

Left ventricular relaxation and filling in hypertrophic cardiomyopathy

*An echocardiographic study*¹

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SUMMARY Echocardiograms showing left ventricular cavity and mitral valve cusps simultaneously were recorded in 36 patients, apex cardiograms being obtained in 26 of them. These were digitised and continuous plots made of left ventricular dimension, its rate of change, and anterior mitral leaflet velocity, and were compared with those in 20 normal subjects. Peak mitral diastolic closure rate was reduced to 120 ± 80 mm/s, compared with normal (250 ± 60 mm/s). Peak rate of increase of dimension was normal (13.4 cm/s), though the pattern of filling was disturbed, with the duration of rapid filling prolonged in 5, and shortened in 15, suggesting restriction. Mitral valve opening, normally synchronous with minimum dimension, was delayed by a mean of 76 ms, and during this period there was an abnormal increase in dimension. Dimension also increased by 50 ± 25 per cent of the total diastolic excursion before the 'O' point of the apex cardiogram compared with 21 ± 7 per cent in normals, and the timing of peak rate of increase of dimension was delayed by 50 ± 20 ms instead of being synchronous with the 'O' point as normal. None of these findings correlated with the reduction in peak mitral diastolic closure rate. Noninvasive methods thus show that relaxation may be abnormal in hypertrophic cardiomyopathy. Delay in mitral valve opening and disturbances in the rate, duration, and co-ordination of wall movement during filling suggest the presence of segmental abnormalities of left ventricular function.

Echocardiography has been of considerable value in defining anatomical abnormalities in patients with hypertrophic cardiomyopathy, so that asymmetrical septal hypertrophy, a small cavity size, and anterior displacement of the mitral valve are now regarded as characteristic of the condition (Epstein *et al.*, 1974). Mitral valve movement may also be abnormal (Moreya *et al.*, 1969), and it has been suggested that slow left ventricular filling may cause a reduction in the diastolic closure rate of the anterior cusp. This conclusion, though supported by indirect haemodynamic evidence (Stewart *et al.*, 1968), has not been confirmed in a series of angiographic studies (Holt *et al.*, 1969; Hammermeister and Warbasse, 1974; Sanderson *et al.*, 1977). In the present study, therefore, we have taken advantage of the ability of echocardiography to make direct observations of

mitral valve and left ventricular wall movement to gain further information about relations between the two. This approach has allowed a number of diastolic abnormalities to be defined in patients with hypertrophic cardiomyopathy, and their relation to mitral valve movement determined.

Subjects and methods

PATIENTS

Thirty-six patients with hypertrophic cardiomyopathy were studied. In 28 patients, the diagnosis was based on angiographic criteria, and in the remainder the typical echocardiographic features of hypertrophic cardiomyopathy were present: asymmetrical septal hypertrophy, small cavity size, and anterior displacement of the mitral valve, with or without systolic anterior movement (Epstein *et al.*, 1974). One patient was in atrial fibrillation at the time of examination, and the remainder were in sinus rhythm. There were 23 men, their mean age was 44 years, with a range of 17 to 66 years; 23

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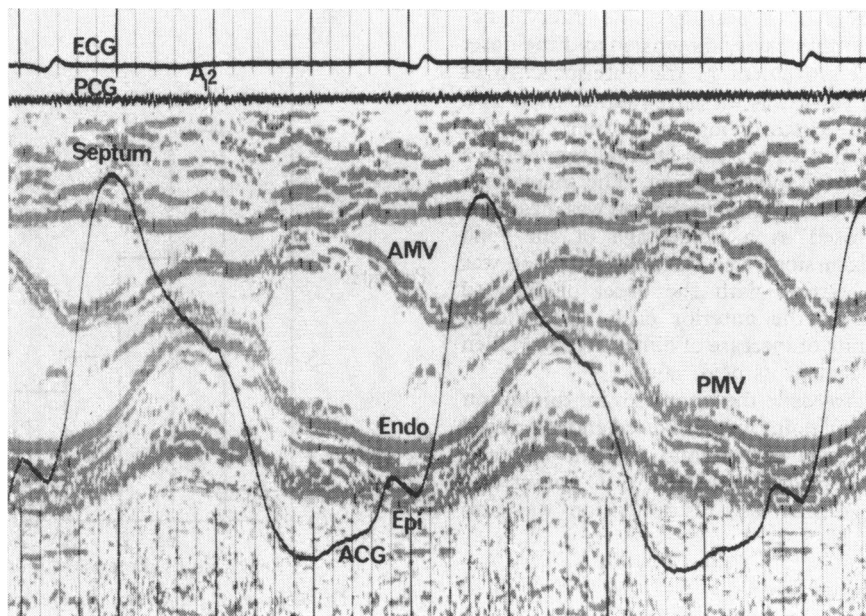


Fig. 1 Echocardiogram of patient with hypertrophic cardiomyopathy showing septum, posterior wall, and mitral valve cusps. Simultaneous apex cardiogram (ACG), and phonocardiogram (PCG) have been recorded. A2, aortic valve closure; AMV, anterior mitral valve leaflet; PMV, posterior mitral valve leaflet; Endo and Epi, endo- and epicardial surfaces of the posterior wall.

were taking propranolol at the time of the examination. Twenty normal volunteers were also studied, and results from this group served as the basis for comparison.

METHODS

Echocardiograms were recorded with an Ekoline 20 ultrasonoscope (frequency 2.25 MHz, repetition frequency, 1000/s). The output was displayed on a Cambridge strip chart recorder, operating at a paper speed of 100 mm/s, with a simultaneous electrocardiogram. Where possible, a phonocardiogram, to define aortic valve closure (A2), and an apex cardiogram were also recorded (Fig. 1). Subjects were studied supine or in the slightly left lateral position, with the transducer at the left sternal border. Echoes were obtained simultaneously from the septum, posterior wall, and anterior cusp of the mitral valve. Measurements were made only on records showing clear continuous endocardial echoes.

APEX CARIOGRAMS

These were recorded from the point of maximum impulse with a Cambridge Scientific Instruments transducer with a 3 cm cup, a time constant of 4 s, and a lower frequency limit of 0.05 Hz. Satisfactory records were obtained in 26 patients.

DIGITISING METHODS

Echocardiograms were digitised as previously described, tracing echoes from the left side of the septum, endocardial surface of the posterior wall, anterior mitral valve leaflet, and apex cardiogram using a Summagraphics digitising table, interfaced with a Prime 300 computer (Upton *et al.*, 1976a; Venco *et al.*, 1977). Strings of approximately 100 co-ordinates were generated for each of these traces together with calibration signals representing 0.5 s and 1 cm and the RR interval of the beat being studied.

From the digitised data, plots were made of the position of the wall and mitral valve echoes, left ventricular dimension (D), rate of change of dimension (dD/dt), and rate of change of anterior leaflet position. When available, the apex cardiogram was superimposed. From these traces, the following measurements were made:

- (1) *Left ventricular dimension*: end-systolic and end-diastolic dimensions were measured directly, along with the peak rate of increase of left ventricular dimension during diastole. The time when the peak rate of increase of dimension had fallen to 20 per cent of its peak value was noted and taken to represent the end of rapid filling.
- (2) *Mitral valve movement*: peak closing velocity of the anterior cusp was taken from the curve of

first differential of position. The interval between minimum cavity dimension and the onset of forward movement of the anterior cusp of the mitral valve was measured: since these two events are synchronous in normal subjects (Upton *et al.*, 1976a), this interval represents a delay in mitral valve opening. The increase in dimension occurring in this period was measured and expressed as a percentage of the total diastolic excursion. The rapid filling period was taken as starting with the onset of forward movement of the anterior cusp, and ending when the rate of increase of dimension had fallen to 20 per cent of its peak value.

- (3) *Apex cardiogram*: the increase in dimension before the 'O' point was measured and expressed as a percentage of the total diastolic increase. The time interval between the 'O' point and peak rate of increase of dimension was also noted.

STATISTICAL METHODS

Normal values were taken as those lying within a range of 2 standard deviations of the corresponding mean values from the normal group. The statistical significance of differences between means of normally distributed populations was assessed by Student's *t* test.

Results

(1) LEFT VENTRICULAR DIMENSION

In patients with hypertrophic cardiomyopathy the mean end-diastolic dimension was 4.2 ± 0.9 cm (mean ± 1 standard deviation) which was not significantly different from normal (4.7 ± 0.3 cm). End-systolic dimension was significantly reduced at 2.4 ± 0.6 cm, compared with 3.0 ± 0.4 in normal subjects ($P < 0.01$). Peak rate of increase of dimension had a mean value of 13.4 cm/s, compared with 16.0 ± 3 cm/s in normals, and values were not normally distributed (Fig. 2). In 14 patients, values were significantly lower, and in 3 patients they were significantly higher than the normal range (Fig. 3). The duration of the rapid filling period was 190 ± 85 ms, compared with 160 ± 30 ms in normals. The mean values were not significantly different, but the dispersion about the mean was greater in the patients with hypertrophic cardiomyopathy, so that the rapid filling period was abnormally prolonged in 5 patients, and abnormally short in 15.

(2) MITRAL VALVE MOVEMENT

Peak closing rate of the anterior mitral cusp was significantly reduced to 120 ± 80 mm/s compared

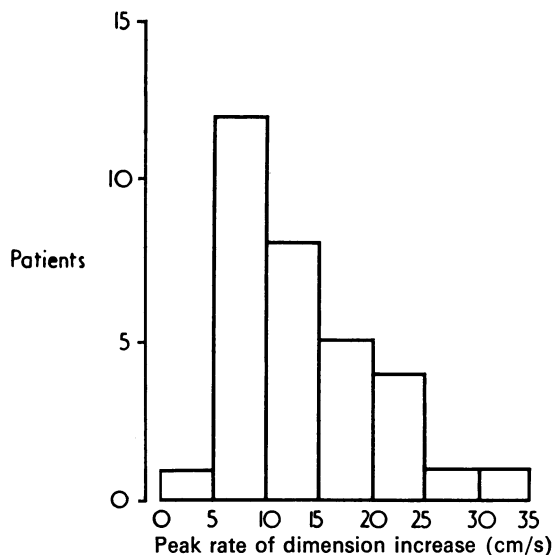


Fig. 2 Distribution of peak rate of increase of dimension in the patients with hypertrophic cardiomyopathy.

with normal (250 ± 60 mm/s, $P < 0.01$). There was no statistically significant relation between peak early diastolic closure rate and any aspect of relaxation or filling studied in the patients with hypertrophic cardiomyopathy.

The onset of mitral valve opening was appreciably delayed, by a mean value of 76 ms with respect to the time of minimum cavity area (Fig. 4), compared with 2.6 ms in normals, so that in only 2 patients were values within the normal range recorded. During the interval between minimum dimension and mitral valve opening a mean of 10 ± 8 per cent of total diastolic increase in wall movement occurred which was significantly greater than normal (1 ± 2 , $P < 0.01$).

(3) APEX CARDIOGRAM

An abnormal increase in dimension before the 'O' point of the apex cardiogram was common, the mean value being 50 ± 25 per cent total diastolic increase compared with 21 ± 7 per cent in normals. Values within the normal range occurred in only 7 patients, while in 1 there was abnormal inward wall movement during this period. The relation between the 'O' point of the apex cardiogram and the timing of the peak rate of increase of dimension was variable. In general, peak rate of increase was significantly delayed by 50 ± 20 ms, compared with 6 ± 9 ms in normal ($P < 0.01$), but the scatter was wide, and in 3 patients it preceded the 'O' point.

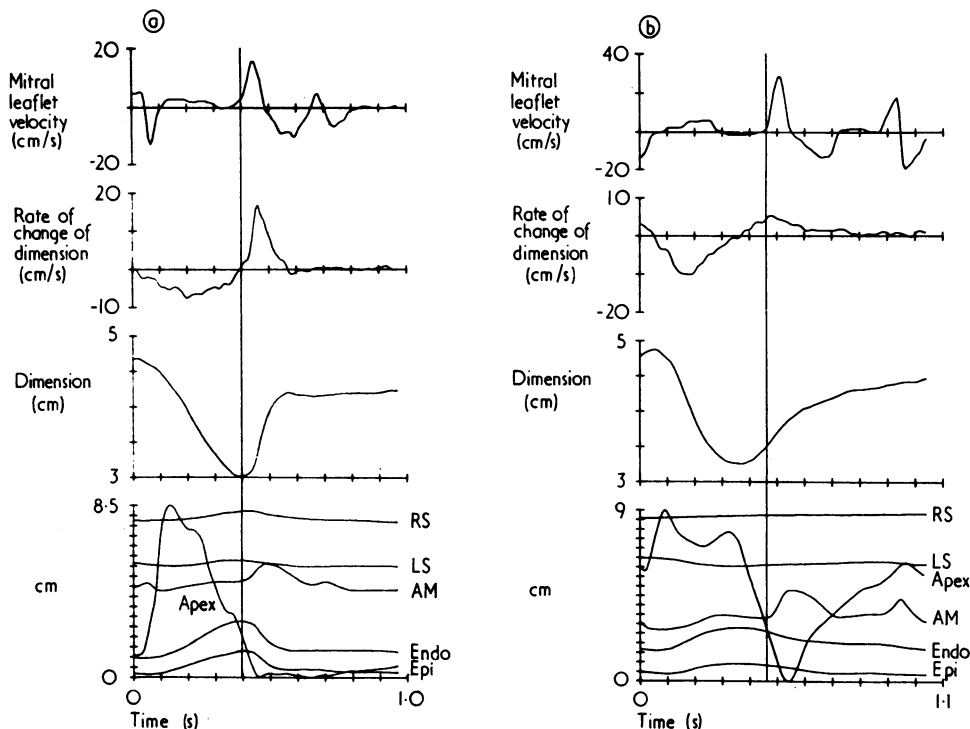


Fig. 3 (a) Computer output of the echocardiogram of the left ventricular cavity of a patient with hypertrophic cardiomyopathy showing digitised echoes from right (RS) and left sides (LS) of the septum, endo- and epicardial (epi) surfaces of the posterior wall, and anterior mitral valve cusp (AM). An apex cardiogram (apex) is superimposed. Above is shown left ventricular internal dimension; above this, rate of change of dimension, and (top) mitral leaflet velocity. Vertical line represents the timing of mitral valve opening. The pattern of dimension change during filling is normal. (b) Computer output from a patient with hypertrophic cardiomyopathy; layout as Fig. 3a. Mitral valve opening is delayed, peak rate of increase of dimension is reduced, and filling period is prolonged.

Discussion

In normal subjects, the co-ordinated series of events during early diastole defined by noninvasive methods suggests the underlying presence of a highly organised process (Upton *et al.*, 1976a; Venco *et al.*, 1977). Minimum left ventricular dimension coincides with the onset of forward movement of the anterior cusp, and dimension increases rapidly thereafter for a period of approximately 0.16 s. The rate of increase then drops abruptly, so that by 0.22 s, it has returned to 20 per cent of its peak value, when there is usually a clear-cut discontinuity on the trace of the first derivative of dimension against time, apparently representing the end of rapid filling and the onset of diastasis. Anterior cusp movement is co-ordinated with that of the wall throughout this period. Not only the start, but also the peak rate of cusp movement coincides with the corresponding event on the dimension trace, and both show a discontinuity at the end of rapid filling. The timing of the apex

cardiogram is also closely related, with mitral valve opening occurring during its downstroke, and the 'O' point coinciding with the timing of peak rate [of increase of dimension (Prewitt *et al.*, 1975). It is only after these events, during diastasis, that the mitral valve shows its characteristic mid-diastolic closing movement, reaching a peak value of 250 mm/s.

In hypertrophic cardiomyopathy, these characteristic interrelations were disrupted. In the group as a whole, mitral valve opening was delayed with respect to minimum dimension by nearly 80 ms, and during this period significant outward wall movement occurred, accounting for 10 per cent of the total increase in dimension during diastole. This late mitral valve opening was associated with loss of the normal time relations between changes in anterior cusp motion and dimension throughout early filling. Left ventricular wall movement, as reflected in the transverse dimension, was also abnormal after mitral valve opening in the majority of the patients studied. In 15, the rapid filling period was short, partly because of late mitral valve open-

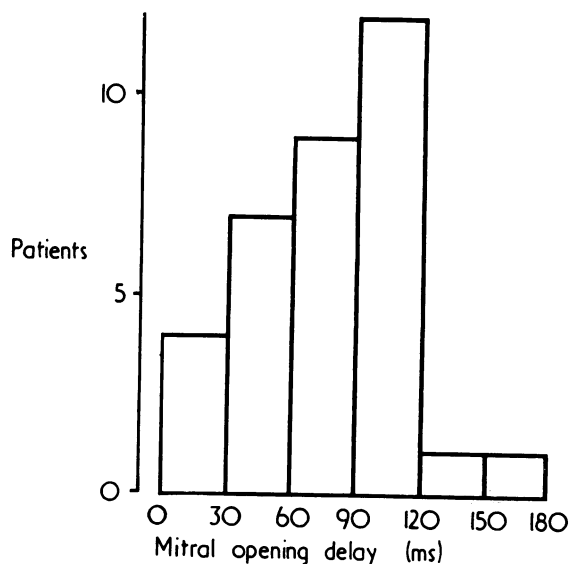


Fig. 4 *Distribution of mitral valve opening delay in patients with hypertrophic cardiomyopathy.*

ing, and partly because its end occurred early with respect to the time of minimum dimension. This shortening was not associated with any increase in the peak rate of dimension increase, so that it could be interpreted as a restrictive pattern of left ventricular filling. By contrast, in 5 patients, rapid filling was prolonged, even allowing for delayed mitral valve opening, though peak filling rates were normal. Peak rates of increase of dimension showed a wider dispersion about the mean than in normal subjects, with values both higher and lower than the normal range being recorded. The timing of the apex cardiogram was also abnormal in that the 'O' point no longer coincided consistently with the peak rate of increase of dimension, and was delayed with respect to mitral valve opening by up to 120 ms. In addition, there was a considerable increase in dimension during the downstroke of the apex cardiogram. The results thus show that it is not only the rate or duration of outward wall movement that is disturbed in patients with hypertrophic cardiomyopathy, but that an additional major abnormality is loss of co-ordination between the different processes involved, and that considerable heterogeneity was present in the group of patients studied.

It is well recognised that the mid-diastolic closure rate of the mitral valve may be reduced in hypertrophic cardiomyopathy (Moreya *et al.*, 1969) and this was confirmed in the present study. The

mechanism of this reduction, however, is not clear. It has been suggested that it may be caused by a low rate of ventricular filling, but the evidence for this is indirect (Stewart *et al.*, 1968), and has not been confirmed by angiographic studies. In addition, peak diastolic closure rate occurs during diastasis, and thus bears no relation to the time of peak filling. It has also been observed that the diastolic closure rate is reduced in conditions with abnormal left ventricular pressure-volume relations (Quinones *et al.*, 1974), but this does not imply that the relation between the two is a direct one. It seems more likely that in hypertrophic cardiomyopathy, a reduced diastolic closure rate results from some aspect of the disease not detected in the present observations, possibly related to anatomical abnormalities of the left ventricular outflow tract which may interfere with movement of the valve (Popp and Harrison, 1969).

The observations described here are compatible with a recent angiographic study (Sanderson *et al.*, 1977). Though only a limited region of the left ventricular cavity can be studied by echocardiography, endocardial position can be defined unequivocally by this method during late systole and early diastole when angiographic results have been questioned (Hugenholtz *et al.*, 1969; Mitchell *et al.*, 1969). In addition, mitral valve movement can be studied more effectively and its relation to wall movement investigated. Both studies indicate the presence of a number of separate diastolic abnormalities in hypertrophic cardiomyopathy (Goodwin, 1970), which resemble those recorded in the same period in ischaemic heart disease (Upton *et al.*, 1976b; Venco *et al.*, 1977). In both conditions, mitral valve opening is delayed with respect to minimum dimension, with loss of the normal relation between wall motion and that of the anterior mitral valve cusp or apex cardiogram, and in both there is considerable variation in these measurements between patients in whom the clinical picture is very similar. There are differences between the two, in that the amplitude of wall movement before mitral valve opening in ischaemic heart disease may be considerably greater than in hypertrophic cardiomyopathy, and may account for up to 50 per cent of the total diastolic increase in dimension. In addition, mitral diastolic closure rate is usually normal in ischaemic heart disease in spite of these other abnormalities, suggesting that they are not responsible for the reduction seen in hypertrophic cardiomyopathy. Nevertheless, the striking similarities between the two conditions strongly suggest that regional abnormalities of function may also occur in patients with hypertrophic cardiomyopathy. Though our studies provide only indirect

evidence for their presence, their existence would be compatible with previous histological observations showing wide variation in myocardial histology and architecture in different regions of the ventricle (Van Noorden *et al.*, 1971; Maron *et al.*, 1974). If such regional variation in structure was associated with corresponding variation in function, it would go far to explain abnormalities of left ventricular function occurring in this condition.

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