Left ventricular angiography on exercise

A new method of assessing left ventricular function in ischaemic heart disease

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Left ventricular function was studied in 17 patients with ischaemic heart disease and compared with 4 patients with normal left ventricular function. The patients in the homogeneous group of ischaemic heart disease were further subdivided into those 'without angina' (n=5) and those 'with angina' (n=12), depending upon the presence of angina during supine leg exercise at the time of definitive study. At rest there was no significant difference in the heart rate, cardiac output, stroke volume, and left ventricular end-diastolic pressure (LVEDP) in the three groups. During exercise the cardiac output and stroke volume were significantly depressed and LVEDP was significantly raised in the ischaemic heart disease group as a whole but within this group failed to show any significant difference in patients with and without angina. The left ventricular end-diastolic volume (LVEDV) and end-systolic volume (LVESV) measurements showed clear separation of these three groups only on exercise. On exercise, there was decrease in LVEDV and LVESV ($P < 0.05$; $P < 0.02$) in the group with normal left ventricular function, no change in the group with ischaemic heart disease without angina, and striking increase in LVEDV and LVESV in the group with ischaemic heart disease and angina ($P < 0.01$ and $P < 0.02$, respectively). This angiographic method of assessing left ventricular function shows clear separation of the three groups and also highlights the significance of angina. Ejection fraction (EF), a commonly measured parameter of left ventricular function, failed to reflect consistent changes on exercise as compared to values at rest which emphasizes the limitations of the measurement of ejection fraction at rest.

Coronary artery bypass surgery in patients with ischaemic heart disease is expected to prevent myocardial ischaemia and to increase or restore coronary blood flow to the underperfused areas, thereby improving left ventricular function. But there are many reports indicating that the improvement in ventricular function studied at rest has not been shown to be consistent with the symptomatic relief achieved by the surgical treatment (Achuff *et al.*, 1972; Miller *et al.*, 1972; Bourassa *et al.*, 1972; Shepherd *et al.*, 1974). Probably one of the main reasons is that left ventricular function in coronary artery disease at rest is often within the normal range and, therefore, does not allow an accurate definition of the functional reserve (Roskamm *et al.*,

1970). Hence, evaluation of left ventricular function in patients with ischaemic heart disease under stress is important. The following study was designed to assess ventricular function and pressure/volume changes during the physiological stress of exercise in patients with ischaemic heart disease who were being investigated for consideration of coronary artery bypass surgery.

Subjects and methods

Patients

Seventeen male patients with ischaemic heart disease were studied for consideration of coronary artery bypass graft surgery. The average age of the group was 41 years (range 29 to 60), average weight 76 kg (range 67 to 82), and average surface area was 1.74 m² (range 1.64 to 1.93). The average length of the history of angina was 5 years (range 1 to 12); none had valvular heart disease, hyper-

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tension, or diabetes. A reliable and definitive history of myocardial infarction was present in 8 patients; none had present or past evidence of heart failure. At the time of study, on clinical examination, a third heart sound was present in 1, and a fourth heart sound was audible in 6 patients. The resting 12-lead electrocardiogram was normal in 9 patients; definitive evidence of old myocardial infarction was present in 7 patients (pathological Q wave and ST-T changes); non-specific ST-T changes were present in the precordial leads in 1 patient; definitive evidence of anterolateral infarction was found in 5, inferior infarction in 1, and combined anterior and inferior infarction in 1 patient. During treadmill exercise, angina was provoked in all, associated with horizontal or downward sloping ST segment depression of 1 mm or more in lead V5. This ST depression induced by exercise, rapidly reverted back to the pre-exercise level with complete resolution of chest pain during recovery period. The chest radiograph was normal and the cardiothoracic ratio was less than 50 per cent in all. None had received any drug other than nitroglycerin for 2 days before the study.

Four male patients, referred for suspected heart disease, were also included. None was found to have any haemodynamic or electrocardiographic abnormality either at rest or during exercise. All had normal coronary and left ventricular angiograms; none had mitral or aortic valve lesions. Thus, all were considered to have normal left ventricular function. The average age of these patients was 40 years (range 28 to 52), average weight 75 kg (range 62 to 81), and average surface area 1.78 m² (range 1.70 to 2.05). Thus, the patients with ischaemic heart disease and normal left ventricular function were homogeneous in age, sex, weight, and body surface area.

The haemodynamic investigations were an essential part of the diagnostic procedure in each patient. The purpose of the extension of the diagnostic investigations by exercise left ventriculography was explained to each patient. The procedures involved were demonstrated during a rehearsal session and their possible significance in the understanding and treatment of angina were specifically discussed with each patient. The voluntary nature of their co-operation was emphasized without inducement (Medical Research Council Report, 1964; Ormrod, 1968).

Design of investigation

Before the definitive study, patients were familiarized with the investigative techniques and, at the same time, trained to do supine leg exercise. A bicycle ergometer was used in 11 patients and the remaining 10 patients were trained to raise their legs alternately, approximately 12 times a minute against adjustable weights suspended on pulleys. Exercise was equal and sub-maximal in all and judged by measuring oxygen uptake during the final 2 minutes in 11 patients. The predetermined level of exercise enabled us to predict the onset of angina in the definitive study. The normal left ventricular function group underwent a similar programme.

On the day of the study, selective coronary arteriography was performed first. Haemodynamic measurements at rest were followed by left ventriculography. Fifteen to twenty minutes were allowed to elapse for the return of circulatory changes to the pre-angiography level. Patients were then exercised at the predetermined level until the onset of angina, or for a total period of six minutes. Haemodynamic measurements were repeated during the final 2 minutes of exercise and left ventriculography was repeated immediately after exercise: no time was allowed to elapse between the conclusion of exercise and the injection of contrast medium into the left ventricle as the patients continued exercise during positioning for angiography in the right anterior oblique position. Cardiac output was measured in 11 patients by the Fick method during the rest period and during the final 2 minutes of exercise. At the end of the study, glyceryl trinitrate was given sublingually to all those patients who developed angina during exercise.

Haemodynamic methods

Blood samples for arteriovenous oxygen differences were collected from pulmonary and brachial arteries through small nylon catheters introduced percutaneously into the brachial artery and via the median antecubital vein for the pulmonary artery. An additional nylon catheter (75 × 0.1 cm) was introduced into the left ventricle percutaneously via the brachial artery for simultaneous and continuous measurement of the left ventricular pressure during angiography in 11 patients. In the remaining 10 patients the left ventricular pressures were recorded by multilumen angiographic catheter (Ducor, Cordis, 8F). Pressures were measured by Stratham P32 strain gauge transducers. The manometers were calibrated over the range 0 to 80 and 0 to 20 mmHg (0 to 10.6 kPa and 0 to 2.7 kPa) for the measurement of left ventricular systolic and left ventricular end-diastolic pressures, respectively, which was arranged to span 10 cm on the recording paper; over this scale the manometers were linear within 2 per cent; the maximum undamped natural frequency of the nylon catheter in the left ventricular pressure measurement was found to be 60 Hz, with damping ratio 0.5. The natural frequency of the multilumen 'pigtail' angiographic catheter was found to be 30 Hz, with damping ratio of 0.25. From high frequency recording of left ventricular pressures in dogs, Gersh, Hahn, and Prys-Roberts (1971) demonstrated that the first six harmonics of Fourier analysis contain sufficient data for measurement of systolic and diastolic pressure to be made with ± 5 per cent. At a heart rate of 90 to 120 faithful reproduction of sixth harmonics is achieved with catheter manometer systems response of 9 to 12 Hz. Using such methods under similar conditions of study, duplicate measurement of cardiac output, left ventricular end-diastolic pressure agreed to within 5 and 8 per cent, respectively, of the mean value both at rest and during exercise. The electrocardiogram was recorded with a disc adhesive electrode from chest lead V5 and calibrated externally (0.1 mV = 1 mm). The intravascular pressures and

electrocardiogram were continuously monitored on the oscilloscope and recorded at minute intervals on a multichannel recorder.

Angiographic method

Left ventriculography was performed through a multi-lumen angiographic catheter (Ducor, Cordis, 8F) inserted percutaneously into the femoral artery and retrogradely positioned into the left ventricle under radiological screening control. The radio-opaque contrast media (76% Urografin) was infused by electro-mechanical pump (Conrac, Contraves, Zurich) at a rate of 10 ml/s for 5 seconds at rest and 15 ml/s for 5 seconds for the exercise left ventriculography. Simultaneous biplane cineangiograms were recorded in 11 patients; single-plane right anterior oblique angiograms in the remaining 10 patients. The patient held his breath in inspiration during filming. Left ventriculograms were studied for abnormal left ventricular contraction by viewing; details of this method of assessing dykinesia are given elsewhere (Sharma *et al.*, 1975b).

The measurement of left ventricular volumes was made at end-diastole and end-systole. During biplane filming simultaneous frames were identified by electronic integration. Biplane filming was at a speed of 75 frames per second and single-plane recordings were made at a speed of 48 frames per second, both on 35 mm films. The values for volume measurements represent the average mean of the first three beats during angiography.

Simultaneous measurement of left ventricular pressures and volumes were made in 11 patients. In the rest of the 10 patients, left ventricular pressures in the first 5 beats immediately before angiography were analysed. Left ventricular volumes were calculated by the semi-area-length method by assuming that the left ventricular chamber can be represented as an ellipse (Kasser and Kennedy, 1969). The films were projected on a Vanguard analyser onto a screen. Chamber length and area were determined by a cursor connected to an Olivetti 602 programmable calculator which transferred the area measurements by Simpson integration into volume measurement automatically. The magnification factors were predetermined for film and heart height combination; analysis showed that there was insignificant pin cushion distortion (J. Darman, 1974, personal communication). The left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV) were identified in each beat by volume time curve. Further angiographic calculations were:

$$\begin{aligned}\text{Stroke volume (SV)} &= \text{LVEDV} - \text{LVESV} \\ \text{Ejection fraction per cent (EF)} &= \frac{\text{SV}}{\text{LVEDV}} \times 100 \\ \text{Cardiac output (CO)} &= \text{SV} \times \text{heart rate}\end{aligned}$$

The LVEDP was measured at the nadir of the atrial wave just before the systolic contraction in the left ventricular pressure curve. Electrocardiographic ST depression in chest lead V5 was measured from the J point to the isoelectric line joining two consecutive PR intervals.

Measurement, calculations, and statistical analysis

Statistical analyses were based on the orthodox methods; within the group probability of statistical significance of difference was calculated by the t-test for paired data; significance of difference between the groups relates to the comparison of means (unpaired t-test).

Results

Of 17 patients with ischaemic heart disease, 12 developed chest pain associated with ischaemic ST depression. The average time of onset of pain was 285 ± 20 seconds (range 180 to 360) and average ST depression was 2.4 ± 0.4 mm (range 0.1 to 3.6). These patients were subgrouped as *ischaemic heart disease with angina*. The other 5 patients with ischaemic heart disease developed neither angina nor ST depression during exercise at the time of the study and were subgrouped as *ischaemic heart disease without angina*. The four patients in the normal left ventricular function group had neither angina nor ST depression during similar exercise.

Selective coronary angiography

In the normal left ventricular function group, the coronary arteriograms were normal in all; there were no obstructive significant lesions in the right and left coronary arteries. In patients with ischaemic heart disease, significant lesions (>50% obstruction) of the left anterior descending artery were found in 7 patients, and of the right coronary artery in 1 patient; two-vessel disease of left anterior descending and right coronary artery in 2 patients; left anterior descending and left circumflex in 2 patients, and left circumflex and right coronary artery in 2 patients. Three-vessel disease was found in one patient. The coronary artery lesions were comparable in both subgroups of ischaemic heart disease, with or without angina at the time of definitive study.

Effects of left ventriculography (Table 1)

Left ventriculography at rest and immediately after exercise was carried out without any complication in all patients. In 11 patients, haemodynamic measurements were made before, during, and 2 minutes after the injection of radio-opaque contrast medium. There was no significant change in the heart rate and left ventricular peak systolic (LVSP) and end-diastolic pressure measured just before and during ventriculography, either at rest or during exercise. But 2 minutes after angiography at rest there was a significance increase in

TABLE 1 Haemodynamic effects of left ventriculography (11 patients)

Variable	Rest			Exercise		
	Preangio ¹	During angio ²	Post-angio ³	Preangio ¹	During angio ²	Post-angio ³
Heart rate/min	75±3	76±3	80±5	124±8	124±8	125±9
LV Peak systolic pressure (mmHg)	144±8	143±8	137±7*	185±15	179±10	167±12**
LV end-diastolic pressure (mmHg)	8±1	10±2	18±2***	32±4	29±3	34±4

Significance in difference relates to the preangio measurements at rest and during exercise:

*P < 0.05; **P < 0.03; ***P < 0.01.

¹Average mean of first 5 beats just before injection of radio-opaque contrast media into the left ventricle.

²Average mean of first 3 beats during injection.

³Average mean of 5 beats after 2 minutes of angiography.

Conversion factor from Traditional to SI units: 1 mmHg ≈ 0.133 kPa.

LVEDP ($P < 0.01$) and a decrease in LVSP ($P < 0.05$). During left ventriculography on exercise there was no significant change in the heart rate or LVEDP, but LVSP was significantly lower ($P < 0.02$) as compared to the preangiographic values. These results indicate that radio-opaque contrast medium during the first three beats produces insignificant haemodynamic change. Thus, preangiographic haemodynamic measurement can be taken to represent haemodynamic changes during angiography. Therefore, in the remainder of the 10 patients it was decided not to measure simultaneous pressures with angiography because it required two catheters in the left ventricle. Volumetric analysis during the first three beats has been regarded as true left ventricular volume devoid of any effect of the contrast medium (Carleton, 1971). By contrast the left ventricular dysfunction produced by contrast medium 2 minutes after injection in patients with ischaemic heart disease is in agreement with the findings of Rahimtoola, Gau, and Raphael (1970).

Reliability of volumetric analysis

The biplane method of measuring left ventricular volume is an established method for the quantitative assessment of left ventricular function (Dodge *et al.*, 1966; Dodge and Baxley, 1969; Arvidsson, 1961; Kennedy *et al.*, 1968). In this study left ventricular volumes were estimated by biplane technique in 11 patients (in 4 normals and 7 patients with ischaemic heart disease) and single plane technique in 10 patients. In clinical practice, single plane right anterior oblique cineangiography is more commonly employed for assessment of myocardial function and localization of abnormal left ventricu-

lar contraction in patients with ischaemic heart disease. Good correlation exists between single plane and biplane angiographic measurements (Sandler *et al.*, 1965; Sandler and Dodge, 1968; Herman and Bartle, 1968). Cardiac output measured at rest and during exercise by the angiographic method correlated well with cardiac output measured by the Fick method in 11 patients (correlation coefficient = 0.922; Fig. 1). The cardiac outputs of 10 patients were derived from the volume measurements which have been shown to be extremely reliable (Dodge, Hay, and Sandler, 1962). The

FIG. 1 Shows good correlation between direct Fick and biplane angiographic method of measuring cardiac output; dotted line— $x=y$; solid line—regression line.

TABLE 2 Haemodynamic, angiographic, and electrocardiographic data

Variable	Normal left ventricle (n=4)		Ischaemic heart disease (n=17)			
			Without angina (n=5)		Angina (n=12)	
	Rest	Exercise	Rest	Exercise	Rest	Exercise
Heart rate/min	68±1.5	112±3	70±4	118±8	71±1	110±4
Cardiac output (angio.) (l/min per m ² BSA)	3.3±0.1	7.8±0.2	3.1±0.1	6.3±0.4	2.9±0.1	6.6±0.3
Stroke volume (angio.) (ml/beat per m ² BSA)	51±0.6	68±1.7	45±2	54±4	43±2	60±2
LV peak systolic pressure (mmHg)	136±5	175±8	140±5	185±9	138±5	186±8
LV end-diastolic pressure (mmHg)	8±1	14±5	12±2	25±3	13±1	34±3
LV end-diastolic volume (ml per m ²)	78±3	70±1	80±3	84±4	97±2	139±3
LV end-systolic volume (ml per m ²)	27±3	6±2	34±4	30±3	46±3	76±4
Ejection fraction (%)	63±4	92±4	58±3	66±3	54±2	46±2
S T depression (V5) (mm)	0.0±0.0	0.2±0.2	0.0±0.0	0.5±0.4	0.6±0.4	2.4±0.4

Data expressed as mean ± SEM; Significance of difference between rest and exercise within the same group: *P < 0.05; **P < 0.03; ***P < 0.02; ****P < 0.01; *****P < 0.001. Conversion factor from Traditional to SI units: 1 mm Hg ≈ 0.133 kPa.

duplicate error by 2 independent observers in the measurement of left ventricular volume was ±4.2 ml (n = 42).

Haemodynamic changes (Tables 2 and 3; Fig. 2)

At rest, there was no significant difference in the heart rate, cardiac output, stroke volume, LVEDP, and the LVSP when compared in the 3 groups. Though there was no significant difference in the average values of resting LVEDP in patients with ischaemic heart disease as compared with normal subjects, data from individual patients revealed that only 4 had an LVEDP higher than 15 mm Hg (2.0 kPa) at rest.

During exercise, the average oxygen uptake was 645 ± 11 ml/min per m² BSA; heart rate and LVSP were similar in all 3 groups. The cardiac output and stroke volume were depressed in the ischaemic heart disease group as a whole, but within this group there was no statistically significant difference in patients with and without angina. Similarly, LVEDP during exercise rose significantly to higher levels in all patients with ischaemic heart disease (P < 0.03) as compared to the patients in the normal left ventricular function group, but within the ischaemic heart disease group the rise in LVEDP showed no statistically significant difference in patients with and without angina.

Thus, haemodynamic values at rest in patients with ischaemic heart disease were in no way any

different from those with normal left ventricular function. It was only exercise that separated patients with ischaemic heart disease from normal subjects.

FIG. 2 LVEDP during exercise is raised significantly in all patients with ischaemic heart disease. There is no significant difference in LVEDP in patients with ischaemic heart disease with and without angina; R—rest; Ex—exercise; P value related to the significance between rest and exercise.

TABLE 3 Statistical analysis between groups

Variable	Normal ventricle group		Normal left ventricle		Ischaemic heart disease without angina	
	vs. Ischaemic heart disease without angina		vs. Ischaemic heart disease with angina		vs. Ischaemic heart disease with angina	
	Rest	Exercise	Rest	Exercise	Rest	Exercise
Heart rate/min	NS	NS	NS	NS	NS	NS
Cardiac output (angio.) (l/min per m ²)	NS	<0.03	NS	<0.03	NS	NS
Stroke volume (ml/beat per m ²)	NS	<0.05	NS	<0.05	NS	NS
LV end-diastolic pressure (mmHg)	NS	<0.05	NS	<0.02	NS	NS
LV end-diastolic volume (ml per m ²)	NS	<0.03	NS	<0.001	NS	<0.01
LV end-systolic volume (ml per m ²)	NS	<0.02	NS	<0.001	NS	<0.01
LV peak systolic pressure (mmHg)	NS	NS	NS	NS	NS	NS
Ejection fraction (%)	NS	<0.02	NS	<0.001	NS	<0.05
ST depression (mm)	NS	NS	NS	<0.01	NS	<0.03

NS = Statistically not significant.

Left ventricular dyskinesia

Localized diminished, absent, or paradoxical areas of myocardial contraction of the left ventricle, as observed from the angiogram, were defined as 'dyskinesia'. At rest and during exercise none of the patients with normal left ventricular function showed dyskinesia. In the ischaemic heart disease with angina group, 6 had dyskinesia at rest; in these the area of dyskinesia was further extended during exercise. The remaining 6 patients with normal left ventricular contraction at

rest developed new areas of dyskinesia during exercise. The details of these findings and their implications have been discussed elsewhere (Sharma *et al.*, 1975b).

Left ventricular volume changes (Fig. 3 to 6; Tables 2 and 3)

Left ventricular end-diastolic volume (LVEDV)

At rest the LVEDV was within normal range in all three groups. The LVEDV in ischaemic

FIG. 3 Effect of submaximal exercise on LVEDV. During exercise LVEDV falls in normal subjects, remains the same in ischaemic heart disease without angina, and increases considerably in ischaemic heart disease with angina; NS = not significant.

FIG. 4 Effect of submaximal exercise on LVESV. During exercise LVESV decreases in normal subjects, remains the same at rest in ischaemic heart disease without angina, and increases in ischaemic heart disease with angina.

heart disease with angina tended to be higher than in the other groups, but because of wide scatter this difference did not reach statistical significance. During exercise there was a 10 per cent decrease in LVEDV in the normal left ventricular function group ($P < 0.05$), no significant change in the ischaemic heart disease group without angina, and a 43 per cent increase in the ischaemic heart disease group with angina ($P < 0.01$), all being compared to the values at rest. Between the groups during exercise the LVEDV was higher in the ischaemic heart disease without angina ($P < 0.03$) and ischaemic heart disease with angina ($P < 0.001$) compared to the group with normal left ventricular function, showing clear separation of the 3 groups.

Left ventricular end-systolic volume (LVESV)

All 3 groups showed normal ranges of LVESV at rest. Though the values of LVESV tended to be higher in patients with ischaemic heart disease with angina, the differences were not statistically significant. During exercise LVESV decreased in the group with normal left ventricular function ($P < 0.02$), did not change in the ischaemic heart disease group without angina, and showed a significant increase in ischaemic heart disease with angina ($P < 0.02$) indicating insufficient emptying of the left ventricle in patients with ischaemic heart disease. There was a statistically significant difference in LVESV during exercise in the group with normal left ventricular function, those with ischaemic heart disease without angina, and those with ischaemic heart disease with angina when these groups were compared with each other.

Ejection fraction

This is the conventional angiographic method of assessing left ventricular function. Ejection fraction did not differ significantly at rest in all three groups. Though the average mean was lower in patients with ischaemic heart disease with angina, it failed to reach statistically significant difference. During exercise the group with normal left ventricular function increased their ejection fraction significantly as compared to the values at rest ($P < 0.03$) and also when compared with other groups (ischaemic heart disease without angina, $P < 0.02$; ischaemic heart disease with angina, $P < 0.001$); within the ischaemic heart disease group, patients with angina had lower ejection fractions at rest than patients without angina ($P < 0.05$).

Ejection fraction failed to reflect consistent changes during exercise in the patients with ischaemic heart disease with angina. In this group

FIG. 5 Effect of submaximal exercise on ejection fraction. This study shows that ejection fraction at rest does not predict the state of left ventricular function during exercise.

some patients having an ejection fraction less than 50 per cent, indicating poor left ventricular function at rest, were found to increase ejection fraction above 50 per cent. On the other hand, the majority of the patients in this group had an ejection fraction greater than 50 per cent and decreased their ejection fraction during exercise. All patients with new or extended areas of dyskinesia and angina were found to have a significantly depressed ejection fraction ($P < 0.05$).

Assessment of left ventricular function

The ejection fraction and LVEDV in the clinical situation represent the indirect evidence of myocardial fibre shortening and initial diastolic fibre length, respectively (Hamilton, Murray and Kennedy, 1972). A left ventricular function curve has been constructed by plotting ejection fraction against LVEDV (Fig. 7). Data in patients with normal left ventricular function showed good function during exercise with increase in ejection fraction and decrease in LVEDV. In patients with ischaemic heart disease with angina, the increase in LVEDV was associated with a decrease in ejection

fraction, but patients with ischaemic heart disease without angina showed a flat response (no change in either LVEDV or ejection) during exercise. On the basis of left ventricular function these 3 groups have shown clear separation only on exercise.

In order to assess the relation between systolic and diastolic volume of the left ventricle, LVESV was plotted against LVEDV. These volumes represent the end results of systole and diastole, respectively (Fig. 8). These findings indicate that in patients with ischaemic heart disease, there is proportionate systolic and diastolic dysfunction of the left ventricle.

Discussion

This study has confirmed that in ischaemic heart disease in the absence of myocardial ischaemia at rest, ventricular function can remain within the normal range; exercise has been shown to unmask the impairment of the left ventricular function as evidenced by the presence of abnormally raised LVEDP, depressed stroke volume, and cardiac output. When exercise was accompanied by angina, cardiac output, LVEDP, and stroke volume did not change any further, but there were statistically significant increases in ventricular volumes as

FIG. 6 Left ventricular cineangiograms performed at rest and during myocardial ischaemia (angina and ST depression 2.1 mm in lead V5) induced by exercise in a patient (J.S.; 48 years) with a 5-year history of ischaemic heart disease, who was assessed for coronary artery bypass surgery. This patient shows ventricular dilatation, incomplete left ventricular emptying, and fall in ejection fraction during angina induced by exercise. ED, ES and EF represent end-diastole, end-systole, and ejection fraction, respectively (see text).

FIG. 7 Comparison of the left ventricular function by plotting LVEDV and ejection fraction as indices of diastolic fibre length and systolic fibre shortening, respectively. The results in normal left ventricular function (top left), ischaemic heart disease without angina (middle), and ischaemic heart disease with angina (bottom right corner of the diagram), show clear separation of these groups during exercise, indicating good function in normal left ventricle group and poor left ventricular function in the ischaemic heart disease with angina group.

FIG. 8 Correlation between LVEDV and LVESV shows no disproportionate impairment in these two measurements at rest and during exercise.

measured angiographically. These changes clearly separated the patients with angina on effort from those without angina and the normal left ventricular group. Thus, certain haemodynamic and angiographic investigations during exercise were proved to be of value in assessing the functional cardiac reserve and significance of angina.

In normal subjects, supine exercise causes an increase in sympathetic tone and thus a rise in the heart rate and contractility, which together with the decrease in peripheral resistance and simultaneous increase in venous return (Topham and Warner, 1967) results in an increase in cardiac output and stroke volume, corresponding to the demand of the periphery (Ross *et al.*, 1966). The present study has shown similar changes in cardiac output, stroke volume, and heart rate measurements, confirming these observations. In normal subjects the values of volumetric analysis (LVESV, LVEDV, and ejection fraction) at rest are in agreement with others (Kennedy *et al.*, 1966; Miller and Swan, 1964; Sanmarco and Bartle, 1964). During supine submaximal exercise there was a small decrease in LVEDV, a striking decrease in LVESV, and, consequently a significant increase in ejection fraction. A similar physiological response to exercise has been reported by others (Rushmer, Smith, and Franklin, 1959; Holmgren and Ovenfors, 1960). Harrison, Goldblatt, and Braunwald (1963) observed decrease in the left ventricular dimensions by an average of 13 per cent during supine submaximal leg exercise.

FIG. 9 Pressure-volume relation at rest and during exercise. This study indicates left ventricular dilatation during exercise-induced angina.

In patients with ischaemic heart disease the haemodynamic and angiographic measurements at rest were not significantly different from normal subjects, which indicates that assessment of left ventricular function at rest alone may be of only limited value for the management of such patients. During exercise, the patients with ischaemic heart disease have been shown to respond differently. The conventional methods of assessing the resting function of the heart (cardiac output, stroke volume, and LVEDP) do separate patients with ischaemic heart disease from those with normal function but fails to separate ischaemic patients with and without angina of effort. The deterioration in left ventricular function, shown by volume measurement on effort, clearly separates the angina group from the group without angina.

Though exercise in patients with ischaemic heart disease is associated with abnormally raised LVEDP and the symptoms of angina (Müller and Rørvik, 1958; Wiener, Dwyer, and Cox, 1968; Sharma and Taylor, 1970), the precise significance of LVEDP to the onset of exercise-induced angina is far from clear. It is apparent in this study, and shown by others (Lichtlen, Baumann, and Albert, 1969), that LVEDP can be raised during exercise irrespective of angina in patients with ischaemic heart disease. Before the onset of pain, the LVEDP frequently rises far earlier during the course of exercise and reaches a plateau, thus bearing no relation to angina (Lichtlen, 1971). Furthermore, when LVEDP, one of the haemodynamic determinants of myocardial oxygen consumption, was either altered or controlled as discretely as possible with the help of right atrial pacing, propranolol, phentolamine, and ouabain, and the effects of these changes were observed on the onset and total duration of angina, there was no consistent relation between the LVEDP and angina (Sharma, Majid, and Taylor, 1975a). On the other hand, exercise left ventriculography and data on the ventricular volumes in this study have defined the significance of angina. The presence of angina was associated with an area of abnormal left ventricular contraction (dyskinesia) related to major obstructions of the corresponding coronary artery (Sharma and Taylor, 1975); these dyskinetic segments were not present in either the normal left ventricular function group or patients with ischaemic heart disease without angina (Sharma *et al.*, 1975b). Also in the presence of angina of effort there were large increases in LVESV and LVEDV. Eubanks *et al.* (1970) have also shown similar changes in the ventricular volume during exercise-induced pain in patients with ischaemic heart disease. There is also suggestive evidence that the magnitude of changes in

LVEDV may play a role in both the production and amelioration of pain in patients with angina pectoris (Parker *et al.*, 1970).

The question whether raised LVEDP during pain in patients with ischaemic heart disease is associated mainly with loss of compliance or largely reflects ventricular dilatation, remains debatable. This study supports the view that angina induced by exercise is accompanied by ventricular dilatation (Fig. 9), hence left ventricular failure, which is also supported by another study (Eubanks *et al.*, 1970). The concept of loss of compliance emerges from the studies carried out by atrial pacing (Dwyer, 1970; Barry *et al.*, 1974). Though atrial pacing is a safe and useful technique for producing angina and ST depression (Sowton *et al.*, 1967), it is by no means physiological, for atrial pacing causes abrupt shortening of diastole and prevents adequate and complete relaxation of the ventricle. Experimental evidence in dogs suggests that encroachment upon the diastolic period results in incomplete relaxation which in turn leads to changes in diastolic compliance (Monroe and French, 1961; Mitchell, Linden, and Sarnoff, 1960; Templeton, Ecker, and Mitchell, 1972) so that results obtained by atrial pacing are difficult to interpret in physiological terms.

Traditionally, LVEDP is a widely used haemodynamic measurement for the evaluation of the left ventricular function in clinical practice and therefore deserves further comment in relation to ischaemic heart disease. The decision to carry out revascularization surgery in ischaemic heart disease often depends on the LVEDP, yet there is a lack of positive correlation between LVEDP and post-operative results (Johnson and Lepley, 1970; Chatterjee *et al.*, 1971). Furthermore, LVEDP has not been shown to be an absolute index of left ventricular function (Chatterjee *et al.*, 1971), and the present study has distinctly revealed that LVEDP may not necessarily reflect changes in LVEDV (Fig. 9). The LVEDP should be regarded as a poor substitute for LVEDV (a measure of diastolic fibre length) in constructing Frank Starling's ventricular function curve in man.

Another widely accepted measure of left ventricular function is the ejection fraction (EF). Ejection fraction of 50 per cent or more is regarded as a normal ventricular response at rest. The limitation of ejection fraction at rest is clearly shown in this study (Fig. 5). Ejection fraction measured at rest does not predict the response to exercise in patients with ischaemic heart disease. In the group of patients with ischaemic heart disease and angina the majority of patients with an ejection fraction of 50 per cent or more at rest have

decreased their ejection fraction during exercise and vice versa; this further highlights the limited value of the measurements at rest.

Experimental evidence suggests that a definite relation exists between end-diastolic and end-systolic volume in a given set of circumstances (Tyberg *et al.*, 1970). During an enhanced contractile state of the heart the decreased end-diastolic volume and decreased vascular impedance to ejection induces smaller end-systolic volumes (Tyberg *et al.*, 1970). Similarly the physiological response to exercise in man is characterized by reduced end-diastolic volume and increased ejection fraction (Rushmer *et al.*, 1959), all of which result in a decrease in end-systolic ventricular volume. The present study has shown a close relation between LVEDV and LVESV in patients with ischaemic heart disease and normal left ventricular function at rest as well as during exercise (Fig. 8). There was no dissociation between systolic and diastolic impairment of left ventricular function as judged by LVESV and LVEDV. This relation may be explained on the concept of an equilibrium volume (volume at zero pressure) as elucidated by Brecher, Kolder, and Horres (1966) under set animal experimental conditions. Small LVESV (less than equilibrium volume) is more likely to be achieved by a small LVEDV and vice versa. Though the present study was not designed to elucidate this fact and none of the variables was controlled, it clearly shows that a relation between LVEDV and LVESV exists in normal subjects as well as patients with ischaemic heart disease during variable inotropic state of the heart.

Left ventricular volume analysis by angiographic methods has been shown to provide useful information in coronary artery disease with wide varieties of ventricular dysfunction present at rest (Hamilton *et al.*, 1972), but its usefulness during exercise has been clearly demonstrated in this study. Thus, volume measurements should not be regarded purely as an academic exercise for assessing the inotropic and contractile state of the myocardium but they have valuable uses in determining the surgical and medical management of patients with ischaemic heart disease.

The results of this study point quite clearly to the limitations of the assessment of left ventricular function at rest and the value of studying the heart on exercise in order to evaluate improvement of the functional cardiac reserve after coronary artery bypass surgery. It is our intention to restudy these patients after successful coronary artery bypass graft at the level of exercise similar to those obtained before operation, to determine if surgery improves left ventricular function.

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