Early clinical experience with the Hancock porcine xenograft valve prosthesis

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SUMMARY In a 2-year period, 75 Hancock porcine xenograft valves were inserted in 66 patients, 33 male and 33 female. Their average age was 55 years (range 14 to 69 years). The indication for operation was rheumatic heart disease (30 patients), prosthetic valve dysfunction (8 patients), papillary muscle dysfunction (8 patients), degenerative valve disease (13 patients), subacute bacterial endocarditis (3 patients), luetic valve disease (2 patients), congenital heart disease (1 patient), and traumatic valve damage (1 patient).

Forty-five valves were placed in the mitral, 28 in the aortic, and 2 in the tricuspid position; 9 patients required double valve replacement. Additional operative procedures included coronary artery vein bypass grafts (12 patients), tricuspid annuloplasty (6 patients), left ventricular aneurysmectomy (4 patients), open mitral valvotomy (3 patients), replacement of ascending aorta (1 patient), and closure of ventricular septal defect (1 patient). There were 2 hospital deaths (3%). Oral anticoagulation was continued for approximately 6 weeks postoperatively, when it was discontinued in all but 8 patients.

In the follow-up period—mean 16 months (range 8 to 31 months)—there were 4 late deaths, 2 of which were sudden. There was no documented episode of thromboembolism or valve degeneration. All except 2 patients were clinically improved from NYHA class III or IV preoperatively to class I or II postoperatively.

Initial results with Hancock porcine xenograft valves are most satisfactory and compare more than favourably with other commercially available valve substitutes.

The ideal heart valve substitute should be readily available, easily inserted, free from thromboembolic and infectious complications, haemodynamically satisfactory, and durable in the long term.

Dissatisfaction with the thrombogenicity, haemodynamic performance, and long-term durability of many mechanical prostheses (Stanford *et al.*, 1972; Vidne *et al.*, 1973) has led to the increasing use of many different types of tissue valves (Ionescu *et al.*, 1974; Wallace, 1975).

Of the tissue valves commercially available, the porcine aortic xenograft prepared by the 'stabilised glutaraldehyde process' and mounted on a flexible polypropylene Dacron-covered stent (Hancock

Laboratories) has gained wide clinical acceptance. This valve was first used in Edinburgh in November 1973 and we report our initial clinical experience with it.

Subjects and methods

In a two-year period from November 1973, 75 Hancock valves were inserted into 66 consecutive patients at Edinburgh Royal Infirmary. There were 33 male and 33 female patients. The patients' ages ranged from 14 to 69 years (mean 55 years) (Fig. 1). Preoperatively, all patients were in class III or IV (New York Heart Association classification) (Fig. 2).

Forty-five valves were placed in the mitral position, 28 in the aortic, and 2 in the tricuspid position. Valve sizes ranged from between nos. 29 and 35 in the mitral position, nos. 21-29 in the aortic position, and no. 33 in the tricuspid position.

Of 57 single valve replacements, 36 patients had

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Fig. 1 Age and sex of patients.

Fig. 2 Symptomatic improvement (NYHA classification).

mitral valve replacement and 21 aortic valve replacement.

Seven patients had double valve replacement (aortic and mitral) and 2 patients underwent mitral and tricuspid valve replacement (Table 1).

Additional procedures in 27 patients included 1 to 4 saphenous vein aortocoronary bypass grafts (12 patients), tricuspid annuloplasty (6 patients), resection of left ventricular aneurysm (4 patients), open mitral valvotomy (3 patients), replacement of the ascending aorta (1 patient), and closure of ventricular septal defect (1 patient).

In 53 patients in whom coronary artery disease was either excluded by selective coronary angiography or was not suspected, there was 1 death (mortality 1.9%) after a single aortic valve replacement (Table 2).

In 13 patients, the presence of ischaemic heart disease was proved preoperatively by selective coronary angiography and left ventricular angiography. In 12 of these patients, valve replacement was combined with coronary artery vein bypass grafting without mortality. One patient, submitted to aortic and mitral valve replacement and left ventricular aneurysmectomy without coronary artery grafting, died intraoperatively, giving a hospital mortality for this group of 7.7 per cent (Table 3).

The aetiology of the valvular disease in the different patient groups is shown in Tables 4, 5, 7, and 8.

Table 2 Valve replacement in patients without ischaemic heart disease

Mitral valve replacement	28
Aortic valve replacement	18*
Mitral + aortic valve replacement	5
Mitral + tricuspid valve replacement	2
Total	53
*Hospital death	1 (1.9%)
Additional procedures:	
Tricuspid annuloplasty	6
Mitral valvotomy	2
Replacement ascending aorta	1
Total	9

Table 1 Valve replacement and prosthetic size

	No. of patients	Valve(s) replaced	Valve replaced	No. of patients	Prosthetic size (range)
Single valve	57	MV 36; AV 21	Mitral	45	Nos. 29-35
Double valve	9	MV + AV 7; MV + TV 2	Aortic	28	Nos. 21-29
			Tricuspid	2	No. 33
Total	66		Total	75	

Table 3 Valve replacement in patients with ischaemic heart disease

Mitral valve replacement + coronary artery bypass graft	6
Aortic valve replacement + coronary artery bypass graft	2
Mitral valve replacement + coronary artery bypass graft + LV aneurysmectomy	1
Aortic valve replacement + coronary artery bypass graft + LV aneurysmectomy	1
Mitral valve + aortic valve replacement + coronary artery bypass graft	1
Mitral valve + aortic valve replacement + LV aneurysmectomy	1*
Mitral valve replacement + coronary artery bypass graft + LV aneurysmectomy + closure of VSD	1
Total	13
*Hospital death	1 (7.7%)

Table 4 Aetiology of valve disease

Rheumatic heart disease	30
Prosthetic valve dysfunction	8
Papillary muscle dysfunction	8
Degenerative valve disease	13
Subacute bacterial endocarditis	3
Luetic valve disease	2
Congenital heart disease	1
Traumatic valve damage	1
Total	66

Table 5 Indications for mitral valve replacement

Rheumatic heart disease	22
Prosthetic valve dysfunction	4
Papillary muscle fibrosis	1
Papillary muscle rupture	4
Ruptured chordae tendineae	4
Q fever endocarditis	1
Total	36
Hospital mortality 0	

Table 6 Previous operations performed in 35 patients with rheumatic mitral valve disease

Operation	No. of patients
Closed mitral valvotomy × 1	9
× 2	2
× 3	1
Closed mitral valvotomy + mitral valve replacement	2
Closed mitral valvotomy × 3 + mitral valve replacement	1
Closed mitral valvotomy + aortic valve replacement	1
Closed mitral and aortic valvotomy + mitral and aortic valve replacement	1
Mitral valve replacement	2
Replacement of mitral valve prosthesis	1
Total (32 operations)	20

Table 7 Indications for aortic valve replacement

Rheumatic heart disease	5*
Calcific aortic stenosis	11
Subacute bacterial endocarditis	2
Luetic valve disease	2
Traumatic valve rupture	1
Total	21
*Hospital mortality	1 (4.8%)

Table 8 Indications for double valve replacement

Rheumatic heart disease	3
Prosthetic valve dysfunction + rheumatic heart disease	3
Double prosthetic valve dysfunction	1
Marfan's syndrome	1
Calcific aortic stenosis + ischaemic mitral regurgitation	1*
Total	9
*Hospital mortality	1 (11.1%)

Of the 35 patients whose first presentation for cardiac surgery had been with rheumatic mitral valve disease, 20 had already been submitted to a variety of surgical procedures (Table 6).

SURGICAL TECHNIQUE

Standard bicaval-aortic route cardiopulmonary bypass, using a disposable bubble oxygenator and roller pump, was employed. Flow rates varied between 2 and 3.5 litres/min with a mean arterial pressure between 40 and 70 mmHg. Mild hypothermia down to 31°C was reached in most patients.

All operations were performed through a vertical median sternotomy incision. The aorta was cross-clamped throughout the intracardiac procedures, the myocardium being protected by continuous irrigation with cold saline solution at 4°C. Horizontal mattress sutures were used to secure all valves and the struts of the mitral and tricuspid prostheses were orientated so as to produce minimal obstruction to ventricular outflow.

Oral anticoagulation with warfarin was started on the first postoperative day and was discontinued after 6 weeks, except in those patients with a previous history of an embolism, left atrial thrombus at operation, or a giant left atrium.

Results

There were 2 hospital deaths (mortality rate 3%). One patient with calcific aortic stenosis and mitral regurgitation with coronary artery disease did not have a preoperative left ventricular cineangiogram as the aortic valve could not be crossed. At operation

Table 9 Late mortality

Patient	Operation	Survival (mth)	Cause of death	Valve histology
1	Mitral valve replacement + coronary artery vein bypass graft $\times$ 4	2	Congestive cardiac failure; left atrial clot at necropsy	Normal
2	Replacement of aortic valve prosthesis + mitral valve replacement + tricuspid annuloplasty	3	Cause unknown	Normal
3	Mitral valve replacement	4	Congestive cardiac failure with gross cardiomegaly; left atrial clot at necropsy	Normal
4	Replacement of mitral valve prosthesis	20	Congestive cardiac failure with gross cardiomegaly; extensive myocardial fibrosis and left ventricle thrombus at necropsy	Normal

Table 10 Long-term follow-up

No. of patients	64
Period of follow-up	8 to 31 months (mean 16 months)
Total follow-up period	1026 months
Long-term anticoagulation	8 patients
Valve failure	0
Valve infection	0
Episodes of thromboembolism	1

he was found to have a large left ventricular aneurysm with mitral valve papillary muscle dysfunction. After left ventricular aneurysmectomy, aortic and mitral valve replacement, the operation was concluded without incident. He suddenly developed ventricular fibrillation after wound closure and could not be resuscitated. The second hospital death occurred in a 69-year-old man submitted to aortic valve replacement, and was the consequence of laceration of the subclavian artery during insertion of a central venous pressure monitoring line. He was reopened on several occasions for bleeding before the bleeding point was identified, had massive blood transfusion, and died after 24 days from multiple system failure.

During the mean follow-up period of 16 months (range 8 to 31), there were 4 late deaths at 2, 3, 4, and 20 months. All occurred in patients with a long preoperative history of heart disease and congestive cardiac failure.

Necropsy was carried out in all patients. In 2, thrombus was found in the left atrium and in a third, with myocardial fibrosis and gross cardiomegaly, thrombus was found in the left ventricle. No thrombus was found on the prosthetic valves which were macroscopically and microscopically normal in every case.

FOLLOW-UP

Sixty-four patients were discharged and followed up for a total of 1026 months or 16 months/patient (range 8 to 30 months). Long-term anticoagulation

was continued after 6 weeks in only 8 patients. There was no incidence of valve failure or infection or of paraprosthesis leak. One patient had transient blindness of one eye during the first 6 weeks while still on anticoagulation, from which he fully recovered. No other known or suspected embolic episodes were experienced.

SYMPTOMATIC IMPROVEMENT

Of 31 patients in class III (NYHA classification) preoperatively, 3 died, 24 improved to class I, and 4 to class II. Thirty-five patients were class IV preoperatively; 25 improved to class I, 6 to class II, and 1 to class III. One patient remained in class IV until death at 20 months and 2 other patients died.

Actuarial survival curves show an overall survival rate of just under 80 per cent at 2½ years. Over this period, survival after mitral valve replacement was 80.2 per cent and survival for valve replacement in association with ischaemic heart disease was 84.6 per cent at 36 months. For double valve replacement survival was 85.7 per cent at 2 years, and for single aortic valve replacement survival was 94.5 per cent at 18 months.

Discussion

The results of this study confirm the findings of others (Ionescu *et al.*, 1972; Brown *et al.*, 1974; Carpentier *et al.*, 1974; Horowitz *et al.*, 1974; Stinson *et al.*, 1974; Zuhdi, 1974; Zuhdi *et al.*, 1974; Cohn *et al.*, 1975; Pipkin *et al.*, 1976) that the porcine aortic xenograft bioprosthesis (Hancock Laboratories) functions very well as a heart valve substitute in the mitral, aortic, and tricuspid position in man.

A particular feature in these patients was the rapid and smooth immediate postoperative recovery that the majority enjoyed and which was attributed

to the very favourable haemodynamic characteristics of these valves. Improvement in at least two functional classes was seen in 98 per cent of the surviving patients. Failure to obtain symptomatic improvement was related in one patient to myocardial disease after 3 previous mitral valve procedures, and to non-cardiac causes in another patient with osteoarthritis.

Serious valve-related problems were extremely few. In particular, there was no incidence of valve failure or infection over the first 2½ years post-operatively and there was only one probable episode of systemic embolisation. This occurred during the first 6 postoperative weeks while the patient was still on oral anticoagulation, a time when the valve sewing ring is not yet endothelialised and when the risk of systemic embolisation is known to be highest with all prostheses.

After this first 6-week period, anticoagulation with its attendant morbidity and mortality (Stanford *et al.*, 1972; Cleland and Molloy, 1973; Vidne *et al.*, 1973) was avoided in the large majority of patients (87%). It is possible that thrombus formation in the left atrium may have had a part to play in the sudden death of 2 patients comparatively soon after their oral anticoagulation had been discontinued. Because of our experience with these patients, we are now inclined to keep most patients on long-term oral anticoagulation after mitral valve replacement with a Hancock prosthesis if they have more than moderate left atrial enlargement and are in atrial fibrillation, and particularly if there is clot in the left atrium at the time of operation.

The durability of these valves, with not one single valve failure occurring throughout the follow-up period, has been most encouraging and is in striking contrast to the experience with many other earlier forms of tissue valve prosthesis, where there has been a steady attrition rate from the early post-operative period (Wallace, 1975). This improved durability has been largely attributed to 2 factors. The use of a flexible stent has been shown to reduce stress at the cusp edges on closure up to 90 per cent (Reis *et al.*, 1971); secondly, the glutaraldehyde process used to 'tan' the valve is known to produce much more stable cross-linkage between the collagen fibres of the leaflets than has been achieved with previous preservation methods (Carpentier *et al.*, 1969).

In our opinion, the Hancock porcine xenograft prosthesis fulfils many of the characteristics of an ideal human valve substitute and compared more than favourably with other commercially available valve substitutes.

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