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Midterm Results of Aortic Valve Replacement with Cryopreserved Homografts

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ABSTRACT

Objective: The aim of this study was to analyze the midterm clinical results of aortic valve replacement with cryopreserved homografts.

Materials and Methods: Aortic valve replacement was performed in 40 patients with cryopreserved homograft. The indications were aortic valve endocarditis in 20 patients (50%), truncus arteriosus in 6 patients (15%), and re-stenosis or regurtitation after aortic valve reconstruction in 14 (35%) patients. The valve sizes ranged from 10 to 27mm. A full root replacement technique was used for homograft replacement in all patients.

Results: The 30-day postoperative mortality rate was 12.5% (5 patients). There were four late deaths. Only one of them was related to cardiac events. Overall mortality was 22.5%. Thirty-three patients were followed up for 67±26 months. Two patients needed reoperation due to aortic aneurysm caused by endocarditis. The mean transvalvular gradient significantly decreased after valve replacement ($p<0.003$). The last follow up showed that the 27 (82%) patients had a normal left ventricular function.

Conclusion: Cryopreserved homografts are safe alternatives to mechanical valves that can be used when there are proper indications. Although it has a high perioperative mortality rate, cryopreserved homograft implantation is an alternative for valve replacement, particularly in younger patients and for complex surgical problems such as endocarditis that must be minimalized.

Key Words: Aortic valve replacement, cryopreserved homograft, endocarditis, heart valve banking

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Introduction

For 35 years, many mechanical and biological heart valves have been used successfully for aortic valve replacement (AVR). Despite ongoing investigations and clinical applications, the ideal aortic valve substitute remains elusive. Stented bioprosthesis manufactured to provide a standard device that is easily implanted and provide reproducible results in the aortic position have been associated with good short- and mid-term results (1). Unfortunately, stented heterograft tissue failures with calcificat ion and cusp rupture become apparent with longer follow-up, particularly in younger patients.

Homografts are useful tools for valve replacement, especially in juveniles, in the presence of contraindications for anticoagulation and in endocarditis. The use of a homograft represents the ideal standard in the aortic valve replacement (2). However, its clinical use is severely restricted by its limited availability; hence studies demonstrating the clinical results of these grafts are also limited. The purpose of this study was to examine the durability of cryopreserved homografts and to determine the clinical outcome.

Material and Methods

Patients included in this study were selected from the Department of Cardio-Thoracic Surgery with the diagnosis of isolated aortic valve disease. Informed consent was obtained for all patients. Cryopreserved homografts were used in 40 patients (26 male, 14 female) (aged 0-79, median: 40 years). The indications for a surgical approach were aortic valve endocarditis in 20 (50%) patients, truncus arteriosus in 6 (15%) patients, repeat surgery for aortic valve reconstruction in 14 (35%) patients. Eighteen patients (45%) were in a condition of cardiac decompensation before operation and had class IV angina, the other 14 (35%) had class III, and 8 (20%) had class II angina according to the New York Heart Association functional classification. Surgery was performed as an emergency procedure in 14 (35%) patients. The valve size ranged from 10 to 27 mm and median diameter was 21 mm. Homograft valves were harvested under sterile conditions from cardiac transplant recipients, beating-heart or nonbeating-heart donors, with a maximum age of 65 years. Dissection of the heart was performed generally within 24 hours after circulatory arrest. After dissection, the valves were decontaminated by in-

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cubation in a medium with an antibiotic mixture for 24 hours at 4°C. Thereafter, valves were cryopreserved in a medium containing 10% dimethylsulfoxide (DMSO) frozen at a controlled rate of -1°C/min up to -100°C and stored on the vapour of liquid nitrogen (-150° to -196°C). All tissues were cryopreserved within 48 hours after circulatory arrest of the donors. All donors were seronegative for human immunodeficiency virus, hepatitis B surface and core antigen, cytomegalovirus or treponema pallidum. For implantation, ABO compatibility or HLA type matching was not required.

All operations were performed through a median sternotomy under moderate hypothermic cardiopulmonary bypass. Myocardial protection was achieved via injection of antegrade cold blood cardioplegia into the aortic root or into the coronary ostia, and in retrograde fashion through the coronary sinus. Root replacement technique (RRT) was used for homograft replacement in all patients. The hospital records, operative and follow-up notes were reviewed in this report.

A low dose of acetylsalicylic acid (5mg/kg/day) treatment as antithrombotic therapy was administered to all patients for 3 months postoperatively. All patients were followed up with serial echocardiographic measurements performed at discharge, at 6 months, at 1 year and annually thereafter. Graft failure was defined as the need for explantation and valve related death. The aortic insufficiency (AI) with grade 1 was considered of mild severity. Mean gradient across the aortic valve was used to define the severity of aortic stenosis (AS) (mild, <25mm Hg; moderate, 25-50 mm Hg; severe, >50mm Hg). Valve related dysfunction was defined as an insufficiency of grade 3-4 and a transvalvular gradient of 45 mmHg or greater.

Statistical analysis

All data analyses were performed with SPSS.13 for windows statistical package. Continuous variables were expressed as median and range, means and standard deviations. Categorical data were given as percentages. Paired and unpaired Student's *t* tests were used as appropriate to analyse continuous data, and the χ^2 and Fisher's exact tests were used to analyse discrete data. In all cases p values less than 0.05 were considered to be significant.

Results

Root technique was used for AVR in all patients. The mean cardiopulmonary bypass time was 96±31.6 minutes and cross clamp time was 82±53 minutes. Mean intensive care unit stay and mean total post operative stay durations were 3.8 and 12.1 days, respectively. The 30-day-operative mortality rate was 12.5% (5 patients). None of these events were valve related and 4 of them were emergency procedures. 31 patients were examined by Doppler echocardiography before discharge. Tables 1, 2 demonstrate the mean gradients and the grade of valve insufficiency grades with respect to valve sizes.

There were 4 (10%) late deaths. Only 1 (2.5%) of these was cardiac related. Overall mortality rate was 22.5% (9 patients). 33 (82.5%) patients were followed-up for 67±26 months (median: 18 months). 2 (5%) patients needed reoperation for endocarditis and newly developed aortic aneurysm. The mean transvalvular gradient decreased significantly after valve replacement (p<0.003). The last follow up showed that 27 (82%) patients had normal left ventricular function. Tables 1-4 demonstrate the mean gradients, the grade of valve insufficiency and left ventricle end-diastolic diameters according to valve sizes.

Discussion

Although it has been a half century since Hufnagel implanted the first mechanical prosthesis; valve surgery continues to have challenges for cardiac surgeons. Ideal aortic valve prosthesis has not yet been found. Theoretically, such a substitute should provide hemodynamic comparable to the natural human aortic valve, have the ability to remodel, be resistant to infection, must not propagate thromboemboli, be free from the hazards of anticoagulation and must be feasible.

According to the internationally approved literature, mechanical prostheses with diameters smaller than 21 mm are not preferred due to the risk of providing suboptimal hemodynamic (3). Moreover, hemolysis and thromboembolic events can occur due to mechanical prosthesis applications. Thromboembolic events seen in mechanical valve replacements are the second leading cause of mortality after cardiac insufficiency (4). Along with these, complications due to use of anticoagulant agents and postoperative endocarditis are encountered more often in these patients (1, 5). In our series, we implanted

Table 1. Early postoperative echocardiography results for aortic insufficiency with respect to the homograft size

n=31	10-18 mm n=3	19-21 mm n=13	22-23 mm n=12	>23 mm n=3
Grade 0		1	1	1
Grade 1	3	12	11	2

Table 2. Early postoperative echocardiography results for mean gradients

Mean Gradient	11.3±4.6
Peak Gradient	18.6±7.6

Table 3. Last follow-up echocardiography results for aortic insufficiency with respect to valve size

n=33	10-18 mm n=3	19-21 mm n=13	22-23 mm n=13	>23 mm n=4
Grade 0	-	1	1	
Grade 1	3	12	12	2
Grade 2	-	-	-	2

Table 4. Last follow-up echocardiography results for mean gradients

Mean Gradient	8.3±3.8
Peak Gradient	14.1±7.4

cryopreserved homografts with diameters smaller than 21 mm in twelve patients. During our follow up, we did observed no major hemodynamic deterioration or structural valve deterioration. Only two patients among the survivors had grade II AI. This could be related to the quality of the harvested donor valve. Since these two valves had diameters greater than 23 mm, we may assume that they might have been harvested from enlarged hearts and had the possibility of being insufficient initially.

The first surgical conduit option in the treatment of endocarditis is a homograft (6-13). One of the main advantages of a homograft is its durability in the setting of native or prosthetic valve endocarditis. Homograft heart valves can be used after several conservation techniques (14, 15). Cryopreservation technique has improved the durability as compared to other techniques such as irradiation, fresh or freeze storage in antibiotic solution, and immediate transplantation (16). In our study, we used cryopreseved homografts and prosthesis endocarditis was the indication for homograft use in 20 (50%) patients. Three (7.5%) patients with endocarditis died due to septicemia in the early postoperative period. One (2.5%) patient had infective endocarditis at the postoperative 15th month and had to be reoperated. Riberi and colleagues and Niwaya and colleagues have reported excellent results with the use of homografts in these patients, with no recurrent infection (17, 18). The risk of reinfection after homograft implantation is low (19). We determined 2.5% reoperation rate for infective endocarditis. However, no clear evidence exists that the homograft is more resistant to reinfection than other valve types, and the most important issue in the surgical treatment of patients with severe endocarditis is radical resection of all infected tissues, rather than the type of valve implanted (20).

The potential limiting factor for routine use of homografts is the limited donor supply, establishing valve banks, and mastering the techniques of homografts. In our study, 28 cryopreserved homografts (70%) were supplied from our own homograft bank. Many centers do not have experience with these grafts and hence technical mistakes are often made in the hands of inexperienced surgeons during operations. However, once the valve banks are established and the technical skills are improved, the procedure is highly favorable and cost effective (21).

There is debate about the best technique for homograft aortic valve replacement (22, 23). This root replacement technique (RRT) decreases the risks of geometrical distortion due to technical error since the homograft is implanted as a functional unit. The sub coronary technique (ST) carries the advantage of an easier reoperation in the event of structural deterioration as compared to the RRT (24). However, the technique is difficult, has a learning curve, and the technique itself has a higher incidence of early reoperation risks if the exact geometry is not maintained. Willems and colleagues showed that the learning curve associated with ST is a major reason for early reoperation (24). RRT is easier to perform but reoperations after this technique are difficult. Most authors advocate use of RRT (25, 26).

RRT, which was applied in our all procedures, was preferred for its low postoperative valve insufficiency rate. The results for aortic valve insufficiency derived from similar studies are in agreement with our study. Another point which is conspicuous is the discrepancy between the postoperative gradients. Although the sizes of the implanted valves are the same, the mean gradients in our study are higher when compared with other clinics. This can be due to the chosen implantation technique or the duration of endocarditis infection and related fibrosis. RRT can be associated with increased gradients across the homograft and distortion of coronary anastomosis because of a blood filling space between the homograft and the native aortic wall (27).

Despite the improvements in medicine, treatment of valve diseases is still considered as a problem. There has been a significant increase in the number of aortic valve diseases due to multifactorial causes. Investigators are trying to increase the life span and life quality by the treatment of these diseases. Because of the hemodynamic disadvantages and need for anticoagulation, there have been many investigations to replace the widely used mechanical prosthesis. Usage of the biological prosthesis used to be limited because of the resistance problems, but it has become popular recently. Our experiences showed that the difficulties of providing the homografts can be overcome by informing and encouraging the public about organ donation and increasing the number of tissue banks country wide.

Homografts are ideal biological grafts, especially for surgical treatments of endocarditis and young patients because of the physiological characteristics and superior hemodynamics. As seen in the literature, despite high perioperative mortality rates, aortic homograft applications are safe and reliable alternatives for surgical procedures with favorable short and mid-term results. As a surgical technique, root implantation is superior when compared with the aforementioned techniques.

Conflict of Interest

No conflict of interest was declared by the authors.

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