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Bicuspid mitral bioprosthesis

E BODNAR, N L R BOWDEN, P J DRURY, E G J OLSEN, I DURMAZ, AND D N ROSS

From the Department of Surgery, Cardiothoracic Institute, Guy's Hospital Medical School, and the Department of Pathology, National Heart Hospital, London

ABSTRACT A bicuspid mitral bioprosthesis was prepared by mounting glutaraldehyde-processed porcine pericardium onto commercially available Brownlee-Yates stents. The bioprostheses were inserted into 17 dogs. Haemodynamic performance and long-term function of the valve was assessed. Of the 11 animals in the survival group, eight died within the 24–72 hour postoperative period. The clinical picture of these animals revealed progressive left ventricular failure although the bioprostheses were tested and found competent both at insertion and at necropsy. The causes of the late deaths were deterioration of the porcine pericardium in two, and cerebral embolism in another. The acute haemodynamic studies showed a significantly high closing reflux from within the tubular bioprosthesis, and this reflux was found to be inherent in the design. It was concluded that any stented bicuspid valve where the stent assumes the function of the papillary muscles, has to be tailored so that parts of the tissue can assume the function of the chordae tendineae to minimise the closing reflux.

A bicuspid mitral bioprosthesis was prepared from autologous fascia lata and inserted into a limited number of patients by Brownlee and Yates in 1971.[1] The valve had the principal advantages of non-thrombogenicity and of unrestricted central flow. Although early clinical results,[1 2] were encouraging, no data have been reported on the long-term performance of these valves. There is also no information either on the use of biological material other than fascia lata, or on the haemodynamic characteristics of such bicuspid valvular prostheses.

In the present study, glutaraldehyde-processed porcine pericardium was used instead of autologous fascia lata for constructing the bicuspid mitral bioprosthesis. Haemodynamic performance and long-term function of the valve were assessed.

Methods

PREPARATION OF VALVES

Porcine pericardium was dissected within six hours of slaughter, rinsed in normal saline, and processed in 0·2% glutaraldehyde solution. The processed material was sewn onto commercially available Brownlee-Yates stents of 22 mm or 24 mm diameter. The tissue was attached to the strut asymmetrically to form a truncated cone with a larger anterior and smaller posterior cusp. The anterior leaflet was also slightly longer than the posterior so that the valve would follow the normal angle of the mitral annulus (fig 1). Unlike the original Brownlee-Yates valve there was no Dacron reinforcement around the atrial circumference of the tissue. Before insertion of the bioprosthesis it was sterilised in 1·0% glutaraldehyde solution.

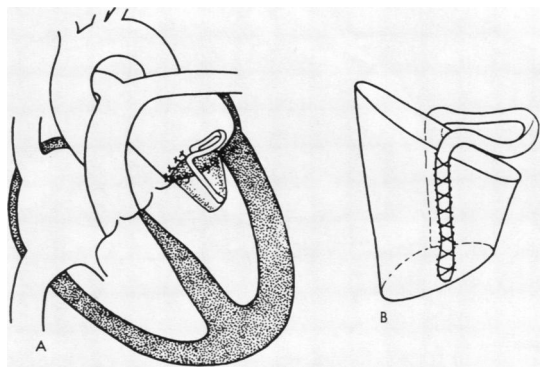

Fig 1 *Schematic drawings of (A) the bicuspid bioprosthesis inserted into the mitral orifice and (B) the bicuspid mitral bioprosthesis.*

Address for reprint requests: Dr Endre Bodnar, Department of Surgery, Cardiothoracic Institute, 2 Beaumont Street, London W1N 2DX.

SURGICAL PROCEDURE

Eleven mongrel dogs of either sex and of 25–30 kg body weight were studied as a possible survival group. The animals were anaesthetised with etorphine/methotrimeprazine (Immobilon: 0·1 ml/kg), and thiopentone sodium (Intraval sodium), intubated and ventilated with room air. The left chest was opened, and, after systemic heparinisation, cardiopulmonary bypass was established with general hypothermia via the right atrial appendage and right femoral artery. At a body temperature of 30°C the aorta was cross-clamped, the left atrium opened through an L-shaped incision, and the mitral valve replaced by the bioprosthesis using multiple interrupted 2/0 Ethibond sutures. The orientation and competence of the inserted valve was tested by filling the left ventricle with blood. The coronary circulation was restored and the animal rewarmed. After closing the atriotomy wound, the air was removed from the heart and, shortly after defibrillation, bypass was discontinued, protamine administered, and the chest closed in layers with a chest drain in place. Tetracycline (500 mg) was given intravenously during chest closure and the same dose repeated three times during the first 48 hours. Three co-trimoxazole tablets per day were given until the chest drain was removed. No anticoagulant of any kind was administered. The animals were kept under constant supervision and were killed electively when their condition deteriorated.

The bioprosthesis was removed immediately after death and examined for macroscopic as well as microscopic appearance. Suitable areas were selected for histology and were embedded in paraffin. Sections 5 μm thick were stained with haematoxylin and eosin, Weigert's van Gieson stain, Alizarin red, van Kossa and Gram where appropriate.

HAEMODYNAMIC INVESTIGATION

Six male greyhounds of 30±2 kg body weight were studied in an acute experiment. The surgical procedure was identical to that already described for the survival group of animals. After stabilisation of the circulation, aortic, left atrial and left ventricular pressures were recorded. A catheter-tip velocity probe was introduced into the left atrium and led across the mitral bioprosthesis. By retracting the probe from the left ventricle into the atrium, the flow in various areas of the tubular valve was recorded. Finally, cineangiograms from the left atrium, left ventricle, and inside the valve itself were recorded. This protocol was repeated at least twice in every case. The animals were then killed, the hearts removed, and the competence of the valve again tested.

Results

Of the 11 animals in the survival group there were eight early deaths within 24–72 hours after operation. The clinical picture of these animals revealed progressive left ventricular failure and pulmonary oedema corresponding with severe mitral incompetence, although the bioprostheses were tested and found competent both at insertion and at

Fig 2 *Left ventricular aspect of a bicuspid bioprosthesis 17 months after insertion. Arrows point to massive thrombotic apposition on both cusps.*

necropsy. The remaining animals survived four weeks, 18 weeks, and 17 months respectively. The cause of death in the first two cases was valve failure from deterioration of the glutaraldehyde-processed porcine pericardium. In the last case, thrombotic apposition inside the valve with consequent renal and cerebral embolism made termination of the experiment necessary (fig 2).

PATHOLOGY

Hearts from two animals were available for study, one having survived for four and a half months and the other for 17 months after operation.

Specimen 1

Macroscopic examination showed that all the sutures were intact and well sited. The bicuspid valve measured 24 mm in diameter. Two holes were present on the anterior leaflet, one at the base measuring 12 mm and the other in the middle zone measuring 10 mm. Calcification had caused distortion of the leaflet. The only pathological change of the posterior leaflet was slight fibrous thickening of the tissue.

Microscopically there was some thickening and distortion of the normal architecture in the anterior leaflet (fig 3). Extensive degeneration of collagen tissue was present with a severe reduction in the number of nuclei. There were several foci of calcification, particularly in the proximal and distal third of the leaflet, and no normal architecture was observed surrounding these areas. In the mitral annulus adjacent to the suture line there was one focus of ossification. The areas around the holes showed degeneration of collagen tissue with no evidence of inflammatory reaction. Vascularity of the leaflet was not increased. There was mild thickening of the posterior leaflet and degeneration of collagen tissue but this was less severe than that observed in the anterior leaflet. Collagen superimposition had occurred at the free edge of the leaflet. There was one focus of ossification which was again in the mitral annulus adjacent to the suture line. Vascularity of the leaflet was not increased.

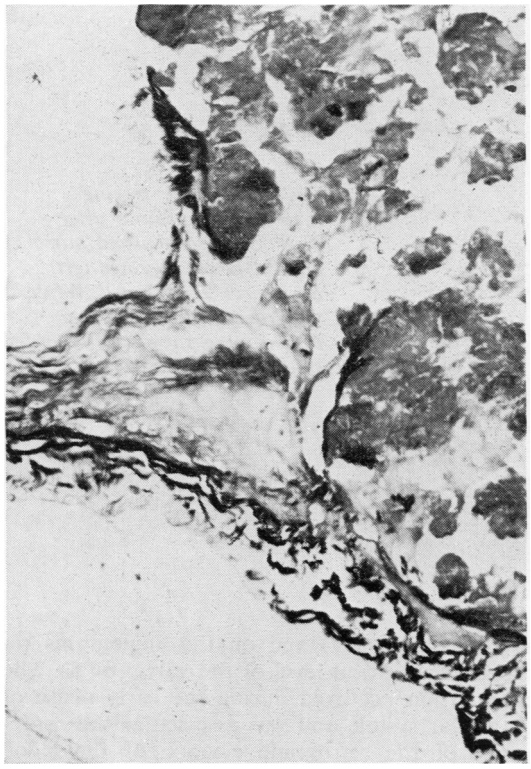

Fig 3 *Photomicrograph of porcine pericardium (lower part of picture) four and a half months after insertion as bicuspid mitral bioprosthesis. Extensive degeneration of the collagen tissue is apparent. H and E, original magnification ×80.*

Specimen 2

Macroscopic examination showed that there was left ventricular hypertrophy and severe dilatation of that chamber. The bicuspid valve measured 25 mm in diameter. A 10 mm hole was present at the base of the anterior leaflet near the mitral annulus. It was difficult to identify the posterior leaflet, the site of which was slightly raised and covered with granular, friable material.

Microscopically, the normal architecture of the proximal third of the anterior leaflet was shown to have been preserved. There was also preservation of collagen with a normal complement of nuclei. In the rest of the leaflet there was severe degeneration and absence of nuclei (fig 4). Gram positive bacteria in the fibrin tissue were shown to be present by the haematoxylin and eosin stain. Small granules of calcium were also observed. There was sparse, mononuclear cell reaction in the pericardium and a more inflammatory cell infiltrate which included neutrophils was present superficial to the superimposed fibrin. A focus of cartilage was present at the base of the leaflet near the mitral annulus. Changes similar to those of the anterior leaflet were observed in the posterior leaflet, but the degree of architectural and degenerative change as well as the superimposition of fibrin was more severe.

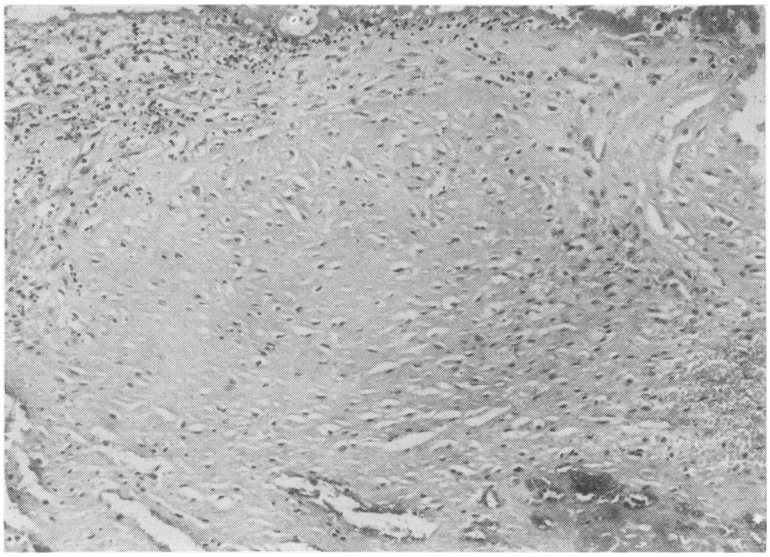

Fig 4 *Photomicrograph of porcine pericardium 17 months after insertion as bicuspid mitral bioprosthesis showing severe distortion of the normal architecture and absence of nuclei. H and E, original magnification ×128.*

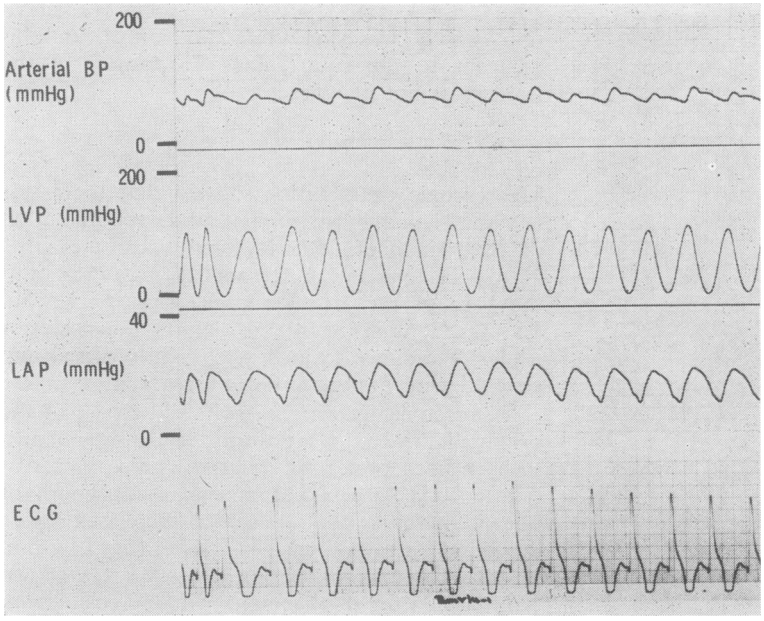

Fig 5 *Pressure tracings recorded 60 minutes after insertion of a bicuspid mitral bioprosthesis. Elevated left atrial pressure is noted. While the tracings do not appear synchronous they were recorded simultaneously.*

HAEMODYNAMIC STUDIES

Although normal intracardiac pressures were recorded before insertion of the bioprosthesis, an elevated left atrial pressure characteristic of moderate or severe mitral incompetence was observed in every animal on completion of the surgical procedure (fig 5). While no reflux was shown on the cineangiograms taken from the left ventricular cavity (fig 6), significant reflux was observed as a bidirectional flow both on the flow tracings (fig 7) and on the angiograms recorded at the atrial level of the valve (fig 8). The regurgitation occurred during the early phase of ventricular systole and was assessed as the consequence of the retrograde ejection of the blood column enclosed by the valve at the end of the ventricular diastole. The maximum volume of this reflux was calculated to be 13·3 ml/stroke for the 22 mm valve, and it was considered to be independent of the left ventricular stroke volume.

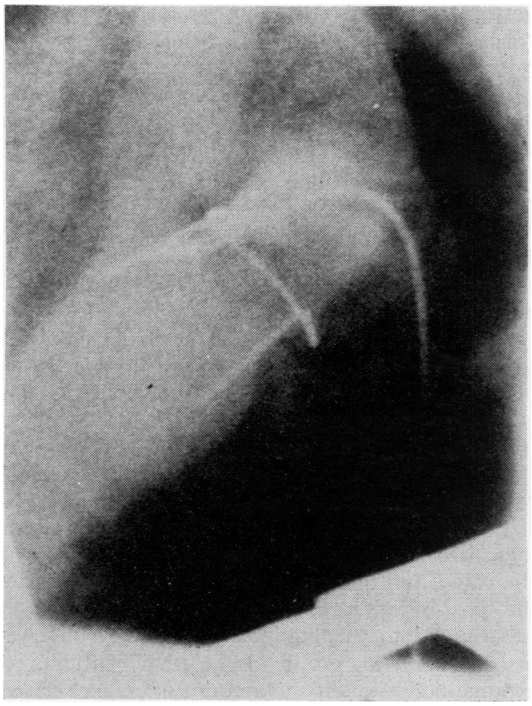

Fig 6 *Left ventriculogram showing no reflux across the bicuspid mitral bioprosthesis when the contrast medium is injected into the ventricular cavity. Opacification in the left ventricle and ascending aorta.*

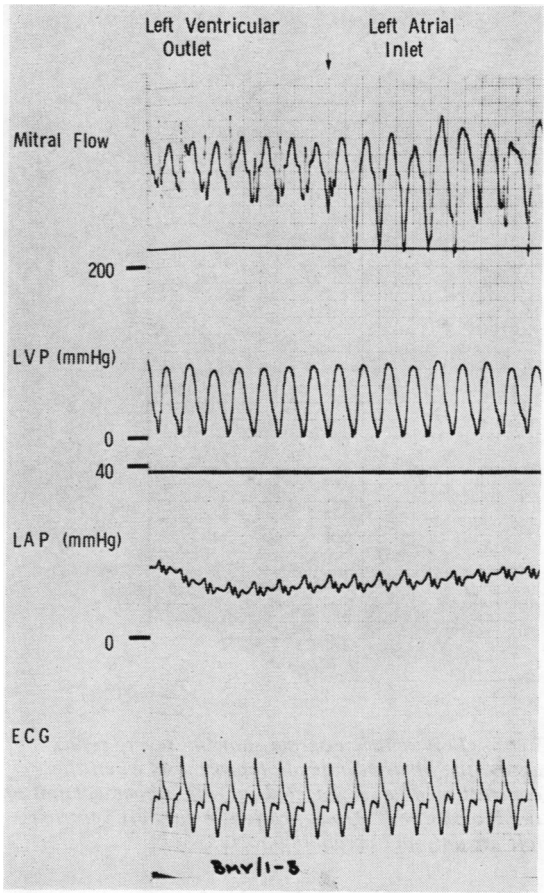

Fig 7 *Flow velocity tracing recorded at the outlet and at the inlet level of a bicuspid mitral bioprosthesis. Significant retrograde flow is present at the atrial level.*

Discussion

Current methods for bioprosthetic replacement of the mitral valve in clinical cardiac surgery involve the use of porcine aortic valves,[3] human dura mater,[4 5] bovine pericardium,[6] and human aortic homografts.[7] All of these bioprosthetic valves are tricuspid and the first three necessitate the insertion of a rigid ring into the mitral annulus. Fresh homografts reinforced by a Dacron tube do not contain rigid parts, but the level of the inserted aortic valve is within the left atrium and well above the level of the mitral annulus.[7]

For almost 20 years there has been a desire either to transplant the mitral valve or to replace it by an unsupported bicuspid tissue valve. Attempts to transplant the mitral valve have failed mainly because of the unreliability of the suture line between host and donor papillary muscle.[8 9] Biological tissue such as pericardium and fascia lata was tailored into the shape of the mitral valve with chordae tendineae and attached to the remnant of the resected papillary muscle or onto the left ventricular wall.[10 11] Technical difficulties as well as tearing of the ventricular sutures proved to be the main obstacles and the idea was never generally adopted.

The main advantage of the frustum mitral valve as described by Brownlee and Yates is that it becomes bicuspid in the closed position yet it can be inserted with a single suture line.[1] It was assumed by these authors that the vortex formation in the left ventricular cavity that occurs parallel to the deceleration of the blood column inside the tubular valve will cause collapse of the pericardium and at least partial closure of the valve. Nevertheless, a retrograde flow at closure was observed but not quantified during mock

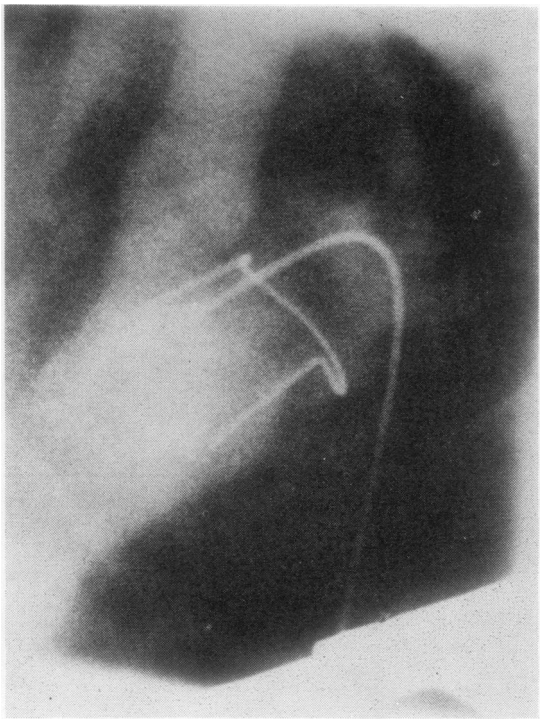

Fig 8 *Left ventriculogram showing severe reflux across the bicuspid mitral bioprosthesis when the contrast medium is injected into the upper portion of the bioprosthesis. Opacification in the left ventricle, left atrium, and ascending aorta.*

circulatory testing of the valve.[2]

The results of the present study agree with the experience of Brownlee and Yates[1] as far as the surgical technique is concerned. The insertion of these valves is simple and does not require surgical skills other than those used for implantation of prosthetic valves. However, the performance of the frustum valve in animal experiments was found to be less appealing.

Raised left atrial pressures were recorded in every animal although anatomical stenosis and reflux from within the left ventricular chamber were excluded. The only factor responsible for the abnormally high left atrial pressure was the functional reflux of the blood column enclosed by the pericardial tube at the end of the ventricular diastole. This reflux was observed persistently on the flow tracings and recorded on the cineangiograms when the contrast medium was injected into the atrial portion of the bioprosthesis.

Any valve of a tubular shape closes from the bottom (ventricular) to the top (atrial), with the consequence that the enclosed fluid is ejected in a retrograde direction. With a frustum valve closing properly the amount of regurgitant blood depends only on the size of the valve and on the actual approximation of the pericardial sheets at the end of the ventricular diastole. Neither pressure conditions nor ventricular stroke volume influence it. The maximum volume of reflux possible for any given frustum valve can be calculated by multiplying the orifice area by the length of the pericardial tube (the calculation neglects the conical widening of the frustum). This volume can be described as the morphological dead space of the valve, and the functional dead space—that is, regurgitation as ml/minute—can be calculated by multiplying the former by the heart rate. Thus, the percentage loss of cardiac output through the reflux at valve closure can be assessed from valve size and heart rate at any given time. It seems logical to conclude that this particular feature of the valve, and the fast heart rate of the dog during the post-bypass and early postoperative period, contributed to the high early mortality observed in the survival group. In cardiac patients of average body weight the amount of reflux relative to the stroke volume of the left ventricle is much less than it is in the dog. It is for this reason, perhaps, that neither the theoretical possibility of the regurgitation at closure nor its clinical importance have been reported in the original description of the frustum valve.[1] The negative left ventricular cineangiogram is misleading in this respect because the blood enclosed by the valve is part of the atrial fluid system rather than of the ventricular one. Previous reports of the mock circulatory testing of such a valve have not attempted to quantify the amount of back-flow nor have they attached any importance to it.[2]

The glutaraldehyde-processed porcine pericardium gave obvious unsatisfactory results. Final conclusions cannot be drawn from the present data as to whether the direct attachment of the pericardium onto the heart, thus deliberately creating the opportunity for cellular invasion, or the insufficient strength of the porcine pericardium in the mitral position, was the principal cause of the tissue deterioration. Previous publications give equal evidence for both assumptions.[12 13]

In consideration of future work it might be suggested that any stented bicuspid valve, where the stent assumes the function of the papillary muscle, has to be tailored so that parts of the tissue should assume the function of the chordae tendineae. With regard to the selection of the

biomaterial, both human dura mater and glutaraldehyde-treated calf pericardium are more promising for the replacement of the mitral valve than glutaraldehyde-processed porcine pericardium.

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