result in a need for excessive inotropic and IABP supports. Preoperative left ventricular function is accepted as a key determinant of surgical outcome in patients with severe AS, while the development of left ventricular hypertrophy in terms of an increase in LVMI is recognized as an independent cardiac risk factor (12). Patients with severe AS constitute a challenging group. Patients with low LVEF have two different reasons for LVD:afterload mismatch, which generally respond well to surgery and immediately normalizes left ventricular afterload; and advanced left ventricular systolic dysfunction, which causes a high operative risk group. Increased LVMI could be responsible of higher mortality by means of contractile impairment, diastolic dysfunction, abnormalities of coronary flow reserve or cardiac arrhythmias. A significant decrease in LVMI after operation shows better survival (12, 13). In our study, survivors had a significantly decrease in LVMI after operation. Serial measurements of left ventricular mass may be helpful for assessing the efficacy of therapeutic intervention and in determining the timing of surgery for patients with chronic aortic valve disease.

5. CONCLUSION

Left ventricular ejection fraction and symptoms improve after AVR in patients with severe isolated AS and LVD with acceptable operative mortality and satisfactory long-term survival.

Particularly, patients with severe AS and LVD should undergoAVR in the earliest phase of LVD, because preoperative worsening of functional capacity can increase operative mortality. Likewise, impaired left ventricular function affectslong-term survival, especially the need for IABP support is one ofthe important predictors for late death.

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