Regional left ventricular wall movement in hypertrophic cardiomyopathy

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SUMMARY Left ventriculograms of 20 patients with hypertrophic cardiomyopathy were digitised frame by frame and analysed using a contour display. Abnormalities of regional wall movement were present in 17, and included an abnormal sequence of inward movement during systole (13), regional delay in the onset of inward movement (10), and an abnormal dispersion of peak velocities (5). Diastolic wall movement was disturbed in 13, because of abnormal peak velocities in 7 and regional asynchrony in 6. Abnormal wall movement during the two isovolumic periods was rare in hypertrophic cardiomyopathy, unlike ischaemic heart disease. These disturbances may reflect underlying structural abnormalities.

One of the most important mechanisms interfering with left ventricular function in hypertrophic cardiomyopathy is the hypertrophy itself. This may be severe and asymmetrical, causing distortion of cavity shape, particularly at end-systole (Braunwald et al., 1964); and histological studies have shown the presence of areas in the septum and free wall, where normal myocardial architecture is lost (Olsen, 1971; Van Noorden et al., 1971; Ferrans et al., 1972). These morphological abnormalities may have functional significance by causing incoordinate contraction, and indirect evidence that this does occur has been obtained from echocardiographic observations (Sanderson et al., 1978). It was the purpose of the present study to gain more direct information about left ventricular wall movement in hypertrophic cardiomyopathy using information derived from left ventriculograms. This made it possible to assess the nature, timing, and distribution of a series of abnormalities and to assess the extent to which they modified overall left ventricular function.

Methods

Observations were made on 20 patients with hypertrophic cardiomyopathy, in whom diastolic events had been studied in detail and reported elsewhere, along with clinical and haemodynamic data (Sanderson et al., 1977). In the present study, regional endocardial movement was assessed from their left ventriculograms by construction contour displays showing variation of the position of the cavity outline throughout the cardiac cycle. This method is based on a series of plots of wall movement against time (Gibson et al., 1976). The angiographic cavity outline was digitised successively on each frame of the beat to be studied. End-diastolic and end-systolic cavity outlines were identified as those with the largest and smallest areas, respectively. With the outlines from successive cine frames superimposed on one another with respect to an external reference point, 40 equally spaced points were selected on the end-diastolic outline, starting from the mitral aspect of the aortic root, and proceeding anticlockwise. From each of these, the nearest point on the end-systolic outline was identified, and endocardial position noted along the lines thus defined for each frame of the cycle to be studied. This procedure results in 40 plots of wall movement against time, and the resulting information was more easily assimilated if a contour display was used (Figs 1-6). Here, inward movement of the cavity outline from its position in the end-diastolic frame is shown by a series of contour lines, each representing a displacement of 1 mm. The timing of minimum cavity area and mitral valve opening was superimposed, the latter determined by direct inspection of the angiogram. On such a display, the timing, velocity, and extent of wall movement can be appreciated from the position, spacing, and number of contour lines along the horizontal line corresponding to the region being studied. Once such

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regions of interest had been identified by inspection of the contour on a visual display unit, selected plots of endocardial position against time could be constructed, along with their rates of change, in order to quantify regional behaviour. From these displays, the following information was extracted:

1. The site of onset of inward movement at the start of systole. Normally movement begins in the anterior region of the cavity just below the aortic root, followed by the interior wall, and finally the apex (Gibson et al., 1978).

2. The time interval over which inward movement started in different regions of the cavity, normally less than 100 ms (Gibson et al., 1978). When this interval was exceeded, the site of segments showing delay was noted.

3. The extent and peak velocity of inward movement during systole, from single plots of endocardial position against time. At least one plot was studied from the anterior and one from the inferior region of the cavity. When segmental abnormalities were present, representative plots were taken from different regions, so that all types of abnormal behaviour appearing in the cavity were included.

4. The pattern of wall movement after mitral valve opening, with particular reference to regional abnormalities of velocity.

5. The duration of the rapid filling period in different parts of the cavity, measured as the time interval between mitral valve opening and the end of rapid phase wall movement. This latter point is readily visible in normal subjects, and also in all the patients studied, except the one represented in Fig. 2.

Information was also obtained about overall left ventricular function. Angiograms were examined directly for the presence of cavity obliteration and mitral regurgitation. Peak rates of change of volume were estimated from plots of the first derivative of volume against time. The period of isovolumic relaxation was taken as that between minimum cavity area and mitral valve opening. The duration of the QRS complex was estimated from the resting electrocardiogram.

REPRODUCIBILITY
The reproducibility of the method of angiographic analysis was assessed in 8 patients in whom there were 2 beats available for digitisation. Not surprisingly, comparison of the pairs of displays showed minor differences in the distribution of contour lines. However, there was satisfactory agreement between them with regard to the main features. Thus, comparison of systolic events showed that the root mean square difference between estimates of the time interval over which the onset of contraction occurred in different regions of the cavity was 20 ms, over a range of 20 to 160 ms. There was complete agreement with respect to localisation of hypokinetic segments and areas of reduced velocity of wall movement. There was also agreement over the site of onset of inward wall movement in all, though in 3 there was disagreement over the second and third areas to move. In each of these latter patients the overall duration of the onset of inward movement was 40 ms or less. During diastole, the root mean square difference between the two estimates of the duration of the rapid phase of outward wall movement was 20 ms, over a range of 80 to 220 ms. Areas of significant prolongation, or reduced rate of outward wall movement, were also similarly localised on all 8 pairs of displays.

Results
OVERALL LEFT VENTRICULAR FUNCTION
In all patients studied, the ejection fraction was normal or greater than normal (84 ± 4%, mean ± 1 standard deviation). The mean value of peak ejection rate, measured as the maximum rate of reduction of ventricular volume during systole, was 690 ± 280 ml/s, compared with a normal value of 690 ± 270 ml/s. Values from 2 patients lay outside the 95 per cent confidence limits of normal: one of 140 ml/s, whose plot is shown in Fig. 2 in whom generalised diastolic abnormalities of wall movement were also present, and one of 1320 ml/s from a patient with moderate mitral regurgitation. Cavity obliteration occurred in 12 patients.
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**Fig. 2** Hypertrophic cardiomyopathy. Systolic wall movement is normal, but there is a generalised reduction in the rate of outward movement during diastole.

**REGIONAL LEFT VENTRICULAR FUNCTION**

Regional abnormalities were common in the patients studied, and occurred in all but 3. Their properties are described in greater detail below, but in general they were those of timing or velocity of movement rather than of amplitude. Representative plots are shown in Figs 1-5 with a normal plot in Fig. 6 for comparison.

*(1) Order of onset of inward movement*

The normal sequence of inward movement, starting in the anterior wall, followed by the inferior region and finally the apex was seen in only 7 patients. In all of the remainder, premature inward movement occurred at the apex, which was the first region to move in 3, and which failed to show its accustomed delay with respect to the inferior wall in 8. In 2 patients, movement in the inferior region preceded that in the anterior wall as well as at the apex.

*(2) Timing of onset of inward movement*

Abnormal segmental delay in the onset of inward movement occurred in 10 patients. In 4, the anterior part of the cavity was involved, in 4 the apex, and in 2 the inferior region. All but 3 of these ventriculograms showed cavity obliteration. The

**Fig. 3** Contour display of left ventriculogram from a patient with hypertrophic cardiomyopathy, showing regional abnormalities of wall movement. The onset of inward movement is delayed anteriorly, but its peak velocity here is increased. Outward wall movement occurs slowly, inferiorly.

**Fig. 4** Hypertrophic cardiomyopathy. There is abnormal delay in the onset of inward wall movement during systole. Diastolic wall movement is normal.

**Fig. 5** Hypertrophic cardiomyopathy. There is premature inward wall movement at the apex, and inferior hypokinesis.
mean ejection rate in these patients, however, was 660 ± 220 ml/s, not significantly different from those in whom the onset of inward movement was normal (730 ± 390 ml/s). However, there was inverse correlation between the delay in onset of inward movement of the most retarded segment (y) and peak filling rate (x) given by the equation: 
\[ y = 0.17x - 41 \text{ ms}, r = 0.75, P < 0.001 \] (Fig. 7). In addition, prolonged onset of inward movement (y) was weakly correlated with the duration of the QRS complex (x), \[ r = 0.64 \] (P < 0.01). Representative examples of abnormal systolic movement are shown in Figs 3-5. In Figs 3 and 4, the abnormal regions appear demarcated from one another, while in Fig. 5 this is not so, and the pattern is similar to that occurring in ischaemic heart disease.

(3) Regional velocities of inward movement
In normal subjects, peak rate of inward movement in the anterior region of the cavity has a mean value of 10 ± 3.5 cm/s, rather higher than the inferior region, where the mean value is 8.3 ± 1.7 cm/s. Though considerable variation may occur in a single cavity, values differing by a factor of more than 2 are not found in normal subjects. In patients with hypertrophic cardiomyopathy, values greater than the 95 per cent confidence limit of normal (17 cm/s) occurred in 6 in the anterior region, and in 5 inferiorly (12.7 cm/s). Three of these segments had also shown abnormal delay in the onset of inward movement. In 5 patients there was abnormal dispersion of velocities with peak values differing by a factor of more than 2 occurring in the same cavity, examples being shown in Figs 1 and 3.

(4) Diastolic wall movement
In normal subjects, rapid outward wall movement normally ends within 160 ± 50 ms of mitral valve opening, and in different regions of the cavity, within 95 ± 20 ms of one another. In 7 patients, these variables were outside the normal range. In one, Fig. 2, there was no recognisable rapid outward wall movement anywhere in the cavity, but instead, filling continued slowly throughout diastole. In a further 6, there was increased regional variability in the duration of the rapid filling period. The mean value of peak filling rate was 770 ± 360 ml/s in these patients, not significantly different from those in whom this was normal (790 ± 300 ml/s). Velocities of outward wall movement greater than the 95 per cent confidence limit of normal (15 cm/s) were recorded in the anterior region in 7 patients and in 2 in the inferior region.

Discussion
The present study has shown a series of regional abnormalities of left ventricular wall movement occurring in hypertrophic cardiomyopathy. These were not apparent from inspection of the original angiograms or from superimposed cavity outlines, but were demonstrable by using contour lines to express regional displacement of endocardium from its end-diastolic position. This process led to loss of information about cavity size and shape, since the end-diastolic cavity outline itself was used as the zero reference for position. In addition, the overall amplitude of wall movement between end-diastolic and end-systole was less obvious than when the appropriate cavity outlines were superimposed. On
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the other hand, by showing continuous movement in terms of discontinuous contour lines, the method emphasised the time relations of its onset and cessation. It also allowed regional differences in the velocity of wall movement to be perceived from variation in the number of contour lines occurring in unit time, and their relation to the phase of the cardiac cycle or position in the cavity to be determined. The uniformity and degree of organisation implicit in these patterns was immediately evident on direct inspection. It became apparent that appreciation of the timing of changes in the speed or direction of wall movement depended not only on the positions of the single contour line that divided different regions, but also on what could be described as a process of visual integration of their behaviour for a significant time before and after the change had occurred, leading to increased certainty in the definition of such boundaries. It may have been this particular suitability of the contour method in demonstrating the distribution of wall velocities that led to its usefulness in these patients, since the velocity of contraction is a significant factor in describing the physiological state of the muscle itself. The properties of these displays must be borne in mind when interpreting the results, since though they contain no more information than that present on the original angiogram, they introduce an element of selection by facilitating the appreciation of certain types of abnormality.

Assessment of endocardial position in hypertrophic cardiomyopathy may present several difficulties. Cavity obliteration at the apex was represented in the present study by increased amplitude of inward wall movement in the affected area. Abnormal pocketing may cause the cavity outline to be ragged, and thus not completely digitisable when 80 to 100 points are used for each cavity outline. Abnormal movement of the outer border of the cavity may result from displacement of the papillary muscles, or from local collapse and extrusion of dye, and thus not represent correspondingly rapid myocardial contraction. All these mechanisms may have affected the present results. However, regional abnormalities of wall movement were as common at the base of the heart as at the apex, where such artefacts might be expected to be more frequent. In addition, these mechanisms operate when cavity size is small and so cannot explain the delay in the onset of inward movement at the start of systole or the strikingly reduced velocities of wall movement in some patients. Finally, there was satisfactory agreement between pairs of displays prepared from successive beats in 8 patients. Thus the abnormal patterns of change in the position of the cavity outline seen in patients with hypertrophic cardiomyopathy are reproducible, and seem mainly to reflect endocardial movement, though other effects, themselves related to the myopathic process such as cavity obliteration or regional collapse, may contribute.

The disturbances of left ventricular behaviour shown in this study differ in a number of ways from those in ischaemic heart disease. Regional delay in early systolic wall movement was common in both conditions, but lack of associated outward movement during isovolumic contraction in patients with hypertrophic cardiomyopathy differed sharply from its high incidence in those with ischaemic heart disease (Gibson et al., 1978). In the latter condition, this delay in onset of movement may be a sign of local disease, when it is associated with a reduction in the peak velocity of inward movement of affected segments during ejection. This was not the case in hypertrophic cardiomyopathy, where some of the highest velocities of inward movement occurred in regions where their onset was delayed. In ischaemic heart disease, further inward movement of these delayed segments may occur during isovolumic relaxation, particularly when their systolic function is preserved, leading to delay in mitral valve opening. Again, this was not seen in patients with hypertrophic cardiomyopathy, where the reverse was the case, so that the greater the delay in the onset of inward movement in different regions of the cavity during systole, the shorter the period of isovolumic relaxation and the more rapidly did filling proceed. Finally, though diastolic abnormalities of wall movement occurred in both conditions, their nature was different. In ischaemic heart disease, they were seen mainly during the period of isovolumic relaxation (Gibson et al., 1976; Upton et al., 1976), reverting to normal after the mitral valve opened, while in hypertrophic cardiomyopathy, wall movement during isovolumic relaxation was of small amplitude, even when this period was prolonged, but asynchronous wall movement after mitral valve opening was found in approximately one-third of the patients. In ischaemic heart disease, therefore, abnormalities of wall movement other than a simple reduction in amplitude, took place predominantly in the isovolumic periods, whereas in hypertrophic cardiomyopathy they occurred during filling and ejection.

The nature of these abnormalities thus gives some indication of their genesis. In view of the differences discussed above, it seems unlikely that they result from regional ischaemia, whether caused by large or small vessel coronary artery disease, by a degree of hypertrophy inappropriate to the blood supply, or by compression of coronary arteries within the septum. The relation between the width of the QRS complex and the delay in the onset of inward move-
ment in different regions of the cavity raises the possibility that abnormal activation may be responsible. Though this explanation would be compatible with normal peak velocities of systolic movement in delayed segments, it would not explain the absence of prolongation of isovolumic relaxation in such patients resulting from corresponding asynchrony in the onset of relaxation. It seems more probable, therefore, that electrical and mechanical abnormalities are both aspects of local disease.

One of the most characteristic features of hypertrophic cardiomyopathy is the presence of structural abnormalities of the left ventricle. At the macroscopical level, free wall and septal thickness are increased, and the cavity is small, particularly at end-systole. Even in normal subjects, left ventricular wall thickness is of the same order of magnitude as transverse dimension, so that thickening during systole can only be brought about by an orderly process of muscle shortening in order to avoid buckling and structural distortion within the wall. These constraints are likely to be greater when its thickness is increased as in hypertrophic cardiomyopathy. In addition, the myocardium itself is abnormal in hypertrophic cardiomyopathy, with regions where the muscle bundles are disorganised and their orientation disturbed. The cells are shorter than normal, with increased branching, and their myofibrils abnormal in architecture and insertion (Olsen, 1971; van Noorden et al., 1971; Ferrans et al., 1972). It seems possible, therefore, that these regional abnormalities of structure are accompanied by corresponding abnormalities of function. Instead of the normal orderly pattern of wall thickening during systole, regional wall movement becomes disorganised because of increased wall thickness and abnormal fibre orientation. The absence of wall movement during the two isovolumic periods indicates that the onset and course of contraction was likely to have been synchronous throughout the ventricle, so that regional delay in the onset of inward movement resulted from tension development initially being isometric in these affected areas. As ejection proceeded, however, wall movement later became possible at normal or even increased velocity with changing cavity shape. Myocardial architecture is thus likely to have been distorted, even with local collapse, at end-systole, particularly in those patients in whom the onset of inward movement was asynchronous, with a correspondingly increased tendency for the ventricle to return to its diastolic configuration once relaxation began. This mechanism is compatible with previous suggestions that much of the tension developed during systole in hypertrophic cardiomyopathy is isometric (Bulkley et al., 1977), and would also explain the relation between peak filling rate and asynchronous onset of contraction.

The present study illustrates that regional abnormalities of left ventricular wall movement occurring in disease are not random, but that specific patterns may occur in different conditions. The picture seen in ischaemic heart disease, mainly involving the isovolumic periods, is distinct from that of hypertrophic cardiomyopathy. Recognition of these characteristic features may allow similar disturbances to be detected in other conditions, such as secondary left ventricular hypertrophy. It may also provide the basis for more detailed analysis of left ventricular function when both conditions coexist, as in aortic stenosis or hypertension complicated by coronary artery disease. Finally, the results are potentially applicable to those non-invasive techniques that detect endocardial position and movement, increasing their diagnostic precision, and allowing separation of conditions that may be clinically similar, but whose pathological basis, management, and prognosis are widely different.

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