Heart 2001;**86**:467–475

HYPERTENSION

Essential hypertension: the heart and hypertension

K E Berkin
St James's Hospital, Leeds, UK

S G Ball
Institute for Cardiovascular Research, Leeds General Infirmary, Leeds, UK

Hypertension:

- Is a common risk factor for ischaemic heart disease and heart failure
- Is suboptimally detected and treated
- In the elderly is often systolic only, and treatment reduces risk of coronary heart disease

The heart and hypertension are intimately linked. Hypertension predisposes to coronary heart disease, myocardial hypertrophy, and cardiac dysfunction. Other organs and systems are also important in hypertension but this article concentrates on the effect of hypertension on the heart. The impact of hypertension on the heart is much more important than its effect in causing stroke and renal failure in terms of numbers of patients affected. There is still undue emphasis on diastolic pressure, with little attention paid to isolated systolic hypertension, and treatment remains inadequate for many patients. Cardiologists have a responsibility in this regard. The perspective taken in this article is that of the physician in the outpatient clinic.

Background

General practitioners deal with most hypertension. Patients are usually sent to the hospital clinic because the blood pressure has not been controlled despite multiple drug treatment, for loss of previously good control, where it is felt that a cause for hypertension should be sought, or because of an overt cardiovascular event. The extent and tempo of investigation of the elevated pressure are determined by the clinical situation. Hypertension also presents as an incidental finding in other clinical situations and as a result is often suboptimally managed or even ignored. Attention to blood pressure is surprisingly cavalier in cardiac clinics given its importance as a risk factor. Undoubtedly, it is more difficult to deal with than the measurement of cholesterol and the reflex—albeit appropriate—prescribing of a statin in the patient with known ischaemic heart disease. In light of the cost of coronary angioplasty and bypass graft surgery, especially to the patient, it seems inappropriate not to pursue rigorously the best management of hypertension. Blood pressure recordings after myocardial infarction, revascularisation, and rest in hospital are unlikely to be representative of subsequent levels. Follow up is essential.

Even when undertaken, the measurement of blood pressure is sometimes casual and imprecise. Nonetheless, attaching a number to the reading is important. Inspection of the hospital notes for previous recordings can be useful in determining past levels and the need for treatment. The British Society of Hypertension (BSH) guidelines have been incorporated into the joint British guidelines on the prevention of coronary heart disease,[1] and recommend formal assessment of 10 year coronary heart disease risk as a guide to the treatment of high blood pressure.[2] Cardiac hypertrophy can alter that risk and is not accounted for in the standard risk tables currently in use for primary prevention. Other articles in this series deal with risk assessment and drug treatment.

The level of the pressure and time of exposure appear to be key factors in determining the effect on the heart. However the response of the individual seems varied and the length of exposure is rarely known accurately. This leads to an imprecise relation between the level of pressure recorded in the office and the state of the heart. The underlying *cause* of the hypertension seems unimportant in the development of cardiac problems, except in the rare case of phaeochromocytoma. Here a cardiomyopathy may ensue of such severity that the patient may no longer have raised blood pressure. All patients with cardiomyopathy, irrespective of blood pressure, should therefore have a 24 hour urine collection for measurement of noradrenaline and adrenaline (norepinephrine and epinephrine). Renal artery stenosis should be sought in hypertensive patients with vascular disease, particularly if presenting with recurrent pulmonary oedema and relatively preserved left ventricular systolic function.

Isolated systolic hypertension

Elevation of systolic pressure not accompanied by the expected diastolic rise carries cardiovascular risk, which can be reduced with treatment. In large population surveys systolic pressure continues to rise whereas diastolic pressure peaks in the sixth decade (50–59 years). Systolic pressure is the major determinant of the workload of the heart and cardiac hypertrophy. The wider pulse pressure associated with isolated systolic hypertension (ISH) is associated with an increase in risks from cardiovascular disease and mortality[3] (fig 1). Systolic pressures continue to be ignored by some practitioners and patients, but in numerical terms ISH is probably responsible for more morbidity than the less frequent diastolic hypertension.

Correspondence to:
Professor SG Ball, Institute for Cardiovascular Research, Yorkshire Heart Centre, G Floor, Leeds General Infirmary, Leeds LS1 3EX, UK
cvssgb@leeds.ac.uk

Pathophysiology

Coronary artery disease is one of the most frequent accompaniments of raised arterial pressure. Atheroma is not seen in the pulmonary arteries unless there is pulmonary hypertension, indicating a central role for pressure itself in the genesis of atherosclerotic lesions. Even so, the importance of large vessel coronary heart disease complicating hypertension has probably been underestimated. Modest pressure elevation is common in the population. In this substantial group coronary heart disease, not stroke, is the major clinical issue. In severe pressure elevation the problems of stroke and cardiac failure dominate. Framingham data showed that hypertension was the most common cause of heart failure, but this reflects the poor detection and treatment of hypertension 30–50 years ago. Hypertension is now second to ischaemic heart disease as a cause of heart failure.[4] However, the two conditions frequently co-exist. High pressure initially induces useful compensatory hypertrophy but later decompensation results in heart failure. Myocardial infarction may also play an important part in this decompensation.

Structural changes

Increase in left ventricular mass is a consistent feature of hypertension. Cardiac myocyte cell number does not increase but there is cell hypertrophy. In addition there is considerable interstitial change and fibroblast proliferation. The myocytes account for 70% of the normal cardiac mass but represent only 25% of the cell content.

The changes in small vessel structure are akin to those seen in other tissues in response to pressure elevation, with increase of wall thickness and relative reduction of lumen. However, the haemodynamics of the coronary vessels and the smaller arterioles are different from other organs. Flow is greatest in diastole but the pressure curve in the epicardial coronary arteries follows that of the proximal aorta with which they are contiguous. The smaller intracardiac vessels are subject to extrinsic pressure from contracting cardiac muscle, their feeding pressure and pressure within the ventricular cavity.

An increasing mass of myocardium, made up of larger cells with increased deposition of surrounding collagen, requires more blood supply and relative ischaemia ensues. Exercise tests may indicate ischaemia when the epicardial vessels show no narrowing. Compensatory hypertrophy turns to myocardial failure, with increasing subendocardial ischaemia and subsequent fibrosis.

Additional ischaemia occurs from narrowing of the large epicardial arteries. A stenosis of less than 70% is usually compensated for by dilatation of the smaller arterioles distal to the lesion. However, when the small distal vessels are hypertrophied and subject to increased extrinsic pressure from hypertrophied myocardium, along with raised ventricular pressure, the flow reserve diminishes. Ischaemia occurs at lower workloads. Occlusion of a major vessel may further damage heart muscle and precipitate overt failure in an already compromised vulnerable hypertrophied heart.

Numerous hormonal and neurogenic factors have been postulated to contribute to these changes. The benefit in morbidity and mortality from treatment with both β antagonists and angiotensin converting enzyme (ACE) inhibitors in patients with impaired systolic function, clinical heart failure after myocardial infarction or at high cardiovascular risk suggest at least two important adverse processes amenable to partial correction with treatment. Nevertheless, the reduction of blood pressure itself, irrespective of the mechanism of drug action, appears to both prevent myocardial infarction and reduce the incidence of heart failure.[5]

Hypertrophy is initially concentric. Wall thickness and muscle mass increase, systolic wall stress remains unchanged. At this stage coronary reserve is already compromised. Asymmetric hypertrophy is reported in some 10–15%, affecting the anterior wall, apex, base, and septum. Confusion can then occur with hypertrophic cardiomyopathy, although other distinctive features should be evident on echocardiography. In time the concentrically hypertrophied ventricle dilates and so-called (confusingly) eccentric hypertrophy is observed.

Haemodynamic changes

In young adults with established hypertension, increased heart rate and stroke volume with normal peripheral resistance are reported. Increased peripheral resistance (from the smaller resistance vessels) and loss of compliance (increased stiffness) of large arteries is seen with a consequent increase of mean pressure and pulse pressure, largely through systolic elevation (fig 1). Endothelial dysfunction plays a part in flow modulation via impaired nitric oxide synthesis by the coronary endothelium. Coronary reserve decreases. Myocardial compliance (ventricular distensibility),

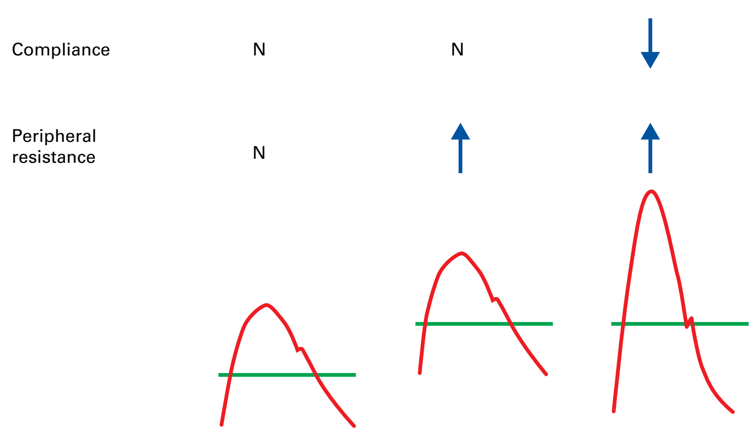


Figure 1. Pressure wave effects of compliance and changes in peripheral resistance. Increase in peripheral resistance is the major cause of the increase in mean blood pressure (horizontal bar) with age. In addition the loss of "distensibility" of the large vessels—that is, the decrease in compliance with age—leads to the change in shape of the blood pressure curve as shown, with relative enhancement of the systolic pressure (right hand curve). When loss of compliance is severe diastolic pressure may even fall as seen in patients in their last decade of life. N = normal; ↑ = increase; ↓ = decrease.

Raised pressure leads to:

- Myocyte hypertrophy, interstitial changes, and fibrosis
- Reduction in flow in intracardiac vessels and endothelial dysfunction—"small vessel disease"
- Epicardial (large vessel) coronary disease
- Increased peripheral resistance and loss of compliance in arteries

measured by the pressure–volume relation, can remain normal even with severe hypertrophy. Decompensation of the ventricle is associated with loss of compliance. The product of the systolic wall stress and the stroke volume is increased but the forward pump function is lessened. The heart function can be supported by reducing afterload, reducing preload (thereby reducing volume so increasing the mass:volume ratio), and inotropes.

Causes of cardiac and vascular changes

Undoubtedly increased blood pressure itself enhances the vessel and cardiac changes alluded to above. The proof is the reversibility of many of these by the lowering of pressure by a variety of means.[6] What initiates and augments the elevation remains largely unknown though extensively investigated.

Clinical approach to the heart in the patient with hypertension

The patient with high blood pressure should be assessed clinically and with selected investigations. Much of this assessment is rightly directed to the heart and is expanded upon below.

Clinical information

Hypertension should be assessed in the context of all the other standard risk factors. Cardiac symptoms and age are clearly relevant as regards any likely underlying heart disease. Obesity, especially if increasing in recent years, is a common cause of worsening breathlessness and blood pressure control (1 mm Hg systolic for each 1 kg increase in weight). The heart may be enlarged on clinical examination with associated third and fourth heart sounds. The presence of a systolic ejection murmur in the elderly without significant gradient increases the risk of cardiovascular death and myocardial infarction by 50%.[7] An accentuated second heart sound, referred to in standard texts, helps little, but any auscultatory abnormality pointing to cardiac involvement in hypertension should stress the need for good blood pressure control. Hypertension is a common cause of atrial fibrillation, which carries its own risks and requires specific treatment. Concomitant cerebrovascular and peripheral vascular disease and other evidence of "end organ damage" increase the likelihood of the presence of cardiac involvement.

Clinical assessment should:

- Establish presence of sustained hypertension if necessary by 24 hour measurement
- Elicit symptoms and signs of coexistent heart disease
- Include assessment of standard risk factors
- Include an ECG
- Consider need for cardiac ultrasound, stress testing, and coronary angiography

The ECG

The ECG is inexpensive, informative, and available routinely. However, lead placement is too often approximate, even on the limbs. This can alter interpretation, particularly for voltage measurement but also for ischaemia (poor R wave progression in the chest leads may be caused by incorrect placement of V2–4). Computer algorithms for interpretation can help to alert the clinician to left ventricular hypertrophy (LVH), which is sometimes overlooked. Silent myocardial infarction is surprisingly common in males in the 40–59 year age group and may be more common in the hypertensive population.[8]

Interpretation, particularly for LVH, must take account of the patient's age and build. In particular the chest lead voltages are increased in young, slim, and athletic individuals and reduced in obesity. Racial differences alter the usefulness of the standard ECG criteria of hypertrophy. Specificity is decreased in blacks.[9] See table 1 for commonly used voltage criteria and fig 2 for ECG examples.

The overall reliability of the ECG in the detection of hypertrophy ranges from less than 10% up to 50% when compared to measurement by cardiac ultrasound, depending on the population screened and ECG criteria chosen. This is well illustrated when electrocardiographic criteria were compared with ultrasound derived evidence of cardiac hypertrophy in 4684 subjects of the Framingham heart study.[10] Voltage criteria combined with borderline and definite repolarisation changes had a sensitivity of only 6.9% but a specificity of 98.8%. Nevertheless, the presence of voltage criteria of LVH *and repolarisation changes* (fig 2) on ECG criteria adds a risk similar to that for a patient with a previously documented myocardial infarction.[11] Indeed, investigation of asymptomatic hypertensive patients with ECG LVH strain shows a high prevalence of epicardial coronary disease. Sudden death is claimed to be six times more common for any given level of blood pressure and is thought more likely to relate to ischaemia rather than a primary arrhythmia, although long QT intervals are seen. LVH based on voltage criteria

ECG

- Inexpensive, informative, and available routinely
- Misplacement of leads may mislead
- Normal ECG does not exclude significant coronary heart disease or hypertrophy
- May detect "silent myocardial infarction"
- Voltage criteria for left ventricular hypertrophy (LVH) are reasonably specific (table 1)
- Voltage criteria for LVH with a strain pattern (table 1) carry risk equivalent to a previous myocardial infarction

without ST/T wave change carries less risk and seems to reflect largely the risk associated with the duration and severity of the hypertension. Non-specific ST/T changes alone carry no more risk than the presence of voltage criteria alone and are less clearly related to pressure levels. The finding of left bundle branch block (LBBB) or left axis deviation in hypertension is not uncommon but the significance is uncertain unless caused by ischaemia. Finally, a normal ECG cannot exclude significant ischaemic heart disease or heart failure in the patient with high blood pressure.

The calculation of independent risk associated with ECG change depends on the use of multiple logistic regression analysis to take account of other factors—for example, age—which themselves exert notable effects. The approach has well described limitations and serves to emphasise the importance of the controlled clinical trial to determine best clinical practice. Observational studies support the notion that antihypertensive treatment reduces the prevalence of high blood pressure and ECG voltage evidence of LVH with mild/moderate repolarisation changes.[12]

Chest *x* ray

An enlarged heart shadow may represent LVH but equally may be caused by chamber dilatation, pericardial fat or technical factors such as poor inspiration and projection. Conversely, an apparently normal sized heart may be hypertrophied or have impairment of function, especially if induced through ischaemia. However, chest radiography can still be important in the assessment of the hypertensive patient and may show left atrial enlargement, pulmonary venous hypertension as a consequence of increased left atrial pressure, abnormalities of the aorta and rarely rib notching.

Cardiac ultrasound

Cardiac ultrasound is not generally recommended in the assessment of all hypertensive patients, but it can be informative in certain situations. The assessment of the LVH is an important but difficult task. Modern ultrasound machines have better capability for

Table 1 Commonly used criteria for ECG left ventricular hypertrophy (LV)

25–50% sensitive*
95% specific*

Chest lead
R wave in V_5 or V_6 exceeds 25 mm
S wave in V_1 or V_2 exceeds 25 mm
Tallest R wave in V_5 or V_6 + deepest S wave in V_1 or V_2 exceeds 35 mm
Ventricular activation time (onset of QRS to peak R) exceeds 0.04 s

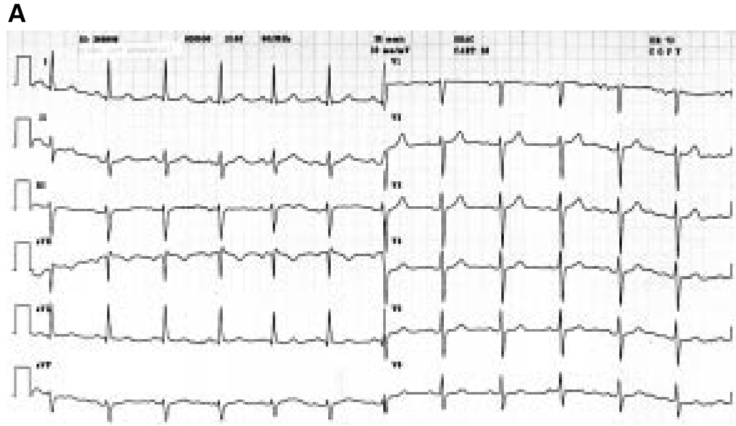
Limb lead
R in aVL exceeds 11 mm
R in I exceeds 12 mm
R in aVF exceeds 20 mm
R in I + S in III exceeds 25 mm
R in aVL + S in V_3 exceeds 13 mm

Repolarisation changes (see note)
Mildly abnormal:
ST-T segment flattening, isolated ST depression or T wave inversion
Severely abnormal:
ST depression with inverted or biphasic T waves
- V_4 to V_6 (that is, leads facing left ventricle)
- 1 and aVL (facing left ventricle when heart horizontal) or
- 11 and aVF (facing left ventricle when heart vertical)

Additional points
LVH results in only slight shift to the left of the frontal plane QRS axis
Horizontal heart: axis = +30° to −30°
Vertical axis: axis = +60° to +90°
There is often counterclockwise rotation—that is, qR complexes appear in the chest leads before the usual V_4 to V_6
Prominent u waves may be seen in the mid and right precordial leads in LVH
Remember digoxin can produce ST/T wave changes and u waves

*Vary with criteria used and population screened—see text.
Note: "strain" refers to the *additional* presence of ST/T wave changes, usually definite ST depression (1 mm) and T wave inversion or biphasic T wave, which are of particular prognostic importance in *the presence of* voltage changes—see text.

A



B

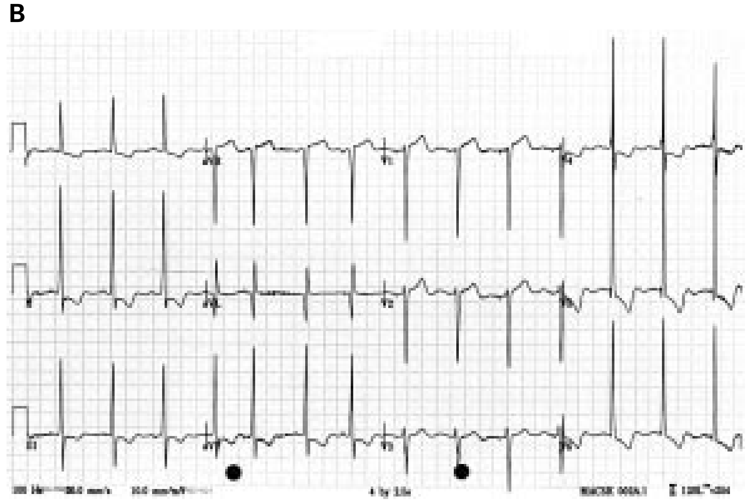


Figure 2. (A) Twelve lead ECG showing left ventricular hypertrophy (LVH) in the limb leads only. The patient was obese, which reduces the sensitivity of the chest leads for LVH. (B) Twelve lead ECG showing LVH and widespread strain pattern. The strain pattern denotes a worse prognosis. Ischaemia (large and/or small vessel) is likely to be present.

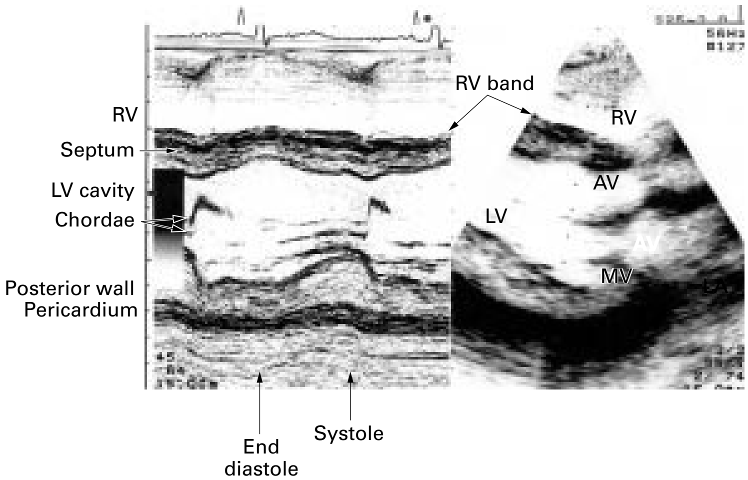


Figure 3. M mode (left panel) and two dimensional (right panel) echocardiography (parasternal long axis view) demonstrating concentric LVH in a female patient (septum 13 mm; left ventricular (LV) cavity 48 mm; posterior wall 13 mm). The measurements (leading edge to leading edge) are taken just beyond the tips of the mitral valve (MV) leaflets at end diastole. Care must be taken not to include the right ventricular band in the septal measurement. RV, right ventricle; AV, aortic valve.

endocardial border detection but accurate measurements of wall thickness can still be difficult and involve a degree of subjectivity. The use of harmonic imaging (present on many of the machines currently on the market) improves image quality but can alter the subjective appearance of wall thickness and must be allowed for by the echocardiographer. Measurements of septal and posterior wall thickness at end diastole (fig 3) or subjective assessment by an experienced echocardiographer usually suffice, but eccentric hypertrophy (chamber enlargement but left ventricular wall thickness remains within normal units despite increased left ventricular mass) may be missed. Greater accuracy is introduced by estimating left ventricular mass using septal, posterior wall, and left ventricular M mode dimensions in diastole, calculating volumes, and correcting for height or body surface area (table 2[13]). Few UK echocardiography laboratories do this routinely because of time constraints and uncertain impact on clinical decisions.

Systolic ejection murmurs are common in the hypertensive. High pressure and loss of vascular compliance can mask the slow rising pulse of aortic stenosis, and echo assessment of the valve and gradient is important. Missed significant aortic incompetence as a cause of systolic hypertension would embarrass most clinicians, but it occurs. Echocardiography is useful in the assessment of associated atrial fibrillation. Detection of regional wall motion abnormalities is useful confirmatory evidence for associated ischaemic damage and may be found in the absence of a history of coronary ischaemia.[14] Increased left atrial size and pulmonary artery pressure may indicate hypertensive damage but are not specific. Non-invasive estimates of left atrial or end diastolic ventricular pressures are not sufficiently robust for clinical use. Calcified aortic cusps—"aortic sclerosis"—are found more frequently in the hypertensive and may be a marker of increased risk through coronary disease.[7]

The ultrasound examination may also give useful information on cardiac function and consequently prognosis. Should the presence of myocardial dysfunction influence the choice of treatment or management? Impaired systolic ventricular function was a major reason to justify treatment with an ACE inhibitor and perhaps to avoid treatment with a β blocker. The recent HOPE (heart outcomes prevention evaluation) study has emphasised that high cardiovascular risk alone is sufficient to warrant use of an ACE inhibitor.[15] The recent β blocker studies[16] now mandate the use of β blockade in patients with heart failure, assuming clinical stability and careful titration of dose. Thus knowledge of left ventricular systolic function does not necessarily influence treatment decisions.

Cardiac ultrasound can sometimes help sort out the breathless hypertensive patient, particularly if there is clear cut evidence of systolic dysfunction or significant valve disease. Patients may, however, be more breathless than expected for a given level of systolic dysfunction, raising the possibility of associated diastolic dysfunction, particularly if LVH is present. Patients with hypertension are often old, and age and hypertension are particularly associated with "stiff ventricles" and consequent breathlessness. The assessment of diastolic dysfunction is controversial and has been the subject of many reviews.[17] Its reported frequency ranges from 10–40%, depending on selection criteria and measurement techniques. Diastolic dysfunction is difficult to establish using current echocardiography techniques, many of which are unduly influenced by fluid loading conditions in the patient. The finding of an apparently normal heart or one with obvious hypertrophy, dilatation or impaired systolic function on echocardiography is helpful in assessing the breathless hypertensive patient. Indeterminate findings are more difficult to interpret clinically.

Magnetic resonance imaging

Assessment of left ventricular wall thickness and overall left ventricular mass using magnetic resonance imaging (MRI) is probably the most accurate non-invasive method for the assessment of LVH. Assessment of left ventricular systolic function and tissue blood flow at rest and with pharmacological stress can also be undertaken. However, there are no substantial studies linking measurements by this approach to outcome. Limited availability and patient acceptance restrict its use at present, but future

Table 2 Echo criteria for LVH and formula for left ventricular mass calculation

Septal and posterior wall thickness are measured just beyond the tips of the mitral valve leaflets Abnormal S > 13 mm men; > 12 mm women Abnormal PW > 12 mm men; > 11 mm women
Left ventricular mass formula (using American Society of Cardiology guidelines, measuring leading edge to leading edge) Left ventricular mass (g) = $0.83\ [(S + PW + LVDD)^3 - LVDD^3] + 0.6$
*Left ventricular mass > 134 g/m^2 (men) *Left ventricular mass > 110 g/m^2 (women)

*Corrected for body surface area. Correction by height in metres is preferred in Framingham outcome studies.
S, septal thickness; PW, posterior wall thickness; LVDD, left ventricular diastolic diameter.

protocols may allow for a single complete investigation of the hypertensive patient, giving information not only on the presence of LVH, but also coronary disease, myocardial structure and function, valve disease, and other important pathology including evidence of renal artery narrowing or adrenal pathology (fig 4).

Ambulatory blood pressure measurement

It seems logical that multiple measurements of blood pressure give a better estimate of "hypertensive load" than a single measurement.[18] This is borne out in the consistency of such 24 hour readings, which have allowed definitions of day and night time normality, and exhibit a closer relation to ventricular mass estimates and coronary events.[19] The daytime average is most usefully compared with the clinic reading. Guidelines suggest adding 10/5 mm Hg to accord with clinic/office readings. The early readings after initial cuff application, if unduly elevated, indicate the presence of the "alerting reaction"; it may be seen again in the hour preceding return of the pressure measuring device. This measurement seems most useful when clinic readings show unusual variability, when blood pressure is resistant to treatment, when there are symptoms suggestive of *hypotension* in the absence of an obvious postural fall, or when "white coat hypertension" is suspected.

Stress testing and the hypertensive

Exercise ECG can be helpful in the diagnosis of associated ischaemia. Generally, the stress test should not be undertaken if the blood pressure is very high (> 220 mm Hg systolic or 115 mm Hg diastolic, or both) and should be stopped if the pressure increases greatly during exercise. It may not be possible to stop antihypertensive drug treatment before exercise testing, thus reducing the sensitivity of the test. The prognostic value of the increase in blood pressure with exercise does not seem greater than for resting blood pressure, even though it is claimed to relate more closely to cardiac hypertrophy. A fall in the level of the patient's usual pressure (in contrast to the "settling" of pressure elevated by anxiety) with increased

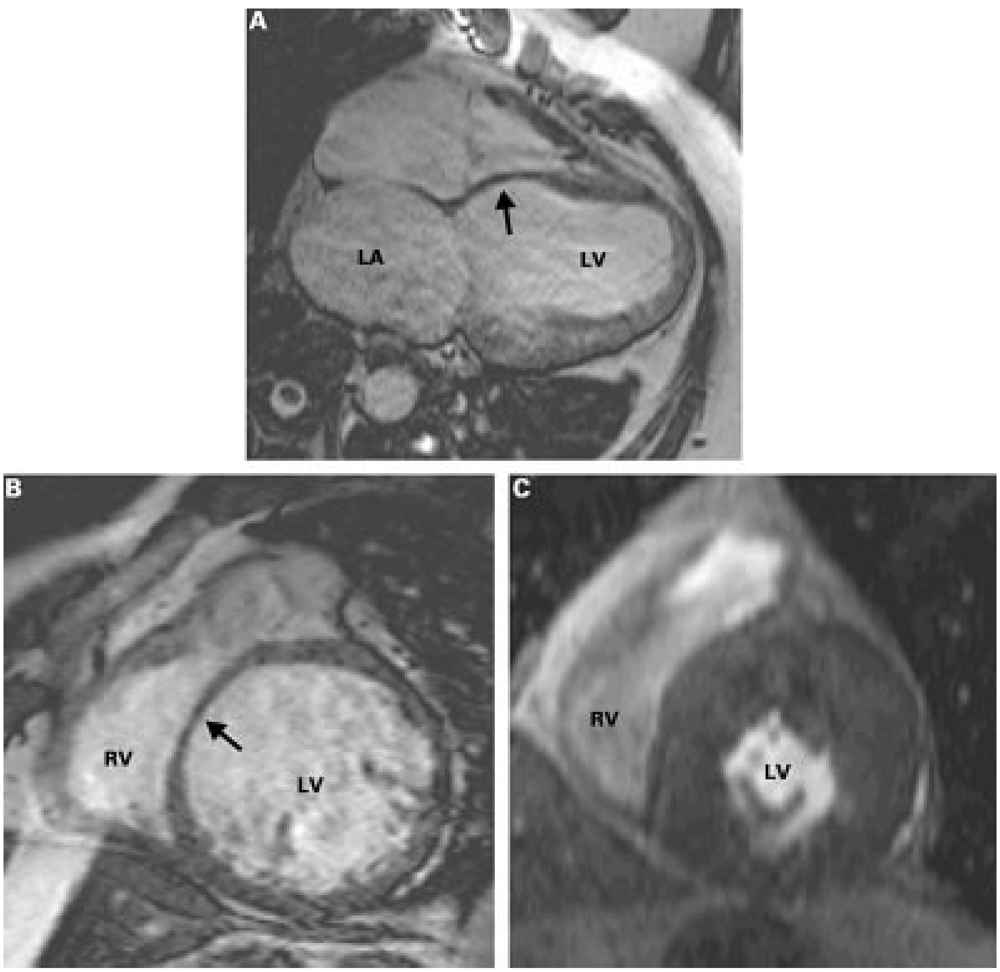


Figure 4. Magnetic resonance images. (A) Long axis view showing pronounced left ventricular dilatation and thinning of the interventricular septum (arrow) (True-FISP acquisition). (B) Mid-ventricular short axis view of the same patient as in (A), showing the dilated left ventricle with thinning (arrow) of the septum (True-FISP acquisition). (C) Another patient but a similar view to (B) acquired from a single phase gradient echo cine and in contrast showing pronounced hypertrophy of the left ventricle. The thin walled right ventricle can be seen wrapping around the left ventricle, lying superiorly and to the left on the cross sectional views. The views are similar to a cross sectional two echo view. Note the clarity of the endocardial border, allowing accurate estimation of left ventricular volume and mass. LA, left atrium; LV, left ventricle, RV, right ventricle. (Images provided by Dr U M Savananthan.)

workload can indicate serious cardiac impairment. The test can be repeated after improved blood pressure control or an alternative stress test method used. The ECG may be difficult to interpret if repolarisation abnormalities or LBBB are present, but the exercise time, symptoms, and blood pressure response can still provide useful information. Alternative stress tests using either pharmacological agents or exercise with echocardiography or nuclear imaging can improve the sensitivity and specificity of ischaemia detection, but are more costly and generally less available. ST segment depression, abnormal response of ejection fraction, and perfusion defects occur without evidence of obstructive epicardial vessel disease in the presence of hypertrophy.[20] Stress echo techniques may be more specific than nuclear techniques for epicardial vessel as opposed to small vessel narrowing.

Coronary and left ventricular angiography

This can be undertaken when significant coronary and/or valve disease is suspected. Blood pressure control should be optimised before arterial puncture. LVH and dysfunction may be evident from the left ventricular angiogram, but in general the non-invasive tests provide this information. Increases in left atrial and left ventricular end diastolic pressures may indicate cardiac involvement in hypertension. Small vessel disease is inferred when stress tests are abnormal but no narrowing of major vessels is seen on angiography.

Left ventricular hypertrophy

How important is the presence of LVH? The relation of LVH with the level of pressure is complex. In part this may relate to never knowing how long blood pressure elevation has been present at any particular level in an individual. The prevalence of hypertrophy increases considerably with age. Many other factors are involved in its development. Black patients were thought to be more at risk for developing LVH for a given level of pressure, but Lee[9] has shown reduced specificity for ECG criteria for LVH in black patients. In general, hypertensive black patients have a lower incidence of cardiac events than whites.[19] In 3220 subjects in the Framingham heart study, apparently free of cardiovascular disease and over the age of 40 years at enrolment, the relative risk of an increment in cardiac mass of 50 g per metre height (substantial), adjusted for age, diastolic blood pressure, pulse pressure, antihypertensive treatment, cholesterol, cigarette smoking, diabetes, body mass index, and ECG evidence of LVH with repolarisation change, was associated with a 49% risk increase in cardiovascular disease in men but at the same time a 49% risk increase in mortality from all causes. For women the cardiovascular and all cause mortality rates were doubled.[21] Given that the accepted clinical approach is to produce optimal pressure reduction in all patients, especially encouraged by the findings of the recent HOT (hypertension optimal treatment) trial,[5] how useful is the knowledge about the presence of LVH in the individual patient? There are no drugs currently to treat cardiac hypertrophy itself, even if echo diagnosed hypertrophy is accepted as carrying risk additional to the pressure measurement. Its findings may encourage the physician and patient to try harder and with more drugs, and sway a treatment decision for "borderline" pressure recordings, but the guide will remain the level of pressure achieved. At the moment there is no convincing trial evidence that reduction of hypertrophy carries any more benefit than that from reduction of the blood pressure per se. It is difficult to see how this hypothesis can be tested without the use of agents that reduce ventricular hypertrophy independent of their effect on blood pressure.

Reduction of blood pressure leads to regression of hypertrophy, measured by a variety of techniques. Extrapolation from animal studies suggests that the reversal is only partial both in the quantity of mass reduced and the quality of the remaining myocardial tissue compared with a normal heart. The dominating factor is the extent of blood pressure reduction. Claims for the superiority of one agent compared with another in reducing hypertrophy, particularly the effectiveness of ACE inhibitors as a group compared with other agents, continue to be debated.[11]

Choice of drug in the hypertensive with concomitant heart disease

Modern treatment of hypertension is centred on the concept of treating according to risk, not simply the pressure level. Traditional trials in hypertension are characterised by the low cardiac event rates, and the evidence for reduction in myocardial infarction or death has been disappointing compared to prevention of stroke. However, the consensus now from many studies is that reduction of blood pressure reduces not only the occurrence of heart failure but also myocardial infarction rates. Fears associated with the J shaped curve and reduction of blood pressure have been largely allayed by the HOT study.[5] Nevertheless patients with a critical stenosis of a coronary vessel, especially if flow reserve is compromised by LVH and its accompanying pathological changes, can develop worsening ischaemia if pressure is greatly lowered.

The HOPE population carried a risk of death, stroke or myocardial infarction of about 4% per year.[15] Those included with hypertension were treated with conventional drugs excluding an ACE inhibitor. Overall blood pressure control was better in the ACE inhibitor treated patients, but those randomised to the ACE inhibitor showed a significant reduction in cardiac event rates well beyond that predicted from the small added blood pressure fall. Previous trials to find superiority of one drug over another have not found differences; the reduction of pressure rather than the agent seems paramount. However, this does not sit easily with the studies after myocardial infarction and in heart failure patients where clear benefit has been seen from ACE inhibitors and β blockers in reducing cardiovascular mortality and myocardial infarction rates. The recent CAPP (captopril prevention project) study specifically compared treatment including or excluding the ACE inhibitor captopril and found no difference in events.[22] However, the study has been heavily criticised. The Swedish STOP-2 (Swedish trial in old patients with hypertension 2) study superficially also appeared to find no difference between agents on event rates.[6] Nevertheless, subgroup analysis does suggest that a regimen including an ACE inhibitor might be beneficial in reducing rates of myocardial infarction.[6] Furthermore the doxazosin arm of the ALLHAT (antihypertensive and lipid lowering treatment to prevent heart attack) study has been stopped, on the basis that fewer patients in the diuretic arm developed heart failure than those on doxazosin. Whether this is because of "pre-treatment" of heart failure by the diuretic or a genuine lack of effect of doxazosin is speculative.[23] The overall mortality and cardiovascular risk is not reduced by treatment to the level of the normotensive.[24] Clearly attention to other risk factors (diabetes, smoking, increased cholesterol) is also important and absolute risk varies widely between populations.[25]

Most patients require at least two agents to control blood pressure adequately, and some three or more. A regimen that includes a β blocker and an ACE inhibitor might be expected to offer some cardiac protection when risk is present. The β blocker will also help control the symptoms of angina. Addition of a vasodilating calcium antagonist may improve symptoms and further reduce pressure. Diuretics remain unequalled for symptom control in the patient breathless from heart failure, offer blood pressure control equal to other agents used alone, combine well with other drugs, and—although they have side effects—are remarkably well tolerated by the majority of patients. Spironolactone no longer has a licence in the UK for the treatment of hypertension, but the recent findings of benefit from this drug in those with severe stable chronic heart failure would justify its use in the hypertensive with heart failure.[26] Lifestyle measures are also important in the reduction of blood pressure levels and thereby LVH.

Aspirin and heart disease

Aspirin is usually prescribed in those with known ischaemic heart disease. Clopidogrel is an alternative in patients genuinely intolerant of aspirin. Aspirin as primary prevention is controversial. The HOT study suggests a relative risk reduction of about 15% for major cardiovascular events, but at the cost of an excess of major bleeding events.[5] When the individual's overall absolute cardiovascular risk is high then the 15% relative risk reduction becomes worthwhile when set against the risk of a serious bleed. The BHS guidelines[2] advocate statin prescription to those with angina or previous myocardial infarction at a total cholesterol concentration of 5 mmol/l or higher under the age of 75 years.

Treatment of hypertension:

- By any agent, if effective, will reduce risk of ischaemic heart disease (IHD)
- Should include β blocker or ACE inhibitor, or both, if heart disease present
- Usually requires two or more agents
- Should include attention to lifestyle and modifiable risk factors
- Should include aspirin for those with IHD, or at high risk of developing IHD

Summary

The effect of hypertension on the heart and therefore prognosis is highly variable and depends not only on the pressure level but also on other factors including age, sex, cholesterol, and smoking. High blood pressure can severely damage the heart, reducing the quality of life as well as longevity. Significant protection is offered to the heart by good control of blood pressure and other risk factors. The higher the risk the greater the absolute benefit the patient can expect. Doctors should not exaggerate the risks of pressure elevation to the individual patient and thereby over claim the benefit likely to accrue from treatment; however good the treatment, it cannot be expected to more than compensate for the associated risk. Understanding of these concepts by both patients and physicians should lead to improved care and protection of the heart through the early detection and rigorous control of high blood pressure.

1. **British Cardiac Society, British Hyperlipidemia Association, British Hypertension Society.** Joint British recommendations on prevention of coronary heart disease in clinical practice. *Heart* 1998;**80** (suppl 2):S1–29.

2. **Ramsay LE, Williams B, Johnston DG,** ***et al.*** Guidelines for management of hypertension: report of the third working party of the British Hypertension Society, 1999. *J Hum Hypertens* 1999;**13**:569–92.
- *The latest guidelines emphasise that the 10 year risk of coronary heart disease (> 15%), diabetes, and target organ damage should be taken into account rather than isolated blood pressure levels. The target level of 140/85 mm Hg should be achieved by standard treatment and lifestyle measures, and control of other risk factors is important.*

3. **Blacker J, Staessen JA, Girerd X,** ***et al.*** Pulse pressure not mean pressure determines cardiovascular risk in older hypertensive patients. *Arch Intern Med* 2000;**160**:1085–9.
- *A meta-analysis of three large trials in systolic hypertension showed that after controlling for mean pressure, a 10 mm wider pulse pressure increased the risk of cardiovascular mortality by 20%. The probability of a cardiovascular end point increased with lower diastolic pressures for any given systolic pressure suggesting that the wider pulse pressure is driving the risk of major complications.*

4. **McMurray JJ, Stewart S.** Epidemiology, aetiology, and prognosis of heart failure. *Heart* 2000;**83**:596–602.

5. **Hansson L, Zanchetti A, Carruthers SG,** ***et al*** **for the HOT Study Group.** Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the hypertension optimal treatment (HOT) randomised trial. *Lancet* 1998;**351**:1755–62.

6. **Hansson L, Lindholm LH, Ekbom T,** *et al.* Randomised trial of old and new antihypertensive drugs in elderly patients: cardiovascular mortality and morbidity. The Swedish trial in old patients with hypertension-2 study. *Lancet* 1999;**354**:1751–6.
- *A prospective randomised trial in 6614 patients comparing traditional (β blocker, diuretics) with newer (ACE inhibitor and calcium antagonists) drugs on cardiovascular events and mortality found a significant and similar decrease in both groups.*

7. **Otto CM, Lind BK, Kitzman DW,** *et al.* Association of aortic-valve sclerosis with cardiovascular mortality and morbidity in the elderly. *N Engl J Med* 1999;**341**:142–7.

8. **Kannel WB, Dannenburg AL, Abbott RD.** Unrecognized myocardial infarction and hypertension: the Framingham study. *Am Heart J* 1985;**109**:581–5.

9. **Lee DK, Marantz PR, Devereux RB,** *et al.* Left ventricular hypertrophy in black and white hypertensives. *JAMA* 1992;**267**:3294–9.

10. **Levy D, Labib SB, Anderson KM,** *et al.* Determinants of sensitivity and specificity of electrocardiographic criteria for left ventricular hypertrophy. *Circulation* 1990;**81**:815–20.
- *The sensitivity and specificity of ECG LVH in 4684 subjects in the Framingham heart study was examined, using echo estimates of left ventricular mass. The sensitivity of the ECG was low, and further reduced in females, obese individuals, and smokers, but increased with age.*

11. **Dunn FG, Pfeffer MA.** Left ventricular hypertrophy in hypertension. *N Engl J Med* 1999;**340**:1279–80.
- *A recent editorial reviewing the risks associated with ECG LVH and the likelihood of regression of LVH with blood pressure control.*

12. **Mosterd A, D'Agostino RB, Silbershatz H,** *et al.* Trends in the prevalence of hypertension, antihypertensive therapy, and left ventricular hypertrophy from 1950 to 1989. *N Engl J Med* 1999;**340**:1221–7.
- *Almost 40 years of follow up on over 10 000 subjects in the Framingham heart study! Over the observation period the use of antihypertensive medication increased, and the prevalence of hypertension (blood pressure > 160/100 mm Hg) reduced as did the prevalence of ECG LVH/strain. It is suggested that the improved detection and treatment of hypertension has contributed to the decline in mortality from cardiovascular disease observed in the USA.*

13. **Devereux RB, Alonso DR, Lutas EM,** *et al.* Echocardiographic assessment of left ventricular hypertrophy: comparison with necropsy findings. *Cardiol* 1986;**57**:450–8.

14. **Gardin JM, Siscovick D, Anton-Culver H** *et al.* Sex, age, and disease affect echocardiographic left ventricular mass and systolic function in the free-living elderly. The cardiovascular health study. *Circulation* 1995;**91**:1739–48.

15. **Heart Outcomes Prevention Evaluation Investigation.** Effects of an angiotensin converting enzyme inhibitor, ramipril, on cardiovascular events in high risk patients. *N Engl J Med* 2000;**342**:145–53.

16. **MERIT-HF Study Group.** Effect of metoprolol CR/XL in chronic heart failure: metoprolol CR/XL randomised intervention trial in congestive heart failure (MERIT-HF). *Lancet* 1999;**353**:2001–7.

17. **Brutsaert DL.** Diagnosing primary diastolic heart failure. *Eur Heart J* 2000;**21**:94–6.
- *This editorial reviews the "minefield" of diastolic dysfunction and failure, emphasising that ventricular relaxation times used for assessment are very variable and dependent on systolic contraction times. Hence abnormal relaxation times are probably caused by early systolic dysfunction, and "pure" diastolic dysfunction is rare (and difficult to measure with current echo techniques).*

18. **O'Brien E, Coates A, Owens P,** *et al.* Use and interpretation of ambulatory blood pressure monitoring: recommendations of the British Hypertension Society. *BMJ* 2000;**320**:1128–34.
- *This recent position paper gives clear guidelines on the application and interpretation of ambulatory pressure, reviews devices available, and includes references to the advantages of ambulatory blood pressure monitoring.*

19. **Khattar RS, Swales JD, Senior R,** *et al.* Racial variation in cardiovascular morbidity and mortality in essential hypertension. *Heart* 2000;**83**:267–71

20. **Frohlich ED.** State of the art lecture. Risk mechanisms in hypertensive heart disease. *Hypertension* 1999;**34**:782–9.
- *An up-to-date review of the contributory factors and pathophysiology of hypertensive heart disease from a world authority.*

21. **Levy D, Garrison RJ, Savage DD,** *et al.* Prognostic implications of echocardiographically determined left ventricular mass in the Framingham heart study. *N Engl J Med* 1990;**322**:1561–6.
- *A total of 3220 subjects in the Framingham heart study with no apparent clinical heart disease had left ventricular mass determined by echo. Over a four year follow up a strong correlation was found with left ventricular mass and adverse outcome, despite correcting for age, blood pressure, treatment, smoking, diabetes, obesity, cholesterol, and ECG LVH. There was a 50% increase in risk for each 50 g per metre in left ventricular mass (corrected for height). Echo is a more sensitive method for the detection of LVH than ECG, and left ventricular mass > 140 g/m indicates a higher risk of adverse events.*

22. **Hansson L, Lindholm LH, Niskanen L,** *et al.* Effect of angiotensin-converting enzyme inhibition compared with conventional therapy on cardiovascular morbidity and mortality in hypertension: the captopril prevention project (CAPP). *Lancet* 1999;**353**:611–5.

23. **Ball SG.** Discontinuation of doxazosin arm of ALLHAT. *Lancet* 2000;**355**:1558.

24. **Andersson OK, Almgren T, Persson B,** *et al.* Survival in treated hypertension: follow up study after two decades. *BMJ* 1998:**317**:167–71.
- *Over 20 years follow up on 686 treated hypertensive men, compared with 6810 non-hypertensives. Despite treatment the hypertensives had increased cardiovascular and total mortality. Regression analysis suggested that the incidence of coronary heart disease was related only to cholesterol concentrations.*

25. **MacMahon S.** Blood pressure and the risk of cardiovascular disease. *N Engl J Med* 2000;**342**:50–2.

26. **Pitt B, Zannad F, Remme WJ,** *et al.* The effect of spironolactone on morbidity and mortality in patients with severe heart failure. *N Engl J Med* 1999;**341**:709–17.