İzmir Eğitim ve Araştırma Hastanesi Tıp Dergisi, 2015; 19(1): 21-26

ARAŞTIRMA MAKALESİ

SURGERY ON SEVERE AORTIC INSUFFICIENCY WITH HIGHLY ENLARGED LEFT VENTRICLE: IS THIS A REAL PROBLEM FOR AORTIC VALVE REPLACEMENT

SOL VENTRİKÜL FONKSİYONLARI İLERİ DERECEDE BOZULMUŞ AORT YETMEZLİĞI HASTALARINDA CERRAHİ: AORT KAPAK REPLASMANI **İÇİN ÖNEMLİ BİR SORUN**

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ABSTRACT

In this study, we investigated the long term results of aortic valve replacements performed on patients with aortic insufficiency whose left ventricular functions were severely impaired.
Twenty nine patients with aortic insufficiency that were operated between April 2001 and May 2003, whose left ventricular functions were severely impaired, were included in this study. In this retrospective study, previously recorded preoperative and postoperative (1st, 12th, 36th and 60th months) echocardiographic examinations were evaluated for long term cardiac functions.
Mean left ventricular end-systolic diameter (LVESD) was 65.8 mm preoperatively, whereas it was calculated as 40.3 mm in the 12th month and 45.1 mm in the 36th month, postoperatively. This difference was statistically significant ($p<0.005$). Mean left ventricular end-diastolic diameter (LVEDD) was 80.7±9.53 mm preoperatively, whereas it was calculated as 55.4±10.40 mm in the 12th month, 60.6±16.46 mm in the 36th month and 61.9±19.90 mm in the 60th month, postoperatively. This difference between pre- and postoperative values was statistically significant ($p=0.001$). In addition, mean preoperative functional capacity was NYHA Class 3.1, whereas it was calculated as 2 at the end of 1st month, 1.4 in the 12th month, 1.8 in the 36th month and 2.1 in the 60th month, postoperatively. This improvement during the postoperative period was statistically significant ($p<0.005$).
Aortic valve replacement is a successful method in terms of both functional capacity and cardiac functions for treatment of patients with aortic regurgitation and severely impaired left ventricular function.

Key words: left ventricle, aortic regurgitation, dysfunction, myocardial protection

ÖZET
Bu çalışmada sol ventrikül fonksiyonları ileri derecede bozulmuş aort yetmezlikli hastalarda yapılan aort kapak replasman ameliyatlarının uzun dönem sonuçlarını incelemeye çalıştık.
2001 – 2003 yılları arasında sol ventrikül fonksiyonları ileri derecede bozulmuş aort yetmezliği nedeniyle opera edilen 29 hasta çalışmaya dahil edildi. Bu retrospektif çalışmada daha önceden kaydedilmiş ekokardiyografik değerleri (1., 12. , 36.ve 60. ay) değerlendirildi.
Ortalama sol ventrikül end sistolik çapı preoperatif 65.8mm iken postoperative 12.ayda 40.3mm, 36.ayda 45.1mm ölçüldü ve istatistiksel olarak bu değişim anlamlı bulundu. ($p<0.005$)

Yazının alınma tarihi:23.10.2014, Kabül tarihi:26.12.2014,Online basım:01.01.2015

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Ortalama enddiastolik çap preoperative 80.7±9.53 mm iken postoperatif 12.ayda 55.4±10.4mm, 36.ayda 60.6±16.46mm ve 60.ayda 61.9±19.9 mm ölçüldü. Budeğerlerde istatistiksel olarak anlamlı bulundu. (p=0.001) Ek olarak ortalama preoperative fonksiyonel kapasite ortalama NYHA Class 3.1 iken postoperatif 1.ay sonunda Class 2 , 12.ayda Class1.4 , 36.ayda 1.8 , 60.ay sonunda 2.1 idi ve bu gelişme istatistiksel olarak anlamlıydı.
Aort kapak replasmanı sol ventrikül fonksiyonları ileri derecede bozulmuş aort yetmezliği hastalarında kardiyak fonksiyonlar ve fonksiyonel kapasite göz önüne alındığında başarılı bir metoddur.

Anahtar kelimeler: sol ventrikül , aort yetmezliği , disfonksiyon , kardiyak koruma

INTRODUCTION

Among patients with aortic regurgitation and impaired left ventricular functions, possible benefits of aortic valve replacement are controversial. Some authors indicate that aortic valve replacement have unfavorable long term results and increased mortality rates. On the other hand, may authors emphasize the favorable results of such cases (1,2,3,4,5). The treatment of choice for these patients is a significant issue. Because the alternative treatment modality beside valve replacement is cardiac transplantation which itself has a high mortality and comorbidities. In this study, we reviewed the results of aortic valve replacement in such cases under the light of literature.

METHODS

In this study, 29 patients with aortic regurgitation and severely impaired left ventricular function that underwent aortic valve replacement between April 2001 and May 2003 were investigated retrospectively. There were 2 female and 27 male patients with a mean age of 35.36±9.68 (20-53).
Inclusion criteria of these patients were; diagnosis of severe aortic regurgitation during preoperative period, left ventricular end-systolic diameter (LVESD) >50 mm, left ventricular end-diastolic diameter (LVEDD) > 70 mm and an ejection fraction (EF) < 40%. Aortic valvular pathology was isolated regurgitation. Exclusion criteria included coexistent aortic stenosis and coronary artery disease. Preoperative echocardiographic findings of these patients were summarized in Table 1.
Etiological factors included rheumatic heart disease in 21 cases, infective endocarditis in 3 cases, degenerative valvular disease in 2 cases, dilated cardiomyopathy in 2 cases and Marfan syndrome in 1 case. Nine cases had mitral insufficiency requiring surgical correction. Beside aortic valve replacement; 8 cases underwent mitral valve replacement. One case underwent mitral valve repair and 1 case underwent Bentall operation due to aneurysm of ascending aorta. Clinical characteristics of the patients were shown in Table 2.
Clinical conditions and echocardiographic cardiac performances of the patients were recorded preoperatively and at the end of 1st, 12th, 36th and 60th postoperative months. In addition, patients under risk of coronary artery disease or with multivalvular involvement underwent cardiac catheterization and coronary angiography.

Surgical technique: All the patients were operated under general anesthesia. Median sternotomy was routinely applied. The patient was cannulated via the aorta and a single atrial venous cannula. For patients intended to repair the mitral valve, venous canulae were inserted bicavally. All the patients were cooled down to 28-30°C. After aortic cross-clamping, a transverse aortotomy was made approximately 1 cm above the take off of the right coronary artery, slightly above the level of the sinotubular ridge. The incision was extended three-quarters of the way around the aorta, leaving the posterior one-quarter of the aorta intact allowing excellent visualization of the native aortic valve and annulus. Isothermic hyperpotassemic blood cardio plegia solution was introduced initially through coro nary ostia as antegrade, and then as retrograde for maintenance. As explained before, initial cardio plegic solution contained potassium (30 mEq/L), bicarbonate (10 mEq/L) and magnesium sulphate (6 mEq/L) in 1000 ml of pump blood; whereas maintenance cardioplegic solution contained potassium (10-12 mEq/L) and bicarbonate (5 mEq/L) in 500 ml of pump blood (6). The leaflets of the aortic valve were excised to the level of the annulus. Suspending 3-0 polypropylene sutures were placed at three commissures. Braided 2-0 sutures with pledgets were utilized for suturing the valve. Beginning at the noncoronary commissure, the annulus was encircled with interrupted mattress sutures extending from the aortic to the ventricular surface (everting). Mechanical valve of proper size was placed on annulus. Then the aortotomy was closed with a double layer of polypropylene suture consisting of an underlying mattress suture and a more superficial over-and-over suture and, if necessary, the remaining procedures were completed. Aortic cross-clamp was removed. An inotropic support was initiated when necessary during weaning from cardiopulmonary bypass (CPB). Mean CPB time was 89.03±18.65 minutes (65-125) and mean cross-clamping time was 56.68±15.34 minutes (35-88). Intraaortic balloon pump was used whenever necessary. No perioperative mortality was observed. Patients were observed under mechanical ventilation support with invasive monitoring.
Patients received angiotensinogen converting enzyme inhibitors (ACEI), diuretics and warfarin starting from 1st postoperative day. The dose of warfarin sodium was regulated by monthly follow-up of INR levels (2-2.5). Echocardiographic examinations were arranged every 6 months.
Statistical analyses: All the analyses were conducted via SPSS 15.0 for Windows program. Our data were summarized in tables. Suitability of variables for normal distribution was investigated by Kolmogorov-Smirnov analysis. For normally distributed variables from preoperative and

postoperative 1st, 12th, 36th and 60th month evaluations were examined by Repeated Measures, posthoc statistical analyses. P<0.05 was considered as statistically significant.

RESULTS

Mean duration of follow-up was 62.9 months. Four patients died of heart failure during this period. Remaining 25 patients are still under control. Thus, 5-year survival rate is 86%.

During follow-up, no thromboembolic event was observed. No reoperation was necessary. Six patients were hospitalized due to heart failure during this period. Four of them were lost. Characteristics of these patients were shown in Table 3. Five patients were hospitalized due to high INR values; but, no serious complication developed and they were discharged again.

The clinical status of patients was evaluated preoperatively and in 1st, 12th, 36th and 60th postoperative months by New York Heart Association (NYHA) classification. The cardiac status was evaluated by echocardiographic parameters.

NYHA classes were found to be statistically significant among different follow-up periods ($p<0.05$). Mean preoperative NYHA value was found to be significantly higher than those of other periods ($p<0.05$) (Table 4).

In evaluation of the mean LVESD values of the patients, statistically significant difference was found among follow-up periods ($p<0.05$). Assessment of between what follow-up periods this difference was indicated that mean preoperative values were significantly higher than that of 12th and 36th months ($p<0.05$)(Table 5).

In evaluation of the mean LVEDD values of the patients, statistically significant difference was found among follow-up periods ($p<0.05$). Assessment of between what follow-up periods this difference was indicated that mean preoperative values were significantly higher than that of 12th, 36th and 60th months ($p<0.05$)(Table 5).

No significant difference was found in evaluation of mean left atrial diameter (LA) and mean pulmonary arterial pressure (PAP) values among follow-up periods ($p>0.05$)(Table 5).

In evaluation of the mean EF values of the patients, statistically significant difference was found among follow-up periods ($p<0.05$). Assessment of between what follow-up periods this difference was indicated that mean preoperative values were significantly lower than that of 12th month ($p<0.05$)(Table 5).

During postoperative follow-up period, pressure gradients across the mechanical valves showed no significant differences among the periods.

Preoperative Echocardiographic Characteristics

LVESD, mm	65.8 (54-79)
LVEDD, mm	80.7 (72-93)
EF, %	34.9 (30-35)
PAP, mmHg	43.1 (28-76)
AR, Grade	3.6 (3-4)
Left atrium, mm	53.2 (41-58)

LVESD: left ventricular end-systolic diameter. LVEDD: left ventricular end-diastolic diameter. EF: Ejection fraction. PAP: Pulmonary arterial pressure. AR: Aortic regurgitation

Table 1: Preoperative echocardiographic characteristics of the patients

Patient characteristics	n
Age	35.36±9.68 (20-53)
Etiology	
Rheumatic	21 (72%)
Endocarditis	3 (10%)
Degenerative	2 (6%)
Idiopathic dilated cardiomyopathy	2 (6%)
Marfan Syndrome	1 (3%)
Additional operation	
Mitral valve replacement	8 (27%)
Mitral valve repair	1 (3%)
Bentall procedure	1 (3%)
Preoperative findings	
NYHA class	3.18±0.6
Pulmonary arterial pressure	44.4±15.5
Atrial fibrillation	5 (17%)
Ejection fraction (%)	34.09±2.02 (30-35)
Thromboembolic events	1 (3%)
Replaced valve sizes	
21 mm	3 (10%)
23 mm	9 (31%)
25 mm	10 (34%)
27 mm	7 (24%)

Table 2: Preoperative patients' characteristics

Patient Nr.	Age	Sex	Preoperative LVESD, mm	Preoperative LVEDD, mm	Preoperative EF, %	Survival
1	46	F	69	88	30	16 mo
2	58	M	72	91	35	8 mo
3	41	M	66	78	30	21 mo
4	62	F	68	77	35	19 mo

LVESD: left ventricular end-systolic diameter. LVEDD: left ventricular end-diastolic diameter.
EF: Ejection fraction

Table 3: Clinical characteristics of patients who died

Group	Duration (months)	N	Mean	±	Std. Deviation	Sig.
NYHA	preoperative	25	**3.18**	±	0.60	**<0.001**
	1	25	2.00	±	0.45	
	12	25	1.45	±	0.69	
	36	25	1.82	±	0.75	
	60	25	2.18	±	1.17	

Sig: significance, std: standard

Table 4: NYHA functional classes of patients

Parameter	Duration(mo)	N	Mean	±	Std. Deviation	Sig.
LVESD, mm	preoperative	25	***65.82***	±	8.54	***0.002***
	1	25	50.91	±	6.14	
	12	25	***40.36***	±	9.80	
	36	25	***45.18***	±	18.63	
	60	25	49.82	±	21.84	
LVEDD, mm	Preoperative	25	***80.73***	±	9.53	***0.001***
	1	25	64.91	±	5.97	
	12	25	***55.45***	±	10.40	
	36	25	***60.64***	±	16.46	
	60	25	***61.91***	±	19.90	
LA,mm	Preoperative	25	53.27	±	15.23	0.091
	1	25	44.55	±	6.65	
	12	25	41.91	±	8.78	
	36	25	44.27	±	7.35	
	60	25	49.45	±	11.75	
PAP, mmHg	Preoperative	25	43.18	±	16.91	0.062
	1	25	33.64	±	12.89	
	12	25	31.18	±	8.28	
	36	25	28.91	±	7.61	
	60	25	31.73	±	11.19	
EF, %	Preoperative	25	***34.09***	±	2.02	***0.014***
	1	25	40.45	±	8.66	
	12	25	***52.27***	±	8.76	
	36	25	47.27	±	15.87	
	60	25	46.36	±	18.99	

LVESD: left ventricular end-systolic diameter. LVEDD: left ventricular end-diastolic diameter.
EF: Ejection fraction. PAP: pulmonary arterial pressure. LA: left atrium. Mo: months, Sig: significance, std: standard

Table 5: Evaluation of patients with echocardiographic parameters

DISCUSSION

The success of the medical therapy is not promising in patients with advanced left ventricular dysfunction and severe aortic regurgitation. Five-year survival rate in medical treatment of severe AR ranges between 20 and 60% (2). Two treatment modalities become prominent. These are aortic valve replacement and cardiac transplantation. Although the results of cardiac transplantation are promising, its use is limited to donor availability (7,8).

Current guidelines recommend aortic valve replacement for severe aortic regurgitation in following circumstances: symptomatic patients, asymptomatic patients with deteriorating left ventricular functions, patients with EF<35% or LVEDD of 75 mm and LVESD of 55 mm. Recently, aortic valve replacement is recommended even for patients with very low EF (9,10).

In patients with significant left ventricular dysfunction, aortic regurgitation (AR) and prominent left ventricular dilation; aortic valve replacement is performed with a reasonable mortality rate of 8-15%. Five-year postoperative survival rates approach 75%. In case where these patients received only medical therapy, survival rates remain about 50%. Therefore, patients with advanced left ventricular dysfunction and dilation show a better prognosis if they undergo valve replacement than the ones with medical therapy (7,11,12,13).

Chaliki *et al.* evaluated 450 patients with AR undergoing valve replacement. Perioperative mortality rate was calculated as 5.5% for cases with normal EF, whereas 23.5% for cases with low EF. In the same paper, it was reported that 5-year survival rate was 85% and and 63%, for patients with normal and low EF, respectively (2). In our study, 5-year survival rate was found to be 86%.

Bonow et al. evaluated 50 patients with severe AR undergoing aortic valve replacement. Mean age was 46, mean left ventricular EF was 37% and 5-year survival rate was found to be 63% (7). In a study by Acar et al, 46 patients with poor left ventricle and severe AR undergoing aortic valve replacement were evaluated. Mean EF was below 40% and 5-year survival rate was found to be 84% (11). Rothenburger evaluated patients (mean age: 61 years) with EF below 30% and severe AR undergoing aortic valve replacement and found the 5-year survival rate as 74% (12).

Many studies demonstrated that patients with excessively dilated ventricle and AR initially have significantly reduced left ventricular diameters after the repair of insufficient valve (2,7,13,14). According to the results of the study conducted by Chaliki, mean preoperative LVEDD was calculated as 74 mm, becoming 63 mm in 6th postoperative month. In the same manner, mean preoperative and postoperative LVESDs were 61 and 51 mm, respectively. Postoperative regression was identified as 14% and 13%, for LVEDD and LVESD, respectively (2). Bonow found out that in patients with valve replacement, mean preoperative and postoperative 6th month's LVEDDs were 76 and 64 mm, respectively. LVEDD showed 15% of regression postoperatively with a 5-year survival rate of 63% (7). Again, Klodas calculated the mean preoperative and postoperative 6th month's LVEDDs as 83 and 59 mm, respectively.

Mean preoperative LVESD was 61 mm and became 42 mm in 6th postoperative month. Postoperative regression ratios were calculated as 29% and 31%, for LVEDD and LVESD, respectively. Five-year survival rate was 83% (13). Henry calculated the mean preoperative and postoperative 6th month's LVEDDs as 73 and 56 mm, respectively. Mean preoperative LVESD was 51 mm and became 40 mm in 6th postoperative month. Postoperative regression ratios were calculated as 23% and 21%, for LVEDD and LVESD, respectively. Five-year

survival rate was about 71% (14). The results of our study coincided with that of literature. Postoperative regression ratios were calculated as 20% and 23%, for LVEDD and LVESD, respectively. Five-year survival rate was 86%. In all these studies, there were statistically significant differences between mean preoperative and postoperative LVEDDs and LVESDs. But there was no correlation between regression and 5-year survival rates.

One of the most important factors affecting long-term survival among patients with severe AR and poor left ventricle is preoperative left ventricular diameters. A study investigated the results of the aortic valve replacement performed on patients with excessively dilated left ventricles and AR. A total of 49 patients were included. Mean preoperative LVEDD and LVESD were 76 and 67 mm, respectively, among patients died of congestive heart failure during late postoperative period (14). In another study, mean preoperative LVEDD and LVESD were 75 and 60 mm, respectively, among 11 patients died postoperatively (7). In our study, mean preoperative LVEDD and LVESD of 4 cases that died were 84 and 69 mm, respectively. In the conducted studies, no limit value was pointed regarding the effect of preoperative left ventricular diameters on postoperative mortality in this kind of patients. Nevertheless, the mortality rate seems to be higher among patients with preoperative LVESD of over 65 mm and LVEDD of over 80 mm. On the other hand, as in this study, many studies showed that many patients with excessively dilated left ventricle benefited from the operation.

Another issue to be underlined is that perioperative myocardial protection of these patients. Concomitant use of intermittent antegrade blood cardioplegia and continuous retrograde blood cardioplegia was recommended as in our study (6,15,16,17,18,19,20).

As a conclusion, aortic valve replacement performed with meticulous myocardial protection on patients with severely impaired left ventricular functions and AR reduces the left ventricular diameters significantly. It also improves the functional capacity and prolongs the 5-year survival rates. Therefore, regardless of how poor the left ventricular functions are, patients with severe AR should be given a chance for operation.

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