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Determinants of angina in aortic stenosis and the importance of coronary arteriography

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Coronary arteriography was performed in 140 patients with aortic stenosis (peak systolic gradient > 50 mmHg). Coronary artery disease was found in 32 patients (23%) of whom 9 (6%) had no history of angina. Fifty-six patients (40%) presented with angina but had normal coronary arteriograms. Effort syncope was a presenting symptom in 34 patients of whom 9 had coronary artery disease.

Patients with angina but normal coronary arteriograms had significantly greater peak left ventricular pressures, peak systolic gradients, left ventricular end-diastolic pressures, and left ventricular masses than angina-free patients with normal coronary arteriograms. The ratio of diastolic pressure-time index (DPTI) to tension time index (TTI) and the aortic valve area were less in the patients with angina and normal coronary arteries than in angina-free patients. These findings support the concept of oxygen demand exceeding supply in patients with severe aortic stenosis and normal coronary arteries.

Two surgical problems were related to operative mortality: a long bypass time and difficulty with coronary artery perfusion. High quality selective coronary arteriograms are essential in all patients undergoing cardiac catheterisation for aortic stenosis if anatomical problems with coronary artery perfusion are to be avoided.

Angina pectoris has long been recognised as a presenting symptom of aortic stenosis (Contratto and Levine, 1937; Lewes, 1951; Mitchell *et al.*, 1954; Wood, 1958; Braunwald *et al.*, 1963), often in the presence of normal coronary arteries (Levine, 1951; Linhart *et al.*, 1968). Angina in this situation is clinically indistinguishable from that caused by occlusive coronary artery disease (Wood, 1968).

Many patients with severe aortic stenosis may have additional coronary artery disease (Basta *et al.*, 1975; Mandal and Gray, 1976), and this is known to be a major factor in left ventricular function after aortic valve replacement (Linhart and Wheat, 1967). Saphenous vein bypass grafting is now possible with aortic valve replacement (Loop *et al.*, 1972; Merin *et al.*, 1973). Preliminary results vary, some groups reporting a higher earlier mortality (Berndt *et al.*, 1974; Callard *et al.*, 1976), and others a reduced mortality (Moraski *et al.*, 1976).

Coronary arteriography carries a small but definite morbidity and mortality (Emanuel, 1975), and several workers have attempted to delineate which patients with aortic stenosis should have coronary arteriography at cardiac catheterisation. Bonchek *et al.* (1973) suggest it may be omitted in patients with no symptoms of ischaemic heart disease, while Mandal and Gray (1976) suggest it may be omitted in patients under 40. Nevertheless it is recognised that patients without angina may have coronary artery disease (Harris *et al.*, 1975).

This study presents our findings at cardiac catheterisation in 140 patients with aortic stenosis, all of whom had selective coronary arteriography at cardiac catheterisation.

The surgical results are presented of 122 patients, both elective and emergency, who proceeded to aortic valve surgery in this hospital, between 1971 and 1976. Factors involved in the operative mortality are discussed.

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Patients and methods

Studies were made on 140 patients aged 18 to 75 (mean age 60) with full informed consent; 50 of these patients were women.

The most common presenting symptom was exertional dyspnoea in 116 patients; 79 patients

had angina. Effort syncope had occurred in 34 patients and 9 presented with systemic emboli. Three patients were asymptomatic.

Patients were premedicated with atropine 0·6 mg and diazepam 10 mg intramuscularly. Pressures were measured by Statham P23 Gb transducers using the sternal angle as a reference point, and were recorded on a Cambridge 12-channel instrument. Aortic valve area was calculated using the method of Gorlin and Gorlin (1951) from simultaneous recordings of aortic and left ventricular pressure. In these studies the left ventricular pressure was obtained from a catheter advanced via a 'teflon' sheath across the atrial septum and down through the mitral valve (Brooksby *et al.*, 1974). This technique of transseptal puncture avoids haemodynamic changes produced by a catheter through a narrow orifice, and the risk of producing systemic emboli by knocking plaques of calcium off the aortic valve.

Cardiac output was measured by indocyanine green-dye dilution from duplicate curves using a Gilford densitometer.

In patients with mild aortic regurgitation the cardiac output used for the calculation of aortic valve area was derived from angiographic volume analysis. Patients with more than mild aortic regurgitation were excluded from calculations of valve area. Left ventricular volumes were calculated using the single plane area-length method and a light pen-computer system. Left ventricular mass was calculated using the method of Kennedy *et al.* (1970).

The diastolic pressure-time index (DPTI) and the tension time index (TTI) were derived from simultaneous aortic and left ventricular pressure recordings using the methods of Sarboff *et al.* (1958 and Buckberg *et al.* (1975). The ratio of DPTI:TTI is thus calculated as:

$$\frac{\text{Mean (Ao-LV) pressure in diastole} \times \text{diastolic filling time} \times \text{heart rate}}{\text{Mean LV pressure in systole} \times \text{LV ejection time} \times \text{heart rate}}$$

and represents myocardial oxygen supply : myocardial oxygen demand.

Selective coronary arteriography was performed using the Judkins technique in 128 patients and the Sones technique in 12.

Aortic stenosis was defined as a peak systolic gradient >50 mmHg or a calculated aortic valve area of $<0{\cdot}5$ cm^2.

Only left ventriculograms and pressure recordings of high quality were used for analysis, and 10 successive cycles were used for calculations of valve area and DPTI:TTI.

Results were statistically analysed using Student's unpaired t test.

Results

(1) CARDIAC CATHETER RESULTS

Of the 140 patients studied, 79 had angina (Table 1). Of these, 56 had normal coronary arteriograms. Sixty-one patients had no history of angina and of these 9 had abnormal coronary arteriograms. The youngest patient with coronary artery disease was aged 38.

Table 2 shows the results in the patients with normal coronary arteriograms divided into those with a history of angina and those who were free of angina. There was a significantly greater peak left ventricular pressure, peak systolic gradient, and left ventricular end-diastolic pressure in those patients with angina. The left ventricular end-diastolic volume index was similar in the two groups. Patients with angina had smaller aortic valve areas, a smaller DPTI/TTI ratio, and a greater left ventricular mass than patients without angina.

Table 3 shows the results in the patients with angina divided into normal and abnormal coronary artery groups. In this study the only significant differences were that patients with abnormal coronary arteries had a lower peak left ventricular pressure and a lower peak systolic gradient across the aortic valve. Other variables were similar in the two groups.

Table 4 shows the results in the 25 patients who had experienced syncope compared with 83 patients who had not had this symptom (all patients with normal coronary arteriograms). Patients with a history of syncope on effort had higher resting peak systolic gradients and higher peak left ventricular pressures than the non-syncopal group. In those patients in whom good left ventriculograms were obtained, the left ventricular end-diastolic volume index was found to be smaller in the syncopal group.

(2) SURGICAL RESULTS

One hundred and twenty-two patients proceeded to aortic valve surgery at this hospital. The mean time from cardiac catheterisation to operation was 40 days. One hundred and one patients received Starr-Edwards prostheses, 19 had Bjork-Shiley prostheses, 1 patient had an aortic homograft, and 1 patient had an aortic valve decalcification. Two patients had a triple valve replacement, 8 had aortic and mitral valve replacements, 2 had aortic valve replacement plus open mitral valvotomy, and 6 patients had an aortic valve replacement plus one or more saphenous vein bypass

grafts. There were 14 deaths (hospital mortality 11%).

Table 5 shows two main factors that were found to be important during operation in the 14 patients who died: coronary artery perfusion problems and a long bypass time. Coronary artery perfusion problems were pre-existing coronary artery disease (in 3), local anatomical problems such as double left coronary ostia (in 2), small right coronary ostia (in 3), or very heavy valve calcification involving the coronary ostia (in 2). A long bypass time occurred in those patients requiring additional mitral valve surgery. One of these also had a small right coronary ostium. Of the 6 patients requiring saphenous vein bypass grafting, 1 died.

Of the remainder 3 patients refused operation and 2 died within 19 months of cardiac catheterisation. Four patients died suddenly before aortic valve replacement could be performed. Two of these patients had severe coronary artery disease in addition to aortic stenosis, and the other 2 had a peak systolic gradient >95 mmHg. Six patients were considered unsuitable for heart operation; 3 of these had widespread coronary artery disease and poor left ventricular function, 1 had severe renal disease, 1 had grossly impaired lung function, and 1 had generalised arteriosclerosis. Three of these patients considered inoperable have died. Three patients are on the urgent surgical waiting list. Two patients were operated on elsewhere.

Discussion

Angina is a common symptom in patients with severe aortic valve stenosis who have normal coronary arteries proven by selective arteriography (Basta *et al.*, 1975; Mandal and Gray, 1976). The demonstration of lactate production or decreased lactate uptake in such patients under haemodynamic stress suggests that myocardial oxygen consumption exceeds the available supply (Fallen *et al.*, 1967).

Three factors predominantly determine myocardial oxygen consumption: heart rate (Laurent *et al.*, 1955), velocity of contraction (Sonnenblick

Table 1 *Incidence of angina syncope and coronary artery disease in 140 patients*

	Normal coronary arteriograms	*Abnormal coronary arteriograms*
Angina	56 (40%)	23 (16%)
No angina	52 (37%)	9 (6%)
Syncope	25 (18%)	9 (6%)

Table 2 *Aortic stenosis and normal coronary arteriograms*

	Angina	*No angina*	*Significance*
	n=49	n=42	
Peak LVP (mmHg)	209 ±26	191 ±32	P=0·003
Peak systolic gradient (mmHg)	94 ±25	79 ±26	P=0·007
LVEDP (mmHg)	15 ±9	10 ±7	P=0·005
LVEDVI (ml/m²)	92 ±39	98 ±43	NS
	n=26	n=24	
Aortic valve area (cm²)	0·51 ±0·16	0·62 ±0·17	P<0·008
DPTI/TTI	0·49 ±0·18	0·62 ±0·24	P<0·04
LV mass (g)	362 ±143	266 ±82	P<0·006

LVP, left ventricular pressure; LVEDP, left ventricular end-diastolic pressure; LVEDVI, left ventricular end-diastolic volume index; DPTI, diastolic pressure-time index; TTI, tension time index.
Results are expressed as mean ±1 SD.

Table 3 *Aortic stenosis and angina*

	Normal coronaries	*Abnormal coronaries*	*Significance*
	n=49	n=23	
Peak LVP (mmHg)	209 ±26	194 ±38	P<0·05
Peak systolic gradient (mmHg)	94 ±25	80 ±26	P=0·04
LVEDP (mmHg)	15 ±9	13 ±8	NS
LVEDVI (ml/m²)	92 ±39	88 ±45	NS
	n=26		
Aortic valve area (cm²)	0·49 ±0·18	0·53 ±0·17	NS
LV mass (g)	362 ±143	291 ±129	NS

LVP, left ventricular pressure; LVEDP, left ventricular end diastolic pressure; LVEDVI, left ventricular end diastolic volume index.
Results are expressed as mean ±1 SD.

Table 4 *Aortic stenosis, syncope, and normal coronary arteriograms*

	Effort syncope	*No effort syncope*	*Significance*
	n=25	n=83	
Peak systolic gradient (mmHg)	98 ±23	81 ±26	P=0·005
Peak LV pressure (mmHg)	208 ±27	194 ±32	P<0·05
LVEDP (mmHg)	11 ±7	13 ±9	NS
	n=20	n=50	
Aortic valve area (cm²)	0·52 ±0·16	0·58 ±0·17	NS
LVEDVI (ml/m²)	79 ±34	100 ±43	P<0·05

LVEDP, left ventricular end-diastolic pressure; LVEDVI, left ventricular end-diastolic volume index.
Results are expressed as mean ±1 SD.

Table 5 *Operative problems in deaths from aortic valve replacement*

	No.
Hospital deaths	14
Problems with coronary artery perfusion	
Pre-existing coronary artery disease	3
Double left coronary ostia	2
Small right coronary ostia	3
Ostial calcium extending from valve	2
Long bypass time	
Additional mitral valve surgery	5

et al., 1965), and left ventricular wall tension (Rodbard *et al.*, 1964). Exercise or emotion which most commonly precipitate angina increase all three factors. The dangers of provoking angina or syncope in patients with aortic stenosis precluded studies during exercise. Data are presented from studies at rest of two determinants of wall tension: left ventricular volume and systolic pressure. From the law of Laplace the wall stress of a chamber is related directly to the square of the radius and to the intracavity pressure, and inversely to the wall thickness (corresponding, in this instance, to the left ventricular volume, systolic pressure, and mass, respectively). In the patients studied who had angina but normal coronary arteriograms both the mean left ventricular mass and the peak systolic gradient were significantly higher and the aortic valve area significantly lower than in those without angina. The significant correlation of these three closely related variables suggests that increased wall tension is related to the occurrence of angina. It is of interest that no correlation was found with left ventricular volume.

It is likely, but by no means obvious from either this series or others (Fallen *et al.*, 1967; Buckberg *et al.*, 1975), that the aortic valve area is the critical factor. A small aortic orifice requires high left ventricular pressures to maintain flow across the valve in systole and results in inefficient conversion of pressure energy into flow energy because of losses caused by increasing turbulence of the jet (Bellhouse, 1972). The raised left ventricular pressure will lead to an increase in mass by hypertrophy.

Myocardial blood supply is also affected by aortic valve stenosis. Studies in mechanical models indicate that a decrease in aortic valve area will result in a low aortic perfusion pressure (Bellhouse and Bellhouse, 1969). The effective coronary perfusion pressure will be further reduced by the higher than normal diastolic pressure in the hypertrophied ventricle and by the increased wall thickness itself. In addition, a Venturi effect at the coronary ostia may impair or even reverse coronary flow during systole (Bellhouse and Bellhouse, 1969). The calculation of aortic valve area is subject to many pitfalls, but the correlation of decreased area and its dependent variables (peak gradient and left ventricular mass) with angina in our cases does suggest that this ominous symptom is related to the severity of the valve stenosis.

The combination of decreased coronary flow and increased left ventricular work leads to a lower oxygen supply with a higher demand. The ratio of DPTI:TTI represents this supply to demand ratio and was lower in the angina group. However, the standard deviations overlap, and we have not found it to be as specific as others in studies of ischaemia in aortic stenosis (Fallen *et al.*, 1967). Studies of Hoffman and Buckberg (1975) in dogs suggest that a ratio of 0·5 or less indicates subendocardial ischaemia. In this study of patients with normal coronary angiograms 54 per cent of 26 patients with angina had a ratio of less than 0·5, but 33 per cent of 24 patients without angina also had a ratio less than 0·5.

Effort syncope in aortic stenosis may be caused by the high ventricular pressure firing baroreceptors to produce reflex bradycardia and vasodilatation (Johnson, 1971). In this series, patients with syncope had higher peak left ventricular pressures and higher peak systolic gradients than those who did not have this symptom.

It may not be necessary to invoke baroreceptor activity. The normal vasodilatation in skeletal muscle during exercise in patients who are unable to increase their cardiac output sufficiently may be enough to cause a dramatic fall in blood pressure. This hypotension with no rhythm disturbance on exercise has been recorded clinically (Flamm *et al.*, 1967), but only in the standing position.

Patients with a history of syncope on effort and normal coronary arteriograms had smaller left ventricular end-diastolic volume indices than those without the symptom. These volumes were measured in the recumbent patient and probably represented the maximal end-diastolic volumes on upright exertion (Wang *et al.*, 1960). Because of the lower left ventricular end-diastolic volume indices in this group, the stroke volume would be smaller for any given ejection fraction. An increased ejection fraction with exertion (if it occurred at all in these patients) would also produce little increase in stroke volume. It is likely, therefore, that on exertion the cardiac output would be lower, and almost entirely rate dependent, in the group with syncope.

Coronary arteriography was performed routinely on all patients, with no mortality. The only haemodynamic variables which differed in patients with and without coronary artery disease were the peak left ventricular pressure and peak systolic gradient which were lower in patients with coronary artery disease (Table 3). This agrees with previous studies (Mandal and Gray, 1976), but could not adequately predict coronary artery disease. The absence of angina does not preclude coronary artery disease, which was present in 6 per cent of our patients without angina. Age has been suggested as a helpful guide, and that patients under 40 do not need coronary arteriography (Mandal and Gray, 1976). However, one of our patients who needed saphenous vein bypass grafting for coronary artery

disease as well as aortic valve replacement was aged 38. In our experience coronary arteriography has three principal roles:

(1) To exclude patients from operation in whom the combination of severe aortic stenosis, widespread diffuse coronary artery disease, and impaired left ventricular function presents an unacceptable surgical risk. In this series 3 patients were excluded on this basis.

(2) To delineate stenotic coronary lesions which may require saphenous vein bypass grafting. In our series this was performed on 6 patients, 5 of whom survived.

(3) To define the anatomy of the coronary ostia. Analysis of the surgical problems in the 14 patients who died (Table 5) showed that in 7 patients great difficulty was experienced at intubating the coronary ostia at cardiopulmonary bypass. The ventricular mass in these patients is high and even minor defects of coronary perfusion during bypass jeopardise myocardial function. Myocardial infarction has been reported to occur in 15 to 18 per cent of patients during aortic valve replacement (Follath and Ginks, 1972; Sharratt *et al.*, 1976), and accounted for 80 per cent of the deaths in a recent series (Sharratt *et al.*, 1976).

High quality coronary arteriograms are needed to differentiate between a left coronary artery which bifurcates immediately and one which has two ostia. In the latter situation the ostia may be too small to admit perfusion cannulae, when only one may be perfused. In this series 2 out of 3 patients who had a left coronary artery with 2 ostia, died. The condition was diagnosed preoperatively in only 1. There may be considerable difficulty in perfusing the left coronary artery which bifurcates immediately (Fox *et al.*, 1973).

We consider coronary arteriography is essential in all patients before aortic valve replacement if the surgical mortality for this condition is to be reduced.

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