Clinical and haemodynamic evaluation of mounted porcine heterograft in mitral position

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SUMMARY Clinical and haemodynamic assessment has been made of 24 patients with porcine heterograft mitral valve replacements. Twenty patients had a good clinical result and were studied electively and 4 patients had persistent symptoms caused either by poor left ventricular function, aortic paraprosthetic regurgitation, mitral paraprosthetic regurgitation, or impaired left ventricular function with a rather small mitral valve area of 1.4 cm². The mean left ventricular end-diastolic pressure was 17.8 ± 1.2 mmHg and the mean mitral valve diastolic gradient was 5.9 ± 1.0 mmHg. The larger prostheses had the smaller gradients. The average mitral valve area was 3.2 cm² for 35 mm valves, 2.8 cm² for 33 mm valves, 2.1 cm² for 31 mm valves, and 2.3 cm² for 29 mm valves. Two patients showed significant mitral regurgitation on left ventricular cineangiography but in the remainder the valves were competent.

An apical diastolic murmur was audible in 9 of 24 patients but there was no correlation between the presence of a murmur and the magnitude of the mitral valve gradient or mitral valve area. Nine patients with soft apical systolic murmurs had no evidence of mitral regurgitation but 2 patients with louder murmurs had significant regurgitation.

We conclude that the haemodynamic indices observed with porcine heterograft valves are similar to those observed with other mitral valve prostheses and that though most patients have distinct symptomatic improvement significant haemodynamic abnormalities persist. Apical systolic and diastolic murmurs can be present with normal prosthetic valve function.

Carpentier and Dubost (1972) suggested glutaraldehyde as a method of stabilising porcine aortic valves and Reis and his associates (1971) described the use of a flexible stent on which such valves could be mounted and used as prostheses. These advances were followed by the successful use of mounted porcine heterograft valves in many centres (Brown *et al.*, 1974; Carpentier *et al.*, 1974; Horowitz *et al.*, 1974; Cohn *et al.*, 1975; Johnson *et al.*, 1975; McIntosh *et al.*, 1975; Hannah and Reis, 1976; Sang *et al.*, 1976; Stinson *et al.*, 1977). Their major advantage has been the diminished need for long-term anticoagulation (Cohn *et al.*, 1975; Stinson *et al.*, 1977), while the main disadvantage, as with other tissue valves, has been concern about their long-term durability (Roberts, 1976). As yet few clinical and haemodynamic studies of these valves have been available. This report concerns the appraisal of a group of

patients in whom the clinical and haemodynamic function of their implanted mounted porcine heterografts has been assessed. All of the prostheses described in this report were manufactured by Hancock laboratories.

Subjects and methods

Twenty-four patients were studied 4 to 32 months (mean 14 months) after implantation of a mounted porcine heterograft in the mitral position. In 4 patients postoperative haemodynamic assessment was indicated because of continuing symptoms. The other 20 were restudied electively after giving informed consent.

At cardiac catheterisation simultaneous pulmonary capillary wedge pressure and left ventricular pressure were recorded at the same gain with zero level set at mid chest. Left atrial pressure was recorded in case 24. Pulmonary artery wedge pressures were accepted if the pressure contour was distinctly different from, and the phasic and mean pressure were lower than, those recorded

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from the pulmonary artery. The 8 patients in sinus rhythm had a biphasic pulmonary artery wedge pressure trace. Mean mitral valve gradient was obtained by averaging values for 5 cardiac cycles. Mitral valve area was calculated using the Gorlin formula (Gorlin and Gorlin, 1951). Cardiac output was measured by the Fick principle using measured oxygen uptake and arteriovenous oxygen

difference. Left ventricular angiography was performed in the right anterior oblique position. The ejection fraction was measured by the area length method of Greene (Greene *et al.*, 1967), and the competence of the mitral valve was assessed. A proportion of patients had preoperative haemodynamic data which have been tabulated with the postoperative results. Four patients had pre-

Table

Case no.	Age (y)	Sex	Diagnosis	Rhythm	HR (beats/min)	MPA (mmHg)	PAW (mmHg)	LVEDP (mmHg)	CI (l/min/m ²)	MVA (cm ²)	MVG (mmHg)	Ring EF size (%)	Other procedure	NYHA class	Angiography MR AR
1	57	F	RHD MS MR	AF	82	32	18	18	NA	NA	0	31 53	—	I	0
2	61	F	RC MR	NSR	75	36	26	24	3.6	3.3	7	33 52	—	I	0
3	69	M	RHD MS MR	AF	53	32	22	21	2.4	1.7	4	31 63	TA	I	0
4	43	F	RHD MS	NSR	77	37	30	27	2.9	2.1	10	29 51	—	I	0
5	51	M	RHD MS	AF	50	40	30	25	1.7	—	0	33 44	—	I	0
6	54	M	RC MR	AF	70	20	15	16	2.0	3.6	1	35 73	—	I	0
7	60	F	RHD MS MR	AF	75	27	22	20	2.0	2.1	5	31 73	—	II	2/3
8	58	M	Cleft MV	AF	51	31	24	23	1.4	2.1	3	33 10	—	II	0
9	66	F	IHD RPM	AF	78	32	22	15	3.1 ^E	2.6	6	31 52	CABG	I	0
10	57	M	RHD MS MR	AF	66	27	19	17	3.6	3.1	3	35 74	—	II	0
11	50	M	RHD AS MPS	AF	77	30	24	20	2.3	1.6	8	29 49	AVR	III	0 2/3
12	49	F	RHD MS MR	AF	97	36	23	16	2.5 ^E	2.0	8	31 39	—	I	0
13	36	M	RHD MR AR	AF	59	30	24	15	3.7	2.4	15	31 29	AVR	III	0 0
14	35	M	RHD MS MR	NSR	71	19	9	8	4.1	3.5	5	33 50	—	I	0
15	39	F	RHD MS	NSR	66	23	15	15	4.0	3.3	6	29 62	—	I	0
16	34	F	RHD MS MR	NSR	75	23	17	10	5.4	—	0	33 73	—	I	0
17	55	M	RHD MS	AF	68	22	12	14	2.6	1.8	4	31 59	—	I	0
18	54	F	RHD MS MR	AF	61	32	23	19	4.1	2.1	10	31 88	—	I	0
19	66	M	RHD SBE	NSR	72	37	33	25	3.1	1.3	21	31 61	—	II	0
20	41	F	AR MR	AF	61	15	8	8	2.5	2.2	3	33 63	—	II	0
21	43	M	RHD MR MS AR	AF	69	20	15	14	3.7	3.1	3	35 58	—	I	0
22	51	F	RHD MS	NSR	98	35	20	13	3.2	1.7	10	31 53	—	II	0
23	59	M	IHD MR	NSR	120	42	36	30	2.3	3.0	1	35 10	CABG	III	0
24	36	F	RHD MPR	AF	115	40	35	15	5.0	3.0	8	31 NA	—	III	2/3
Mean	51				74.4	29.9	21.7	17.8	3.1	2.46	5.9	53.9			
±SEM	2.1				3.6	1.5	1.5	1.2	0.21	0.15	1.0	3.9			

AF, atrial fibrillation; AR, aortic regurgitation; AS, aortic stenosis; AVR, aortic valve replacement; CABG, coronary artery bypass graft; CI, cardiac index; E, estimated; EF, ejection fraction; HR, heart rate; IHD, ischaemic heart disease; LVEDP, left ventricular end-diastolic pressure; MPA, main pulmonary artery mean pressure; MPR, mitral prosthetic regurgitation; MPS, mitral prosthetic stenosis; MR, mitral regurgitation; MS, mitral stenosis; MV, mitral valve; MVA, mitral valve area; MVG, mitral valve gradient; NA, not available; NSR, normal sinus rhythm; PAW, pulmonary artery wedge mean pressure; RC, ruptured chordae; RHD, rheumatic heart disease; RPM, ruptured papillary muscle; SBE, subacute bacterial endocarditis; SEM, standard error of mean; TA, tricuspid annuloplasty.

Fig. 1a-1d Preoperative and postoperative haemodynamic data of mounted porcine heterografts in the mitral position.

operative coronary angiography which was normal in 2.

Postoperative results

HAEMODYNAMICS

Individual values are shown in the Table and Fig. 1 and standard errors of the mean are given in the text.

The mean left ventricular end-diastolic pressure (Fig. 1a) was 17.8 ± 1.2 mmHg (range 8 to 30 mmHg) compared with an almost identical preoperative mean value of 17.2 ± 2.4 mmHg (range 8 to 40 mmHg) in the 13 patients in whom these data are available. Seven patients showed a rise in left ventricular end-diastolic pressure and in 7

the postoperative values fell. Mean pulmonary artery wedge pressures postoperatively (Fig. 1b) averaged 21.7 ± 1.5 mmHg (range 9 to 36 mmHg) which is almost identical to the preoperative average of 21.8 ± 1.0 mmHg (range 16 to 26 mmHg). The average mean pulmonary artery pressure postoperatively (Fig. 1c) was 29.9 ± 1.5 mmHg (range 15 to 42 mmHg) while the average preoperative mean pulmonary artery pressure was 31.2 ± 1.7 mmHg (range 22 to 72 mmHg). The mean mitral diastolic gradient postoperatively averaged 5.9 mmHg (range 0 to 21 mmHg) (Fig. 1d). The average gradient for the 35 mm stent mounted valve was 2.0 mmHg (range 1 to 3 mmHg), for the 33 mm stent was 3.0 mmHg (range 0 to 7 mmHg), for the 31 mm stent was

Fig. 2 Mitral valve gradient related to stent diameter. X, apical mid-diastolic murmur; O, apical pansystolic murmur.

8.3 mmHg (range 0 to 21 mmHg), and for the 29 mm stent was 8.0 mmHg (range 6 to 10 mmHg). The relation between mitral valve gradient and stent diameter was statistically significant ($r = 0.69$, $P < 0.05$) as shown in Fig. 2.

Two patients (cases 9 and 13) were unable to perform expired air collection and an estimated oxygen uptake was used to calculate cardiac output (Robertson and Reid, 1952) and to derive mitral valve area. The cardiac index ranged from 1.4 to 5.4 l/min per m^2 with an average of 3.1 ± 0.21 l/min per m^2 . The average mitral valve area for 21 patients in whom it could be calculated postoperatively was 2.5 cm^2 (range 1.3 to 3.6 cm^2). The average area for the 35 mm diameter stent valves was 3.5 cm^2 (range 3.0 to 3.6 cm^2), that for the 33 mm stents was 2.5 cm^2 (range 1.1 to 3.5 cm^2), that for the 31 mm stent valves was 2.0 cm^2 (range 1.3 to 3.0 cm^2), while that for the 29 mm stent valves was 2.2 cm^2 (range 1.6 to 3.0 cm^2). Discounting the patients in whom the area could not be calculated (3 patients) the valve area cor-

related significantly with the stent diameter ($r = 0.56$, $P < 0.01$).

The ejection fraction averaged 53.9 ± 3.9 per cent (range 10 to 88%). Left ventricular angiography showed important mitral regurgitation in 2 patients but the prosthesis was competent in the remaining 22 patients. Aortography showed important aortic regurgitation in 2 other patients.

Clinical results

Functional improvement from preoperative class III or IV to functional class I or II was noted in 20 of the 24 patients studied (Fig. 3). Of the 4 patients with a poor clinical result, 1 was found to have important mitral paraprosthesis regurgitation (the mean mitral valve gradient was 8 mmHg) and another had severe aortic paraprosthesis regurgitation (mean mitral valve gradient 8 mmHg). A third patient had a mean mitral diastolic gradient of 15 mmHg (valve area 2.4 cm^2) combined with an ejection fraction of 29 per cent. The fourth patient had severe coronary artery disease and an ejection fraction of 10 per cent with a satisfactory prosthesis.

Clinical examination revealed a grade 1 to 2 out of 6 apical mid-systolic murmur in 9 patients, none of whom had angiographic evidence of mitral regurgitation. Two patients with important mitral paraprosthesis regurgitation had grade 3 out of 6 pansystolic murmurs.

Diastolic murmurs were audible at the apex in 9 of the 24 patients. Seven of the murmurs were grade 1 or 2 out of 6, 2 were grade 3 out of 6. There was no correlation between the stent diameter of the mitral valve implanted or the mitral valve area and the presence of a murmur, nor was there

Clinical class (NYHA)

Fig. 3 Clinical class (NYHA) pre- and postoperatively.

Fig. 4 Mitral valve area related to stent diameter. X, apical mid-diastolic murmur; O, apical pansystolic murmur.

any correlation between the presence of a murmur and the size or indeed the presence of a mitral diastolic gradient (Fig. 2 and 4).

Discussion

The majority of patients undergoing mitral valve replacement with a mounted porcine heterograft have a good clinical result (Sang *et al.*, 1976; Stinson *et al.*, 1977). This is also true of other widely used mitral valve prostheses (Winter *et al.*, 1972; Böök, 1974; Brown *et al.*, 1974). The main advantage of the heterograft valve has been the relatively low incidence of thromboembolic complications (Wallace, 1975; Roberts, 1976; Stinson *et al.*, 1977). Our practice has been to anticoagulate our patients for 6 weeks postoperatively and then to stop anticoagulants unless a massive left atrium or atrial thrombus has been found at operation. In this series we have noted no embolic phenomena though we have encountered several major emboli in our total heterograft experience.

The haemodynamic findings in this series are similar to those found by other investigators (Horowitz *et al.*, 1974; Johnson *et al.*, 1975; McIntosh *et al.*, 1975; Hannah and Reis, 1976). Hannah and Reis (1976) found average gradients of 5.2 mmHg, 2.3 mmHg, 2.5 mmHg, and 2.7

mmHg across the 29 mm, 31 mm, 33 mm, and 35 mm stent diameter prostheses, respectively. Johnson and his colleagues (1975) found an average gradient of 5.5 mmHg in the 14 patients they studied while Brown *et al.* (1974) and later McIntosh *et al.* (1975) of the Bethesda group found gradients of up to 15 mmHg, but emphasised that many patients had no gradients. No report of a gradient as high as 21 mmHg found in one of our patients has been made previously. The resting cardiac output was 6.8 l/min and the mitral valve area 1.3 cm². This is similar to other patients and the large gradient presumably reflects the high resting cardiac output rather than prosthetic valve dysfunction. Postoperatively this patient had a good clinical result, improving from functional class IV to class II and therefore no further intervention has been contemplated. With this one exception the atrioventricular gradients found with the porcine heterografts are similar to those found across the other commonly used prostheses (Winter *et al.*, 1972; Böök, 1974; Brown *et al.*, 1974; Angell *et al.*, 1977; Ionescu *et al.*, 1977).

Many of our patients had abnormally high left ventricular end-diastolic pressure postoperatively, and reduced ejection fractions. These indices of left ventricular dysfunction did not correlate significantly with the total cardiopulmonary bypass time or with the aortic cross clamp time. Deterioration in left ventricular function after mitral valve replacement has been well documented previously (Hultgren *et al.*, 1968; Gold, 1974; Maloney *et al.*, 1975) but is not fully understood though it may be related to the bypass technique. In this series myocardial preservation with local hypothermia using ice-cold saline was the technique employed. It is striking that in spite of the frequency of significant haemodynamic abnormalities postoperatively, both in terms of left ventricular and valve function, the majority of patients have such obvious symptomatic improvement. This discrepancy between clinical and haemodynamic results is not an infrequent finding after mitral valve surgery, and an abnormality of left ventricular compliance has been suggested as an explanation for the increased left ventricular end-diastolic pressures sometimes encountered (Feigenbaum *et al.*, 1968). Recently Sutton *et al.* (1977) have mentioned several patients with small or absent mitral valve gradients in whom symptoms were relieved by mitral valve surgery. They postulate that removal of the subvalve apparatus is responsible for the improvement and this may be a factor in our cases also.

The presence of systolic murmurs in patients with normally functioning mitral porcine hetero-

grafts and no other valvular disease was noted by Horowitz and his colleagues (1974) in 11 of 14 patients. One patient had a mid-diastolic murmur and he had a pannus of tissue interfering with the function of an otherwise normal heterograft, effectively causing mitral prosthetic obstruction. Nine of our patients had systolic murmurs similar to those described by Horowitz *et al.*, with no evidence of mitral regurgitation. In addition, we found mitral diastolic murmurs in 9 of the 24 patients. These murmurs gave no guide to the severity or presence of a transvalvular gradient. In 2 of the patients it is possible that the diastolic murmur was caused by increased flow associated with concomitant mitral regurgitation. Another patient with a mid-diastolic murmur had mild aortic regurgitation and this may have been an example of the Austin Flint phenomenon, which can occur with mitral prostheses (Epstein and Coulshed, 1975; Schaefer *et al.*, 1975). In the other 6 patients with apical mid-diastolic murmurs, however, no such explanation is available and we conclude that apical systolic and diastolic murmurs may be associated with normal prosthetic valve function.

References

- Angell, W. W., Angell, J. D., and Sywak, A. (1977). Selection of tissue or prosthetic valve: a 5 year prospective, randomised comparison. *Journal of Thoracic and Cardiovascular Surgery*, **73**, 43–53.
- Böök, K. (1974). Mitral valve replacement with the tilting disc valve—clinical and haemodynamic studies in isolated mitral valve lesions. *Scandinavian Journal of Thoracic and Cardiovascular Surgery*, Suppl. 12, 1–28.
- Brown, J. W., Myerowitz, P. D., Cann, M. S., Colvin, S. B., McIntosh, C. L., and Morrow, A. G. (1974). Clinical and hemodynamic comparisons of Kay-Shiley, Starr-Edwards No. 6520, and Reis-Hancock porcine xenograft mitral valves. *Surgery*, **76**, 983–991.
- Carpentier, A., Deloche, A., Relland, J., Fabiani, J. N., Förman, J., Camilleri, J. P., Soyer, R., and Dubost, C. (1974). Six year follow up of glutaraldehyde preserved heterografts. *Journal of Thoracic and Cardiovascular Surgery*, **68**, 771–782.
- Carpentier, A., and Dubost, C. (1972). From xenograft to bioprosthesis: evolution of concepts and techniques of valvular xenografts. In *Biological Tissue in Heart Valve Replacement*, p. 515, ed M. I. Ionescu, D. N. Ross, and G. H. Wooler. Butterworth, London.
- Cohn, L. H., Lambert, J. J., Castaneda, A. R., and Collins, J. J., Jr. (1975). Cardiac valve replacement with the stabilised glutaraldehyde porcine aortic valve: indications, operative results and follow up. *Chest*, **68**, 162–165.
- Epstein, E. J., and Coulshed, N. (1975). Murmurs and prostheses (correspondence). *Circulation*, **52**, 965.
- Feigenbaum, H., Linback, R. E., and Nasser, W. K. (1968). Hemodynamic studies before and after instrumental mitral commissurotomy. *Circulation*, **38**, 261–276.
- Gold, R. G. (1974). Deterioration in left ventricular function after mitral valve replacement (abstract). *British Heart Journal*, **36**, 1038–1039.
- Gnorla, R., and Gorlin, S. G. (1951). Hydraulic formula for calculation of the area of the stenotic mitral valve, other cardiac valves and central circulatory shunts. *American Heart Journal*, **41**, 1–29.
- Greene, D. G., Carlisle, R., Grant, C., and Bunnell, I. L. (1967). Estimation of left ventricular volume by one plane cineangiography. *Circulation*, **35**, 61–69.
- Hannah, H., III, and Reis, R. L. (1976). Current status of porcine heterograft prostheses: a 5 year appraisal. *Circulation*, **54**, Suppl. III, 3–27.
- Horowitz, M. S., Goodman, D. J., Fogarty, T. J., and Harrison, D. C. (1974). Mitral valve replacement with the glutaraldehyde-preserved porcine heterograft: clinical, hemodynamic and pathological considerations. *Journal of Thoracic and Cardiovascular Surgery*, **67**, 885–895.
- Hultgren, H., Hubis, H., and Shumway, N. (1968). Cardiac function following mitral valve replacement. *American Heart Journal*, **75**, 302–312.
- Ionescu, M. I., Tandon, A. P., Mary, D. A. S., and Abid, A. (1977). Heart valve replacement with the Ionescu-Shiley pericardial xenograft. *Journal of Thoracic and Cardiovascular Surgery*, **73**, 31–41.
- Johnson, A. D., Daily, P. O., Peterson, K. L., Le Winter, M., DiDonna, G. J., Blaire, G., and Niwayama, G. (1975). Functional evaluation of the porcine heterograft in the mitral position. *Circulation*, **51** and **52**, Suppl. I, 40–48.
- McIntosh, C. L., Michaelis, L. L., Morrow, A. G., Itscoitz, S. B., Redwood, D. R., and Epstein, S. E. (1975). Atrio-ventricular valve replacement with the Hancock porcine xenograft: a 5 year clinical experience. *Surgery*, **78**, 768–775.
- Maloney, J. V., Jr., Cooper, N., Mulder, D. G., and Buckberg, G. D. (1975). Depressed cardiac function after mitral valve replacement: problem of myocardial preservation during operation. *Circulation*, **51** and **52**, Suppl. I, 3–8.
- Reis, R. L., Hancock, W. D., Yarbrough, J. W., Glancy, D. L., and Morrow, A. G. (1971). The flexible stent: a new concept in the fabrication of tissue heart valve prostheses. *Journal of Thoracic and Cardiovascular Surgery*, **62**, 683–689.
- Roberts, W. C. (1976). Choosing a substitute cardiac valve: type, size, surgeon. *American Journal of Cardiology*, **38**, 633–644.
- Robertson, J. D., and Reid, D. D. (1952). Standards for the basal metabolism of normal people in Britain. *Lancet*, **1**, 940–943.
- Sang, C., Caves, P. K., Davidson, K. G., Miller, H. C., and Kitchin, A. H. (1976). Initial clinical experience with a stented porcine aortic valve xenograft (abstract). *British Heart Journal*, **38**, 875–876.
- Schaefer, R. A., McAnulty, J. H., Starr, A., and Rahimtoola, S. H. (1975). Diastolic murmurs in the presence of Starr-Edwards mitral prosthesis, with emphasis on the genesis of the Austin Flint murmur. *Circulation*, **51**, 402–409.
- Stinson, E. B., Griep, R. B., Oyer, P. E., and Shumway, N. E. (1977). Long-term experience with porcine aortic valve xenografts. *Journal of Thoracic and Cardiovascular Surgery*, **73**, 54–63.
- Sutton, M. G. St. J., Traill, T. A., Ghafour, A. S., Brown, D. J., and Gibson, D. G. (1977). Echocardiographic assessment of left ventricular filling after mitral valve surgery. *British Heart Journal*, **39**, 1283–1291.
- Wallace, R. B. (1975). Tissue valves. *American Journal of Cardiology*, **35**, 866–871.
- Winter, T. Q., Reis, R. L., Glancy, D. L., Roberts, W. C., Epstein, S. E., and Morrow, A. G. (1972). Current status of the Starr-Edwards cloth-covered prosthetic cardiac valves. *Circulation*, **45** and **46**, Suppl. I, 14–24.

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