PREVALENCE OF LEFT VENTRICULAR HYPERTROPHY IN HYPERTENSIVE PATIENTS UNDERGOING ECHO CARIOGRAPHY

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ABSTRACT
Left ventricular hypertrophy is an important predictor of cardiovascular risk, and its detection contributes to risk stratification. The aims of the study were to evaluate the prevalence of left ventricular hypertrophy in hypertensive patients and to assess the accuracy of electrocardiography in its diagnosis. Left ventricular hypertrophy (LVH) is an important predictor of cardiovascular risk, and its detection contributes to risk stratification. The aims of the present study were to estimate the prevalence of echocardiographic LVH and to evaluate the influence of echocardiography (ECHO) on cardiovascular risk stratification in hypertensive patients presenting in Khanaqin general hospital.

KEYWORDS: LVH and ECHO.

INTRODUCTION
Left ventricular hypertrophy (LVH) is defined by the increased left ventricular mass; with myocardial cell hypertrophy and an increase in collagen within myocardium.[1] Multifactor etiology for LVH has been implicated including, age, sex, body size, blood pressure and diabetes.[2]

Age, race, gender and body size can influence cardiac mass; this might occur through cardiac load.[3] Hypertensive LVH is a risk factor for high insulin level and insulin resistance. Significant correlation between left ventricular mass, insulin-like growth factor–I (IGF-I) and insulin was observed in a cohort study.[4] Correlation between LVH in first-degree relatives than in second-degree relatives or couples is shown in analyzing of left ventricular mass heritability in the Framingham Heart Study, suggesting that about 30% of left ventricular mass variance is determined by genetic.[5]
Pathological changes induced by chronic pressure overload include an increase in the size of the cardiac myocytes, changing composition of the extracellular matrix with increase of collagen fibers and abnormal changes in intramyocardial coronary vessels. However, most attention has been put on risk factors associated with LVH, and on the beneficial effects of pharmacological treatment, as there is detrimental contribution of LVH to cardiovascular events and survival.

Physical examination may show signs of hypertension and LVH like high blood pressure measurement, augmented aortic sound on auscultation and displaced cardiac impulse palpation. Yet, ECG may be an effective tool in the diagnosis of LVH. Precordial leads may show a negative P wave, anterior leads may have large QRS amplitudes while lateral leads demonstrating deep S and high R as a consequence of LVH. The most popular ECG criteria are the Cornell voltage, the Cornell product, the Sokolow-Lyon index and the Romhilt-Estes point score system (Table 1). Electrocardiography (ECG) limitations are; first, variable diseases present with near similar changes. Second, inaccuracy in some patients like morbid obesity and emphysematous chest. Echo, if available, should be the test of choice to assess for LVH and detect other abnormalities such as left ventricular dysfunction and valvular disease.

Cardiac magnetic resonance imaging (MRI) scan is more accurate for measuring left ventricular mass and is assessed in well-designed epidemiological and clinical studies but ECG and Echo are the cheapest and most readily available tests for LVH.

The development of LVH leads to left ventricular diastolic dysfunction, an important factor in the evolution of congestive heart failure. Furthermore, interstitial myocardial fibrosis and an increased myocardial mass reduce coronary flow reserve leading to impaired tolerability and myocardial ischemia. Also there is enough evidence showing that LVH causes arrhythmia. The aim of this study is to evaluate and show the prevalence of LVH in hypertensive cases and to assess the accuracy of ECG in diagnosing LVH.

**HYPERTENSION AND LEFT VENTRICULAR HYPERTROPHY**

In hypertension, left ventricular hypertrophy (LVH) is initially a useful compensatory process that represents an adaptation to increased ventricular wall stress; however, it is also the first step toward the development of overt clinical disease. The Framingham study has shown that
the prevalence of LVH, according to EKG criteria, is quite low in a general population sample (about 3%). Using the echocardiographic technique, it has been demonstrated that the prevalence of LVH in the Framingham population increases from 5% in subjects younger than 30 years to 50% in those older than 70 years. The Framingham study has also shown that the prevalence of echocardiographic LVH is 15.20% in mild hypertensive patients and increases further in patients with more severe hypertension.\(^1\) The increase of LV mass with age might reflect the influence that other risk factors exert with time on the development of LVH. The relationship of echocardiographic LV mass with clinical blood pressure is usually weak. Twenty-four hour blood pressure recordings have shown a much closer correlation between LV mass and average daily blood pressure.\(^2\) Non-haemodynamic factors, such as age, sex, race, body mass index, diabetes, or dietary salt intake may contribute to determining whom, among hypertensive patients, develop LVH and to what degree LVM is increased.

In fact, the coexistence of hypertension with diabetes increases the prevalence of LVH. Moreover, insulin resistance and high insulin levels are associated with the development of LVH in hypertensive patients. Other major cardiometabolic risk factors, notably hypercholesterolemia and hyperglycaemia, may also modify the extent of LVM and the prevalence of LVH in the hypertensive population. Genetic factors might also exert a powerful modulation of LV mass; in fact, monozygotic twins have more similar LV mass values than dizygotic twins.\(^3\)

**Diagnosis of LVH**

Several diagnostic criteria for LVH diagnosis can be used. Electrocardiography has a low sensitivity for LVH detection, but nonetheless LVH diagnosed by the Sokolow-Lyon index or the Cornell voltage-duration product has been shown to be an independent predictor of cardiovascular events.\(^4\) Electrocardiography can also be used to detect patterns of repolarization abnormalities and arrhythmias, including atrial fibrillation. Echocardiography is a specific, repeatable and far more sensitive measure of LVH in comparison with EKG. Proper evaluation includes calculation of LV mass according to M-mode measurements, under two-dimensional control, of LV internal diameter and wall thickness, according to ASE recommendations or the. Penn Convention.

These methods have been validated with measurements obtained by necroscopic examination. Measurements of LV wall thickness and internal dimensions from 2D images can be also performed. Although the relationship between LV mass and incidence of
cardiovascular events is continuous\textsuperscript{[5]}, ESH/ESC guidelines indicate that the thresholds of 125 g/m\textsuperscript{2} BSA in men and 110 g/m\textsuperscript{2} in women may be used for conservative estimates of LVH.\textsuperscript{[6]} An assessment of LV mass reproducibility, one of the major technical limitations of echocardiography, has shown that LV mass changes of 10 to 15\% may have true biological significance in individual patients.\textsuperscript{[7]} Geometric adaptation of the left ventricle to increased cardiac load may differ among patients. Concentric hypertrophy is characterized by increased mass and increased relative wall thickness, whereas eccentric hypertrophy is characterized by increased mass and relative wall thickness < 0.42; concentric remodelling occurs when there is increased thickness with respect to radius, in the presence of normal LV mass.\textsuperscript{[8]} These LV geometric patterns are associated with different haemodynamic characteristics, and peripheral resistances are greater in patients with concentric geometry, while cardiac index is increased in those with eccentric hypertrophy. Evaluating LV mass increase by taking into account gender and cardiac loading conditions has been proposed in order to discriminate the amount of LV mass adequate to compensate the haemodynamic load (adequate or appropriate) from the amount in excess to loading conditions (and therefore inappropriate or non-compensatory). LV mass is inappropriate when the value of LV mass measured in a single subject exceeds the amount needed to adapt to the stroke work for that given gender and body size.\textsuperscript{[9]}

**Prognostic value of LVH and its regression by treatment**

A large number of studies have reported on the relationship between LVH at baseline examination, measured either by EKG or by echocardiography, and the risk of subsequent morbid or mortal events in clinical or epidemiological populations.\textsuperscript{[4]} Despite the fact that electrocardiography has a low sensitivity for LVH detection, LVH diagnosed by the Sokolow-Lyon index or the Cornell voltage-duration product is an independent predictor of cardiovascular events.\textsuperscript{[4]} Direct measurement of LV mass by echocardiography (M-mode, under twodimensional control) has proved to be a strong predictor of the risk of cardiovascular morbidity and mortality; subjects with LVH consistently have 2 to 4 or more -fold higher rates of cardiovascular complications, independent of other risk factors such as hypercholesterolaemia, age, and blood pressure measured in the clinic or by 24-hour blood pressure monitoring.\textsuperscript{[4]} Concentric hypertrophy appears to carry the highest risk and eccentric hypertrophy an intermediate risk. The presence of inappropriate LV mass is also associated with an increased number of cardiovascular events, even in hypertensive patients without LVH.\textsuperscript{[10]} The prognostic significance of changes in EKG criteria of LVH has been
demonstrated in the Framingham population\textsuperscript{[11]}, in high CV risk patients\textsuperscript{[12]}, in hypertensives with isolated systolic hypertension\textsuperscript{[13]} or with EKG-LVH\textsuperscript{[14]} (Table 1). Other observational, prospective studies have examined the potential clinical benefits of regression of echocardiographic detectable LVH, and have demonstrated that changes in LV mass, during treatment, may imply an important prognostic significance in hypertensive patients (Table 2). The results of these studies\textsuperscript{[15,18]} have also been analysed in a metaanalysis.\textsuperscript{[19]} They have clearly shown that subjects who failed to achieve LVH regression, or in whom LVH developed during follow-up, were much more likely to suffer morbid events than those in whom LVH regressed or never developed. In these studies, LV mass changes during antihypertensive treatment and age were the most important factors related to the occurrence of cardiovascular fatal and non-fatal events in hypertensive patients. Further information was obtained in the LIFE echocardiographic sub-study, performed according to a prospective, interventional, controlled design. In this study, including 930 patients with EKG LVH, a decrease of 25 g/m\textsuperscript{2} (i.e. one standard deviation) of LV mass index was associated with a 20\% reduction of the primary end-point, adjusting for type of treatment, basal and treatment BP, and basal LV mass index.\textsuperscript{[20]}

Table 1: LVH and risk of cardiovascular (CV) events.

<table>
<thead>
<tr>
<th>Reference</th>
<th>N\textdegree patients</th>
<th>Average follow-up yrs</th>
<th>CV events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levy et al. 1994</td>
<td>524 Framingham population 1</td>
<td>36 EKG bi-annual examination</td>
<td>Decrease in voltage vs no change OR 0.46 (95% CI 0.26, 0.84) male OR 0.56 (95% CI 0.30, 1.04) female Increase in voltage vs no change OR 1.86 (95% CI 1.14, 3.03) male OR 1.61 (95% CI 0.91, 2.84) female</td>
</tr>
<tr>
<td>Matthew et al. 2011</td>
<td>8281 High CV risk patients</td>
<td>2.8</td>
<td>12.3% in patients with LVH regression/absence 15.8% in patients with LVH persistence/development</td>
</tr>
<tr>
<td>Fagard et al. 2004</td>
<td>4159 Older patients with systolic hypertension</td>
<td>6.1</td>
<td>14% decrease in cardiac events for 1 mV change in EKG voltage</td>
</tr>
<tr>
<td>Okin et al. 2004.</td>
<td>9193 Patients with EKG LVH</td>
<td>4.8</td>
<td>20.4% decrease in composite endpoint for 10.5 mm (1 SD) Sokolow Lyon Index 15.4% decrease in composite endpoint for 1050 mm × × msec (1 SD) Cornell product</td>
</tr>
</tbody>
</table>

The information obtained in the metaanalysis and in the LIFE study should be considered complementary. In fact, while the observational prospective studies have analysed younger patients, with or without LVH at baseline, with follow-up examinations by their family doctors, in the LIFE study all patients had EKG-LVH and were older, at higher cardiovascular risk, were randomized to receive antihypertensive treatment and were followed according to a clinical prospective protocol. The prognostic significance of LVM
changes in subgroups of patients at higher CV risk (diabetics, patients with previous stroke or MI) deserves further investigation. Changes in geometric adaptation seem to imply a prognostic value, independent of changes in LV mass. The persistence, or development of, a concentric geometry during treatment has been found to be associated with a greater incidence of cardiovascular events, independent of changes in LV mass.\(^{[21]}\)

The LIFE study has provided results that confirm the prognostic influence of LV geometry, in addition to changes in LV mass.\(^{[22]}\) A better prognosis associated with regression of LVH may be related to the improvement of systolic and diastolic function, to the increase of coronary flow reserve and to the decrease of cardiac arrhythmias. ESC/ESH guidelines suggest that echocardiography should be performed in patients at low or intermediate CV risk in order to better identify global cardiovascular risk, and to start more appropriately pharmacological treatment.\(^{[6]}\)

In fact, it has been shown that an increase of echocardiographic LV mass can be identified in 25.30% of hypertensive patients with a low or moderate CV risk (based on risk factor evaluation and EKG), thus substantially changing the original risk stratification.\(^{[23, 24]}\) There is no evidence that an echocardiographic study may modify the therapeutic strategy in patients at high or very high CV risk. In patients at high CV risk, and in particular in patients with aortic valve disease, or in patients with asymptomatic LV dysfunction, echocardiography may be useful to better define and follow cardiovascular anatomical and functional alterations.

At this time, the echocardiographic instrumentation for LV mass measurements is widely available in most western countries; hopefully, with reduction of price, its use will be expanded worldwide. Among other diagnostic procedures, usually reserved for specific indications, nuclear magnetic resonance provides the most precise measurements of LV mass and cardiac tissue constitution; however, the cost of NMR prevents large-scale use in hypertension. Techniques based on the reflectivity of cardiac ultrasound imaging have been used in order to assess the degree of cardiac fibrosis and to improve the ability of increased LV mass to predict the outcome, together with the use of new biomarkers such as circulating markers of collagen tissue composition.

It has been demonstrated that an effective, long-term antihypertensive treatment, inducing a gradual, constant and homogeneous control of 24-hour blood pressure values, may determine
a significant reduction and even a normalization of LVH.\textsuperscript{[25]} However, available studies have also suggested that regression of LVH may be more rapidly or more completely obtained by the use of some classes of antihypertensive drugs such as Angiotensin receptor blockers, ACEinhibitors and calcium antagonists.\textsuperscript{[26, 27]} Echo-reflectivity studies have suggested that tissue composition of the left ventricle may vary, and that drugs favouring LVH regression may affect myocardial fibrosis differently.

LEFT ventricular hypertrophy (LVH) plays a dual role in patients with systemic hypertension — being both a necessary adaptation to pump a normal amount of blood against the increased pressure load and a pathologic manifestation of hypertensive cardiovascular disease. For many years, knowledge of the complex status of the heart in human hypertension advanced slowly because of the lack of suitable means of measuring cardiac anatomy and function in unselected hypertensive patients or of following their natural history. The development over the last decade of accurate echocardiographic methods for detection of LVH and characterization of ventricular contractile performance has catalyzed an explosion of information about the heart in hypertension.

In this review, we summarize the available data to provide preliminary answers to the following questions: Do all patients with systemic hypertension exhibit cardiac involvement? Is hypertensive cardiac hypertrophy closely related to the level of blood pressure, or does it convey independent information about disease severity? Are cardiac findings related to cardiovascular dynamics in patients with hypertension? Do neural or endocrine factors directly influence the heart — beyond their influence on hemodynamics.

Detection of LVH by echocardiogram depends not only on the established accuracy of the method in reflecting anatomic findings\textsuperscript{1,2} but also on use of correct normal limits. Although considerable progress has been made in establishing statistically reliable and reproducible normal limits,\textsuperscript{3, 4} no single criterion is yet completely validated and universally accepted. Despite this, tentative conclusions may be drawn about the prevalence of LVH among patients with hypertension by examining the results of studies in which hypertensive patients and normotensive controls were evaluated by identical echocardiographic methods.

This approach can be applied in four available clinical studies of patients with essential hypertension\textsuperscript{5-8} that include comparison groups of apparently normal subjects.\textsuperscript{6-9} In these studies the overall prevalence of LVH was determined by applying identical cutoffs for left
ventricular (LV) mass indexed for body size (e.g., LV mass/body surface area > 120 g/m2) to both patients and control populations. The prevalence of LVH was 23 to 48% in hypertensive patients and 0 to 10% in normal subjects (Figure 1). Overall, 189 of 450 (42%) of hypertensive patients and 9 of 251 (3.6%) of controls exhibited LVH (chi square test = 117.1, p< 10^-6).10 These data establish that LVH occurs in a substantial minority of patients with mild to moderately severe essential hypertension evaluated in a referral center. The finding that LVH was detected by echocardiogram in a slightly higher percentage of apparently normal subjects than had been expected statistically for upper 95% confidence limits (3.6% vs 2.5%) may reflect a slight random fluctuation of results in a moderate sized sample or admixture of a few individuals with clinically undetected heart disease. A recent study” indicates that the prevalence of LVH by the same echocardiographic criteria is somewhat lower — 17% and 21%, respectively — among unselected patients with uncomplicated borderline or established hypertension drawn from an employed population. Further information about the prevalence of LVH in patients with hypertension has been derived from more recent studies of factors that influence normal LV mass or appear to modify the cardiac response to hypertension. Of greatest importance in this regard is recognition of demographic variables that should be taken into account in determining statistically valid upper limits of normal LV mass. All available studies agree that LV mass should be indexed by body size, of which body surface area appears to be the best measure by a narrow margin.4 Similarly, the three largest echocardiographic studies of normal subjects3—**have found that LV mass indexed by body surface area differs significantly between men and women, and the primary LV measurements reported by Valdez et al.12. are in accord with this conclusion. The tentative cutoff values we have proposed for recognition of LVH, representing the 97th percentile of values in apparently normal subjects,4 are 2111 g/m2 in women and a 135 g/m2 in men.

Effect of Sex The prevalence of LVH found in men and women with essential hypertension is strikingly dependent on whether one uses such sex-specific criteria or a single criterion of LV mass indexed for body surface area. When a single cutoff value for hypertension is applied to both sexes, the prevalence of LVH is consistently higher among men (26-56%) than women (18-42%) in clinical studies7’13’14 (Figure 2A). When sex-specific criteria are used, however, a higher proportion of female (43-61%) than male (18—41%) hypertensive subjects exhibit LVH (Figure 2B). We have recently obtained similar results (i.e., a higher prevalence of LVH in women by sex-specific criteria and in men by unified criteria) in a study of
patients with hypertension in an employed population." The reasons for this discrepancy between men and women with hypertension are not clear but might include either a selective reduction in physical activity among men with hypertension or a substantial prevalence of clinically inapparent heart disease, associated with mild LVH, among apparently normal men. Longitudinal studies of physical activity, cardiac status, and cardiovascular morbidity will be needed to determine the cause.

Influence of Race No difference has been detected between normal black and white subjects in any echocardiographic measurement of LV anatomy or function." In contrast, both Dunn etal.16 and our group" 15 have reported that black patients with essential hypertension have a greater degree of LVH than white patients with similar levels of clinically measured blood pressure, but this was not found in a previous study.17 Our findings demonstrate a significant increase in relative wall thickness, an index of concentric LVH, in black patients compared to white patients of similar age, duration of hypertension, and prior treatment status identified through the same worksite clinics (Table 1). In the same group, the greater degree of concentric LVH among black patients was associated with a modest elevation of peripheral resistance (Table 1), whereas white patients from the same population exhibited an increased cardiac output without a significant increase in peripheral resistance.15 This evidence of greater concentric LVH and a hemodynamic pattern felt to characterize more advanced hypertension in black as compared to white patients makes an interesting parallel with the known higher incidence of cardiovascular morbidity in black hypertensive persons,18 although it has not yet been established whether the excess morbidity among blacks is accounted for by the subset with concentric LVH.

Age and Hypertensive Cardiac Hypertrophy Both increasing age and duration of hypertension would logically be expected to be associated with a higher prevalence and greater severity of hypertensive cardiac hypertrophy, but we have not been able to demonstrate this in cross-sectional studies of large clinical6’7 or unselected” populations of patients with systemic hypertension. Evidence does suggest, however, that a small proportion of elderly hypertensive patients develop severe LVH associated with symptoms of cardiac dysfunction. Topol et al.[19] recently reported 21 elderly patients with systemic hypertension, predominantly black women, with a mean age of 73 years, who exhibited severe concentric LVH, supernormal LV systolic function, and severely impaired early diastolic LV filling. In an echocardiographic study of the original Framingham cohort (mean age, 70 ± 7 years),
Savage et al. [20] found that 27 of 1620 (1.7%) exhibited disproportionate thickness of the interventricular septum, associated in nearly all such subjects with a history of at least mild hypertension as well as a high prevalence of heart murmurs and cardiac symptoms. By their design, neither of these reports permits calculation of the prevalence of cardiac hypertrophy among elderly patients in whom system hypertension has been diagnosed by conventional clinical criteria although the Framingham Study has an optimal data base in which to do so.3.

**Hypertensive Cardiac Hypertrophy and Blood Pressure**

Although early studies of highly selected patients suggested that heart weight was closely related to the level of arterial blood pressure, [21] it is now clear that this is not normally the case. In several groups of patients with uncomplicated essential hypertension, physician measurements of systolic blood pressure have been only weakly related to echocardiographic LV mass, with correlation coefficients of 0.24 to 0.45.7'13[22-23] Even weaker correlations were observed in these studies between diastolic arterial pressure and LV mass. A similarly modest relationship (r = 0.43) was observed by Abi-Samra et al. [24] in a study of 74 patients with systemic hypertension.

**Ambulatory Blood Pressure**

Twenty years ago Sokolow et al. [25] reported that evidence of cardiovascular damage in patients with hypertension was more closely related to blood pressure measured by a portable recorder than by physicians. More recently, the same group has reported that ambulatory blood pressure measurements were better predictors than casual determinations of subsequent morbid events in patients with hypertension. [26] Both these studies, however, used an ambulatory recording system that was patient-activated thus precluding complete 24-hour recordings, and also employed indirect means of detecting LVH, such as the electrocardiogram.

Recording blood pressure through the entire 24-hour period has been made possible by development of invasive [27] and noninvasive [28-29] M systems with acceptable accuracy. Because of their greater acceptability and safety, noninvasive systems have been most widely used and have provided important information about blood pressure variability [30] with implications for patient management. [31] Three studies have compared the relationships between echocardiographically determined LV mass and physician or 24-hour blood pressure measurement.7[32-33] In each study average 24-hour systolic blood pressure was the closest
correlate of LV mass (Table 2). To gain further insight into the relationship between cardiac hypertrophy and Blood pressure during normal activity, we categorized ambulatory blood pressures by the setting in which they were recorded (e.g., physician's office, occupational workplace, home, and sleep). The closest relationships were observed between LV mass index and average workplace systolic blood pressure ($r = 0.50, p<0.001$) and between end-diastolic relative wall thickness and average workplace diastolic blood pressure ($r = 0.59, p<0.001$). In this study LV mass was less closely related to peak blood pressure than to the average workplace blood pressure. These data suggest that the blood pressure response to regularly recurring stress may have particular importance in the pathogenesis of hypertensive cardiac hypertrophy.

Other Blood Pressure Measurements

Because obtaining precise 24-hour ambulatory blood pressure recordings is cumbersome and technically difficult, considerable attention has been devoted to finding other methods of obtaining a reliable estimate of patients' average blood pressure. Two recent studies have yielded promising results. In the first, we demonstrated that home blood pressure recordings by trained patients not only provided a better estimate of average 24-hour blood pressure than did physician measurements but also were more closely correlated to indices of LVH. The second study, by Ren et al.,[34] reported a substantially closer relationship of LV mass to maximum systolic arterial pressure during treadmill exercise testing than to blood pressure at rest prior to exercise.

Hypertensive Cardiac Hypertrophy and Cardiovascular Dynamics

Because cardiac hypertrophy is felt to be an important adaptive response to hypertension, consideration must be given to the degree to which LVH is matched to the hemodynamic load and is successful in maintaining cardiac performance in hypertension. In the first studies in this regard, performed by Folkow[35] in experimental animals, the severity of cardiac hypertrophy tended to parallel the severity of peripheral vascular resistance. In a subsequent study by Shkhvatsabaya and coworkers,[36] echocardiographically determined LV mass correlated significantly ($r = 0.60, p<0.001$) with vascular resistance in the calf, measured by plethysmography during maximal vasodilation. Extending this line of investigation to 100 patients with essential hypertension, we examined the relationships between systemic hemodynamics and the pattern of LV anatomy.[13] A significant positive correlation ($r = 0.52$, #
p<0.001) was observed between total peripheral resistance and end-diastolic LV relative wall thickness (Figure 3A). Furthermore, cardiac index was inversely related to relative wall thickness (r = −0.47, p < 0.001) (Figure 3B). Taken together, these experimental and clinical studies suggest that the cardiac pattern of concentric LVH and the hemodynamic pattern of elevated peripheral resistance with low cardiac output are pathophysiologically interrelated.

**Left Ventricular Performance**

To investigate further the relationships between cardiac structure and function, we have performed an additional series of studies. In order to exclude the possibility that excessive or inadequate degrees of LVH in relation to blood pressure load accounted for differences in LV function, we measured myocardial afterload by calculating end-systolic LV wall stress with a catheterization-validated formula.[37] As predicted from basic principles of cardiac mechanics, a close inverse relationship existed in 87 normotensive subjects between end-systolic stress and LV fractional shortening, an echocardiographic index of systolic ventricular performance (r = -0.83, p<0.001). A significant inverse relationship between these variables was also observed in 81 unmedicated patients with essential hypertension (r = -0.78, p<0.001). When the data points from the hypertensive patients were superimposed on 95% confidence limits derived from the normal subjects (Figure 4), a significant proportion of the hypertensive patients exhibited high fractional shortening in relationship to wall stress (19 of 81 or 23%; />0.001 vs 1 of 87 normotensive subjects). Subdivision of hypertensive patients into groups with normal and increased LV performance based on this analysis of cardiac mechanics revealed striking differences in both systemic hemodynamics and LVH (Table 3). Of note, the patients with increased ventricular performance exhibited substantially increased cardiac output, lower peripheral resistance, and an absence of LVH compared to the hypertensive patients with normal ventricular performance. In a more recent study from our laboratory, hypertensive patients who had high fractional shortening in relation to end-systolic stress on baseline measurements exhibited a significantly higher (p< 0.005) slope of the end-systolic force-length line during nitroglycerin-induced reduction in hemodynamic load than hypertensive patients who fell into the normal range of fractional shortening in relation to end-systolic stress.[39] Taken together, these studies suggest that in the majority of mildly hypertensive patients the heart plays a secondary role, undergoing adaptive hypertrophy in proportion to the elevation of blood pressure. In a significant minority of such patients, however, increased myocardial contractility may have pathogenetic importance by allowing the heart to pump an increased cardiac output without need for any hypertrophy.
Since an important capacity of the normal heart is the ability to sustain a strikingly increased hemodynamic load during normal activity, assessment of the heart in hypertension is not complete without evaluation of the cardiac responses to exercise. This has been directly evaluated by means of radionuclide cineangiography at rest and during exercise in several recent studies. Among hypertensive patients with no evidence of coronary artery disease, the prevalence of abnormal LV ejection fraction responses to exercise has ranged from 9 of 37 patients (24%) to 15 of 20 patients (75%). Our studies indicate that a small proportion — approximately 10% — of the hypertensive patients who exhibit abnormal LV functional reserve can be identified by evidence of impaired myocardial contractility (low echocardiographic fractional shortening in relation to end-systolic stress) at rest; whereas in the remainder, LV dysfunction is only revealed by imposition of exercise stress. A preliminary study from our laboratory suggests that LV dysfunction during exercise and LVH are closely linked, with an inverse linear relationship (r = -0.50, p<0.01) between echocardiographically determined LV muscle mass and the change in LV ejection fraction from rest to exercise observed among hypertensive patients with LVH. The ability of the left ventricle to sustain a normal or increased workload is also dependent on its diastolic performance characteristics. Abnormalities of LV diastolic time intervals and filling rates have been well documented in patients with systemic hypertension and may be a more sensitive marker of hypertensive cardiac involvement than echocardiographic LVH. These diastolic abnormalities appear to be manifestations of so-called pathologic LVH since subjects with a similar degree of exercise-induced physiologic hypertrophy exhibited normal LV diastolic properties in one study.

**Blood Viscosity**

Several lines of evidence suggest that altered blood rheology may be importantly related to cardiac findings in hypertension. Hematocrit and blood viscosity have been found to be higher in hypertensive than normotensive individuals. Recently we reported a modest direct relationship between blood pressure and whole blood viscosity in both hypertensive and normotensive subjects. We found that increased whole blood viscosity in unselected patients with mild essential hypertension accounted for the entire increase in peripheral resistance in them as compared with normotensive subjects drawn from the same employed population. Finally, high rates of cardiovascular morbidity have been reported in patients with hyperviscosity due to hypertension or so-called pseudo-polycythemia. No study, however, had related blood viscosity to objective cardiac measurements in patients with
hypertension. Therefore, we recently undertook a study to examine the relationships among arterial blood pressure, whole blood viscosity, and LVH in 24 patients with essential hypertension and 13 age- and sex-matched control subjects. A significant correlation was observed between mean arterial blood pressure and whole blood viscosity in this study population ($r = 0.52, p<0.005$). Similarly, mean blood pressure was modestly related to LV mass in the hypertensive patients ($r = 0.47, p<0.02$) and in the normotensive subjects ($r = 0.44, p = NS$). A close correlation was observed (Figure 5B) between whole blood viscosity at the high shear rate of 104 sec$^{-1}$ and LV mass in the hypertensive patients ($r = 0.80, p<0.001$), which was significantly closer than the correlation between mean blood pressure and LV mass ($p<0.02$). Furthermore, as shown in Figure 5B, the relationship between viscosity and LV mass in normotensive subjects closely resembled that in the hypertensive patients with normal whole blood viscosity.

### Neurohumoral Factors and Hypertensive Cardiac Hypertrophy

Although hemodynamic factors have received the most attention in studies of the pathogenesis of hypertensive cardiac hypertrophy, considerable scatter clearly exists in the relationships between the best available measures of blood pressure and LV muscle mass. The search for nonhemodynamic causes of LVH in hypertensive patients has focused mostly on neurohumoral factors, principally the sympathetic and renin-angiotensin systems.

Evidence in favor of the so-called catecholamine hypothesis of LVH was originally derived from studies using sympathetic agonists and antagonists in intact animals. More recently, Simpson and co-workers have provided evidence that induction of protein synthesis by norepinephrine in tissue-cultured cardiac myocytes is an $a_{1}$-receptor-mediated phenomenon. Limited studies in patients with essential hypertension have suggested a positive relationship between plasma norepinephrine concentration and LV mass and a greater reduction in LV mass than blood pressure during treatment with sympatholytic drugs. These results have not been consistently observed, however, and recent observations in patients with pheochromocytoma suggest that applicability of the catecholamine hypothesis to clinical hypertension may be limited. The suggestion that renin-angiotensin system activity directly stimulates myocardial hypertrophy is also based primarily on experimental observations. Thus, Robertson et al. reported that radiolabeled angiotensin II rapidly localized in nuclei of cardiac and smooth muscle cells, while
Khairallah and Kanabus\cite{65} have documented a significant increase in ventricular weight after 6 days of angiotensin II infusion at a mildly pressor dose. Some studies of patients treated with angiotensin converting enzyme inhibitors have suggested that echocardiographic LV mass may decrease more than expected for the induced reduction in blood pressure,\cite{6*} but this finding has not been consistent.\cite{67} Our studies suggest that the renin-angiotensin system may have more important effects on LV function than on its structure. Thus, patients with low-renin essential hypertension had higher LV fractional shortening and cardiac index than those in normal and high-renin subgroups,\cite{6} while relief of vasoconstriction by captopril in those with high-renin essential hypertension was associated with an increase in cardiac index.\cite{68} In a separate study,\cite{69} we observed an inverse relation between plasma renin activity and LV fractional shortening, an index of systolic performance. We have subsequently documented that patients with renovascular hypertension, the overwhelming majority of whom have high plasma renin levels, have significantly poorer LV systolic function than age-, sex- and blood pressure-matched patients with essential hypertension.

**Limitations of M-Mode Echocardiography in Abnormally Shaped Ventricles**

Since M-mode echocardiography only delineates the LV along its anteroposterior minor axis, accurate estimation of chamber and myocardial volume is possible only if the ratio between measurements along this and other axes remains within a relatively narrow normal range. Fortuitously, none of the\cite{34} patients in our initial necropsy validation study\cite{12} exhibited severe distortion of LV geometry. Admixing patients with LV aneurysms due to coronary artery disease or other causes of altered LV geometry has undoubtedly contributed to the slightly greater error of M-mode echocardiographic LV mass estimates reported more recently by Woythaler et al.\cite{3} and by our group.\cite{3} Direct confirmation of the effect of altered LV geometry on the accuracy of M-mode myocardial mass estimates has been provided by Reichek et al.\cite{8} Of their 21 patients,\cite{5} had current or previously resected LV aneurysms,\cite{7} had transmural myocardial infarctions, and\cite{11} had right-heart dilatation and failure. M-mode echocardiography substantially overestimated anatomic LV mass (Figure 3), but a reasonable correlation ($r = 0.86$, $p<0.001$) was preserved between echocardiographic and necropsy mass in the 18 patients with technically adequate M-mode echocardiograms.

In addition to fixed distortion of cardiac shape, functional abnormalities may cause marked alteration of LV geometry between end diastole and end systole. This may be produced both
by regional LV dyssynergy and abnormal overall heart motion, which causes the M-mode echo beam to lose its normal orientation along the left ventricle's minor axis during part of the cardiac cycle. These abnormalities would cause LV muscle mass calculated from end-diastolic and end-systolic echo dimensions in the same patient to differ significantly. As shown in Figure 4, end-diastolic and end-systolic LV mass estimates were quite close in patients with symmetric LV wall motion studied in our laboratory, whereas greater differences were observed in five patients with paradoxical septal motion or swinging of the heart within large pericardial effusions.

DEVELOPMENT OF LV HYPERTROPHY

The myocardium has three morphological compartments: (1) the muscular compartment consisting of myocytes, the dominant cell type of the normal heart comprising, 30% of the myocardial cells and 70% of cardiac tissue volume; (2) the interstitial compartment formed by fibroblasts and collagen; and (3) the vascular compartment with smooth muscle and endothelial cells. An increase in LV wall stress—for example, caused by hypertension induced increase in afterload—will stimulate myocyte hypertrophy, collagen formation and fibroblasts, and thus remodelling of the myocardium with a disproportionate increase in fibrous tissue. These changes will subsequently reduce LV compliance, leading to diastolic dysfunction. Structural changes of the coronary arteries and the increase in both interstitial myocardial fibrosis and in myocardial mass contribute to reduce the vascular coronary flow reserve. In addition, myocardial ischaemic episodes cause transient diastolic dysfunction (figs 3 and 4).

An increase in LV wall stress is the principal mechanical factor in the development of LV hypertrophy, and blood pressure the most powerful determinant of LV mass. However, some additional haemodynamic factors play important roles in the development and maintenance of LV hypertrophy (fig 5).[4] Thus, volume overload also contributes importantly to the development of cardiac hypertrophy. Although the exact mechanism by which sodium intake influences LV mass is unclear, a high salt intake could expand intravascular volume and increase LV preload. Hypertrophy of the arterial resistance vessels with an increased peripheral vascular resistance is present in established hypertension.w5 Also the carotid arteries and other large arteries show structural changes. These structural vascular changes with increased arterial stiffness lead to enhanced reflection of the arterial pulse wave, and the
resulting increase in systolic blood pressure may promote the development of LV hypertrophy. While diastolic blood pressure is more.

Figure 1: Left ventricular hypertrophy, a condition with variable background. AMI, acute myocardial infarction; CMP, cardiomyopathy.

Closely related to LV wall thickness probably reflecting pure pressure load, systolic blood pressure is more closely related to LV mass, suggesting an influence of both pressure and volume load. However, the modest correlation between blood pressure and LV mass suggests additional important factors. Important non-haemodynamic factors for the development of LV hypertrophy include trophic influence mediated by the sympathetic nervous system and the renin–angiotensin–aldosterone (RAA) system. Noradrenaline (norepinephrine) and other substances with α1 adrenergic agonist activity have been shown to induce myocyte hypertrophy in vitro and in vivo. Recent results suggest that an increased cardiac sympathetic neurotransmission plays a part in the increase in LV mass in human hypertension. However, it is likely that direct haemodynamic effects from sympathetic augmentation in hypertension also contribute to the development of LV of insulin and insulin resistance is more common in patients with cardiovascular disease, including hypertension. Although insulin may have peripheral haemodynamic actions that could increase afterload, it appears that it does not have a direct growth promoting effect on the myocardium. Circulating plasma
concentrations of aldosterone and angiotensin II are related to the extent of LV hypertrophy. Angiotensin II promotes myocyte cell growth, and aldosterone increases the collagen content and stimulates the development of myocardial fibrosis.[6] Circumstantial evidence suggesting an important role for the RAA system is also the greater reduction in LV mass and of myocardial fibrosis by antihypertensive treatment with drugs that interfere with the actions of the RAA system.[7-8,9] Furthermore, gene polymorphisms of various components of the RAA system also predict the response in LV mass to antihypertensive treatment.[9,10]

Demographic determinants such as age, sex, race, and body size also play a role in the development of LV hypertrophy.[4] Taken together, genetic as well as non-genetic influences on haemodynamic and non-haemodynamic factors seem to cause intracellular stimulation of protein synthesis ultimately influencing the development of LV hypertrophy.

Definition of LVH and LV geometry In all studies, LVH was defined by LV mass echocardiographically assessed and indexed to body size: body surface area (BSA) or less frequently to height or height to the allometric power of 2.7. Cut-off criteria for LVH definition were either: (a) associated with increased risk of CV events,[13-17,19-21, 23-26, 28, 29, 31-36, 41,42] or (b) above the reference limits or percentile values (that is, 95%) in apparently healthy individuals.[18,22,27,30-40] LV diameters and wall thickness were measured by M-mode technique (in almost all instances under two-dimensional control) in all studies but one[39] according to ASE[13,14,16,22,23,25-27,30-33,37,39,41,42] or PENN15,[17-21,29,36,38,40] convention. LV mass was calculated in all studies using necropsy-validated equations.[43,44] Finally, increased relative wall thickness characterizing LV concentric geometry was defined according to partition values ranging from 0.43,[refs 15,27,36,38,40] to 0.50.[ref. 39]
LVH criteria

As shown in Table 2, LVH prevalence was defined according to 23 criteria, all but two based on LV mass indexed to BSA (n=12), height2.7 (n=45) or height (n=42), BSA1.5 (n=41) and height2.13 (n=41). In about one-third of trials (n=12), more than one LVH definition was provided (range 2--7). In these studies, criteria providing the highest figures of LVH were considered less conservative; conversely, criteria providing the lowest figures of LVH were considered more conservative. Gender-specific partition values and indexation of LV mass to BSA were used in the majority of trials, the BSA/height and gender/ non-gender ratio being 1.6 and 1.9, respectively. LV mass indexes equal or exceeding 125 gm_2 in men and 110 gm_2 in women (n=49) and 125 gm_2 in both sexes (n=49) were the prevalent LVH diagnostic criteria, followed, in ranking order, by 51 g h_2.7 (n=48) and 49/47 g h_2.7 (n=44).

Prevalence of LVH In the whole study population, mean LV mass index ranged from 96(ref. 18) to 135 gm_2 (ref. 35) and from 39(ref. 41) to 63 g h_2.7.(ref. 23) Overall, 13 433 patients (35.6%) were found to have LVH by conservative criteria and 15 431 (40.9%) by the less restrictive ones, according to thresholds indicated in Table 2. The prevalence of LVH consistently varied among studies (9--77%) as well as in single studies defining this
phenotype according to multiple criteria. Prevalence rates of LVH were lowest in population-based studies (10--19%), \cite{14,18} intermediate (19--48%) in untreated hypertensive cohorts \cite{28,31,38} and, as expected, greatest in highrisk hypertensive patients (58--77%), that is, subjects with electrocardiographic LVH, \cite{13} severe hypertension, type-2 diabetes mellitus, or a history of previous CV events \cite{34} refractory hypertension. \cite{35}

LVH was less prevalent in untreated patients than in their treated counterparts. Prevalence rates of LVH, indeed, varied from 30.5 to 33.1%, according to different diagnostic criteria in studies (n=140) including as many as 8397 untreated patients. \cite{14,15,17,19,21,24,26,28,36} In contrast, LVH ranged from 43.6 to 52.8% (P=0.03 for comparison between more sensitive criteria) in the four studies (n=46427) with the highest proportion of patients on antihypertensive treatment (X85%). \cite{16,29,35,40} Table 3 shows the findings of 13 studies (n=416 033 patients) providing LVH rates according to a gender-based analysis. \cite{13,14,17,21,22,24,28,30,32,36,38,40} In 8 out of 12 studies, LVH prevalence was higher in women; in 2 reports the trend was opposite and in the remaining 3 LVH was more prevalent in men according to some but not all criteria. Prevalence rates of LVH in the 8229 men ranged from 36.0 to 43.5%, the corresponding values in the 7804 women were 37.9 and 46.2%; these differences did not attain statistical significance.

**Figure 5: Multiple determinants for left ventricular hypertrophy.**
Type of LVH As for LV geometric patterns, the eccentric pattern was more prevalent than the concentric one in 14 out of 18 studies (n=420,656 patients) providing this kind of information. On the whole, 5608 (27.1%) and 4905 patients (23.7%) were found to fulfill the more and less conservative criteria for eccentric LVH, respectively; the corresponding numbers for concentric LVH were 3575 (17.3%) and 3998 (19.3%), respectively. These differences were significant regardless the criteria used (P=0.04 for more restrictive criteria, P=0.03 for less restrictive ones). Finally, information on gender-related LVH patterns were limited to a few studies (n=45 including 4384 patients, 2259 men).13,14,17,21,36 Eccentric LVH prevalence tended to be higher in women than in men (42--61 versus 32--45%, respectively, P=0.13); concentric hypertrophy had a similar range in both genders (24--33 versus 25--32%).

**Patients and Methods**

A cross sectional study was carried out at a single center (khanaqin general hospital) for a period of six months, from 1st of January 2018 to 1st of July 2018, all patients underwent transthoracic Echo. Inclusion criteria: All hypertensive patients, free from exclusion criteria, during the study period, were included. Exclusion criteria: Cor pulmonale, myocardial infarction, valvular heart disease, bundle branch blocks, pre-excitation syndrome and cardiomyopathy are excluded.

**Intervention and data collection**

The data were obtained from the patient’s case notes and through direct questioning. Physical examination of each patient was carried out including precordial examination and taking blood pressure in a proper way. All patients underwent Echo. The estimation of left ventricular mass (LVM) was based on the formula derived by Devereux et al.\[12\]

\[
LVM = 0.8 \times (1.04 \times [(LVIDd + PWTd + IVSTd) - (LVIDd)]^3) + 0.6\ g
\]

where, LVIDd = Left ventricle internal dimension in diastole

PWTd = Posterior wall thickness in diastole,

IVSTd = Interventricular septal thickness in diastole,

1.04 = specific gravity of the myocardium

Also by incorporating height and weight, LVM index calculated, LVM index was defined as LVM divided by body surface area (LVM/BSA, g/m²). BSA was calculated according to the formula.

\[
BSA = 0.6 \times \text{height (m)} + 0.0128 \times \text{weight (kg)} - 0.1529.
\]
Left ventricular hypertrophy was defined by LVM of ≥ 162 grams for women and ≥224 grams for men, or LVM index of ≥ 95 g/m² for women and ≥115 g/m² for men and graded according to Table 2.

**Statistical analysis**

Data analysis was done by computerized statistical software; Statistical Package for Social Sciences (SPSS) version.\(^{[22]}\) Descriptive statistics presented as (mean±standard deviation) and frequencies as percentages. Normality of the data set was verified. Multiple contingency tables conducted and appropriate statistical tests were performed, chi-square test was used for categorical variables and independent t-test was used to compare between means. In all statistical analysis, level of significance (p-value) was set at ≤ 0.05.

**RESULTS**

The study included 311 patients, 132 (42%) cases were male and 179 (58%) patients were female, the age ranged between 50–80 years with mean age of 62.7±7.

**Table 1:** Left ventricular hypertrophy grading.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ventricular mass/BSA (g/m²) Women</td>
<td>96–108</td>
<td>109–121</td>
<td>≥122</td>
</tr>
<tr>
<td>Left ventricular mass/BSA (g/m²) Men</td>
<td>116–131</td>
<td>132–148</td>
<td>≥149</td>
</tr>
</tbody>
</table>

**Table 2:** Socio-demographic characteristics of patients.

<table>
<thead>
<tr>
<th>Variable</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>50–59</td>
<td>94</td>
</tr>
<tr>
<td>60–69</td>
<td>150</td>
</tr>
<tr>
<td>≥70</td>
<td>67</td>
</tr>
<tr>
<td>Male</td>
<td>132 (42%)</td>
</tr>
<tr>
<td>Female</td>
<td>179 (58%)</td>
</tr>
<tr>
<td>Weight mean±SD (76.34±10 kg)</td>
<td></td>
</tr>
<tr>
<td>Height mean±SD (162± 7.2 cm)</td>
<td></td>
</tr>
<tr>
<td>BMI mean±SD (28.38± 2.9 kg/m²)</td>
<td></td>
</tr>
<tr>
<td>Anti-hypertensive treatment</td>
<td>243 (70%)</td>
</tr>
<tr>
<td>Duration of hypertension</td>
<td></td>
</tr>
<tr>
<td>1–5 years</td>
<td>94</td>
</tr>
<tr>
<td>6–10 years</td>
<td>138</td>
</tr>
<tr>
<td>11–15 years</td>
<td>57</td>
</tr>
<tr>
<td>≥16 years</td>
<td>22</td>
</tr>
<tr>
<td>Mean systolic blood pressure</td>
<td>158–45</td>
</tr>
<tr>
<td>Mean diastolic blood pressure</td>
<td>87–67</td>
</tr>
</tbody>
</table>
Echo findings

Sixty (30%) patients revealed LVH, among them 211 (65%) patients were female and 66 (35%) patients were male. Eighteen (9%) patients had left ventricular systolic dysfunction, 157 (27%) patients had left ventricular diastolic dysfunction. Table 4 gives details of ECG findings of the patients.

The prevalence of LVH was significantly higher in female, and eccentric type was significantly more prevalent in female as given in Table 5.

<table>
<thead>
<tr>
<th>Echocardiographic finding</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>No left ventricular hypertrophy on echocardiography</td>
<td>214(70)</td>
</tr>
<tr>
<td>Left ventricular hypertrophy on echocardiography</td>
<td>97(30)</td>
</tr>
<tr>
<td>Systolic dysfunction</td>
<td>35</td>
</tr>
<tr>
<td>Diastolic dysfunction</td>
<td>71</td>
</tr>
<tr>
<td>Eccentric left ventricular hypertrophy</td>
<td>58</td>
</tr>
<tr>
<td>Concentric left ventricular hypertrophy</td>
<td>40</td>
</tr>
<tr>
<td>Mild left ventricular hypertrophy</td>
<td>54</td>
</tr>
<tr>
<td>Moderate left ventricular hypertrophy</td>
<td>38</td>
</tr>
<tr>
<td>Severe left ventricular hypertrophy</td>
<td>15</td>
</tr>
</tbody>
</table>

Table 4: Gender specific difference in geometry of left ventricular hypertrophy (LVH).

<table>
<thead>
<tr>
<th>Type of LVH</th>
<th>Male</th>
<th>Female</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVH (ALL)</td>
<td>31(10.5%)</td>
<td>49(19.5%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Eccentric LVH</td>
<td>24(7%)</td>
<td>36(13%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Concentric LVH</td>
<td>22(6%)</td>
<td>18(4%)</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

Table 3: Left ventricular longitudinal strain and strain rate values assessed by 2D strain analysis.

<table>
<thead>
<tr>
<th></th>
<th>Normotensive</th>
<th>Prehypertensive</th>
<th>Hypertensive</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 33)</td>
<td>(n = 41)</td>
<td>(n = 33)</td>
<td></td>
</tr>
<tr>
<td>LV longitudinal 2D strain (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mid septal</td>
<td>$-23.9 \pm 3.0$</td>
<td>$-18.9 \pm 3.4^*$</td>
<td>$-18.0 \pm 3.3^{**}$</td>
<td>0.002</td>
</tr>
<tr>
<td>Mid lateral</td>
<td>$-22.9 \pm 3.3$</td>
<td>$-18.1 \pm 4.7^*$</td>
<td>$-17.1 \pm 4.2^*$</td>
<td>0.003</td>
</tr>
<tr>
<td>LV longitudinal 2D strain rate (s$^{-1}$)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mid septal E 1.5</td>
<td>$\pm 0.3$</td>
<td>$\pm 0.4^{**} 1.1$</td>
<td>$\pm 0.3^{**}$</td>
<td>0.0001</td>
</tr>
<tr>
<td>Mid septal A 0.8</td>
<td>$\pm 0.2$</td>
<td>$\pm 0.3^{**} 1.2$</td>
<td>$\pm 0.3^{**}$</td>
<td>0.0001</td>
</tr>
<tr>
<td>Mid septal E/A 2.3</td>
<td>$\pm 1.9$</td>
<td>$\pm 0.6^{**} 1.0$</td>
<td>$\pm 0.4^{**}$</td>
<td>0.0001</td>
</tr>
<tr>
<td>Mid septal S -1.8</td>
<td>$\pm 0.3$</td>
<td>$\pm 0.2^{*} -1.0$</td>
<td>$\pm 0.2^{**}$</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Normotensive (n = 33)</td>
<td>Prehypertensive with normal LVMh(^2,7) (n = 33)</td>
<td>Hypertensive with normal LVMh(^2,7) (n = 20)</td>
<td></td>
</tr>
<tr>
<td>------------------</td>
<td>-----------------------</td>
<td>-----------------------------------------------</td>
<td>-----------------------------------------------</td>
<td></td>
</tr>
<tr>
<td><strong>Mid lateral E</strong></td>
<td>± 0.4 1.4</td>
<td>± 0.5* 1.3</td>
<td>± 0.4*</td>
<td></td>
</tr>
<tr>
<td><strong>Mid lateral A</strong></td>
<td>± 0.3 0.8</td>
<td>± 0.3 0.8</td>
<td>± 0.3</td>
<td></td>
</tr>
<tr>
<td><strong>Mid lateral E/A</strong></td>
<td>± 1.1 1.9</td>
<td>± 0.8 1.9</td>
<td>± 1.2</td>
<td></td>
</tr>
<tr>
<td><strong>Mid lateral S</strong></td>
<td>−1.3 ± 0.3</td>
<td>−1.1 ± 0.3*</td>
<td>−1.0 ± 0.2**</td>
<td></td>
</tr>
</tbody>
</table>

**LV longitudinal 2D strain (%)**

<table>
<thead>
<tr>
<th></th>
<th>Normotensive (n = 33)</th>
<th>Prehypertensive with normal LVMh(^2,7) (n = 33)</th>
<th>Hypertensive with normal LVMh(^2,7) (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mid septal</strong></td>
<td>−23.9 ± 3.0</td>
<td>−18.8 ± 3.2*</td>
<td>−17.5 ± 3.3**</td>
</tr>
<tr>
<td><strong>Mid lateral</strong></td>
<td>−22.9 ± 3.3</td>
<td>−18.0 ± 4.8*</td>
<td>−16.4 ± 4.2*</td>
</tr>
</tbody>
</table>

**LV longitudinal 2D strain rate (s\(^{-1}\))**

<table>
<thead>
<tr>
<th></th>
<th>Normotensive (n = 33)</th>
<th>Prehypertensive with normal LVMh(^2,7) (n = 33)</th>
<th>Hypertensive with normal LVMh(^2,7) (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mid septal E</strong></td>
<td>± 0.3 1.2</td>
<td>± 0.4** 1.1</td>
<td>± 0.3**</td>
</tr>
<tr>
<td><strong>Mid septal A</strong></td>
<td>± 0.2 1.2</td>
<td>± 0.3** 1.2</td>
<td>± 0.3**</td>
</tr>
<tr>
<td><strong>Mid septal E/A</strong></td>
<td>± 1.9 1.2</td>
<td>± 0.6** 1.1</td>
<td>± 0.4**</td>
</tr>
<tr>
<td><strong>Mid septal S</strong></td>
<td>−1.8 ± 0.3 1.1</td>
<td>± 0.2 -1.0</td>
<td>± 0.2*</td>
</tr>
<tr>
<td><strong>Mid lateral E</strong></td>
<td>± 0.4 1.2</td>
<td>± 0.5 1.3</td>
<td>± 0.3**</td>
</tr>
<tr>
<td><strong>Mid lateral S</strong></td>
<td>−1.3 ± 0.3 -1.2</td>
<td>± 0.3*** -1.0</td>
<td>± 0.2**</td>
</tr>
</tbody>
</table>

A, late diastole; 2D strain, two-dimensional strain; E, early diastole; LVMh\(^2\,7\), left ventricular mass indexed by height; S, systole. *P < 0.05 comparison between prehypertensive, hypertensives, and controls. **P < 0.01 comparison between prehypertensive, hypertensive, and controls. ***P < 0.05 comparison between prehypertensive and hypertensive.

Figure - ventricular (LV) geometry in hypertension: four patterns with different prognostic implications. LV hypertrophy.
DISCUSSION

Left ventricular hypertrophy is associated with increased cardiovascular morbidity and mortality, so its diagnosis is critical, especially for hypertensive patients.\textsuperscript{[16]} Echo criteria for LVH have been shown to have excellent sensitivity, specificity and accuracy when compared with postmortem left ventricular mass, and its reliability has been confirmed angiographically.\textsuperscript{[17]} Based on the population studied and the criteria used for LVH, the prevalence of LVH in hypertensive cases varies from 20–70% in the most studies worldwide.\textsuperscript{[18–20]} In one meta-analysis of Cuspidi et al. of 30 studies published in the last decade provides one of the largest data base on echo LVH prevalence in a hypertensive population of 37700 patients from different hypertensive cohorts and from the hypertensive fraction of the general population. Left ventricular hypertrophy is present in approximately 36% of the pooled population according to more restrictive diagnostic criteria. In another meta-analysis by Pewsner et al. who analyzed 5608 patients in\textsuperscript{[21]} studies, the median prevalence of LVH was 33% (interquartile range 23–41%). In the current study, the prevalence of LVH was 30%, this result is very close to the results of de Simone et al. and Fesler et al. which were 31% and 33% respectively.\textsuperscript{[21–24]} Majority of our patients were female. The data were taken consecutively. Whether it occurred by chance or hypertensive is more As for left ventricular geometric patterns, the eccentric pattern was more prevalent than the concentric one in 14 out of 18 studies in the pre-mentioned meta-analysis, the same proportion was also obtained in this study in which eccentric LVH was 20% while concentric LVH was 10%.\textsuperscript{[21]}

There are too much controversies regarding relationship between gender and LVH. There are studies that showed that females have a positive association with LVH. However, other studies confirmed the reverse of this. At the same time, another series showed that there is no difference between gender and LVH.\textsuperscript{[24–30]} This current series showed that the female gender is a predictor for the development of LVH with an odd ratio of 1.182.

Many studies found that patients with obesity are at risk of developing LVH.\textsuperscript{[31–33]} This study supports these findings with odd ratio of 1.2 for patients with BMI more than 25 compared with a patient who has normal weight at a 95% confident interval of 0.07–2.08. The remodeling process in long-standing hypertension consists of hypertrophy, fibrosis and impaired microvascular circulation with arterial stiffness is accompanied by higher pulse pressure and systolic blood pressure, which are well-known risk factors for cardiovascular
Few studies have assessed the relationship between LVH and cigarette smoking. In the LIFE study, smoking was more common among LVH patients in comparison to control. In the current study, there was no association between LVH and smoking.

The criteria were used to increase the accuracy of the method for diagnosing LVH. In this study, sensitivity of all criteria was low (20–30%).

In the present study, three applicable ECG criteria for LVH diagnosis in hypertensive cases with Echo as the diagnostic standard. Sokolow-Lyon criteria are the oldest criteria revised by Sokolow and Lyon in 1949. It is the oldest, quickest and simplest method for diagnosis of LVH by ECG. According to this study, it has sensitivity of 30%, specificity of 89%, positive predictive value (PPV) of 55%, negative predictive value (NPV) of 75% and accuracy of 71%.

The specificity and sensitivity of Sokolow-Lyon criteria showed different results in different studies, in our study it was very close to the sensitivity/specificity of Norman et al. (1995) and Jaggy et al. (2000) which were 30%/86% and 31%/86% respectively.

In assessing Cornell voltage criteria, sensitivity of 25%, specificity of 93%, PPV of 60%, NPV of 74% and accuracy of 72%.

The sensitivity/specificity of Cornell voltage criteria in the current study was close to Salles et al. which were 24%/89% respectively while the sensitivity of our study was far more than the results of Fragolaw which was 8% and a higher score obtained in Calacaw which was 41%.

In assessing the scores for left ventricular strain pattern, sensitivity of 20%, specificity of 96%, PPV of 67%, NPV of 73%, accuracy of 73%.

There is wide range among studies in evaluation of sensitivity of left ventricular pattern, sensitivity ranging from 11.9–38.6%. Our study took a median position among them and it was very close to Sundström et al. 88 in which sensitivity was 21% and specificity was 92%.

Alfakih et al. analyzed the value of gender specific partition for ECG criteria of LVH recalibrated against cardiac MRI scan, and evaluated that Cornell voltage criterion had highest sensitivities in males (26.2%) as compared to females (16.3%), while the reverse was found in Sergio et al., who assessed both the specificity and sensitivity of Sokolow–Lyon and
Cornell voltage criteria for LVH. In their study, the sensitivity of Cornell voltage criterion was 22.5% for males and 28% for females, Rodrigues et al. reported a similar finding, our results go with Sergio et al. in which sensitivity of Cornell voltage criterion was higher for female.\[^{41, 42}\]

There are limitations for this study; the sample size is small, the duration of the study was short and finally although we assessed risk factors at the time, we could not reliably measure how long the risk factors had been present before, as patients may not seek medical attention.

This study shows that a considerable number of patients recently diagnosed with mild hypertension have LVH determined by ECHO (32%; 95% confidence interval _ 26% to 38%), the frequency of which is underestimated using standard methods of detection, Within this population, the method used to detect cardiac organ damage therefore markedly influences cardiovascular risk stratification.

The prevalence of echocardiographic LVH is highly dependent on the criteria used for diagnosis. Several criteria, based on LV mass (indexed by weight, height, or body surface area) have been proposed.\[^{23}\] We have used sex-specific cut-off values of 134 g/m2 in men and 110 g/m2 in women because the prognostic value of these figures has been clearly shown in previous reports.\[^{17}\] In addition, these criteria have been widely used in epidemiologic studies and are considered a suitable reference standard for detection of LVH in a heterogeneous population.\[^{7}\] The frequency of LVH found in our study was higher than that reported by other authors for mild hypertensive subjects.\[^{8, 10}\] The study by Armario et al.\[^{21}\] performed in a series of 171 untreated mild hypertensive, patients, reported a prevalence of LVH of 23% using 125 g/m2 as the LVMI cut-off point. In a large cross-sectional study of 844 mild hypertensive patients, Liebson et al\[^{5}\] found an even lower prevalence (15%). Variations in prevalence are most likely to be due to demographic differences in the study population (mainly age) and to the threshold values used to define LVH. There is little published information about the frequency of LVH in hypertensive patients attended in primary care settings. The Ventrículo Izquierdo Tensión Arterial Espan˜a (VITAE) study\[^{6}\] was designed to research the prevalence of echocardiographic LVH in a representative cohort of essential hypertensive patients attended by general practitioners in Spain.\[^{6}\] The authors reported a prevalence that ranged from 59% to 73%, depending on the threshold values used. These prevalence figures are approximately twice that found by our group. Possible explanations for this difference include a shorter duration of hypertension and lower clinic
BP, age, and body mass index in our series. In addition, a high percentage of our study patients were diagnosed with white coat hypertension, a condition that is associated with less target organ damage than is sustained hypertension.\textsuperscript{[24,25]} In the former group, 20\% of subjects had LVH, a figure intermediate between those found in two large cross-sectional surveys.\textsuperscript{[26,27]}

We found that LVMI was associated with several clinical factors: biological sex, age, UAE, and different measurements provided by ambulatory BP monitoring. The higher prevalence of LVH in women compared with men observed in our sample is likely due to the use of body surface area in the calculation of LVMI\textsuperscript{1},\textsuperscript{[9]} along with sex-specific definition criteria. By contrast, studies using weight usually report a higher prevalence in men.\textsuperscript{[28]} In hypertensive populations, microalbuminuria has been shown to be associated with several risk factors and the presence of early signs of hypertensive organ damage such as LVH.\textsuperscript{[29]} Furthermore, microalbuminuria, similar to LVH, is a powerful, independent predictor of morbidity and mortality.\textsuperscript{[30]} According to this evidence, routine measurement of urinary albumin excretion could be a useful tool for the stratification of cardiovascular risk in patients recently diagnosed with mild hypertension. In agreement with previous results by our group and others, ambulatory BP was related to LVMI more closely than was clinic BP.\textsuperscript{[24,31]} Nighttime ambulatory BP showed a higher correlation with LVMI than daytime BP. This finding, also observed for microalbuminuria in previous studies,\textsuperscript{[32]} could be related to the fact that nighttime ambulatory BP values are usually more reproducible than daytime values\textsuperscript{[33]} because of the limited physical activity during that period.

In a stepwise multiple linear regression model, with LVMI as the dependent variable, age, sex, and nighttime diastolic BP load were predictors of LVMI. The association with urinary albumin excretion that was found in the univariate analysis did not remain after taking these factors into account. This regression model could explain only 26.2\% of LVMI variability, a slightly lower figure than that described by other authors.\textsuperscript{[10,34]} Obviously, LVM is influenced by other factors that were not considered in our study, such as those of genetics, metabolism, and lifestyle.\textsuperscript{[4]} In a logistic regression model with LVH as the dependent variable, only age and daytime systolic load were predictive factors, after controlling for several potential confounding factors.
The question of whether and when to use ECHO in hypertensive patients has been the subject of considerable controversy.\cite{35-37} The WHO/ISH\cite{14} and the JNC\cite{20} guidelines stress the importance of basing decisions about the management of hypertensive patients not only on BP levels, but also on the presence of other risk factors and target organ damage, such as ECG evidence of LVH. Although ECHO is more sensitive and specific for identifying LVH than ECG, it is presently not recommended in the baseline workup of hypertensive patients.

In our primary-care series, most patients (79\%) were initially classified as having low to medium cardiovascular risk by routine investigations. The detection of LVH by ECHO changed the risk category in 40\% of subjects who were initially classified as being at medium risk. By contrast, shifts from one to another risk level were very few in the remaining categories. As a whole, our data therefore suggest that ECHO evaluation might be particularly useful in the initial work-up of mildly hypertensive subjects classified as medium risk by routine evaluation, that is, those patients with several cardiovascular risk factors but no evidence of target organ disease. Within this group, LVH will be diagnosed by ECHO in approximately 40\% of cases. This information will probably lead to the decision to start treatment with antihypertensive drugs, in accordance with the WHO/ISH guidelines. By contrast, ECHO information might be less useful in patients assigned to a very low or high risk category.

Two recent articles\cite{12,13} have investigated the impact of echocardiography in hypertensive patients judged to be at relatively low risk on the basis of traditional clinical evaluation. These studies, performed in hospital clinics, showed that 29\% to 50\% of individuals would be reclassified as being at high cardiovascular risk after detection of LVH. Our results extend those findings to a primary care setting, where most hypertensive patients receive their medical care and which therefore is the context in which the first therapeutic decision is usually made. The present study has two potential limitations. First, our routine procedures to detect target organ damage did not include funduscopic examination, a procedure recommended by international guidelines (WHO/ISH and JNC). Interestingly, previous studies on hypertensive patients showed significant correlations between retinal vascular changes and LVM\cite{38,39} and a low incidence of retinopathy in subjects with no LVH.\cite{38}

According to this evidence, we could hypothesize that funduscopic findings would not have significantly influenced our results on cardiovascular risk stratification. Second, our additional evaluation of organ damage did not include carotid ultrasonography. It is likely that this assessment had increased the proportion of patients reclassified as being at high risk.
by echocardiography. In the Assessment of Prognostic Risk Observational Survey (APROS) study,[12] the carotid evaluation led to another 16% of patients being reclassified. In conclusion, patients in primary care diagnosed with mild hypertension have a substantial frequency of echocardiographically detected LVH. Our results suggest that ECHO could be particularly useful for improving cardiovascular risk stratification in those patients with multiple risk factors but no evidence of target organ damage using routine evaluations. Prospective primary care–based studies are needed to determine the efficacy and cost of this approach for identifying high risk patients.

CONCLUSIONS

This study found that the prevalence of left ventricular hypertrophy (LVH) was 30% among hypertensive population. Effort should be made for early detection and treatment of LVH since it carries bad prognosis. Left ventricular hypertrophy was more prevalent in female, especially eccentric type. LVH determined by ECHO. Our results suggest that this procedure could significantly improve cardiovascular risk stratification in those patients with multiple risk factors, but no evidence of target organ damage by routine investigations.

Recommendations

1. LVH in hypertensive patiantes need careful follow up to avoid complications.
2. Women more dangerse thane male there fore need more carefully and warning
3. advaise more and more studies of LVH in hypertensive patiantes BY ECHO.

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