LONG TERM RESULTS OF MITRAL VALVE REPLACEMENT WITH BIOPROSTHESIS

Birol YAMAK M.D.
Haldun KARAGÖZ, M.D.
Binali MAVİTAŞ, M.D.
Yaman ZORLUTUNA, M.D.
Oğuz TAŞDEMİR, M.D.
Ahmet ERALP, M.D.
Kemal BAYAZIT, M.D.

Between January 1982-December 1990, 838 bioprostheses were implanted in the mitral position. 163 of these patients had Carpentier-Edwards bioprosthesis (CE), and 675 St. Jude bioimplants (SB). The ages ranged between 16-75 (mean 36.5±3.47). Early mortality rate was 8.5% for CE group and 6.07% for SB group. Paravalvular leak was observed in one patient with SB (0.07%/py). Prosthetic valvular stenosis was encountered in 35 patients (1.78%/py). Besides prosthetic valvular stenosis, twenty four patients developed prosthetic valvular tear (1.22%/py). Twenty-seven thromboembolic events occured in 25 patients (1.37%/py) with 4 deaths (0.20%/py). During the follow up period, 14 patients(0.71%/py). developed serious hemorrhage with 12 fatal outcomes (0.61%/py). Two patients with SB (0.14%/py) developed prosthetic valve endocarditis. Total valve related events were encountered at a linearized rate of 9.9%/py with CE and 3.3%/py with SB protshesis. In conclusion, bioprosthetic valve implantation has a high risk of valve related events in this age group and should be utilized with strict indications.

Key Words: Cardiac valve prostheses, pregnancy.

From: Department of Cardiovascular Surgery Türkiye Yüksek İhtisas Hastanesi, Ankara, Türkiye

Adress for reprints:
Birol YAMAK, M.D.
Kalp Damar Cerrahisi Kliniği Türkiye Yüksek İhtisas Hastanesi
Sıhhiye/ANKARA

Bioprostheses preserved with glutareldehyde have been widely used throughout the world for cardiac valve replacement, because of their low incidence of thromboembolism without anticoagulation[1,2]. Bioprosthetic valves have limited durability, and therefore most patients will need a reoperation[3]. Tissue failure is the most common cause of reintervention. The early occurence of the primary tissue failure which mainly depens on the patients' age at the operation, restricts the indications for implantation of bioprostheses. This report describes the utilization of bioprostheses in a young patient population.

Materials and Methods

Between January 1982-December 1990, 838 bioprostheses were implanted in the mitral position. Of these patients, 163 (19.46%) had Carpentier-Edwards (CE), bioprosthesis between January 1982 - September 1986 and 675 (80.54%) had St. Jude Bioimplants (SB, former Liotta) bioprosthesis from May 1986 untill December 1990. Three hundred and twenty patients (38.18%) were male, and 518 (61.82%) were female, age between 16-75 (mean 36.5 ±3.47).

Ninety eight percent of the patients with CE group, and 100% of the patients with SB group were in NYHA class III or IV preoperatively. Seventy-two percent of the patients with CE and 78% of SB group had atrial fibrillation. The predominant lesion was combined mitral stenosis (MS) and insufficiency (MI) in 46% of the patients. Twenty-five percent of the patients were suffering from MI and 29% from MS.

In CE group 21 patients previosuly had closed mitral valvotomy, 1 patient had open mitral valvotomy and 6 patients underwent MVR operations with various mechanical prostheses. In SB group, previous operations were as follows: 117 closed mitral valvotomy, 5 open mitral valvatomy, and 4 mitral valve replacements with mechanical prostheses.

Coronary angiography was performed for all patients over the age of 50 years. Significant coronary atherosclerosis was diagnosed in 5 patients.

Surgical Technique:

Standart techniques of cardiopulmonary bypass with a membrane oxygenator were used in all cases. Moderate hypothermia (28-32 C), cold potassium cardioplegia and topical hypothermia was used for myocardial protection. Since April 1987, cold crystalloid cardioplegic induction followed by cold intermittant blood cardioplegia and terminal warm blood cardioplegia have been used. All valve replacements were performed with simple interrupted sutures. Pledget supported U sutures were not used except when required. Since 1986, posterior mitral valve leaflet has been preserved when feasible. The technique of posterior valve preservation was reported previosuly[4]. When coronary artery bypass grafting was performed with saphenous vein or IMA, the distal anostomoses were performed first, subsequently valve replacement and finally the proximal anostomoses.

Table I: Associated Procedures

	CE	SB
Aortic Valvotomy	2	24
ASD repair	1	10
CABG	-	5
Tricuspit Recons.	5	42

ASD: Atrial septal defect
CABG: Coronary artery bypass grafting
Recons.: Reconstruction

A total of 89 associated procedures were performed (Table I).

Oral anticoagulant therapy with warfarin was employed in 163 patients with CE bioprosthesis, and the first 187 patients with SB prosthesis 3 months postoperatively. The rest of the SB recipients received dipyridamole and aspirine only. In patients who received warfarin anticoagulation, warfarin was started on the first postoperative day. Dipyridamole and aspirin was added on the second postoperative day. Thereafter all patients received 2.5 mg warfarin, 3x75 mg dipyridamole and 250 mg aspirin daily, regardless of prothrombin time and cardiac rhythm.

Survival distribution was estimated according to Kaplan-Meier method and standard error was calculated for each year followed-up by the Greenwood formula. Parametric values are expressed as mean ± standard deviation.

Results

The early mortality rate was 8.5% (13/163) for CE group and 6.07% (41/675) for SB group (p=not significant (NS)). The vast majority of patients died of LCO (34 patients). Two patients with CE and 1 patient with SB developed left ventricular posterior wall rupture. The other causes of the deaths were cerebrovascular accident (5 patients), respiratory failure (5 pa-

tients), mediastinitis (4 patients), hemorrhage (1 patients), and acute renal failure (2 patients).

Late follow-up:

All survived patients were requested for control on the postoperative second, sixth, twelfth months, and annually thereafter. Late follow-up information was obtained in 90% of the CE group and 95% of the SB group by periodic examinations. Total follow-up period was 1959.4 patient years (py): 574.2 py for CE group (9 monthy-9 years, mean 5.3±1.4 years), and 1385.2 py (1year - years, mean 3.50± 0.9 years) for SB group.

Survival rates were 96%, 87%, 84%, 76%, 74%, and 68% after 6 years for SB group, and 96%, 92% 90%, 84%, 72%, 64%, 54%, 54%, and 50% after 9 years for CE group. Actuarial survival at the fifth year was almost equal for each group (Figure 1).

During the follow-up period 92.3% of the CE group and 93.7% of the SB group were in NYHA class I or II.

After implantation of a bioprosthesis 47 patients had 59 uneventful pregnancies. After delivery, All patients were followed from 1 to 5 years and 12 of them developed primary tissue failure (25.5%).

Non-structural dysfunction:

Paravalvular leak was observed in one patient with SB (0.07%/py). Reoperation was performed with a mechanical prosthesis.

Structural dysfunction:

Prosthetic valvular stenosis due to valve calcification have been encountered in 35 patients (1.78%/py). Twenty five of these patients had CE bioprostheses (4.35%/py), and 10 patients had SB(0.72%/py), ($p<0.001$). The ages of 30 patients who developed stenosis, were between 16 and 32 years at the first operation. Ten patients who developed prosthetic valvular stenosis, had at least one pregnancy period after the operation. Besides prosthetic valvular stenosis,

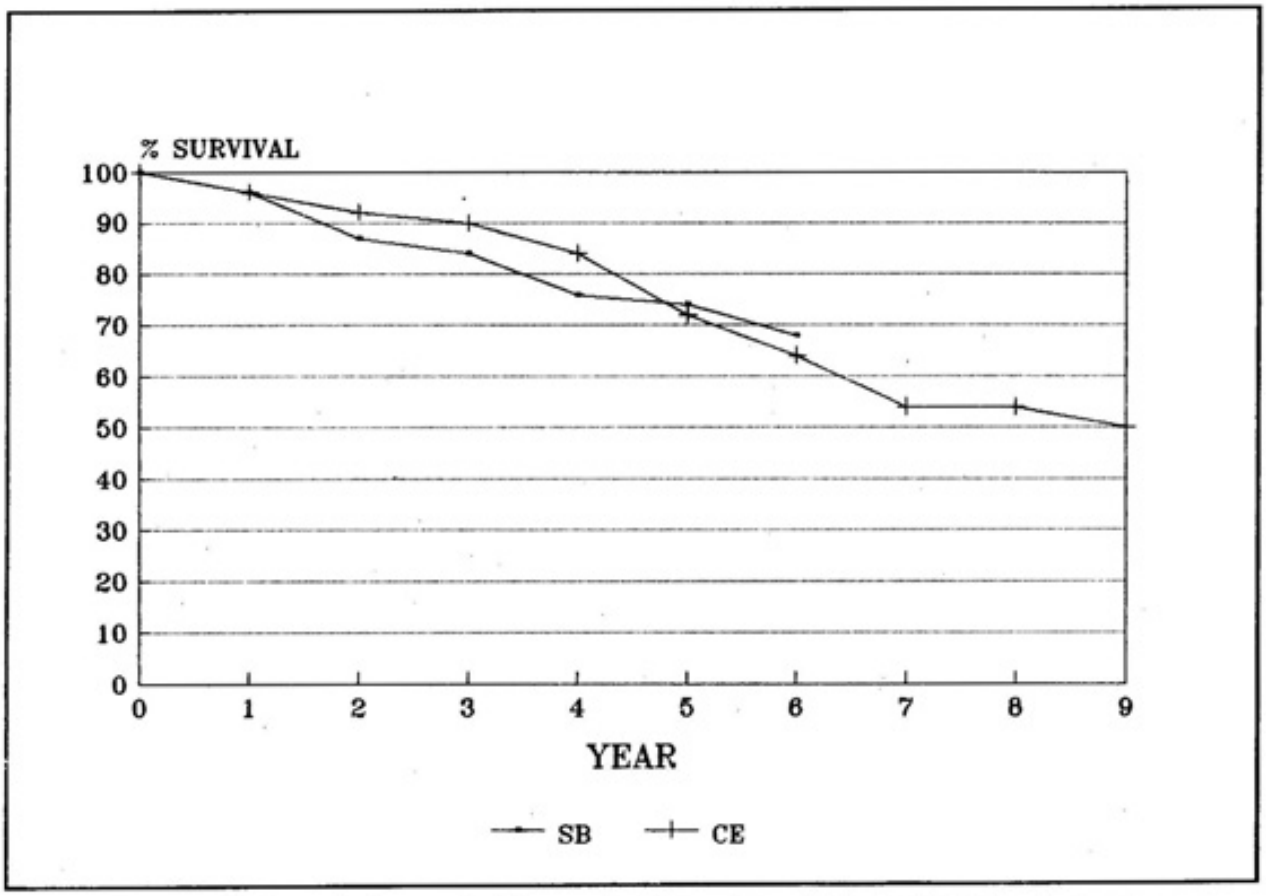

Figure I: Actuarial survival rates for Carpentier-Edwards and St. Jude Bioimplant valve prostheses.

twenty four patients developed prosthetic valvular tears (1.22%/py). Nine patients had CE bioposthesis (1.56%/py), and 15 patients(1.08%/py) had SB, ($p<0.05$). These patient ranged in age from 25 to 38 years. Two of these patients had delivery after the operation, followed by cusp tear. Four of the 59 patients could not undergo reoperation. Two of these patients were lost due to dilated cardiomyopahy, one patient developed multi-system failure, and one patient died of severe hepatic failure. Bioprostetic stenosis and/or tear was confirmed by echocardiography in all patients. Time interval between the bioprosthetic degeneration and reoperation was 5±1.27 years for CE group and 1.5±0.43 years for SB group. Four of the 55 patients who underwent reoperation due to structural dysfunction died of low cardiac output (7.27%). All reoperations were performed with mechanical prostheses.

Thromboembolism:
Twenty seven thromboembolic events occured in 25 patients (1.37%/py) with 4 deaths (0.20 %/py). Nine thromboembolic events(1.15%/py) and 1 death (0.17%/py) occured in the CE group. In SB group 16 thromboemlolic events (1.15%/py) and 3 deaths (0.21%/py) occured, (p=NS). Twenty-three of the 25 patients had atrial fibrillation. Thromboembolic events did not differ in patients who received warfarin and who did not.

Anticoagulation related hemorrhage:
During the follow up period 14 patients(0.71%/py) developed serious hemorrhage with 12 fatal outcomes (0.61%/py). Eleven patients with CE (1.91%/py), and 3 patients with SB (0.21%/py), ($p<0.01$). Hemorrhage was related to warfarin overdosage in all cases. All patients inadvertently received 10 to 15 mg warfarin daily, untill they bled.

Prosthetic valve endocarditis:
Two patients with SB (0.14%/py) developed prosthetic valve endocarditis at the second postoperative year. Both patients underwent succesful reoperation with mechanical prostheses.

Permenant valve related impairment:
There were permanent neurologic deficits in 2 cases with SB (0.14%/py).

Total mortality and morbidity:
Total valve related events were encountered at a linearized rate of 9.9%/py with CE and 3.3%/py with SB prosthesis ($p< 0.01$) respectively.

Discussion

One of the most important decisions for the cardiac surgeon is the choice of a prosthesis for a patient requiring cardiac valve replacement. Several factors should be considered, such as age, fertility, educational level, job, and functional capacity of the patient[5-7].
There is still controversy regarding the use of anticoagulant therapy after valve replacement with a bioprosthesis[8]. In the beginning of our experience, patients who underwent MVR with a bioprosthesis recived 2.5 mg warfarin, 225 mg dipyridamole and 250 mg aspirin daily. The vast majority of these patients were coming from rural areas where prothrombin time is quite difficult to be controlled regularly. Also patient compliance to oral anticoagulants is very low. During this period, unfortunately 14 patients developed serious bleeding complications. The increased risk of bleeding due to anticoagulant management and the inability of appropriate prothrombin time measurements were one of the main causes of bioprosthesis implantation in the mitral position. Bioprosthesis are reported to have lower thromboembolism rates with antiplatelet therapy alone[9-12]. There is no proof that in these patients the incidence of thromboembolism is decreased by the long-term administration of warfarin[8]. We have found the thromboembolic complication rate as 1.56%/py for patients with CE and 1.15%/py for SB prosthesis. Jamieson and Akins had a thromboembolism rate of 1.5%/py and 1.4%/py for patients with CE bioprosthesis[2,13]. Several investigators found that the incidance of thromboembolism was not different between mechanical and bioprosthetic valves as long as

satisfactory levels of anticoagulation is assumed with the mechanical prosthesis. Our results are similar with the results documented by Akins and Jamieson and as well as the results of Czer [5,14-16]. Our current policy is to treat all patients with antiplatelet drugs starting with removal of the chest tubes after the operation. We believe that porcine bioprosthesis do not require warfarin anticoagulation. In this patient population, the risk of thromboembolic events are much lesser and less serious than the risk of bleeding due to warfarin regimens.

All CE bioprosthesis implanted during this study period were first generation and with the high profile stents. These high profile stents caused left ventricular posterior wall rupture in two cases, during the manupulation of the heart for evacuation of the air through the apex. Complications related to excessive protrusion of the stent into the left ventricular cavity were eliminated with the SB bioprosthesis; the peculiar stent configuration, however, was responsible for an increased rate of structural deterioration[17]. The improvement of the functional capacities of patients after the operation strictly depends on the hemodynamic performance of bioprosthesis[18,19]. The CE prosthesis has received particular attention by Pelletier. In his studies, the mitral prosthesis performed satisfactorly. The avarage mean gradients at rest/exercise were 6.5/14 mmHg for 27 to 29 mm valves and 5/12 mmHg for 31 to 33 mm valves. The mean effective orifice areas at rest /exercise for 27 to 29 mm and 31 to 33 mm prosthesis were 2.1/2.8 and 2.5/3.8 cm^2, respectively[18]. In this series, the functional status of the surviving patients was favorable when compared with the status before the operation.

Structural deterioration of bioprosthetic valves begin between 5 and 10 years postoperatively. Catastrophic failures are certainly a problem with mechanical valves, which are seldomly encountered with bioprosthesis. It often develops slowly and is easily recognized. Although not completely proved, pregnancy is generally considered a factor that may accelerate the degenerative process[6,9]. Forty-seven patients with porcine bioprosthesis had 59 uneventful pregnancies and 12 of them developed bioprosthesis degeneration, particularly bioprosthetic calcification. Pregnancy seemed to accelerate bioprosthetic stenosis and calcification in young female patients. In SB group we were able to follow up 95% of the surviving patients. The earliest bioprosthesis degeneration occured 19 months after the operation. But in CE group first tissue failure was diagnosed in the third year postoperatively. The incidance of tissue failure increased in the fifth and sixth years. Structural dysfunction occured in 59 patients. The most significant sign of bioprosthetic failure was development of a new murmur, unless proven to be periprosthetic in origin. Tear, calcification or perforation of the leaflets were considered as degeneration of bioprosthesis. All were diagnosed with echocardiography. Echocardiography has proved to be a very powerful non-invasive tool for detection of prosthetic valve abnormalities. Postoperative echocardiography should be performed annually in all patients receiving bioprosthetic valves, even in asymptomatic patients.

When structural abnormalities were diagnosed in asymptomatic patients, elective reoperation may be performed after any symptomatic progression or with any further structural deterioration. The risk of reoperation is increased by poor NYHA functional class and impaired ventricular function. In this series, almost all patients were operated on electively, with a perioperative mortality rate comperable with primary operations.

In this series of patients, valve related events occured with a linearized rate of 9.9%/py with CE, and 3.3%/py with SB prosthesis. Although SB prostheses showed a more favorable performance then the CE prosthesis, this high incidance of valve related events with both prosthesis, have limited our utilization of bioprosthesis.

The majority of our patients were in 31-40 age group and were female. The enthusiasm for child bearing of female patients in this age group is the only strong indication for bioprosthesis usage. According to our experience to date, bioprosthesis must be concerned in the mitral position only for patients in whom anticoagulation may be difficult or hazardous.

In conclusion, bioprosthetic valve implantation has a relatively high risk of valve related events in this age group, and should be utilized with strict indications.

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