The Use of "Fresh" Unstented Homograft Valves for Replacement of the Aortic Valve

Analysis of 6½ Years Experience

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SUMMARY
Between August 1969 and January 1976, 561 patients underwent homograft replacement of the aortic valve (AVR). Isolated AVR was performed in 339 patients, ranging in age between 18 months and 74 years. The valves were sterilized in antibiotic solution and preserved at 4°C in tissue culture medium. There were 11 early deaths (3.2%) and 23 late deaths (6.8%). Actuarial analysis showed 88% survival at 5 years and 85% at 6 years. Valve failure occurred in 13 patients (3.8%) due to prolapse of one cusp in five patients (1.5%), infective endocarditis in three and degeneration of the graft in five (1.5%). Degenerative valve failure was encountered after the fourth year with an incidence of 3.5% of patients at risk, and occurred only in grafts from donors over the age of 70 years. Diastolic murmurs were present in 22% of patients followed up for more than one month and increased very slightly with time. The clinical result was judged to be good or excellent in approximately 90% of the surviving patients.

THE EARLY AND LONG-TERM SURVIVAL, as well as the quality of life, after aortic valve replacement, can be affected by the type of valve used. We believe that it is essential to continue to evaluate critically the results of different valve substitutes. The purpose of this paper is to analyze our results with the use of unstented antibiotic-sterilized homografts for replacement of the aortic valve over a period of 6½ years at Harefield Hospital.

Patients and Methods

Between September 1969 and June 1976, 561 patients underwent homograft replacement of the aortic valve. Isolated elective aortic valve replacement was performed in 339 patients. This latter group constitutes the subject of this communication. At the time of operation the ages varied from 18 months to 74 years (fig. 1). There were 255 males (with a mean age of 48 years) and 84 females (with a mean age of 51 years) (fig. 1). The dominant lesion was aortic stenosis in 177 patients, aortic regurgitation in 125 and mixed in 37. All were symptomatic except 12 and these had severe aortic stenosis; 218 patients (64.3%) were in functional class III and IV of the New York Heart Association Classification (table 1). The dominant symptom was dyspnea in 178 patients (52.5%), angina and dyspnea in 117 (34.5%) and angina alone in 32 (9.4%). The duration of symptoms varied from 2-84 months with a mean of 27 months. Advanced age or poor general condition were not considered as contraindications to operation. During the period of the study, homograft valves were the only valve substitutes used for aortic valve replacement at Harefield Hospital.

The electrocardiogram showed evidence of severe left ventricular hypertrophy (LVH) with ST and T changes in 239 patients (70.5%), LVH on voltage criteria alone in 64 (18.9%) and was within normal limits in 14 (4.1%). Left bundle branch block was present in 18 (5.3%) and right bundle branch block in 4 (1.2%).

The homograft valves were obtained from routine post-mortem material within 48 hours of death. The ages of the donors varied from 15 to 76 years. The age distribution of 441 consecutive aortic valve donors is shown in figure 2; the majority were between 40 and 70 years, but 25 were aged 71 to 76. Recently we have stopped using valves from donors in this age group because of our finding that all incidents of late valve calcification were in grafts obtained from this age group. The valves were sterilized in antibiotic solution and stored in tissue culture medium containing fetal calf serum and low concentration of antibiotics. The details of the method used for sterilization and storage have been previously reported.1, 2 The period of storage varied from 1 to 42 days (fig. 3); however the majority of valves were used within the first week.

In most cases, the homografts were inserted in the sub-coronary position, without stents, using a method similar to that described by Barrett-Boyes3 and Ross.4 In patients with abnormally large or hypoplastic aortic roots, the aortic root was tailored to accommodate a homograft of optimal size. Large roots were reduced in size by plication or excision of a strip of aortic wall and anulus from the region of the non-coronary sinus. Small roots were enlarged by inserting a gusset of dacron or autogenous aortic wall obtained from the region of the poststenotic dilatation. During the last year, we have used a new method of replacing the aortic valve and root in patients with hypoplastic, distorted or abnormally dilated aortic roots.5 This consists of excising the diseased aortic valve and root and, if necessary, enlarging the root by incising the anulus and subaortic curtain at the mid point of the attachment of the noncoronary cusp. An unstented adult-sized homograft is then inserted as a tube and fixed by two suture lines to the aortic anulus at one end and the ascending aorta at the other. The coronary ostia of the recipient are mobilized with a surrounding rim of the aortic wall. These are anastomosed to the homograft at the site of its coronary ostia. This method has the advantages of avoiding any distortion of the homograft and does not re-
quire matching the size and shape of the components of the homograft to those of the host.

All patients were followed up at regular intervals at our hospital with clinical, radiographic and electrocardiographic examination except in 27 instances when follow-up data were obtained from the referring physician. The follow-up period extended from 3 to 84 months (mean 35 months). Repeat cardiac catheterization was performed in 74 patients randomly selected 6 months to 5½ years after operation.

Results

Early and Late Mortality

There were 11 deaths within the first four weeks after operation, an early mortality rate of 3.2%. Twenty-three patients died within the follow-up period, a late mortality rate of 6.8%. Actuarial analysis of survival (using the method described by Berksen and Cage6) in patients who retained their original homograft is shown in figure 4. Seven patients who underwent a successful second operation were not included in the analysis. The survival rate at 5 years was 88% and at 6 years 85%. Of the 23 late deaths 13 were due to cardiac causes (table 2). Late valve failure was responsible for death in two patients, left ventricular failure not related to valve failure in two, infective endocarditis in six, ventricular arrhythmia in two and coronary heart disease in one (table 2). Of the 10 noncardiac causes, two were due to miliary tuberculosis which could have been related to the valve substitute.7

Valve Failure

Failure of the homograft valve occurred in 13 patients (3.8%) due to different causes (table 3). Sagging or prolapse of one of the homograft cusps developed in five patients (1.5%) between 1 and 3 years after operation (fig. 5) with an incidence of 0.4 to 1.5% of patients at risk during different periods (fig. 5).

Infective endocarditis caused valve failure in three patients. The organism was bacterial in one and fungal in two. This complication was encountered in the first two years with an incidence of 0.7% of patients at risk during the first year and 0.4% of those at risk during the second year. The overall incidence of endocarditis is discussed later.

Calcification of the homograft leading to stenosis and regurgitation occurred in five patients. This occurred after the fourth year with an incidence of 3.6% of the patients at risk (fig. 5). In each of the five cases the valve used was obtained from a donor over the age of 70 years.

Seven patients successfully underwent repeat valve replacement using another homograft valve.

Postoperative Aortic Regurgitation

Diastolic murmurs indicative of a degree of aortic regurgitation were recorded in 72 (22%) of 328 patients who were followed up for a minimum period of one month. The

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<th>Table 2. Causes of Late Mortality following Aortic Valve Replacement</th>
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<tbody>
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<td>Cause of death</td>
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<tr>
<td><strong>Cardiac Causes</strong></td>
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<tr>
<td>Chronic L.V.F.</td>
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<tr>
<td>Candida endocarditis</td>
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<tr>
<td>Bacterial endocarditis</td>
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<tr>
<td>Arrhythmia</td>
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<tr>
<td>Coronary heart disease</td>
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<tr>
<td>Total</td>
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<tr>
<td><strong>Noncardiac Causes</strong></td>
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<tr>
<td>Miliary tuberculosis</td>
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<tr>
<td>Chronic pulmonary disease</td>
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<tr>
<td>Carcinoma</td>
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<tr>
<td>Cerebral hemorrhage</td>
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<tr>
<td>Traffic accident</td>
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<td>Unknown cause</td>
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<td>Total</td>
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Figure 1. Age and sex distribution of 339 patients undergoing elective homograft replacement of the aortic valve.

Figure 2. Age and sex distribution of 441 consecutive aortic valve donors.
murmurs were generally first recorded during the first year. The incidence increased slightly as the follow-up period lengthened (fig. 6). Repeat catheterization to quantify the amount of regurgitation was not performed except in patients who were judged clinically to have a severe hemodynamic lesion. The aortic regurgitation was clinically trivial to mild in 52 (15.9%), moderate in 13 (4%) and severe in seven (21%). At 5 years the incidence of severe regurgitation was 1.2% of patients at risk while that of moderate regurgitation was 3.7% (fig. 6).

Systolic Murmurs

Systolic murmurs were observed frequently. The gradient across the aortic valve in 74 patients, measured at periods between 6 months and 5½ years after operation, did not exceed 10 mm Hg in any patient and was 0 both at rest and exercise in 72. The five patients with stenosis of the homograft due to calcification, referred to earlier, had gradients varying from 40–70 mm Hg.

Systemic Embolism

Systemic embolism did not occur. Routine anticoagulation was not used.

Infective Endocarditis

Ten patients (3%) developed infective endocarditis, five fungal and five bacterial. Bacterial endocarditis occurred shortly after operation in two, within the first year in one and within the second year in one. The infection followed dental treatment in one. One of these died suddenly during antibiotic treatment. Three were cleared bacteriologically but developed signs of valve failure which was successfully treated by repeat homograft valve replacement.

Of the five patients who developed Candida endocarditis four died and one was treated successfully using a combination of 5-fluorocytosine and intravenous amphotericin B for a period of 12 weeks.

Clinical Evaluation

In an attempt to define the result of the operation a set of clinical, electrocardiographic and radiographic criteria were used. These included: 1) absence of symptoms, 2) absence of signs of cardiac failure or need for antifailure treatment, 3) absence of aortic diastolic murmurs, 4) normal pulse pressure, 5) reduction in cardiothoracic ratio as measured from a standard chest film, 6) decrease in electrocardiographic signs of LVH.

Patients were classified as excellent if all criteria were

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<th>Table 3. Etiology of Valve Failure</th>
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<tr>
<td>Cause of valve failure</td>
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<tr>
<td>Stenosis of homograft</td>
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<tr>
<td>Cusp prolapse</td>
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<tr>
<td>Infective endocarditis</td>
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<tr>
<td>Total</td>
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</table>

FIGURE 3. Relationship between time of dissection and time of implantation of aortic homograft.

FIGURE 4. Actuarial analysis of survival following homograft replacement of the aortic valve in patients who have retained their original homograft (seven patients who underwent a successful reoperation are excluded).
present, good if they were asymptomatic and all but one criterion present, fair if two or more criteria were lacking and poor if they had symptoms.

The proportion of patients who were classified as excellent or good were grouped together and expressed as a percentage of the total number of patients followed up for different periods (fig. 7). Six years after operation 90% were judged to be excellent or good (fig. 7). There was no deterioration in the symptomatic status with passage of time (fig. 7).

Electrocardiographic Changes

Complete regression of signs of left ventricular hypertrophy was observed in 215 patients (65.5%). Signs of residual LVH were present in 66 patients (20.1%). Most of these patients had systemic hypertension. The electrocardiogram was unchanged in 15 patients (4.6%).

Left bundle branch block was present in 20 patients (6.2%); of these the abnormality was observed preoperatively in 12.

Perioperative myocardial infarction was seen in two patients who died early after operation.

### Discussion

Analysis of our experience with the use of antibiotic-sterilized unstented homografts for aortic valve replacement has shown that this type of valve substitute gives satisfactory results for periods of up to six years. The main advantages of these valves have been the freedom from thromboembolic complications and the good hemodynamic performance.4, 6

Infective endocarditis involved the homografts in about 3% of cases and still carried a high mortality. If diagnosed early this complication can be successfully treated. The incidence of late degenerative valve failure, to date, had been low and
Hemodynamic Results of Aortic Valvular Replacement with the Porcine Xenograft Valve

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SUMMARY Twenty-three patients were evaluated by cardiac catheterization two to 12 months following aortic valve replacement with the porcine xenograft valve. These hemodynamic studies established a mean peak-to-peak systolic gradient across the prosthesis of 23 mm Hg with a range of 6–58 mm Hg. The mean effective orifice area was calculated to be 1.25 cm². The effective orifice area increased with increasing valve size from 0.99 cm² for the 19 mm prosthesis to 1.44 cm² for the 25 mm prosthesis. While in general the hemodynamics of the porcine xenograft valve are comparable to other available prostheses, the exceedingly small orifice areas (0.99 cm² and 1.03 cm²) calculated for the 19 mm and 21 mm prostheses render their use inadvisable.

Since the era of prosthetic cardiac valves was opened in 1952 with the implantation of the caged ball prosthesis in the thoracic aorta by Hufnagel,1 active investigation of new prosthetic models has continued because of dissatisfaction with the hemodynamic characteristics, the durability, or the thrombogenicity of previously available prostheses. Among the prosthetic valves presently under clinical investigation is the porcine xenograft aortic valve (fig. 1). This prosthesis is a composite tissue valve composed of porcine aortic leaflets mounted on a flexible stent and pretreated with a tanning agent (glutaraldehyde). The glutaraldehyde produces a cross-linkage between the collagen molecules and thus increases tissue strength. While the ease of implantation and the very low thrombogenicity of this particular prosthesis have been substantiated by previous investigations,2–4 its long-term durability remains unproven and its hemodynamic characteristics in the aortic position are untested. The present study defines the hemodynamic characteristics of this prosthesis in the aortic position.

Methods

Patient Population

The study population consisted of 23 patients who had aortic valve replacement with the porcine xenograft aortic valve at Emory University Hospital between July 1974 and July 1975. The patients were selected from the total group of patients receiving the porcine xenograft valve only on the basis of their willingness to participate in this study.

In 14 of these 23 patients valve replacement was performed for amelioration of calcific aortic stenosis; three patients had a mixed valve lesion with thickened, calcific, yet incompetent, leaflets; and only six patients had predominant aortic regurgitation. The valvular calcification extended into the anulus in five of the patients. Two of these patients, in addition, had a heavy bar of calcium extend from the anulus into the anterior leaflet of the mitral valve. Debridement of the calcium was successful in every case and in no instance did residual calcium hinder prosthesis implantation.

Nineteen patients were asymptomatic and in functional class I at the time of the postoperative hemodynamic evaluation. Three patients were in functional class II and one was in functional class III. The average age of the patients with aortic stenosis was 58 years, while the patients with aortic regurgitation and mixed valve lesions averaged 38 years and 42 years, respectively.

Hemodynamic Evaluation

These twenty-three patients were evaluated by left and right cardiac catheterization two to 12 months after valve replacement in order to establish the effective orifice area of the prosthesis and to determine the degree of regurgitant flow across the prosthesis during diastole.

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