Echocardiographic features of secondary left ventricular hypertrophy

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SUMMARY Echocardiograms showing left ventricular cavity and mitral valve were recorded and digitised in 100 patients with secondary left ventricular hypertrophy caused by severe hypertension (23), aortic valve stenosis (21), fixed subaortic stenosis (13), and postoperative aortic stenosis (13), or regurgitation (30). Left ventricular dimension and its rate of change were determined and related to mitral valve opening. These values were compared with those from 30 patients with hypertrophic cardiomyopathy. In the patients with secondary left ventricular hypertrophy, cavity size and peak circumferential fibre shortening rate were normal. In diastole, the peak rate of increase of dimension was reduced in 56, and mitral valve opening, normally synchronous with minimum dimension, was delayed in 78, both the result of abnormal left ventricular relaxation. The septal to posterior wall thickness ratio was greater than 1.3 in 40. Values for delay in mitral valve opening were distributed bimodally in the population of patients with secondary left ventricular hypertrophy, with one subgroup in which it was normal and the other in which it was significantly delayed. The distribution of the latter, along with those of values of peak rate of dimension increase and septal to posterior wall thickness ratio were indistinguishable from those in the patients with hypertrophic cardiomyopathy. Abnormalities similar to those of hypertrophic cardiomyopathy therefore occur in patients with secondary left ventricular hypertrophy, and these echocardiographic criteria cannot separate the two conditions.

Diastolic abnormalities are prominent in hypertrophic cardiomyopathy. Left ventricular end-diastolic pressure may be raised, and disturbances in the timing of wall motion be present, with delayed mitral valve opening, reduced peak rate of dimension increase, prolonged rapid filling period, and evidence of incoordinate relaxation (Sanderson *et al.*, 1978; St John Sutton *et al.*, 1978). Secondary left ventricular hypertrophy, by contrast, has been described as a homeostatic and basically beneficial process (Linzbach, 1960; Goodwin, 1974) in which an increase in wall thickness and mass occur to normalise peak systolic wall stress. It thus appears to be qualitatively different from hypertrophic cardiomyopathy, and it has been suggested that the two can be separated by measurements of the relative thickness of the septum with respect to that of the posterior left ventricular wall (Henry *et al.*, 1973). The purpose of the present study was to investigate the relation between the two processes in greater detail, with particular reference to diastolic events. It was hoped that further criteria for their distinc-

tion might become apparent on the basis of such observations and that these might also be of value in the investigation of those relatively uncommon cases in which the two processes appear to coexist.

Methods

Echocardiograms of 100 patients with secondary left ventricular hypertrophy were studied, and diagnoses are given in Table 1. Those with systemic hypertension all had resting diastolic blood pressures above 120 mmHg before the start of treatment. The severity of the outflow tract obstruction was severe enough to require operation in all the patients with aortic or fixed subaortic stenosis. None had

Table 1 Clinical material

Secondary left ventricular hypertrophy:		100
Severe hypertension	23	
Aortic valve stenosis	21	
Fixed subaortic stenosis	13	
Postoperative:		
Aortic stenosis	13	
Aortic reflux	30	
Hypertrophic cardiomyopathy		30

Received for publication 28 March 1978

Fig. 1 Echocardiogram from a patient with hypertension, showing right (R_s) and left (L_s) sides of the septum, endo- and epicardial surfaces of the posterior wall, recorded with an apex cardiogram (ACG), and phonocardiogram showing aortic valve closure (A_2). The timing of mitral valve opening (MVO) is shown.

significant aortic regurgitation or mitral valve disease. All the patients studied had echocardiographic evidence of left ventricular hypertrophy in that septal or posterior wall thickness, or both, were greater than 12 mm, the upper limit of normal. Results from these patients were compared with those from the echocardiograms of 30 patients with classical hypertrophic cardiomyopathy, diagnosed on angiographic criteria (Steiner, 1964).

Echocardiograms were recorded as previously described (Fig. 1) (Gibson and Brown, 1973), with the patient in the left lateral position using a Smith-Kline Ekoline 20 ultrasonoscope and a Cambridge Instruments photographic recorder, operating at a paper speed of 100 mm/s. Echocardiograms were recorded at the level of the tips of the mitral valve cusps, so that the time of mitral valve opening could be detected as that of initial separation at the start of diastole. The definition of the posterior wall was increased using the switch gain technique, and by a modification of the swept gain to produce a reverse ramp.

Echocardiograms were digitised as previously described (Gibson and Brown, 1973) using a Summagraphics digitiser and a Prime 300 computer system. From these records, the following measurements were made (Fig. 2).

(1) End-diastolic and end-systolic cavity size, wall thickness, and septal thickness. End-diastolic events were taken as simultaneous with the onset of the Q wave of the electrocardiogram, and end-systolic as those simultaneous with minimum cavity dimension.

(2) Peak normalised rate of reduction of dimension during systole (VCF), expressed in s^{-1} .

(3) Peak rate of increase of dimension during diastole.

(4) Early diastolic filling period, as defined in Gibson and Brown (1973).

(5) The time interval between minimum cavity dimension and the onset of mitral valve opening, and the increase in dimension occurring during this time expressed as a percentage of the total increase.

Mean values for each of the 5 groups of patients with secondary left ventricular hypertrophy were derived, and compared with normal, and also with those from the patients with hypertrophic cardiomyopathy. In addition, the distribution of variables was plotted as a histogram from all the patients with secondary hypertrophy taken together so that mean values and distributions could be compared with similar plots of the population with hypertrophic cardiomyopathy. Departures of these samples from normal frequency distributions were investigated using the Kolmogorov-Smirnov test. For normally distributed samples, standard deviations were calculated, and the significance of differences between means checked by t tests.

Results

(1) LEFT VENTRICULAR DIMENSIONS

The results for individual groups of patients with secondary left ventricular hypertrophy are given in Table 2, where they are compared with those from normal subjects and patients with hypertrophic

Fig. 2 Digitised echocardiogram from a patient with aortic stenosis, showing, from below, original data, and above, left ventricular dimension and (top) rate of change of dimension. The cross represents the timing of A2, and the vertical line that of MVO, which is delayed with respect to minimum dimension. The peak rate of increase of dimension is reduced below 10 cm/s, and early diastolic filling period is prolonged.

cardiomyopathy. End-diastolic dimensions did not differ from normal in any of the groups, and end-

systolic dimension was normal in all patients except those with hypertrophic cardiomyopathy, where it was reduced ($P < 0.01$). Posterior wall and septal thickness were greater than normal in all patients, by definition, but were significantly less than those recorded in hypertrophic cardiomyopathy. In general, the ratio of septal to posterior wall thickness was greater than 1.3:1 in patients with hypertrophic cardiomyopathy, but this was not always the case (Fig. 3). Values greater than 1.3:1 occurred in nearly half those with secondary left ventricular hypertrophy, where they were distributed as a single normal frequency curve (Fig. 3). A figure for the ratio of septal to posterior wall thickness of 1.3:1, or indeed any other value did not separate patients with secondary left ventricular hypertrophy from those with hypertrophic cardiomyopathy.

(2) SYSTOLIC WALL MOVEMENT

Systolic rates of wall movement, assessed in terms of peak VCF were normal in all the groups of patients with secondary left ventricular hypertrophy, but somewhat greater than normal in those with hypertrophic cardiomyopathy ($P < 0.05$). This difference was no longer apparent when peak rates of wall movement were expressed in absolute (cm/s) rather than normalised (s^{-1}) units, and so was probably a reflection merely of the reduced end-systolic cavity size.

(3) DIASTOLIC EVENTS

The mean value of peak rate of dimension increase was reduced significantly below normal in all groups of patients with secondary left ventricular hypertrophy, and the distribution of values throughout the whole population of these patients is shown in Fig. 4, where it is compared with that of the patients with hypertrophic cardiomyopathy. Mean values and standard deviations were not significantly different. Significant prolongation of early diastolic filling period occurred in patients with secondary

Table 2 Echocardiographic data

	Normal	Hypertension	Aortic stenosis	Subaortic stenosis	Postoperative		Hypertrophic cardiomyopathy
					AS	AR	
End-diastolic dimension (cm)	4.7 ± 0.32	4.6 ± 1.0	4.9 ± 1.0	4.1 ± 1.1	4.8 ± 1.2	4.9 ± 1.0	4.7 ± 0.3
End-systolic dimension (cm)	2.9 ± 0.35	3.0 ± 1.0	3.3 ± 0.9	2.5 ± 1.1	3.2 ± 0.8	3.5 ± 1.0	2.4 ± 0.3
Peak VCF (s^{-1})	2.4 ± 0.3	2.3 ± 0.9	2.5 ± 1.0	2.5 ± 1.1	2.2 ± 1.0	2.0 ± 0.9	3.2 ± 1.0
Posterior wall thickness (cm)	0.85 ± 0.2	1.2 ± 0.3	1.2 ± 0.3	0.9 ± 0.3	1.1 ± 0.3	0.9 ± 0.3	1.4 ± 0.4
Septal thickness (cm)	0.90 ± 0.1	1.5 ± 0.7	1.5 ± 0.2	1.3 ± 0.6	1.7 ± 0.7	1.5 ± 0.3	2.2 ± 0.5
Septal/PW thickness ratio	1.1 ± 0.1	1.4 ± 0.5	1.3 ± 0.4	1.5 ± 0.5	1.5 ± 0.6	1.8 ± 0.8	1.7 ± 0.6
Peak rate of dimension increase (cm/s)	18 ± 3	10 ± 1	12 ± 5	12 ± 4	11 ± 4	12 ± 6	13 ± 6
Delay in mitral valve opening (ms)	3 ± 5	70	50	25	60	60	75
Outward movement before mitral valve opening (%)	0 ± 2	16	11	7	18	25	28

Mean ± 1 standard deviation, of normally distributed populations.

Fig. 3 Histograms showing the distribution of values of septal/posterior wall ratio. Open columns represent the patients with secondary left ventricular hypertrophy, and solid ones, those with hypertrophic cardiomyopathy. The latter have been displaced slightly to the right for clarity.

left ventricular hypertrophy as well as in those with hypertrophic cardiomyopathy (Table 2). The distribution of the delay in the onset of mitral valve opening with respect to minimum cavity dimension is shown in Fig. 5. For patients with secondary left ventricular hypertrophy, this distribution is bimodal ($P < 0.001$, with respect to normal distribution). This departure is because approximately 40 per cent of the patients with secondary left ventricular hypertrophy have mitral valve opening at the normal time, while in the remainder it is delayed. This latter subgroup showed a distribution in-

Fig. 5 Histograms showing distribution of values of the delay in mitral valve opening. Layout as in Fig. 3.

distinguishable from that occurring in patients with hypertrophic cardiomyopathy. During the period between minimum dimension and mitral valve opening, an abnormal increase in dimension occurred in all groups of patients with secondary left ventricular hypertrophy, particularly those after aortic valve replacement, as well as in those with hypertrophic cardiomyopathy (Table 2). Thus secondary left ventricular hypertrophy could not be distinguished from hypertrophic cardiomyopathy on the basis of these diastolic events.

Discussion

The present study has shown similarities between the echocardiographic features of secondary left ventricular hypertrophy and those of hypertrophic cardiomyopathy. Differences of degree do exist, however; left ventricular cavity size was smaller at end-systole, and the extent of hypertrophy was greater in cases with hypertrophic cardiomyopathy, though this difference is readily explicable on the basis of clinical selection, since in patients with valvular heart disease, symptoms were not necessarily the result of the hypertrophy itself. It was not possible to achieve any useful separation of the two conditions using the ratio of septal to posterior wall thickness. It has previously been suggested that values of this ratio greater than 1.3 are pathognomonic of hypertrophic cardiomyopathy (Henry *et al.*, 1973), but more recently, this view has been questioned (Bulkley, 1977). Not only does the ratio of septal to posterior wall thickness give no indication of the degree of hypertrophy, but normal values have been recorded in hypertrophic cardiomyopathy

Fig. 4 Histograms showing distribution of values of peak rate of dimension increase. Layout as in Fig. 3.

(Rossen *et al.*, 1974), and abnormal ones in normal infants (Larter *et al.*, 1976), weight lifters (Menapace *et al.*, 1977) and other sportsmen, patients with right ventricular hypertrophy (Goodman *et al.*, 1974), and those with reduced posterior wall thickness caused by myocardial infarction. The present results indicate that it cannot be used to distinguish secondary left ventricular hypertrophy from hypertrophic cardiomyopathy. In particular, values greater than 1.3 cannot be taken as diagnostic of additional cardiomyopathy in the presence of a condition capable of causing left ventricular hypertrophy.

Systolic rate of wall movement, assessed in terms of peak VCF, was normal in our patients with secondary left ventricular hypertrophy. This finding confirms previous observations of mean VCF, and is compatible with the idea that hypertrophy is a homeostatic process to normalise wall stress (Hood *et al.*, 1968; Grossman *et al.*, 1975). Left ventricular diastolic properties, however, were clearly abnormal in all groups of patients with secondary left ventricular hypertrophy. Previous studies of diastole in such patients have concentrated on the static pressure-volume characteristics of the cavity or have attempted to assess the material properties of the wall in terms of stress-strain relations (Mirsky, 1976). The present observations show that dynamic aspects of left ventricular filling are also very abnormal in these patients. Peak rate of dimension increase was reduced below the 95 per cent confidence limit of normal in over half, and the period of early diastolic filling was prolonged in a manner exactly resembling that occurring in mitral stenosis. The distribution of these abnormalities was indistinguishable from that in the group of patients with hypertrophic cardiomyopathy (Sanderson *et al.*, 1978; St John Sutton *et al.*, 1978). Since mechanical obstruction to left ventricular inflow is most unlikely in patients with secondary left ventricular hypertrophy, this pattern of diastolic wall movement is likely to be caused by abnormal relaxation. Though its mechanism is clearly different from mitral stenosis, its effects on left ventricular filling are the same, the degree of interference being inversely related to the filling period, and thus worse when heart rate is high.

A third diastolic abnormality, also seen in hypertrophic cardiomyopathy, was delay in mitral valve opening with respect to the timing of minimum dimension. This differed from the two previous ones in that values were not normally distributed in the population of patients studied. In less than half, the timing of mitral valve opening was essentially normal, whereas in the remainder it was delayed by a median value of approximately 90 ms, and this latter group appeared to have a distribution almost

identical with that of hypertrophic cardiomyopathy. In part, this delay appears to represent yet another manifestation of abnormal relaxation, but its bimodal distribution, in comparison with the unimodal one describing values of the peak rate of dimension increase, suggests that additional factors are involved. Significant dimension increase occurs in these patients before mitral valve opening, indicating that a change in cavity shape occurs during isovolumic relaxation. It seems likely, therefore, that this additional factor is a degree of inco-ordinate relaxation. Evidence for this has been presented from analysis of angiocardiograms (Sanderson *et al.*, 1977) and echocardiograms (Sanderson *et al.*, 1978; St John Sutton *et al.*, 1978) of patients with hypertrophic cardiomyopathy. In addition, delayed mitral valve opening is also common in patients with ischaemic heart disease and segmental contraction abnormalities (Upton *et al.*, 1976), and angiographic studies suggest that in this condition also, it is evidence of asynchronous relaxation in different regions of the cavity. We conclude, therefore, that relaxation is commonly abnormal in patients with secondary left ventricular hypertrophy, not only with respect to its rate, but also to its degree of co-ordination in different regions of the cavity.

The present results may have implications in the assessment of the diastolic properties of the left ventricle, either in terms of pressure-volume relations or those between wall stress and strain. Attempts to describe the material properties in terms of simple elastic or viscoelastic models have hitherto assumed that these properties remain constant throughout the period of diastole studied. In patients with left ventricular hypertrophy, relaxation appears to be prolonged and frequently inco-ordinate throughout rapid filling, so that myocardial properties cannot be assumed to be constant during this time. Except in late diastole, therefore, these simple models are likely to be inappropriate.

Secondary left ventricular hypertrophy thus appears to be a more complex condition than is frequently suggested. Peak rates of wall movement are normal during systole, and on this basis it might be said that left ventricular 'function' is unimpaired. However, it is as much a function of the left ventricle to fill as to eject, and the characteristics of filling in these patients are very abnormal. These abnormalities of timing are quite distinct from those of static pressure-volume or stress-strain relations, and are such as to become progressively more significant as heart rate increases. They can be detected non-invasively using the techniques that we have described, and any assessment of overall left ventricular function in such patients seems incom-

plete without knowledge of their presence or absence.

The computing equipment used in this study was provided by the DHSS as part of its experimental programme.

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