Echocardiographic features of malignant hypertension

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SUMMARY Computerised apex- and echocardiography was used to study left ventricular dimensions and function in 13 patients with untreated malignant hypertension and eight with severe benign hypertension.

All patients had normal left ventricular cavity dimensions. Five benign hypertensives and malignant hypertensives with a previous history of hypertension had significant thickening of the septum and posterior wall. In eight malignant hypertensives without a previous history wall thicknesses were normal. The absence of ventricular hypertrophy in some cases of malignant hypertension suggests that it is sometimes of rapid onset and not preceded by a non-malignant phase.

Although fractional shortening and peak Vcf were normal in all the hypertensives, diastolic left ventricular function was frequently abnormal with delayed mitral valve opening, reduced peak rate of filling, and outward endocardial motion during isovolumic relaxation. Malignant hypertensives showed a cavity shape change during isovolumic contraction, and in those without a previous history the aortic second heart sound occurred earlier. The abnormalities of function are probably the result of a combination of factors including pressure overload, abnormal myocardial properties, and myocardial ischaemia, either regional or generalised and secondary to arteriolitis.

Malignant hypertension is a rare disorder which carries a high mortality and morbidity. Heart failure may be a presenting feature and was a common cause of death before the advent of effective hypotensive therapy.¹

Echocardiographic studies in benign hypertension^{2,3} show increased left ventricular wall thicknesses, delayed mitral valve opening, and impaired relaxation.² Disproportionate thickening of the inter-ventricular septum may occur with ventricular hypertrophy in both benign^{2,3} and malignant hypertension.⁴

The purpose of this study was to determine the echocardiographic features of malignant hypertension in patients both with and without antecedent hypertension and to compare them with normal subjects and patients with severe benign hypertension.

Patients and methods

The following groups of patients were studied:

(a) *Normal*: 12 normal subjects (two women, 10 men) aged 29 to 59, mean 42 years. All had a diastolic blood pressure (fifth phase recording with mercury

sphygmomanometer) below 85 mmHg.

(b) *Hypertensives*: none had received drugs for at least three weeks before assessment in hospital and all were investigated before or within 24 hours of beginning a standard antihypertensive regimen of oral atenolol and a thiazide diuretic which ensured a slow reduction in blood pressure. The malignant phase of hypertension was diagnosed in the presence of retinal exudates and haemorrhages with or without papilloedema:

(i) *Severe benign hypertension*: eight patients (three women, five men) aged 26 to 43, mean 37 years: mean blood pressure at presentation was 195/130 mmHg and during investigation 167/119 mmHg.

(ii) *Malignant hypertension with past history of raised blood pressure*: five patients (one woman, four men) aged 36 to 55 (mean 45 years), who had a previous history of hypertension of between six months and nine years: the mean blood pressure at presentation was 250/155 mmHg and during investigation it was 218/132 mmHg.

(iii) *Malignant hypertension with no previous history*: eight patients (one woman, seven men) aged 36 to 51 (mean 45 years), who had no previous history of hypertension: the mean blood pressure at presentation was 245/157 mmHg and during investigation it was 217/126 mmHg.

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A defined cause of secondary hypertension was present in one patient in group (ii) (mild renal failure caused by systemic lupus erythematosus) and two patients in group (iii) (glomerulonephritis and chronic pyelonephritis). Three benign and 10 malignant hypertensives were cigarette smokers. A selective renal arteriogram was normal in all seven malignant hypertensives in whom it was carried out.

ELECTROCARDIOGRAPHY

A standard 12 lead electrocardiogram was performed, and the voltage of the S wave in lead V1 plus the maximum R wave in V5 or V6 was recorded in mm. Left ventricular hypertrophy was diagnosed on voltage criteria if this exceeded 40 mm. The presence of ST-T changes was noted. No subject had electrocardiographic evidence of a myocardial infarction.

CHEST RADIOGRAPHY

Standard two metre posteroanterior chest radiographs were examined, and the cardiothoracic ratio was determined by dividing the cardiac transverse diameter by the internal thoracic diameter, expressed as a percentage.

ECHOCARDIOGRAPHY

Echophonocardiography, with simultaneous apex-cardiography and electrocardiography (standard lead II), was recorded in the partial left lateral position with a SK20 ultrasonoscope and a Cambridge multi-channel photographic recorder with a paper speed of 100 mm/second. A left ventricular echocardiogram at the level of the tips of the mitral valve (to define onset of opening) showing clear continuous echoes from both the septum and the posterior wall was used for further analysis. The thicknesses of the inter-ventricular septum and posterior wall were measured at end-diastole (R wave in electrocardiogram) in cm.

Echocardiographs were digitised as previously described by Gibson and Brown,⁵ using a Summagraphics digitiser and a Prime 3000 computer system. From these records the following measurements were made (Fig. 1).

(1) End-diastolic (EDD) and end-systolic (ESD) cavity dimensions in cm. Fractional shortening was derived as (EDD-ESD)/EDD.

(2) Peak normalised rate of reduction of dimension during systole (peak Vcf).

(3) Peak rate of increase in dimension during early diastole (cm/s).

(4) Early diastolic filling period, defined as the period from minimal left ventricular dimension to the time of reduction in filling to 20% of its peak value (ms).

(5) Time intervals in ms (a) Q wave of the electrocardiogram to aortic second heart sound (A_2),

corrected for heart rate ($QA_2 + \text{heart rate} \times 0.21$ (men) or 0.2 (women))⁶ and expressed as QA_2I . (b) A_2 to minimum dimension was taken as negative if minimum dimension followed A_2 and positive if it preceded A_2 . (c) Minimum dimension to mitral valve opening.

(6) Change in dimension between minimum dimension and mitral valve opening (isovolumic relaxation) expressed as a percentage of the total dimension change during the cardiac cycle.

(7) Change in left ventricular dimension during the time of inscription of the upstroke of the apexcardiogram (isovolumic contraction), expressed as a percentage of the total dimension change during the cardiac cycle.⁷

STATISTICAL METHOD

Normally distributed variables are quoted as mean with one standard deviation and those not normally distributed as mean and range. Student's t test and the Mann-Whitney U test were used to test differences between groups where appropriate.

Results

CLINICAL

All normal subjects had normal electrocardiograms and chest radiographs. The mean heart rate in the normal subjects and benign hypertensives was similar (71 and 76 per minute, respectively). Both groups with malignant hypertension had a higher heart rate (previous hypertensive history 85 per minute and no previous history 89 per minute). All patients with benign hypertension, four of the malignant hypertensives with, and four without a previous history, had electrocardiographic evidence of left ventricular hypertrophy on voltage criteria and all but one each of the latter two groups had ST-T wave changes. The cardiothoracic ratio varied from 42 to 60% in hypertensives; it was greater in the malignant hypertensives with a previous hypertensive history (57%) than in those without (47%). Serum urea concentration was raised above 10 mmol/l (60 mg/100 ml) in seven malignant hypertensives.

LEFT VENTRICULAR DIMENSIONS (Table 1)

The left ventricular cavity dimensions in systole and diastole were normal in all three groups of hypertensives. Seven of the malignant hypertensives with no previous history of hypertension had normal posterior wall and septal thicknesses, and one patient had raised values (Fig. 2). The other two groups of hypertensives showed increased thickness of the posterior wall and septum which were significantly different from normal (benign $p < 0.01$, malignant $p < 0.001$). Two with malignant hypertension and an

Fig. 1 Computer output of apex- and echocardiogram of normal subjects (left) and malignant hypertensive with no previous history (right), showing from bottom upwards the original data, continuous left ventricular (LV) dimension and its rate of change, and an apex- echodimension loop. The horizontal line indicates minimum dimension and crosses on dimension trace A_2 and mitral valve opening, respectively. The normalised rate of dimension change is omitted for clarity. In the malignant hypertensive A_2 occurs early and mitral opening late, and there is inward wall motion during the upstroke of the apexcardiogram.

antecedent history had a thickened septum relative to the posterior wall (ratio septum to posterior wall 1.5:1 and 1.3:1).

LEFT VENTRICULAR FUNCTION (Table 2)

In most hypertensives, A_2 preceded minimum dimension. There was a wide range of values in the malignant groups; in two of the five with a previous history A_2 followed minimum dimension but in those without a previous history A_2 occurred significantly

earlier) $p < 0.05$). Analysis of QA_2I confirmed that A_2 occurred significantly earlier in the cardiac cycle in this latter group ($p < 0.05$).

All hypertensive subjects had a significant delay in mitral valve opening ($p < 0.001$) and reduced peak rate of filling ($p < 0.001$). All hypertensives had a dimension change during isovolumic relaxation. Subjects with benign hypertension showed no significant dimension change during the upstroke of the apexcardiogram, while malignant hypertensives as a group showed a reduction in dimension during isovolumic contraction. Fractional shortening and peak Vcf were normal in all groups.

Discussion

Ventricular hypertrophy is known to occur in hypertension¹ and can readily be shown by ultrasound.²⁻⁴ Myocardial adaption in pressure overload hypertrophy is a controversial subject, but it is probable that wall thickening increases with the systolic left ventricular pressure, tending to reduce peak systolic wall stress.^{8,9} The hypertrophied myocardium in

Table 1 Left ventricular dimensions in hypertensives

	No.	Diastolic dimension (cm)	Systolic dimension (cm)
Normal	12	4.6 ± 0.4	2.8 ± 0.4
Benign hypertension	8	4.7 ± 0.6	2.9 ± 0.8
Malignant hypertension with previous hypertensive history	5	4.9 ± 0.7	3.2 ± 0.5
Malignant hypertension without previous history	8	5.1 ± 0.5	3.1 ± 0.4

Fig. 2 Interventricular septum (open circles) and posterior wall (solid circles) at end-diastole in hypertensives. Bars represent the mean.

essential hypertension and aortic valve disease is capable of maintaining adequate cardiac compensation for a long time.

We have confirmed that patients with severe

essential hypertension and malignant hypertension with a previous hypertensive history have a thickened posterior wall and septum.^{2,3} In two of the latter the ratio of septum to posterior wall thickness exceeded 1.3:1; this disproportionate septal thickening has been shown previously.⁴ The left ventricular dimensions were normal in both groups, so that part of the increased cardiothoracic ratio shown by radiography was probably the result of ventricular hypertrophy. Seven of the eight malignant hypertensives not known to have a previously raised blood pressure had normal wall and septal thickness. This has important implications. The malignant phase may follow essential hypertension but often the presymptomatic history of malignant hypertension is unknown, and visual deterioration and cardiac or renal impairment may lead to presentation. Cigarette smoking may be important in the development of the malignant phase,¹⁰ and most of our patients smoked. Experimental studies suggest that myocardial hypertrophy occurs in several subjects weeks after the induction of severe pressure overload.¹¹ The absence of hypertrophy in some patients with malignant hypertension implies that it is sometimes of acute onset and not usually preceded by a prolonged non-malignant phase. Another hypothesis is that the development of myocardial hypertrophy is in some way prevented by the arteriolitis typically found in malignant hypertension. Though these abnormalities are usually found in the kidney, other tissues, including heart,¹ may show fibrinoid necrosis of arterioles and proliferative endarteritis with resultant ischaemia and focal necrosis.

Computerised analysis of the M-mode echocardi-

Table 2 Left ventricular function

	No.	Fractional shortening	Peak Vcf(s^{-1})	QA ₂ I (ms)	A ₂ to minimum dimension (ms)	Minimum dimension to mitral valve opening (ms)	Early diastolic filling Peak rate (cm/s)	Duration (ms)	Dimension change as a percentage of total During isovolumic relaxation (%)	During up-stroke apex-cardiogram (%)
Normal	12	0.39±0.4	2.5±0.4	540±17	-46 (-38 to -54)	10±3	19±3	166±40	0±3	3±3
Benign hypertension	8	0.38±0.7	2.4±1	542±20	-27 (-14 to -41)	70† (56-90)	12±3†	196±30	15† (5-27)	7 (1-16)
Malignant hypertension with previous hypertensive history	5	0.35±0.9	2.2±1	533±34	-9 (-21 to +14)	76† (60 to 106)	11±2†	191±35	20† (5 to 34)	19† (5 to 43)
Malignant hypertension with no previous history	8	0.39±0.8	2.4±1	505±30*	-87* (-47 to -121)	71† (51 to 111)	9±3†	220±43	16† (8 to 23)	27† (14 to 47)

Difference from normal: * $p<0.05$ † $p<0.001$. ± One standard deviation, values in parentheses indicate range.

gram is an excellent method of studying left ventricular diastolic function.⁵ This was frequently abnormal in hypertensives. The timing of mitral valve opening was significantly delayed relative to minimum dimension because of abnormal left ventricular relaxation.² Ventricular filling was abnormal in all hypertensives, peak rate of dimension increase was significantly reduced, and the early diastolic filling period tended to be prolonged in a manner resembling the pattern of mitral⁵ and aortic valve stenosis.² The impaired filling could not be the result of inflow or outflow tract obstruction and has previously been described by Gibson *et al.*² in benign hypertension caused by the abnormal properties of hypertrophied myocardium. During isovolumic relaxation there was a significant cavity shape change as shown by outward endocardial motion. Impaired relaxation with cavity shape change may be found in ischaemic heart disease^{12,13} and hypertrophic cardiomyopathy,² and a similar mechanism with segmental abnormalities of relaxation could occur in malignant hypertension; the exceptionally high end-systolic pressure and its rapid fall after aortic valve closure, however, may be responsible. Therefore, the abnormal myocardial properties in malignant hypertension could be the result of increased stiffness (from hypertrophy in some cases), myocardial ischaemia (from regional or generalised arteriolitis), or pressure overload.

The apexcardiogram has been shown to represent the timing of the left ventricular pressure trace during isovolumic contraction,⁷ and a change in echo dimension during this period is a sensitive and specific method of detecting cavity shape change during the onset of contraction.¹² Abnormal early systolic wall motion has been shown in ischaemic heart disease,⁷ and in hypertrophic and congestive cardiomyopathies and is thought to make a major contribution to impaired function.¹⁴ In hypertensives fractional shortening and peak Vcf were normal; these variables, however, are not representative of function in a ventricle that does not contract uniformly, and both groups of malignant hypertensives showed a reduction in cavity dimension during the upstroke of the apexcardiogram. This may be because of the very high pressures generated or can be explained by a generalised abnormality secondary to arteriolitis or impaired regional wall motion as found in ischaemic heart disease. Further evidence for the unusual properties of the left ventricle, especially in those without a previous history, was the early occurrence of A₂ and hence a much prolonged isovolumic relaxation period, probably a result of the very high end-systolic pressure. This suggests that though early relaxation and filling are abnormal in all hypertensives, early contraction becomes impaired in the malignant phase and was further disturbed in sub-

jects without adequate ventricular hypertrophy to normalise peak systolic wall stress even though ejection remained normal.

Treatment should not be delayed in malignant hypertension, and in some cases the blood pressure was therefore reduced by beta-adrenergic blockade before investigation. This would not affect myocardial hypertrophy and was unlikely to have greatly influenced function, as peak Vcf and fractional shortening remained normal and a similar therapeutic regimen did not induce cavity shape changes in benign hypertensives.

It is not surprising that patients with malignant hypertension have impaired left ventricular function; the combination of increased work from pressure overload, abnormal ventricular stiffness, impaired perfusion from arteriolitis, and areas of focal necrosis readily explains myocardial dysfunction and the high incidence of heart failure previously reported.¹ The role of coronary atherosclerosis is uncertain but may be important as the greatly increased myocardial oxygen demand may exceed blood flow through narrowed vessels which would not normally limit supply. The absence of wall and septal thickening in some patients with malignant hypertension suggests that this phase is sometimes relatively rapid in onset without a preceding benign phase.

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