Haemodynamic basis for aortic valve replacement¹

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The relation between the increments in mean pulmonary artery wedge pressure and cardiac output during light supine exercise has been correlated with the presence or absence of clinical decompensation in 47 patients with severe aortic valve disease. The most useful indication of compensation or decompensation was obtained from an index which related the increase in cardiac index (ml/min per m²) with exercise to the associated increase in mean pulmonary artery wedge pressure (mmHg). In patients with compensated aortic valve disease the value of this ratio was never less than 283 units, and in those with decompensated disease, never greater than 210 units. Haemodynamic measurements during exercise with calculation of this 'exercise ratio' were most useful in evaluating 11 patients in whom clinical evidence of compensation was equivocal.

Clinicians are well aware that the asymptomatic 'compensated' phase of severe aortic valve disease may be long but once 'decompensation' becomes manifest as clinical left ventricular failure, the prognosis is poor (Cullhed, 1964; Haravon, Delman, and Rosenblum, 1969; Harper, 1967; Hohn *et al.*, 1965; Kay, Suzuki, and Zimmerman, 1963; Ross and Braunwald, 1968; Hegglin, Scheu, and Rothlin, 1968; Takeda, Warren, and Holzman, 1963). Hence decompensation is the commonest indication for aortic valve replacement, and its clinical recognition is accordingly of great importance. Decompensation is not usually difficult to recognize when a careful history and examination are supplemented by ancillary aids such as chest radiograph, electrocardiogram, phonocardiogram, and apex cardiogram. The role of cardiac catheterization is to establish that severe aortic valve disease is the sole haemodynamic burden, and to confirm the existence of left ventricular failure. Haemodynamic evidence of left ventricular failure may be present at rest, or it may only be detectable by stressing the circulation by such means as muscular exercise.

The clinical value of exercise testing at cardiac catheterization depends upon its contribution to the recognition or confirmation of decompensation when all other evidence is equivocal. Previous published reports of the haemodynamic response to exercise in aortic valve disease have concentrated on physiological differences between aortic stenosis, aortic regurgitation, and normal subjects, ignoring

the more clinically useful distinction between compensated and decompensated aortic valve disease (Anderson *et al.*, 1969; Bache, Wang, and Jorgenson, 1971; Cullhed, 1964; Ettinger, Frank, and Levinson, 1972; Gorlin *et al.*, 1955; Lee *et al.*, 1970, 1971; Levinson, Frank, and Schwartz, 1970; Lewis, Bristow, and Griswold, 1970; Sancetta and Kleinerman, 1957). This study provides haemodynamic criteria for the recognition of decompensation, and analyses the contribution of exercise in the assessment of patients for surgery.

Patients studied

Of 131 consecutive patients with isolated severe aortic valve disease who were being considered for aortic valve replacement, 70 were considered fit enough to perform light supine exercise. Fifty-one of these patients were classified as having compensated or decompensated disease from the clinical data alone. For this purpose, decompensation was considered to be present if one or more of the following criteria were satisfied: (1) a definite history of deterioration in exercise tolerance due to dyspnoea for which no alternative cause was found, (2) radiographic evidence of progressive cardiomegaly consistent with an enlarging left ventricle or definite pulmonary venous congestion (Doyle *et al.*, 1957), or (3) unequivocal signs of right heart failure, tachypnoea, pulmonary basal crepitations, pleural effusions, or reduced vital capacity responsive to bed rest, salt restriction, digitalis administration, or diuretic therapy. On the other hand, the presence of a third sound gallop with accentuation of the rapid filling wave of the apical impulse in aortic stenosis or a fourth sound gallop with increase of apical presystolic lift in aortic regurgitation, or the presence of left ventricular strain by electrocardiogram in aortic regurgitation, were regarded as

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valuable confirmatory signs of decompensation in these conditions, but not sufficiently specific to define decompensation. It should also be noted that decompensation was defined in terms of heart failure complicating aortic valve disease. Hence patients with angina pectoris, or those with syncope in the presence of aortic stenosis, could be classified as either compensated or decompensated according to the criteria defined above. The average age of patients with decompensated aortic valve disease was 56 years (range 35 to 67 years) and of those with compensated disease 37 years (range 16 to 59 years). Eleven men with decompensated aortic valve disease were aged 60 or more. Though approximately one-third of the patients with decompensated aortic valve disease showed angiographic evidence of some coronary artery disease, only 3 patients with decompensated aortic valve disease had severe stenosis or occlusions in one major artery. Nine patients with decompensated aortic valve disease were taking digitalis and diuretic preparations at the time of the study.

Patients were only included in this study if their haemodynamic and angiographic data indicated severe aortic valve disease. Pure aortic regurgitation was associated with a gradient across the valve of less than 20 mmHg, and was regarded as severe on the basis of a low diastolic and wide pulse pressure in the aortic root coupled with progressive filling of an enlarged left ventricle by angiographic contrast material injected above the aortic valve (Cohn *et al.*, 1967). Pure aortic stenosis was associated with no widening of pulse pressure and angiographically insignificant aortic regurgitation. The average peak systolic pressure gradient over the aortic valve in pure aortic stenosis was 68 mmHg (range 33 to 126 mmHg).

Methods of study

The clinical assessment was made within 24 hours of cardiac catheterization, which included selective coronary arteriography. For cardiac catheterization, the patient was in the postprandial state and was given sodium pentobarbitone 100 mg orally and promethazine hydrochloride 25 or 50 mg intramuscularly. The right heart was studied from a right antecubital vein, and the left heart retrograde via a brachial arteriotomy. Cardiac output was measured by the indicator dilution technique, injecting indocyanine green through the pulmonary artery catheter and withdrawing blood from the ascending aorta at 22 ml/min via an angiographic catheter with a Gilford 105S pump. The blood was withdrawn through a Gilford 1031R cuvette densitometer and the dye curve was displayed on a pen-writing recorder (RectiRiter, Texas Instruments Co.). Paired estimates of cardiac output agreed, on average, to within 10 per cent of the mean value, both at rest and during exercise. Intravascular pressures were measured by a model 267A Sanborn pressure transducer and a model 350-3000B Sanborn preamplifier. The record was obtained on a polybeam photographic recorder.

These haemodynamic measurements were obtained initially at rest and then in a steady state during the fourth to sixth minute of light supine exercise (25 or 50W) performed on a Lanooy bicycle ergometer. All haemodynamic measurements were obtained before angiography. The response of the heart to exercise was assessed by relating the rise in cardiac index (ΔCI) to the change in the mean pulmonary artery wedge pressure (ΔPW) from the rest to steady state exercise at 25W. The index $\Delta CI/\Delta PW$ was termed the 'exercise ratio'.

TABLE I Comparison of effects of decompensation in aortic stenosis, mixed aortic valve disease, and aortic

Type of lesion	Compensated (C) or decompensated (D)	Average age (yr)	Resting left ventricular pressure (systolic/end-diastolic)	Peak systolic aortic valve gradient (mmHg)	Work load (watt)
Aortic stenosis	C	37 ± 4 (9)	181 ± 11/16 ± 2 (9)	64 ± 9 (9)	0 25 50
Aortic stenosis	D	*58 ± 2 (11)	200 ± 15/21 ± 4 (7)	74 ± 10 (7)	0 25 50
Aortic stenosis, aortic regurgitation	C	45 ± 2 (2)	166 ± 2/14 ± 2 (2)	49 ± 11 (2)	0 25 50
Aortic stenosis, aortic regurgitation	D	*59 ± 3 (7)	182 ± 9/18 ± 4 (7)	69 ± 8 (7)	0 25 50
Aortic regurgitation	C	33 ± 5 (6)	131 ± 8/13 ± 2 (6)	—	0 25 50
Aortic regurgitation	D	*53 ± 3 (12)	134 ± 9/16 ± 2 (11)	—	0 25 50

Results as mean values ± one standard error. Figures in parentheses represent numbers of observations in each group.
* Mean value of D group significantly different from mean value of corresponding C group ($P < 0.05$).

Results

Haemodynamic and clinical classification

Of the 70 patients in whom exercise tests were performed, 51 could be graded as compensated or decompensated from the clinical data alone. By excluding 4 patients in whom atypical results were observed, consistent differences in the pattern of haemodynamic response could be recognized between the compensated (17 patients) and decompensated (30 patients) groups (see Table 1). Thus, decompensation was characterized by a reduction in cardiac index due to a lesser forward stroke volume index, and was associated with higher values of left ventricular end-diastolic pressure and mean pulmonary artery wedge pressure than the compensated state. Such differences due to the decompensation were greatly magnified by exercise. A lesser rise of cardiac output and a greater rise in mean pulmonary artery wedge pressure on effort are known to be features of advancing age in normal subjects (Granath, Jonsson, and Strandell, 1964; Malmberg, 1965). Since 11 patients with decompensated aortic valve disease were older than 60 years, individual haemodynamic changes have been considered separately for patients less than 60 years who had haemodynamic studies at 25W effort (Table 2, Fig. 1-3). Patients with mixed aortic valve lesions were omitted in the interest of clarity. From Table 1, it can be seen that the haemodynamic features of decompensation are superimposed on the

slightly different haemodynamic responses of compensated aortic stenosis and compensated aortic regurgitation. The stroke volume on light supine exercise in compensated aortic stenosis was maintained at near resting levels with moderate rises of mean pulmonary wedge pressure. In compensated aortic regurgitation relatively large rises of stroke volume occurred with very little change in the mean pulmonary artery wedge pressure on effort. Therefore, decompensation with its tendency to depress exercise stroke volume and cardiac index with greater rises of mean pulmonary artery wedge pressure produced greater decreases in exercise ratio in aortic regurgitation than in aortic stenosis.

The effects of exercising on the distinction between the haemodynamic responses of compensated and decompensated aortic valve disease were most clearly shown when the changes in cardiac index and pulmonary artery wedge pressure were combined to calculate the exercise ratio ($\Delta CI/\Delta PW$). The average values of this index in patients with compensated aortic stenosis, mixed aortic valve disease, and aortic regurgitation were 533, 1600, and 2000 ml/min/m² per mmHg. Corresponding values in patients with decompensated disease were 89, 79, and 93 ml/min/m² per mmHg. The use of this index not only accentuated the differences in mean values, but resulted also in a clear distinction between patients with compensated and decompensated disease with no overlap between the groups (Fig. 3). No patient with compensated

regurgitation

Cardiac index (l./min per m ²)	Heart rate	Stroke volume index (ml/m ²)	Mean PAW pressure (mmHg)	Exercise ratio (25W) $\frac{\Delta CI}{\Delta PW}$ (ml/min/m ² per mmHg)
2.9 ± 0.3 (7)	67 ± 3 (9)	43 ± 3 (7)	12 ± 1 (9)	533 ± 222 (4)
4.4 ± 0.1 (4)	100 ± 5 (5)	43 ± 3 (4)	16 ± 2 (5)	
5.1 ± 1.0 (3)	111 ± 10 (4)	42 ± 4 (3)	20 ± 3 (5)	
2.4 ± 0.2 (11)	*80 ± 4 (11)	*31 ± 2 (11)	15 ± 1 (11)	*89 ± 16 (7)
*3.4 ± 0.2 (8)	105 ± 5 (10)	*31 ± 2 (8)	*27 ± 3 (8)	
4.2 ± 0.5 (3)	106 ± 5 (3)	40 ± 7 (3)	*31 ± 1 (3)	
3.1 ± 0.6 (2)	71 ± 1 (2)	44 ± 9 (2)	11 ± 2 (2)	1600 (1)
4.1 ± (1)	114 ± (1)	36 ± (1)	13 ± (1)	
5.8 ± 1.0 (2)	110 ± (1)	54 ± (1)	19 ± 5 (2)	
2.5 ± 0.2 (7)	79 ± 2 (7)	32 ± 3 (7)	17 ± 3 (7)	*79 ± 18 (7)
3.5 ± 0.3 (7)	109 ± 7 (7)	33 ± 3 (7)	33 ± 4 (7)	
2.7 ± 0.1 (6)	72 ± 3 (6)	38 ± 3 (6)	11 ± 2 (6)	∞ (5)
4.7 ± 0.2 (4)	97 ± 3 (6)	49 ± 0 (4)	13 ± 2 (6)	
6.0 ± 0.5 (4)	116 ± 8 (4)	52 ± 3 (4)	12 ± 3 (5)	
2.6 ± 0.2 (12)	75 ± 3 (12)	35 ± 2 (12)	12 ± 2 (12)	*93 ± 19 (12)
4.1 ± 0.4 (9)	110 ± 6 (10)	*36 ± 3 (9)	*28 ± 2 (11)	
*3.1 ± 0.7 (3)	105 ± 2 (3)	*31 ± 2 (3)	*27 ± 4 (3)	

TABLE 2 Individual haemodynamic results in patients less than 60 years old who performed 25 watt exercise*

Type of lesion	Compensated (C) or decompensated (D)	Mean PAW pressure (mmHg)		Cardiac index (l./min/m ²)		Exercise ratio (25W) $\frac{\Delta CI}{\Delta P\bar{W}}$
		Rest	25 Watt	Rest	25 Watt	
Aortic stenosis	C	8	9	3.4	5.6	1200
		9	13	2.9	4.1	300
		12	16	3.0	4.7	283
		12	18	2.1	4.2	350
Aortic stenosis	D	16	28	2.4	3.4	83
		17	26	2.3	3.4	122
		14	36	1.8	3.5	77
		8	16	3.2	4.3	138
Aortic regurgitation	C	15	15	2.4	4.2	∞
		14	13	3.2	5.3	∞
		15	18	2.3	4.6	777
		10	12	3.1	4.7	800
Aortic regurgitation	D	7	33	3.4	4.5	35
		9	17	2.2	3.9	210
		11	27	2.7	4.8	131
		10	36	2.8	3.7	35
		18	29	2.5	2.7	18

* Patients with mixed aortic valve disease excluded for clarity.

FIG. 1 The effect of 25 watt exercise on the mean pulmonary artery wedge pressures (PAW) of patients younger than 60 years with severe aortic stenosis or regurgitation.

disease had an exercise ratio of less than 283 ml/min/m² per mmHg.

Atypical cases

Of 51 patients classified as compensated or decompensated on clinical grounds, 4 showed atypical haemodynamic responses. Of these 4 patients, 2

were decompensated. One had a normal mean pulmonary artery wedge pressure at rest and on effort (8 and 13 mm, respectively), as a result of vigorous diuretic therapy; however, the grossly subnormal cardiac index (1.4 and 1.9 l./min/m² at rest and on effort, respectively) and low exercise ratio (100 units) agreed with the clinical assessment.

FIG. 2 The effect of 25 watt exercise on the cardiac indices of patients younger than 60 years with severe aortic stenosis or regurgitation.

FIG. 3 The clinical value of the exercise ratio ($\Delta CI/\Delta PW$) at 25 watts in distinguishing patients with compensated from those with decompensated aortic valve disease.

The second patient had a normal pulmonary artery wedge pressure and cardiac index at rest and on exercise, and the exercise ratio was in the normal range. Pulsus alternans on exercise was the only haemodynamic abnormality.

Two of the four patients with atypical responses to exercise were clinically compensated. The first, a 66-year-old man with aortic stenosis and an aortic valve area of 0.47 cm^2 , was studied to evaluate syncope on effort. Exercise produced pronounced, though asymptomatic, exertional hypotension apparently due to inappropriate peripheral vasodilatation. The mean pulmonary artery wedge pressure rose from 7 to 22 mmHg and the exercise ratio was 73 units. It is, therefore, probable that effort syncope represented an atypical manifestation of decompensation in this patient. The second patient was a fit, hard working store-keeper with aortic regurgitation who was studied because of the recent development of a fourth heart sound and electrocardiographic evidence of left ventricular strain. 50 watt supine effort was performed at cardiac catheterization without any discomfort but the mean pulmonary artery wedge pressure was 19 mmHg at rest, and 29 mmHg on exercise, and the exercise ratio was slightly below the normal range (244 units); these findings suggested decompensation. For this

reason, the patient was advised to reduce his activity. There has been no evidence of clinical deterioration in two years of follow-up. Though this exercise test may represent the only 'false-positive' case study, it is possible that preclinical decompensation had been detected.

Contribution to clinical assessment

Nineteen of the 70 patients who performed exercise could not be classified into compensated or decompensated groups on clinical criteria alone. These patients were unable to give a clear history, had co-existing respiratory disease, or were severely restricted on medical advice. However, aortic valve replacement was recommended because of angina or syncope in 8 of them, so that there remained 11 patients in whom the decision concerning the presence or absence of decompensation was of paramount importance in deciding whether or not an operation should be performed.

In 5 of these patients, the haemodynamic data were characteristic of compensated disease and none of these patients has shown clinical deterioration during an average follow-up period of 4 years.

Case reports

Case 1

A 51-year-old woman with a past history of asthma, bronchitis, and surgery for empyema, had suffered progressive dyspnoea on exertion for 4 years. She was studied after a severe attack of wheezing at night. Examination showed severe aortic regurgitation as well as signs of pulmonary disease. The chest radiograph showed moderate cardiomegaly with a cardiothoracic ratio of 0.54, but no pulmonary congestion. The left ventricular end-diastolic pressure was 15 mmHg. During exercise at 25W, mean pulmonary artery wedge pressure rose from 10 mmHg to 14 mmHg and the exercise ratio was 375 units. These figures fall in the range consistent with compensation and thus suggested that chronic pulmonary disease was the basis for effort dyspnoea. This was confirmed by spirometry which showed a forced expired volume of 1.7 l./sec and a maximum vital capacity of 2.3 l. when the predicted values were 2.4 l./sec and 2.8 l., respectively.

In 5 patients, the haemodynamic response to exercise was characteristic of decompensation, and aortic valve replacement resulted in clinical improvement in all of them.

Case 2

A 50-year-old farmer with mixed aortic valve disease presented to hospital complaining of vague malaise. This was found to be due to subacute bacterial endocarditis which was treated. Investigation three months later showed an exercise ratio of 83 units. This study was interpreted as showing decompensation which had been masked by the patient's inactivity during treatment for

endocarditis. The heart size was reduced on review 6 months after aortic valve replacement.

There remained one patient in whom the classification remained equivocal even after considering both haemodynamic and clinical data. Aortic valve replacement in this patient neither improved symptoms nor reduced heart size.

Discussion

A rise of venous pressure and a reduction in cardiac output have long been regarded as the hallmarks of cardiac failure, both experimentally and in clinical practice (Hope, 1832; MacKenzie, 1913; McMichael, 1947; Starling, 1918). It might, therefore, be assumed that it would be a simple matter to demonstrate these abnormalities by cardiac catheterization and hence provide objective proof of clinical left ventricular failure in a patient with severe aortic valve disease. However, there are complicating problems in practice. The left ventricular end-diastolic pressure or pulmonary artery wedge pressure may be abnormally raised at rest or during supine exercise in patients who are clinically asymptomatic, possibly as a consequence of reduced compliance of the hypertrophied left ventricle. Continued observation of such patients has confirmed that the abnormal pressure does not imply the progressive deterioration characteristic of the decompensated phase. Furthermore, the present study has shown that there is considerable overlap in the resting values of cardiac output, left ventricular end-diastolic pressure, and pulmonary artery wedge pressure between patients with compensated and decompensated disease. Deliberate case selection has accentuated this overlap, since exercise was only performed in patients who did not manifest obvious left ventricular failure at rest. In these patients, supine exercise clearly accentuated haemodynamic differences between compensated and decompensated disease. The measurement of the mean pulmonary artery wedge pressure is easier and more accurate than the measurement of cardiac output, and provides the basis of most of the distinction between patients with compensated and decompensated disease. However, patients with decompensated aortic valve disease were most clearly distinguished from those with compensated disease when both the tendency for the ventricular filling pressure to rise abnormally during exercise and of the cardiac output to rise subnormally were combined in the calculation of the exercise ratio ($\Delta CI / \Delta PW$).

It should be noted that the exercise ratio is not simply an index which empirically increases the distinction between patients with compensated and

decompensated aortic valve disease, since this index is soundly based on the pathological physiology of heart failure. In normal subjects, the maintenance or augmentation of stroke volume with supine exercise is attributable to both the maintenance of end-diastolic ventricular volume and operation of Starling's law, and also to the increase in myocardial contractility associated with exercise (Braunwald *et al.*, 1967). Reduced myocardial contractility has been demonstrated in the failing left ventricle and to a lesser extent in the non-failing hypertrophied left ventricle (Mason, Spann, and Zelis, 1969; Spann *et al.*, 1967; Simon *et al.*, 1970). Such a reduction in contractility implies that a greater than normal increase in left ventricular end-diastolic volume would be required in order to maintain the stroke volume on exercise. Because of the reduced compliance of the hypertrophied ventricle in aortic valve disease of long standing, this increase in ventricular volume on exercise will result in a correspondingly greater increase in end-diastolic pressure. All of these factors probably combine to cause the larger rise in left ventricular filling pressure in patients with decompensated disease and also in those with compensated disease and myocardial hypertrophy.

Our observations have shown that the changes of ventricular filling pressure and cardiac output during supine exercise are sufficiently abnormal in patients with decompensated aortic valve disease to make them clearly distinguishable from patients without any evidence of decompensation on clinical grounds. This relation, expressed as the exercise ratio, may therefore be used to classify patients into compensated or decompensated categories when the clinical evidence is equivocal.

Aortic valve replacement is generally recommended when clear symptoms of syncope, angina, or decompensation occur in association with haemodynamically severe aortic valve disease. In approximately 10 per cent of cases, the clinical evidence for decompensation is equivocal, and we recommend the use of the exercise ratio to assist with the decision for operation in these patients.

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