Balloon dilatation of the aortic valve in a pulsatile flow model: assessment of the mechanisms and the magnitude and duration of changes in valve area and gradient

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Abstract

Eighteen stenotic aortic valves (17 removed at operation) mounted in a pulsatile flow duplicator were dilated with a balloon catheter. Sequential measurements showed that the valve area initially increased from a mean (SD) of 0.52 (0.16) to 0.78 (0.17) cm². It was 0.73 (0.16) cm² five minutes after dilatation and this was little changed at four weeks (0.70 (0.15) cm²). Initially the mean transvalvar gradient fell significantly from 54 (27) to 32 (8) mm Hg but increased to 35 (10) mm Hg at five minutes and to 40 (11) mm Hg at four weeks. In six valves stretching of the orifice was the only mechanism responsible for the changes while in the remainder there was tearing through commissures with a greater initial increase in area (0.31 v 0.18 cm²) and a smaller decrease in area at five minutes (0.03 v 0.08 cm²). Fractures of calcific deposits in non-commissural positions were seen in one valve only.

This laboratory study of isolated aortic valves showed a significant but small increase in valve area after balloon dilatation, which was greater when commissural tearing had occurred. Recoil of the stretched orifice was complete at five minutes and there was little further change over the next four weeks.

Percutaneous balloon dilatation of the aortic valve in elderly patients with calcific aortic stenosis deemed to be at high risk from conventional operation was first described as a palliative procedure by Cribier *et al* and McKay *et al* in 1986.^{1,2} Their initial encouraging reports were soon followed by larger studies with more impressive results.³⁻⁵ Other reports suggested only a very limited effect from balloon dilatation⁶ and provided evidence of a rapid loss of any haemodynamic improvement.⁷ Recent studies showed that more than half the patients had died, undergone valve replacement or redilatation, or had a recurrence of symptoms at mean follow up periods of 5-8 months⁸⁻¹¹ and the value of the procedure remains uncertain.

Haemodynamic evaluation of dilatation of the aortic valve is confounded by several procedural factors including myocardial

depression during balloon inflation, haemorrhage, arrhythmias, and vagal effects. Aortic valve area estimations by the Gorlin formula may be unreliable at discriminating small changes, especially in patients with low cardiac outputs, and the timing of non-invasive assessments has varied between studies.

Both the procedural and methodological limitations to haemodynamic assessment have contributed to uncertainty about the real and apparent effects of the procedure. Intra-operative simulation was limited to single measurements before and after dilatation⁶ and like most in vitro studies^{12,13} did not measure areas and gradients during flow. We performed balloon dilatation in 18 stenotic human aortic valves mounted in a pulsatile flow duplicator and measured the sequential changes in area and gradient without the constraints present in clinical practice.

Patients and methods

VALVES

Of the 18 valves, seventeen were removed intact at aortic valve operation and one at routine necropsy. Fourteen valves were stored in 10% formaldehyde while four were used fresh from operation and thereafter stored in homograft valve nutrient solution.¹⁴ Pre-operative peak to peak catheter gradients ranged from 50 to 130 mm Hg and significant aortic regurgitation was present in only three patients. Eleven valves were bicuspid, six tricuspid, and one unicuspid. In two patients percutaneous balloon dilatation had been performed without sustained symptomatic improvement (table 1).

TEST APPARATUS

The pulsatile flow duplicator¹⁵ consisted of a roller pump connected to a pulsatile control unit (Stockert Shiley model PFC II; Shiley Ltd, Berkshire) that continuously recirculated saline from a 10 litre reservoir through the stenotic valves when placed in the test chamber (fig 1). The valves were mounted with silk sutures and cyanoacrylic glue on to a truncated polyvinyl chloride cone, cut to the diameter of the valve ring, and the 40 mm diameter base was then clamped into the test chamber. The test chamber had a translucent end plate with eight radial flow outlet ports arranged symmetrically around the circumference, allowing a centrally placed video camera (Hitachi GP 5E/1E; Hitachi Ltd, Tokyo, Japan) to be

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Accepted for publication
8 November 1989

Figure 1 Cross section through the test chamber containing a valve mounted on to a cone fixed in place by the cone retaining plates. Saline at 37°C was continuously pumped at 4 l/min through the valve in the direction indicated by the arrows. The saline left the chamber via radial outlet ports placed symmetrically around the video camera which had an unobstructed view of the valve during flow.

aligned above the valve. The magnified image of the aortic valve was displayed on a video monitor and stored on video tape (Racal Store 7; Racal Recorders, Southampton). The maximal aortic valve area was then measured by planimetry from the monitor screen with a bitpad (Bit Pad 1 digitiser tablet; Summagraphics, Fairfield, USA) interfaced to a Commodore computer (Model 4032; Commodore, USA). A calibration ring set at valvar level was used for reference. Pressure ports in subvalvar and supra-valvar positions allowed measurement of the mean transvalvar gradient by subtraction of the integrated pressure-time curves (Hewlett Packard models HP 1209 A and HP 7754 B). The saline was maintained at 37°C (1°C) and delivered at a constant output of 4 litres per minute with an ejection period of 45% and repetition rate of 70 per minute. The model is capable of delivering up to 5.4 litres per minute but was set at the lower level to reduce the stresses on the valves which were due to undergo repeated measurements. We showed that the valve area of stenotic valves in this model was maximal at a flow of 3 litres per minute.¹⁵

PROCEDURE

The mounted valve was placed in the test cell and saline was circulated for 30 minutes (allowing equilibration of temperature and dissolved gases) before the valve area and mean transvalvar pressure gradient were measured. A 20 mm balloon (Meditech, USA) was advanced anterogradely through the valve over a 0.35 inch J guide wire and positioned with the centre of the balloon inside the valve orifice as

seen from the side view. The balloon was inflated to 3 atmospheres (303 kPa) (manufacturer's limit) during continuous video recording. When obvious commissural tearing occurred the balloon was deflated after 30 seconds; otherwise inflation was maintained for a full minute. During inflation the circulation was temporarily stopped to avoid pressure overload to the circuitry and valve and the circulation was restarted on deflation. Five seconds after the flow had been re-established we measured the valve area and gradient. These measurements were repeated at 5, 10, 15, 20, 25, 30, 60, and 120 minutes while the flow was maintained continuously. The valve was removed from the chamber and stored in the appropriate medium. At 24, 48, and 72 hours and at 1, 2, and 4 weeks the valve was returned to the test chamber and, after 30 minutes of flow, the area and gradient were measured as before. In two valves complete data were not obtained and in one video recordings were inadvertently erased during subsequent recordings.

RADIOGRAPHY

Valves were examined by projection microradiography with a Hilger Watts generator (London) before and after balloon dilatation. The images produced were 3.5 times real size and showed the calcific deposits in fine detail.

DATA ANALYSIS

Changes in valve area and mean pressure gradient were investigated by an analysis of variance for repeated measures with a Genstat Package on the University of London main frame computer. The results are expressed as means (SD) and a p value < 0.01 was considered statistically significant.

Results

AREA AND GRADIENT CHANGES

There was an increase in valve area and decrease in the mean pressure gradient across all the valves studied (table 1). The aortic valve area increased from 0.52 (0.16) cm² to 0.78 (0.17) cm² immediately after balloon dilatation ($p < 0.001$) but had fallen to 0.73 (0.16) cm² five minutes after the procedure ($p < 0.01$). Thereafter there were no significant changes in valve area and at four weeks the area measured 0.70 (0.15) cm²—35% more than before dilatation. The mean transvalvar pressure gradient fell from 54 (27) mm Hg to 33 (8) mm Hg immediately after the procedure ($p < 0.001$) rising to 35 (10) mm Hg at five minutes (NS), with a further slight rise to 40 (11) mm Hg at four weeks ($p < 0.01$ compared with dilatation after). Values at times between those reported were similar, did not affect the statistical analysis, and have been omitted for clarity (fig 2).

MECHANISM OF DILATATION

The balloon totally occluded the orifice (figs 3 and 4) of only five valves (one tricuspid, one unicuspid, and three bicuspid). In six valves

Table 1 Patient and valve characteristics and results of balloon dilatation

No	Age	Sex	Gradient*	AR	Type	Mechanism	Aortic valve area (cm ²)				Mean pressure gradient (mm Hg)			
							Before	After	5 min	4 wk	Before	After	5 min	4 wk
1	62	M	80	0	B	Stretch	0.67	0.87	0.77	0.75	45	38	43	40
2	68	M	80	1	B†	Stretch (O)	0.69	0.83	0.76	0.72	44	38	40	42
3	73	M	70‡	1	B	Split (O)	0.65	0.82	0.83	0.77	58	36	40	38
4	54	M	90	1	T	Split	0.59	0.90	0.87	0.85	36	22	22	26
5	73	M	50	0	T†	Stretch	0.48	0.73	0.66	0.63	40	29	31	36
6	82	F	¶	¶	T	Stretch (O)	0.24	0.49	0.42	0.40	67	46	53	58
7	71	F	—	0	B†	Split (O)	0.34	0.70	0.61	0.58	82	36	38	49
8	47	M	80	1	B	Split	0.55	1.06	1.01	0.82	31	20	20	31
9	48	M	55	1	T	Split	0.60	0.81	0.80	0.81	44	27	27	33
10	30	F	80	1	B†	Split	0.39	0.75	0.70	0.66	53	29	29	36
11	62	M	65	1	T	Split	0.52	0.68	0.64	0.64	53	33	40	44
12	69	M	70	2	T	Stretch	0.36	0.45	0.40	0.40	42	36	42	42
13	35	F	95	2	U	Split (O)†	0.51	0.81	0.76	0.76	53	31	31	33
14	54	M	70	0	B	Split	0.56	0.66	0.65	0.67	53	47	49	49
15	61	M	55	2	B	Stretch	0.90	1.04	0.97	0.91	29	24	24	31
16	55	M	130	1	B	Split§	0.24	0.68	0.67	0.57	149	40	42	71
17	76	M	130	1	B	Split	0.53	0.76	0.76	0.73	47	33	35	33
18	69	M	70‡	0	B	Split	0.53	1.01	0.92	0.91	49	22	24	28
Mean (SD)	61		87				0.52 (0.16)	0.78 (0.17)	0.73 (0.16)	0.70 (0.15)	54.2 (26.8)	32.6 (7.9)	35.0 (9.5)	40.0 (11.3)

*Peak to peak at diagnostic catheterisation.
†Specimen preserved in homograft nutrient medium.
‡Balloon dilatation performed in vivo.
§Pre-dilatation with 9.0 mm balloon.
¶Postmortem valve.
AR, aortic regurgitation; B, bicuspid; O, orifice totally occluded; T, tricuspid; U, unicuspid valves.

Figure 2 Aortic valve area (cm²) and mean systolic transvalvar gradient (mm Hg) plotted against time. Each point represents the mean and the bar the standard deviation.

there were substantial passages (fig 5) around the balloon (up to 60% of the original orifice) (three tricuspid and three bicuspid) while in the remainder only insignificant apertures (<20% of orifice) were present (fig 6). Stretching of the valve orifice was the sole mechanism (figs 3, 4, and 5) in six valves (four tricuspid and two bicuspid) and there was commissural tearing or splitting in 12 valves (figs. 6 and 7). Though the valves with splitting had a greater immediate increase in valve area (0.31 v 0.18 cm²) and fall in valve gradient (28 v 9 mm Hg) than the valves that only showed stretching, these differences did not achieve statistical significance (table 2). Valve areas > 1.0 cm² were seen in only three valves all of which had tearing through commissures. In one heavily calcified valve the deflated 20 mm balloon could not pass through the orifice. Dilatation with a 9 mm balloon allowed subsequent dilatation with the larger balloon and the final valve area was more than doubled. Neither of the two (bicuspid) valves in which clinical balloon dilatation had been performed showed macroscopic changes attributable to

the procedure but both were easily split in vitro. In only one valve was there clearly a fracture of non-commissural calcium (fig 8) while fractures of commissural calcium deposits were found in seven with commissural splitting.

Discussion
Interventional balloon techniques are currently applied to a range of cardiovascular diseases. The favourable results obtained with coronary angioplasty and dilatation of congenital valve obstructions have led to the extension of balloon dilatation to mitral and aortic stenosis in adults.^{16 17} Mitral valvotomy is a well established surgical technique and balloon dilatation in many ways mimics this effective procedure. In contrast, the poor long term results of operative aortic valvotomy¹⁸ mean that many, especially surgeons, doubt the effectiveness of balloon dilatation of such heavily calcified valves.
Immediately after aortic valve dilatation patients are haemodynamically unstable so that the interpretation of changes produced by the procedure is difficult. In particular, myocardial depression during balloon inflation (owing to ventricular overload and coronary underperfusion) may lead to underestimation of the measured gradient. In addition, haemorrhage, arrhythmias, vagal stimulation, and contrast administration may all affect the haemodynamic indices. The Gorlin formula may underestimate aortic valve area in low output states,¹⁹ which are often present in these patients, but more importantly its sensitivity to small changes in aortic valve area is unknown. In the days after balloon dilatation haemodilution and/or transfusion effects may variably alter blood viscosity, cardiac output, and ejection dynamics. Thus even the optimal timing for the early non-invasive assessment is uncertain.
Reports of apparent increases in calculated valve area in the days after balloon dilatation²⁰

Figure 3 Senile tricuspid valve (No 6) obtained at necropsy with an aortic valve area of 0.24 cm² (a). The 20 mm balloon completely occluded the orifice (b) and on deflation valve area had increased to 0.49 cm² (c). By five minutes there has been some recoil and the area measured 0.42 cm² (d). Unless otherwise indicated all frames in this and subsequent figures were taken during systole.

Figure 4 Bicuspid valve (No 2) in which the balloon completely occluded the orifice (b). Immediately afterwards (c) the valve area had increased from 0.69 cm² to 0.83 cm² but at five minutes (d) it had decreased to 0.76 cm².

Figure 5 Tricuspid valve (No 5) in which the inflated balloon (b) did not occlude the orifice and the areas at the commissural angles totalled 60% of the original orifice area. On deflation the valve leaflets rapidly returned towards their original position (c) although the area had increased from 0.48 cm² to 0.73 cm². At five minutes (d) the area had decreased to 0.66 cm².

Figure 6 Tricuspid valve (No 11) showing splitting of a fused commissure during balloon inflation (b). The valve area increased from 0.52 cm² to only 0.68 cm² after dilatation (c) and at five minutes had recoiled to 0.64 cm² (d).

Figure 7 Bicuspid valve (No 10) with an orifice area of 0.39 cm² (a). There is tearing of both commissures during inflation but especially of the commissure at the top left (b). The valve area had increased to 0.75 cm² (c) and the diastolic frame (d) shows the tear and a flail leaflet (black arrow).

Table 2 Area and gradient changes (mean (SD) according to mechanism of dilatation

		Aortic valve area (cm ²)			
	n	Before	After	5 min	4 wk
All	18	0.52 (0.16)	0.78 (0.17)	0.73 (0.16)	0.70 (0.15)
Stretching	6	0.56 (0.24)	0.74 (0.23)	0.66 (0.22)	0.64 (0.20)
Splitting	12	0.50 (0.12)	0.80 (0.13)	0.77 (0.12)	0.73 (0.11)
		Mean systolic gradient (mm Hg)			
	n	Before	After	6 min	4 wk
All	18	54.2 (26.8)	32.6 (7.9)	35.0 (9.5)	40.0 (11.3)
Stretching	6	44.5 (12.4)	35.2 (7.7)	38.8 (10.1)	41.5 (9.1)
Splitting	12	59.0 (30.9)	31.3 (8.0)	33.1 (9.0)	39.3 (12.5)

are countered by reports of decreases^{7 11} and both are explained on the basis of changes in left ventricular function. Cardiac output is variously reported to be decreased,¹¹ unchanged,²¹ or increased^{3 5 8} immediately after the procedure. The procedural effects are likely to vary considerably between patients, depending on their initial left ventricular function and the severity and morphology of their stenotic valve. Variation between centres with their differing techniques, equipment, and experience may also influence these variables while the methodological errors in both invasive and non-invasive assessment will vary according to the timing of the measurements. Serial measurements in consecutive patients have not been reported owing to the variable numbers at any point in follow up and because frequent invasive assessment is inappropriate. These considerations prompted our study of the immediate and short term effects of valve dilatation in vitro.

We found only small changes after balloon dilatation—the magnitude of which was less than that reported in several large clinical series.^{3 8 10 21} In vitro there was almost an immediate recoil of the stretched orifice (whether or not commissural tearing had occurred) but after 5 minutes there was little further recoil. Those studies in patients that show a rapid loss of the haemodynamic gain^{7 11} are likely to be overestimating the immediate benefits and their subsequent measurements are probably a better indication of the immediate effect. The very small changes seen in these patients may reflect inadequate balloon positioning but they would also accord with the valves in which we found no commissural tearing and where gains in area were smaller. It may be that serial assessments would have shown similar findings in many of the patients reported to show “restenosis” by Doppler techniques a few months after dilatation.^{10 11} Postmortem and operative evidence after valve dilatation indicate that commissural tears or fractures persist for some months at least^{11 22–24}; it seems that in isolation stretching or “microfractures” or both do not produce lasting benefit.

LIMITATIONS

The valves obtained at operation were included only if they were removed in a single piece and without damage. Obviously the true aortic valve annulus was not removed and the suture line to the unyielding cone was only an approximation of the in vivo annulus. This may have influenced the results in two opposing directions. A more compliant annulus might

Figure 8 Bicuspid valve (No 18) with splitting through both commissures. There was fracturing of calcium in the commissures but in addition a clear fracture of non-commissural calcium (white arrow) (b). The valve mounting cone appeared as a faint grid with a denser ring where the material was folded.

have prevented tearing through the commissure to the edge of the specimen and so resulted in a smaller orifice area. But at the same time the effect of more force on the remaining parts of the orifice may have caused more stretching, tearing of other commissures, or fractures of calcific deposits and so produced a larger orifice area. In six of the valves (including the necropsy specimen with a true annulus) only stretching was evident and changes were much smaller than in the other valves showing commissural tearing—so on balance it seems that the absence of the annulus might if anything have exaggerated the effects. Ideally, we should have studied postmortem valves with the annulus en bloc but during the nine month study period we found only one suitable case at routine necropsy.

The valves were obtained from a representative group of patients undergoing aortic valve operation who are not typical of patients undergoing balloon dilatation.^{3 8-11 16 19} Our patients were thus younger and this accounts for a higher frequency of men and bicuspid valves. The pattern of calcification is different in bicuspid and tricuspid valves and this may partly explain why we found fewer fractures in calcific deposits than in some,^{12 13 22-24} though by no means all, postmortem or operative studies.^{6 7 11}

We used a 20 mm balloon in this study for a single (though optimally positioned) inflation. In some valves the balloon seemed to be too large and split the “annulus” whereas in those that showed stretching alone it may have been too small. Most clinical procedures, however, have been with 20 mm or smaller balloons and an increase in the balloon size has not always increased valve area after clinical recurrences.⁸ Nevertheless, it is possible that the much larger balloons being used by some more recently would have improved the results in some of our valves.

Leaflet recoil caused an early fall in valve area and only later a rise in gradient. The supralvalvar pressure port in this model is at a fixed distance from the retaining plates that hold the cones, and the distance from the valve to the pressure port varied according to the length of cone left after it was cut down to accommodate the valve annulus area. The distance was nearly always greater than a half of the orifice diameter¹⁵—that is the distance at which the pressure drop is lowest (vena contracta)—so that slight though systematic under reading of the gradients may have reduced the extent of the early changes. The valve area, however, is not the only factor to determine the gradient—orifice geometry and depth are other factors.²⁵ The orifice depth is likely to have increased as the stretching displaced leaflet material and reduced the expected fall in the gradient; recoil of the leaflet thickening would then have offset the rise in gradient. Most of the valves were preserved in formalin—a storage medium used by others for valve dilatation studies^{12 13 26}—and the effects of formalin may provide an alternative explanation for the gradient changes. We have previously shown that the valve area and gradient measured over a wide range of flows does not change within a month of explantation and storage in either formalin or nutrient solution.¹⁵ Nevertheless formalin storage may have had an effect on the gradient measured across *dilated* valves, though the four valves used fresh from surgery (and thereafter stored in nutrient solution) behaved in a similar fashion.

CONCLUSIONS

We found significant though rather small increases in valve area after balloon dilatation of calcific stenotic aortic valves. Commissural splitting seemed to increase the orifice area more than stretching alone, but fractures of calcific deposits unrelated to commissures were

uncommon. Stretching of the valve orifice was followed by a measurable recoil within the first five minutes, irrespective of coexistent commissural splitting. Thereafter, and in the absence of any reparative mechanisms that might be present in vivo, there were no significant changes in valve area over the succeeding four weeks. Assessment of balloon dilatation of the aortic valve in the clinical setting should be performed only when the patient is stable and all the procedural effects can be discounted. In that way it might be possible accurately to document the real effects of the procedure. The changes that we saw suggest that patients who are critically compromised by aortic stenosis may benefit from balloon dilatation. In most patients, however, the improvement in valve area is unlikely to be adequate for definitive treatment.

We thank Peter Liepins (Radiological Sciences Department) for the valve radiographs, Ron Wilson (Dental Research Laboratory) for assistance with the statistical analysis, and Schneider Shiley (UK) for the pulsatile control unit. JKM was supported by the Lions Heart Research Foundation of South Australia. ACP was sponsored by a grant from the Greek State Scholarship Foundation.

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