Experiences with Different Types of Bioprosthetic Heart Valves in the Mitral Position (*)

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An analysis of the experience with different types of bioprosthetic heart valves implanted in the mitral position at the Koşuyolu Heart and Research Hospital in a four year period is given. 330 patients underwent mitral valve replacement alone or with concomittant procedures. Seven different types of valves were implanted. Sex ratio was 60% females and 40% males. The youngest patient was 16, the oldest was 74 years old with an average of 40. Sixty-five percent of the patients had atrial fibrillation. 70% of the patients were in the NYHA functional Class III or IV. 50% of the patients were in congestive heart failure. 60% had cardiac lesions additional to mitral valve disease. Two patients had previous MVR; 5 patients open mitral comissurotomy and 70 had closed mitral comissurotomy. Other cardiac procedures were performed in addition to MVR in 40% of the patients.

Hospital mortality was 8.5% and late mortality was 4%. The predictors of survival were evaluated and 17 preoperative variables were analysed by statistical methods. Factors identified as influencing survival were: advanced age, female sex, concomittant coronary artery disease, giant left atrium, NYHA Class III-IV, atrial fibrillation, congestive heart failure, increased cardiothoracic ratio, prior MVR, prior thromboembolic episodes, diabetes mellitus. Eight patients developed endocarditis, five had thromboembolic episodes. There was no statistically significant difference in early and late mortality between the different types of valves implanted. All of the patients were followed up and an average of 10 mmHg transvalvular gradient was obtained postoperatively either by two dimensional echocardiography or cardiac catheterization. Although statistically insignificant, low profile prostheses had lower transvalvular gradients.

Currently available bioprostheses, especially ones with low profile design, we think are most suitable for mitral valve replacement in patients at risk with anticoagulant therapy.

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Cardiac valve diseases of rheumatic origin affect a major part of the population in underdeveloped countries which acute rheumatic fever could not yet been eradicated. In these countries, cardiac valvular surgical procedures constitute a large number among all cardiac surgical interventions. Surgical attempts directed to cardiac valve diseases were begun in 1925[1]. After 1945, closed mitral valvotomy has been widely performed all over the world[2,3,4]. With the introduction and application, of the heart lung machine, cardiac valvular procedures have been employed widely with more security[5]. These first surgical attempts started by Lillehei and McGoon were mostly directed to the mitral valve reconstruction[6,7]. Shortly after, a new era was started .when A. Starr implanted for the first time the so-called and still in use with its more developed style caged ball mechanical prosthesis for to a patient with aortic insufficiency[8]. It was after this that mechanical prosthetic valve replacement have become the stantard surgical therapy of heart valve diseases and the prostheses were improved by means of technical design and hemodynamic properties and in a very short time various types of mechanical prostheses have become commercially available. But various disadvantages of mechanical prostheses (like thromboemboli, need for anticoagulation and the risks related to it, destruction, mechanical failure etc.) compelled the investigators to research biological prostheses. So, in 1968 Porcine bioprostheses have entered into clinical use by Carpentier[9]. But it was shortly after that some disadvantages of biological prostheses had come to light like calcification in time, early destruction and hemodynamic inadequacy regarding the preference of mechanical or biological prosthetic valves. The only common idea may be summarized as follows:

"The perfect prosthetic heart valve has not been developed yet". The properties of an ideal prosthetic heart valve were reported previously[10].

It is possible to classify the biological prostheses in various ways[11].

Today the most widely used biological prostheses are flexible standed xenografts, sterilized and fixed with glutaraldehyde, low profile ones. The most significant disadvantages of biologicai prostheses are calcification and relatively obstructive construction[11].

The superiority of biologic prostheses over mechanical ones can be summarized as follows[11]:

- Less thrombogenic nature and so no require anticoagulant therapy,
- Noiseless,

But posseses disadvantages like calcification, early destructive properties and production of valvular gradient.

Materials and Methods

Seven hundred twenty open cardiac valve operations were performed between January, 1985-February, 1989 in Koşuyolu Heart and Research Hospital. Three hundred thirty of them were mitral valve replacements with different types of bioprostheses alone or with other concomittant cardiac surgical procedures.

The youngest patient was 16 years old and the oldest was 74 with a mean age of 40±8 years old. One hundred thirty-two patients were male (40%) and the rest were female (60%). All cases demonstrated the symptoms and signs of mitral valve disease. The preoperative profile of the patients are shown in Table I. Two hundred fifteen

Table I: Preoperative status of the patients.

Period: January 1985-February 1989 (720 open heart operations)			
Number of patients	:	330	
Sex			
Male	:	132	(40%)
Female	:	198	(603%)
Age(Years)			
Youngest	:	16	
Oldest:		764	
Mean(±SD)	:	40±8	
Rhythm			
Sinus	:	115	(35%)
Atrial fibrillation	:	215	(65%)
NYHA Class			
I	:	13	(4%)
II	:	86	(26%)
III	:	208	(63%)
IV	:	23	(7%)
Cardiothoracic ratio			
Range	:	53%-78%	
Mean(±SD)	:	64±7%	
Congestive heart failure	:	165	(50%)
Previous cardiac operations			
Closed mitral valvotomy	:	70	
Open mitral reconstruction	:	5	
Mitral valve replacement	:	2	
Prior thromboembolism	:	31	(9.4%)
Prior infective endocarditis	:	16	(5.1%)
Diabetes mellitus	:	19	(5.8%)
Insulin dependent	:	8	
Other organ disorders	:	43	(13%)
Marked pulmonary hypertension	:	198	(60%)
Concomittant other cardiac lesions	:	156	(47%)

patients (65%) had a rhythm of atrial fibrillation. Two hundred eight patients (63%) were in a functional class of NYHA III while 23 (7%) were in NYHA IV. Eighty-six patients (26%) were in Class II and 13 were asymptomatic (4%). One hundred sixty-five patients (50%) were in congestive heart failure when admitted to the hospital and took medical therapy including inotropic and/or vazodilator and/or intraaortic balloon counterpulsation for some periods of time before operation. The mean cardiothoracic ratio according to radiographic examination was 64±7%. Five patients had prior open mitral valve reconstruction; one of them in our center and the others in other clinics. Two patients had previous MVR in other centers. One of them required re-MVR because of thrombosis of the mechanical prosthesis and the other because of the destruction of the biological prosthesis. Seventy patients (21%) had had closed mitral comissurotomy from 11 months to 27 years ago. Thirty-one patients (9.4%) had previous history of thromboembolic events and 11 of them with no sequela. Sixteen patients (51%) had prior infective endocarditis. Forty-three patients(13%) had other organ disorders. Nineteen patients (5.8%) had diabetes mellitus and 8 of them were insulin dependent. Preoperative clinical, electrocardiographic,

radiologic, echocardiographic and hemodynamic examinations revealed moderate or severe pulmonary hypertension in 198 patients (60%). One hundred fifty-six patients (47%) had mitral valve lesion alone. The rest of the patients (33%) had concomittant other cardiac lesions including functionally tricuspid insufficiency.

Operative technique

Median sternotomy was performed in all cases. The conventional cardiopulmonary bypass techniques of our center was established. Membrane oxygenators were used for complicated cases and for whom the operation was thought to be longer with an increasing rate after 1986. Moderate hypothermia was carried out. Hypothermishimic crystalloid cardioplegia with St. Thomas II cardioplegic solution was obtained via the aortic root for the patients with intact aortic valve and via the coronary ostia under direct vision for whom aortic insufficiency was present. Cardioplegic arrest was continued by infusing cold blood cardioplegia intermittantly for every 20-30 minutes intervals. Mitral valve was approached through the left atrium via the inter atrial groove in all cases. Posterior leaflet was protected in 37 cases and the basal chordae of posterior leaflet in 23 cases. In 27 cases with the calcification of the annulus of the posterior leaflet and 9 cases with the calcification of the whole annulus, prosthesis implantation was performed with interrupted teflon pledgeted "U" sutures. In 13 cases implantation was performed with two separate continuous running sutures. In the rest of the cases (221) simple interrupted suture technique was performed. In 132 of the patients (40%) additional cardiac surgical procedures were performed and shown in Table II.

Table II: Additional Cardiac Surgical procedures.

Surgical procedure	No.	%
AVR (Two of Manouguian)	54	16
AR	10	3
TVR	27	8
AR+TVR	6	1.8
LAP	4	1.2
CABG	4	1.2
LAT+LAL	15	4.5
LAT+LAT+TVR	3	0.9
AVR+LAT+LAL	3	0.9
AR+LAT+LAL	2	0.6
Pericardiectomy	3	0.9
Aortorraphy	1	0.3
TOTAL	132	40

AVR: Aortic valve replacement,
AR: Aortic valve reconstruction,
TVR: Tricuspid valve reconstruction,
LAP: Left atrial plication,
CABG: Coronary artery bypass grafting,
LAT: Left atrial thrombectomy,
LAL: Left atrial appendix ligation.

Nine patients (2.7%) had tripple valve procedures. All of the coronary bypass (CABG) patients received left internal mammary artery to left anterior descending coronary artery.

Late follow up

All patients after discharge were given benzathine penicillin every month for prophylaxis. All patients were given anticoagulant therapy together with antiagregant therapy until the second postoperative month, those who were in sinus rhythm, small left atrium, no history of thromboembolism, who had not left atrial thrombi, no concomittant mechanical valve replacement stopped the anticoagulant therapy and continued antiagregant therapy life long. If the patients had prior thromboembolic events, large left atrium, atrial fibrillation, concomittant me-

chanical valve replacement, they continued to take anticoagulant therapy together with the antiagregant therapy life long.

All patients were controlled at 2 months after operation and then at 6 months intervals. Patients who did not come for control examination, were contacted by telephone or letter. Despite these efforts, 22 patients (7.31% of survivors) were lost in the follow-up. The remainder were followed up for 469.16 patient-years with a mean of 2.6±0.9 years per patient with a range of 4-46 months.

Methods of analysis

Linearized incidences (percent per patient-year) include all suspected and confirmed events. The actuarial curves were calculated excluding in- hospital deaths by the method of Grukenmeier and Starr[12]. Statistical significance was established by the student's t test.

Results

Early mortality

We lost 28 patiens in the early postoperative period. Hospital mortality is 8.5%. Death occured in the early postoperative period of 21 patient, (75%) being female and 25% being male. Hospital mortality among female patients was 21/198 (10.6%) and 7/132 (5.13%) for males. It was statistically significant ($p < 0.01$). The youngest nonsurvivor was 16 years old and the oldest was 65 years old. Eighteen patients (64 %) were older than 50 years old. And the mortality rate among the patients older than 50 years old was 18/150 (12%). Five of the nonsurviving patients were diabetic and the mortality among diabetics was 26%. All of the patients who had had prior MVR died at early postoperative periods. Nine non-surviving patients had had prior thromboembolic episodes and the mortality rate among this group of patients was 9/31 (29%). Twenty of the 215 petients who had atrial fibrillation died at early postoperative period. Mortality rate among patients with atrial fibrillation was 11.6%. Twenty-eight of the patients who died in early postoperative period were in NYHA Class III and Class IV before operation and the mortality rate was 10% and 30% respectively. The mortality of previous thromboembolic event was 9/31 (29%) and the majority of them died because of cerebrovascular events.

Other mortality rates among the patients grouped according to the same preoperative properties are:

- Congestive heart failure: 19/165 (11.5%),
- Cardiothoracic ratio greater than 60 (17%),
- Prior open mitral valve repair: 0 %
- Prior closed mitral valvotomy: 8.6 %,
- Prior infective endocarditis: 0 %,
- Giant left atrium: 26 %,
- Moderate / severe pulmonary hypertension: 16/198 (8%),
- Concomittant aortic valve surgery: 5/69 (7.2%),
- Concomittant tricuspid valve surgery:1/30 (3.3%),
- Tripple valve procedures: 1/9 (11.1%),
- Concomittant coronary bypass surgery: 1/4 (25%).

The distrubution of the patients who died at early postoperative period according to the types of prostheses implanted and mortality rate were as follows:

- Pericardial: 1/2 (50%),
- Carpentier-Edwards (Classical): 2/31 (6.1%),

- Carpentier-Edwards (Supra-annular): 3/43 (7%),
- Vessex: 3/39 (7.7%),
- Hanckok: 3/33 (9.1%),
- St Jude: 4/48 (8.3%),
- Biocor: 12/134 (8.8%).
- Excluding pericardial prostheses, there was no statistically significant differences ($p>0.5$).

The causes of early mortality were as follows: Low cardiac output: 2 cases, cerebrovascular events: 6 cases, early prosthetic valve endocarditis: 3 cases, fatal arrhythmia: 1 cases, pulmonary insufficiency: 2 cases and acute renal failure: 1 case, left ventricular posterior wall rupture: 2 cases.

Postoperative complications

Complications in early postoperative periods encountered are as follows: Low cardiac output: 47 cases (11 required intraaortic balloon counterpulsation), arrhythmia: 19 cases, cerebrovascular events: 13 cases, bleeding and/or tamponade requiring reexploration: 16 cases, mediastinitis: 3 cases, wound infection: 9 cases, pulmonary insufficiency: 5 cases, gastrointestinal hemorrhage: 5 cases, prosthetic valve endocarditis: 8 cases, postperfusion delirium: 3 cases, thromboembolism: 6 cases (2 of them with no sequela), renal failure: 2 cases, left ventricular posterior wall rupture: 1 case.

Late mortality

Twelve patients died in 3 to 39 months (mean 21.8 months) after operation, Linearized mortality rate was 8% per patient-year. The cummulative mortality rate at the end of the 4th year was 4%, the late mortality causes were as follows: Late prosthetic valve endocarditis: 3 cases, thrombotic occlusion of the valve: 3 cases, progressive cardiac failure despite normal valve functions: 4 cases, etiology unknown: 2 cases.

Other valve-related complications

Prosthetic valve endocarditis was seen in 8 patients at 4-5-6-9-13-14-20-21th months after operation. Two of them were reoperated and mechanical prostheses reimplanted. But 4 of them died at early postoperative period of second operations. The other two were cured by medical therapy. Five patients had thromboembolic events. Three of them died and the other 2 survived with right hemiplegia sequele. The cummulative valve-related complication rate was 4% at the end of the 4th year. The linearized rate of valve related complications were 17% per patient-year.

Actuarial survival

The actuarial survival curves are shown in Fig.1 and 2. At 4 years 92% of the patients were alive and 83% of the patients survived free from valve related complications.

Valve performance

Echocardiographic findings revealed that 5 of implanted bioprostheses stends (2 Hanckok ,2 Carpentier Edwards and one Vessex) were occluding partially left ventricle outflow tract. The average transvalvular gradients of various types of bioprostheses revealed by echocardiographic examination at late postoperative period are as follows:

- Carpentier - Edwards (Classical): 12 ± 3 mmHg.
- Carpentier-Edwards (Supraannular): 11.4 ± 1.2 mmHg.
- Hanckok: 10.8 ± 2.3 mmHg.
- Vessex 10.7 ± 3.1 mmHg.
- Biocor 10.1 ± 4.1 mmHg.

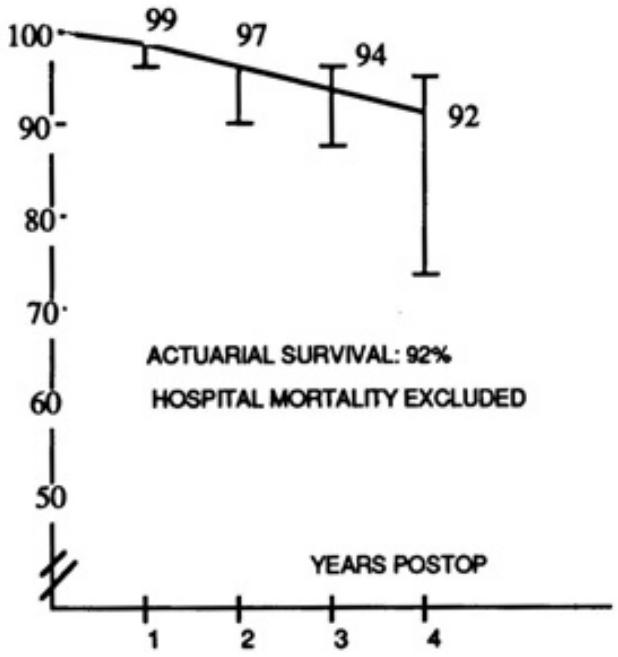

Fig.1: Acturial survival curve of the patients.

Fig.2: The acturial survival freedom from valve related complications.

Postoperative Clinical Picture

Postoperative functional status of the surviving patients is shown in Fig. 3. Most of the patients improved their functional Class to I or II.

Discussion

Prosthetic replacement of the diseased mitral valve is a widely used mode of surgical therapy of mitral valve disease. Biological prosthetic valves are of choice of replacement other than mechanical prosthetic valves. There are still controversies about the preference of these two modes of replacement. However, in patients where anticoagulant therapy wasn't advisable or dangerous or impossible, biological prostheses were the first choice[13]. Because as it can also be seen in our experience, tissue valves have the advantage of lower incidence of anticoagulant therapy dependent complications[13]. So, our policy is to implant biological prostheses to young women in gestational age, to elderly patients, to whom having thromboembolic risks, atrial fibrillation, and to people who couldn't take proper anticoagulant therapy, and patients with bleeding disorders. Our patients' clinical picture reflects this policy.

There are many controversies about using the various types of bioprostheses available today as well. But we couldn't find any differencies among 7 various types of bioprostheses. The main problem about bioprostheses is primary tissue failure(tearing, destruction and calcification) in time. But it is reported that these complications were rarely seen before 7 years after their implantation[11]. Our experience is limited to 4 years. So, that time period is not enough to come to a conclusion about advantages of bioprosthetic valves. But, with these initial observations explained above, bio-

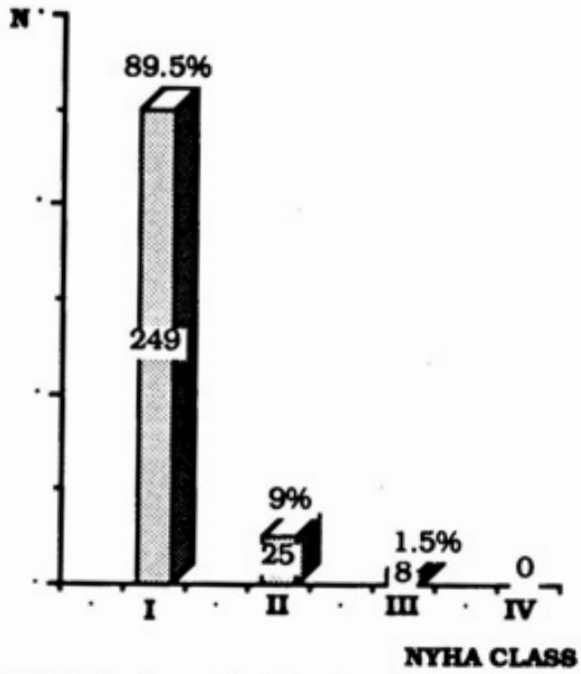

Fig.3: Postoperative functional status of the survivors.

logical prostheses have some advantages over mechanical prostheses. It needs at least 10 years of experience to conclude the preference or abandonment of prostheses in certain situations.

Conclusion

Bioprostheses have an important place in cardiac valvular surgical era. They can be of choice in certain situations and have some advantages over mechanical valves. It seems that the most important disadvantage is primary tissue failure in time[11]. Some investigators reported that biologic prosthetic valves showed relatively more transvalvular gradient in some degree[9,14]. Biotechnology about biologic prostheses has tried to solve these two problems. Nowadays, currently available bioprostheses, especially ones with low profile design-we think are the most suitable for mitral valve replacement in patients under the risk of anticoagulant therapy and thromboembolism.

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