Tissue valves in the mitral position

Five years' experience¹

David A. S. Mary,² Brojesh C. Pakrashi, Roger W. Catchpole, and Marian I. Ionescu

From the Department of Cardiothoracic Surgery, General Infirmary at Leeds, and Leeds University, Leeds

Between April 1969 and November 1973 103 patients underwent isolated mitral replacement with three-cusp stented tissue valves. Autologous fascia lata was used in 50 patients, homologous fascia lata in 21, and heterologous pericardium in 32. The early mortality rate (14.6%) was influenced by age, the extent of preoperative cardiac disability, and low cardiac output. The survivors were followed up for periods varying from 8 to 60 months (average 37 months). In general, a factor in late death (13.6%) was high preoperative pulmonary artery pressure. In the autologous fascial series valve failure and infective endocarditis were significantly related to late mortality.

The results with homologous fascia and pericardium were better than with autologous fascia valves. The incidence of postoperative mitral regurgitation was significantly lower in the homologous fascial and pericardial series and none of these grafts had to be removed. The incidence of thromboembolism was low without anticoagulants. Actuarial analysis showed a survival rate at five years of 82.2 per cent. We no longer use autologous fascial valves. Though better results have been obtained with both homologous fascia and pericardium we prefer the physical characteristics of heterologous pericardium and it is easy to obtain.

Frame-mounted tissue valves for mitral replacement were first used in our department in April 1969 (Ionescu and Ross, 1969). The technique evolved because of dissatisfaction with mechanical prostheses (Duvoisin *et al.*, 1968; Mashhour *et al.*, 1969; Starr, Herr, and Wood, 1967). Advances in operative techniques and better designed valve substitutes have improved the results of mitral replacement (Beall *et al.*, 1972; Behrendt and Austen, 1973; Oxman *et al.*, 1972; Winter *et al.*, 1972; Zerbini, 1973). Mortality rates and the incidence of certain complications, however, are still related to the amount of preoperative cardiac or pulmonary disability (McGoon *et al.*, 1973; Nichols *et al.*, 1972), the type of lesion (Behrendt and Austen, 1973), and the kind of valve substitute used (Cleland and Molloy, 1973; Hylen, 1972; Roberts, Bulkley, and Morrow, 1973; Williams *et al.*, 1971).

Reports of *in vitro* hydraulic studies (Swales *et al.*, 1973), the progress of *in vivo* haemodynamic values (Ionescu *et al.*, 1974), the assessment of valve performance by echocardiography (Mary *et*

al., 1974b), the incidence of clinical postoperative complications, and the histopathological fate of mitral stented tissue valves (Ionescu *et al.*, 1974) have been published.

We report here our five years' experience of isolated mitral replacement with stented fascia lata and pericardial valves.

Patients and methods

From April 1969 to November 1973 mitral replacement with stented tissue valves was undertaken in 103 patients, of whom 45 were men and 58 women. Their ages (Table 1) ranged between 9 and 68 years with a mean ($\pm$ SEM) of 44.5 ± 1 years. The mean ages of patients with mitral stenosis (46 years) and mixed valve disease (44 years) were essentially the same as each other ($P > 0.3$) but lower ($P < 0.05$ and $P < 0.001$, respectively) than that of the patients with pure mitral incompetence (55 years). In 88 patients (85.4%) the appearance of the mitral valve at operation was compatible with a previous rheumatic valvulitis. The aetiology of the mitral valve lesions is shown in Table 2.

The preoperative cardiac disability, assessed according to the New York Heart Association (N.Y.H.A.) classification, was as follows: 20 patients in grade II (19.4%), 69 in grade III (67%), and 14 in grade IV (13.6%). The duration of the disability ranged between two weeks and eight years. In four patients N.Y.H.A. grading was

Received 11 March 1975.

¹ This work was supported by the British Heart Foundation.

² Present address: Cardiovascular Unit, Department of Physiology, University of Leeds, Leeds LS2 9JT.

TABLE 1 Age and sex (M. or F.) distribution of 103 patients who had mitral valve replacement with tissue valves

Age groups (years*)	Autologous fascia lata		Homologous fascia lata		Heterologous pericardium		Total
	M	F	M	F	M	F	
0-10	1	—	—	—	—	—	1
11-20	—	—	—	—	—	—	—
21-30	2	—	1	1	—	—	4
31-40	5	6	2	1	3	6	23
41-50	10	19	2	5	4	10	50
51-60	4	2	6	2	1	6	21
61-70	1	—	1	—	2	—	4
Total	23	27	12	9	10	22	103

* The mean ages of patients having each type of tissue valves (43, 46, 45 years respectively) were not statistically different.

TABLE 2 Aetiology of mitral valve disease in 103 patients

	No. of patients
Rheumatic	88*
additional endocarditis	5
Ruptured chordae tendinae	8
additional endocarditis	1
Valve substitute malfunction†	5
Infective endocarditis	1
Congenital anomaly	1

* History of rheumatic fever in 57 (65%) patients: 37 patients had previous closed mitral valvotomy (35.9%).

† Additional endocarditis constituted 6.8% of the patients with rheumatic valve disease.

‡ Comprised 4 aortic heterografts and 1 Alvarez prosthesis.

TABLE 3 Type of valve lesions in 103 patients

Lesion	Mitral*	Tricuspid†	Aortic‡
Stenosis	17 (8)	—	—
Regurgitation	14	12	17
Mixed disease	66 (32)	—	1
Incompetent aortic heterograft	4	—	—
Thrombosed Alvarez prosthesis	1	—	—
Congenital anomaly	1	—	—
Total	103 (40)	12	18

* Figures in brackets indicate patients with mitral valve calcification.

† Two patients had both aortic and tricuspid valve disease in addition to mitral lesion.

difficult because of coexisting chronic bronchitis. They were, however, included in the series. Angina of effort, systemic embolization, and the presence of left atrial thrombus were encountered in 11, 10, and 13 patients, respectively. The commonest valve lesion was mixed mitral disease, followed by pure mitral stenosis and mitral regurgitation (Table 3). Concomitant aortic and tricuspid valve lesions are shown in Table 3.

Cardiothoracic ratio

The cardiothoracic ratio (CTR) was measured from chest radiographs taken within a fortnight before operation, 6-12 months (average 8.5) postoperatively, and at the latest follow-up 13-55 months (average 39.2) postoperatively. The preoperative CTR ranged between 43 and 83 per cent (mean 58%) for the entire group of patients. It was significantly bigger in patients who had a pericardial valve replacement than in those who had an autologous fascial ($P < 0.05$) but not those who had an homologous fascial replacement ($P > 0.1$). In 40 patients (40.8%) mitral valve calcification was detected on fluoroscopy and its presence confirmed at operation. It was present in 38.3 per cent, 42.1 per cent, and 43.8 per cent of patients receiving autologous fascial, homologous fascial, and pericardial valves, respectively.

Electrocardiography

Before operation 30 patients were in sinus rhythm and 73 in atrial fibrillation. Electrocardiographic evidence of left ventricular, right ventricular, and combined ventricular hypertrophy was present in 36, 16, and 8 patients respectively. The sums of SV_1 or 2 and RV_5 or 6 used as an index of left ventricular electrical forces ranged from 11 to 72 mm, with a mean ($\pm$ SEM) of 34 ± 1 mm, in all the patients except two who had right bundle-branch block. There was no significant statistical difference between these sums in patients having the different types of valve replacement.

Cardiac catheterization and angiocardiology

Preoperative cardiac catheterization was done in 78 patients. The mean cardiac index was lower in patients who had a pericardial than in those who had an autologous fascial ($P < 0.02$) or homologous fascial replacement ($P < 0.02$); the left ventricular end-diastolic pressure was higher in the homologous fascial than in the pericardial series ($P < 0.005$); and the pulmonary wedge pressure was higher in the pericardial than in the autologous fascial series ($P < 0.05$). The differences in the other haemodynamic measurements were not statistically significant. Left ventriculography was carried out during preoperative cardiac catheterization in 58 patients.

Surgical procedure

Three-cusp tissue valves attached to Dacron-covered titanium frames were used. Autologous fascia lata valves were made in the operating theatre under sterile conditions. The homologous fascia lata valves were preserved

TABLE 4 Type of three-cusp tissue valves used for mitral replacement in 103 patients

	Internal diameter (mm)					Valve preparation			Suture to heart valve annulus			Duration of heart lung bypass (min) mean $\pm$ SEM	Total
	22	24	26	28	30	Formaldehyde 4%	Glutaraldehyde 0.2%	Glutaraldehyde 0.6%	Interrupted	Continuous	Mixed		
Autologous fascia lata	1	8	32	9	—	—	—	—	23	27	—	48 $\pm$ 3	50
Homologous fascia lata	—	12	7	1	1	14	7	—	3	14	4	51 $\pm$ 4	21
Heterologous pericardium	—	25	7	—	—	—	8	24	1	21	10	53 $\pm$ 4	32
Total	1	45	46	10	1	14	15	24	27	62	14	50 $\pm$ 2	103

TABLE 5 Distribution of type of three-cusp tissue valves used from April 1969 to November 1973 in 103 patients

	Time of use					Total
	1969	1970	1971	1972	1973	
Autologous fascia lata	34	16	—	—	—	50
Homologous fascia lata	3	15	3	—	—	21
Heterologous pericardium	—	—	8	16	8	32
Total	37	31	11	16	8	103

with either 4 per cent buffered formaldehyde or 0.2 per cent buffered glutaraldehyde. The heterologous pericardial valves were treated with either 0.2 per cent buffered glutaraldehyde or with 0.6 per cent stabilized glutaraldehyde. Calf pericardium was used throughout. The valve sizes varied from 22 to 30 mm inside diameter, 24 and 26 mm being used most often. One continuous suture was nearly always used when inserting valves. The preparation and type of tissue employed and the duration of cardiopulmonary bypass are shown in Table 4. The periods when each type of tissue valve was used are shown in Table 5.

In addition to mitral valve replacement 13 patients had a left atrial thrombus removed, one had an atrial septal defect closed, and one had an internal mammary artery implant into the myocardium.

Definitions

Patients who died within 45 days after the operation were classified as early deaths and those who died later as late deaths. To facilitate correlations between post-operative mortality and preoperative functional or haemodynamic status of the patients deaths attributed to apparent myocardial factors were labelled as cardiac. These do not include deaths due to infective endocarditis or those related to the tissue valve replacement procedure. The latter two complications were analysed separately

under tissue valve-related results. Actuarial analysis was used (Berkson and Gage, 1950).

In infective endocarditis the dividing line of 45 days between early and late was used. It has been shown, however, that infection may remain dormant for weeks or months before becoming clinically evident (Edwards, 1973; Sande *et al.*, 1972). Systemic thromboembolism refers to any neurological deficit or systemic vascular occlusion occurring after the immediate postoperative period or, alternatively, when a thrombus was detected in the left atrium at reoperation. Emboli due to infective endocarditis are detailed elsewhere, and those occurring as a result of heart-lung bypass accidents were not included. Tissue valve failure refers to macroscopic pathological alterations in the valve tissue leading to its malfunction. In two instances of tissue valve dysfunction the tissue appeared unaltered and incompetence was due to technical faults in the construction of the valve.

In order to assess the occurrence of systolic murmurs of mitral origin when associated tricuspid and aortic valve lesions were present the opinions of several observers were considered in addition to phonocardiographic evidence of the quality of the murmurs. The findings were then correlated with the results of left ventriculography. Clinically, however, all these apical systolic murmurs were labelled mitral.

Standard statistical formulae were used.

Results

Nearly all the patients were aged 31 to 60 years, the biggest single group having an age range of 41 to 50 (Table 1). This distribution was influenced by the 37 patients who had previously had one or two closed mitral valvotomies. Most of the patients with pure mitral incompetence had degenerative changes of the valve and, as expected, were older than the other patients (Caves, Sutton, and Paneth, 1973; Pomerance, 1972).

Early deaths

Fifteen patients (14.6%) died between the first and the 40th postoperative days (average 16.8 days). A

post-mortem examination was performed on 14. Two-thirds of the early deaths were due to cardiac causes (Table 6).

There was no significant association between death and the type of tissue valve used, but death was related to the amount of preoperative cardiac disability. A significant statistical relationship was found between the early mortality rate and patients who were in grade IV NYHA as compared with those in grade III ($P < 0.02$) and grade II ($P < 0.05$), and patients in whom the preoperative cardiac index was below $1.6 \text{ l/min per m}^2$ as compared to ($P < 0.02$) those with a higher index. The mean values of cardiac indices in patients who died were lower than in those who survived, but not significantly so ($P > 0.1$). The mean age at operation was higher in the patients who died ($P < 0.02$) than in those who survived. Non-cardiac causes of death as opposed to cardiac causes were significantly associated ($P < 0.01$) with older age. This distribution was influenced by patients with respiratory insufficiency, epilepsy, and gastrointestinal haemorrhage.

Late deaths

Of the 88 patients who were discharged after mitral valve replacement, 12 (13.6%) died 2 to 42 months (average 18.3 months) after the operation. All were

TABLE 6 Causes of early and late deaths in 103 patients after mitral valve replacement

	No. of deaths		Total
	Early	Late	
Heart failure	10	4	14
'Pump' failure	4	3	7
Ventricular dysrhythmia	4		4
Myocardial infarction	1		1
Rheumatic carditis	1		1
Sudden death		1	1
Infective endocarditis	2	4	6
Coliform endocarditis		2	2
Streptococcal endocarditis	2		2
No organisms grown		2	2
Tissue valve failure and replacement with prosthesis		3	3
Homologous serum hepatitis		1	1
Heart failure (periprosthetic leak)		1	1
Oesophageal perforation		1	1
Other causes	3	1	4
Respiratory failure	1	1	2
Status epilepticus	1		1
Gastrointestinal haemorrhage	1		1
Total	15	12	27

examined *post mortem*. The mean interval between operation and death was 23.9 months in the autologous fascial series, 5 months in the homologous fascial series, and 10.3 months in the pericardial series. In some of the patients in the autologous fascial series death occurred a long time after the onset of the relevant complications. In three patients with autologous fascial valve failure regurgitation was noticed immediately after surgery; reoperation and prosthetic replacement was performed after 19, 36, and 38 months, respectively. These patients died 24, 6, and 4 months, respectively, after reoperation. The remaining nine patients died 2–25 months (mean 11.4 months) after operation.

The actuarial analysis of the survival rate of the 88 patients is shown in Fig. 1. In the entire series, including reoperated patients, the survival rate of patients who left hospital was 82.2 per cent and that of only those patients with the original tissue valves *in situ* 73.6 per cent. The follow-up of these patients was for periods of up to 60 months after operation. A significant statistical relationship was found between late death and valve-related factors ($P < 0.001$). The latter were significant with autologous fascial valves ($P < 0.01$) but not with homologous fascial ($P > 0.1$) or pericardial valves ($P > 0.1$). A significant statistical relationship was also found between late death and the development of infective endocarditis ($P < 0.001$) or valve failure ($P < 0.05$). Valve failure occurred only with autologous fascial valves.

There was a statistically significant difference between the mean ($P < 0.01$) or systolic pulmonary artery pressure ($P < 0.01$) in patients who died compared with those who survived. Patients with

FIG. 1 Actuarial representation of survival rate of 88 patients after discharge from hospital following initial valve replacement. Upper curve represents all patients irrespective of the type of valve in the mitral position including reoperated patients with other prostheses; lower curve relates to only those patients with the original tissue valves *in situ*.

FIG. 2 Actuarial representation of survival rate in 103 patients related to their preoperative condition as measured by (a) clinical disability (NYHA), (b) mitral valve lesion, (c) cardiac rhythm, (d) cardiothoracic ratio.

advanced preoperative functional disability, mitral regurgitation, atrial fibrillation, and a CTR above 60 per cent had a relatively higher risk of death at varying periods after operation (Fig. 2).

Thromboembolism

There were five episodes of systemic embolization in four patients. Four were cerebral and one was femoral. They occurred one, three, six, seven, and 30 days, respectively, after mitral valve replacement. Another patient who had a left atrial thrombus removed during the initial mitral valve replacement was reoperated on six months later because of persistent congestive heart failure and low cardiac output; a left atrial thrombus, found at a distance from the mitral valve, was removed. The sequence of events in this patient suggested an early postoperative recurrence of the thrombus. Post-mortem examination of patients who died from other causes showed no sign of systemic embolization, so the occurrence of unrecognized episodes can be excluded (Ullal *et al.*, 1971).

None of the patients with systemic embolization had had preoperative embolism. The left auricular appendage was not obliterated in any patient and anticoagulants were not used. There was no statistically significant relationship between the occurrence of thromboembolism and either the preoperative valve lesion, previous closed valvotomy, presence of calcification, preoperative left atrial thrombus, cardiac disability, any of the haemodynamic values, type of valve substitute, technique of insertion, perfusion duration, re-exploration for haemorrhage, presence of postoperative murmurs, CTR, cardiac rhythm, or DC cardioversion (Cleland and Molloy,

1973; Davila *et al.*, 1966; Roberts and Morrow, 1966).

Infective endocarditis

Beta-haemolytic and non-haemolytic streptococcal endocarditis occurred during the first postoperative month in two patients (1.9%). One had been re-operated on for excessive bleeding. Both died of uncontrollable infection. Five other patients (5.6%) developed endocarditis 2 to 25 months postoperatively. One, who had a coliform bacillus endocarditis, had a persistent thigh wound. In another, coliform organisms were grown from the homologous fascia used for valve construction. In the remaining three patients no organisms were grown. Four patients died, three after prosthetic replacement of the affected valve and one after medical treatment alone. One survived replacement with a prosthesis.

Infective endocarditis therefore had a statistically significant relationship to early and late postoperative mortality. Most of the cases occurred before the introduction of the new policy of bacteriological monitoring and prophylaxis (Freeman, 1974) and were not related to the type of tissue valve used.

Valve failure

Six patients developed tissue valve failure. Significant incompetence was detected at periods ranging from immediately to six months after operation (mean 3.2 months). The valves were replaced with ball valve prostheses after 10 to 38 months (mean 25 months). Three patients died after reoperation (Table 6) and the other three are alive and have a grade I disability (NYHA). Valve failure occurred only in the autologous fascial series. Technical faults in the construction of two homologous fascial valves occurred within the first month of the use of this type of tissue. Regurgitation became obvious shortly after the operation. In both patients the valves were replaced and both are now well. The technical aspect of this complication has been reported (Ionescu *et al.*, 1974).

Postoperative clinical state

Seventy patients with tissue valves were followed for periods of 8 to 60 months (mean 37 months). Of these, 56 (80%) are now in grade I (NYHA), 13 (18.6%) in grade II, and one is in grade III (Fig. 3). The causes of persisting disability in the 14 patients in grade II and III were progressive mitral regurgitation in five patients with autologous fascial valves and chronic bronchitis, associated

that increases in the loudness of murmurs indicated progressive incompetence. Murmurs which increased in loudness were encountered only in patients with autologous fascial valves and in those in whom the murmur appeared early. The association of early systolic murmurs with autologous fascial valves was significantly greater than with pericardial valves ($P < 0.001$). Late systolic murmurs were associated significantly only with autologous fascial valves ($P < 0.05$). When all systolic murmurs (early and late) were considered there was a significant association with autologous fascial valves but not with homologous fascial ($P < 0.05$) or pericardial valves ($P < 0.01$).

The actuarial analysis of the proportion of the 88 survivors still alive at various postoperative periods and without mitral murmurs, regurgitation, or infective endocarditis is shown in Fig. 4. When compared at the same follow-up period of 36 months the three groups of patients showed good results without any complication in 12.1 per cent for autologous fascial, 46.2 per cent for homologous fascial, and 63.7 per cent for pericardial valves.

Discussion

The results of mitral valve replacement vary according to the place of origin of the report and the time of operation (Davila *et al.*, 1966; Harken and Collins, 1969; Starr, 1971). They also depend on, among other factors, the amount of preoperative cardiac disability (Kittle *et al.*, 1969; Litwak *et al.*, 1969; McGoon *et al.*, 1973; Turner, 1968). Our results are therefore not strictly comparable with those from other centres. Nevertheless, in our series the sex incidence of the type of valve lesion and its age distribution were compatible with those reported in the general population and were typical of patients with mitral disease (Caves *et al.*, 1973; Reichel, Shelburne, and Perloff, 1973).

Early death rates after mitral valve replacement vary from 2 to 31 per cent (Aston and Mulder, 1971; Bonchek, Anderson, and Starr, 1974; Kerth *et al.*, 1971; Mullin *et al.*, 1972; Oh *et al.*, 1973; Ross *et al.*, 1973) and are compatible with our mortality rate of 14.6 per cent. As we (Mary *et al.*, 1974a) and others (Kittle *et al.*, 1969; Litwak *et al.*, 1969; McGoon *et al.*, 1973; Yacoub, Towers, and Somerville, 1972) had previously found, advanced preoperative cardiac disability was the main factor influencing early postoperative death. Valve-related deaths were due only to infective endocarditis and the incidence was not statistically significant. The operative mortality in the present series, however, declined to 4.2 per cent during 1972–3. Such a decrease reflects improved operative

technique and postoperative care (Mary *et al.*, 1974a) and is similar to that of others (Aston and Mulder, 1971; Behrendt and Austen, 1973; Starr, 1971).

The introduction of new designs of prosthetic valves has reduced the early and late complications encountered with the earlier models (Björk, 1970; Bonchek *et al.*, 1974; Pluth, Broadbent, and Danielson, 1973). A similar trend has been reported with tissue valves, which have been in use for a shorter time (Lennox *et al.*, 1971; Oh *et al.*, 1973; Talavlikar *et al.*, 1973; Zerbini, 1973). Thus, the duration of our follow up would be comparable with that in reports of the more recently introduced ball and disc prostheses and some types of tissue valves.

Late deaths in our series were mainly due to complications related to the tissue valve or to cardiac factors. Most of these complications occurred in patients with autologous fascial valves and were seen within a year of operation. Autologous fascial valve failure and infective endocarditis were the main valve-related complications. As in other reported series (Kittle *et al.*, 1969; Messmer *et al.*, 1971) cardiac disability and pulmonary hypertension appeared also to be factors affecting late mortality. Late death rates in patients with the more recent types of mitral valve substitutes (who were in general followed up for a different period from ours) have ranged from 3.5 to 22 per cent (Bonchek *et al.*, 1974; Graham *et al.*, 1971; Isom *et al.*, 1972; Lennox *et al.*, 1971; McEnany, Ross, and Yates, 1972; Nichols *et al.*, 1972; Oh *et al.*, 1973; Pluth *et al.*, 1973; Winter *et al.*, 1972; Yacoub *et al.*, 1972). The late mortality rate in our series (13.6%) compares favourably with these reported figures. Actuarially the survival rate in other series with a comparable follow up ranges from 73 to 91 per cent (Nichols *et al.*, 1972; Talavlikar *et al.*, 1973) and is similar to that in our series (82.2%).

No deaths in our series were attributed to thromboembolism. All the episodes occurred within a month of operation. Early postoperative thromboembolism has been attributed to advanced heart disease; cardiac dilatation and low cardiac output; obstruction to blood flow; atrial fibrillation; and surgical trauma inflicted on the left atrial endocardium, especially near the valve ring (Davila *et al.*, 1966; Roberts and Morrow, 1966; Yeh *et al.*, 1967). All our patients had advanced preoperative cardiac disability, an increased CTR, and most remained in atrial fibrillation after their operation. Like others (Cleland and Molloy, 1973), however, we found no significant statistical relationship to these factors in our cases of thromboembolism.

Unlike other recent series of prosthetic or tissue valve replacement (Graham *et al.*, 1971; Isom *et al.*, 1972; McEnany *et al.*, 1972; Pluth *et al.*, 1973; Ross *et al.*, 1973) we did not give our patients anticoagulants routinely for any length of time, even when left atrial thrombus was discovered during surgery. This may explain the early occurrence of thromboembolism in our series. Furthermore, a left atrial thrombus may form in a site unrelated to the inserted valve, whether it is a tissue valve (Angell *et al.*, 1968) or a prosthesis (Pluth *et al.*, 1973; Reis *et al.*, 1970); as happened in one of our patients. The stitched edge and sutures of tissue valves removed or recovered within one month after operation in our department have been completely and evenly covered with a smooth layer of organized fibrin. Encapsulation of the cloth-covered components of prosthetic valves is said to occur between 6 and 12 months after insertion (Nichols *et al.*, 1972; Reis *et al.*, 1970; Spencer *et al.*, 1970). A reduction in the incidence of thromboembolism and the avoidance of the risks of anticoagulation (Bonchek *et al.*, 1974; Isom *et al.*, 1972; McEnany *et al.*, 1972; Spencer *et al.*, 1970) are obvious advantages of the use of tissue valves.

The causes of tissue valve failure have been discussed before (Ionescu *et al.*, 1974). McEnany *et al.* (1972) believed that failure of autologous fascial valves in the mitral position in their cases was due to the unsuitability of a three-cusp valve in the atrioventricular annulus. The two posterior cusps thickened and shrunk owing to a relative lack of diastolic mobility and were therefore subjected to a more severe and irregular stress than the anterior cusp, which, as in a natural mitral valve, maintained a better diastolic mobility. Echocardiographic evidence in our patients has shown that at least two cusps, the anterior and one posterior moved in a similar fashion during ventricular diastole (Mary *et al.*, 1974b). *In vitro* hydrodynamic studies have shown that all three-cusp valves open in a sequential manner, and that this phenomenon is accentuated by irregularities in the shape and size of the cusps or in the thickness and pliability of the material. The order in which the cusps of a particular valve open is maintained irrespective of its circumferential position in relation to the left ventricular outlet. In patients with a low cardiac output postoperatively, mitral valves made of autologous, biologically active tissue may not open fully, and consequently the cusp with little or no mobility may undergo structural changes leading to fibrosis and atrophy (Swales *et al.*, 1973; Ionescu *et al.*, 1974).

Our experience does not support the view that

valve failure is due to lack of anticoagulation (Bernhard *et al.*, 1973) or that it is related to age and sex of the patients (McEnany *et al.*, 1972). Valve failure occurred in our autologous fascial valve series and was not related to the patient's age or sex. It seems that it is not enough to construct a competent valve but that when using autologous, living tissue the valve cusps must be identical in thickness, pliability, elasticity, and shape. Poor valve construction (McEnany *et al.*, 1972) and changes in technique (Talavlikar *et al.*, 1973) have been named as contributory factors causing incompetence. That there were no cases of valve failure in our homologous fascial series corroborates this. All the valves that had to be replaced in our cases were autologous fascial valves. In these cases the mitral regurgitant murmur developed early after operation and increased in intensity. Also patients in our autologous fascial valve group were the only ones in whom mitral systolic murmurs appeared late. The method of preserving tissue valves did not appear to influence our results nor did the type of suture or the size of the valves used.

Mitral reflux could not be demonstrated in our series when there was no apical systolic murmur. Apical or parasternal early systolic and ejection type murmurs seemed to occur whether or not there was angiocardigraphic evidence of mitral regurgitation (Zerbini, 1973). A 'low grade systolic murmur' has been noted in patients with tissue valves in the absence of demonstrable regurgitation (Puig *et al.*, 1972). Possibly turbulence created by the supporting struts of the valve projecting into the left ventricle (Morrow *et al.*, 1964) may cause these systolic murmurs, which occur when there is no associated valve disease or angiocardigraphic evidence of mitral incompetence (Willerson *et al.*, 1972). Obviously labelling all systolic murmurs in our patients as mitral in origin has overestimated the incidence of postoperative mitral regurgitation.

The improvement in cardiac disability in our patients is comparable to that seen in other series of cases (Bonchek *et al.*, 1974).

Our study has shown, therefore, that the patient's age and the amount of preoperative cardiac disability are contributory factors in early mortality after mitral valve replacement. Late mortality in our series was related to high preoperative pulmonary artery pressure, postoperative infective endocarditis, and tissue valve-related complications.

The merit of tissue valves in that they reduce thromboembolic and anticoagulant complications is balanced by the expected durability of prosthetic valves of recent design. The lower incidence of mitral systolic murmurs and incompetence associated with homologous fascial and pericardial valves

has encouraged their use in preference to autologous fascial valves, with which there is a high incidence of failure and regurgitation. Though the results with homologous fascial valves are good the tissue is difficult to procure and the long-term fate of formaldehyde-treated biological tissue is uncertain (Ionescu *et al.*, 1972). Calf pericardium, on the other hand, is easily available, its properties are more suitable for valve construction than fascia lata (Ionescu *et al.*, 1974), and glutaraldehyde seems to produce permanent cross-linkages which enhance tissue durability (Carpentier and Dubost, 1972). A controlled prospective trial to compare the results from tissue valves with those from recent, cloth-covered prosthetic devices has been started.

We are grateful to Miss Beryl Walsh and Mrs. Christine Crowther for invaluable help with this work.

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Requests for reprints to M. I. Ionescu, Esq., F.A.C.S., Department of Cardiothoracic Surgery, The General Infirmary, Great George Street, Leeds LS1 3EX.