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MYOCARDIAL PERFORMANCE IN ASYMPTOMATIC ESSENTIAL HYPERTENSION

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Abstract : Prevalence, determinants, and prognostic value of left ventricular function in subjects with asymptomatic essential hypertension are still incompletely known. The goal of this study was to investigate the effects of asymptomatic untreated essential hypertension on left ventricular structure and function. The left ventricular functions were assessed among 127 hypertensive and 80 healthy subjects. American society of echocardiography (ASE) convention was applied to measure the stroke volume, percentage ejection fraction, percentage fractional fiber shortening, cardiac output and cardiac index. The stroke volume, cardiac output and cardiac index were normal but significantly high among hypertensive compared to normotensive subjects ($P<0.05$). The percentage ejection fraction and fractional fiber shortening were significantly reduced among hypertensives compared to normotensives ($P<0.05$). The significant impairment of percentage fractional fiber shortening is due to alteration in dimension of left ventricular wall thickness, left ventricular cavity and left ventricular geometry. This carries prognostic implication and requires further documentations, investigations and researches. Percentage ejection fraction and fractional fiber shortening is considered a hallmark of normal left ventricular function. The left ventricular contractile state was negatively correlated to left ventricular after load parameters. So the main objective of management of hypertensive subjects should be, to reduce the after load to improve the left ventricular contractile state.

Key words : left ventricular function asymptomatic essential hypertension echocardiography

INTRODUCTION

Hypertension is a potent risk factor for congestive cardiac failure (1). Development of overt congestive cardiac failure (CCF) may be preceded by a phase of asymptomatic left

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ventricular systolic dysfunction (ALVSD) (2). Asymptomatic left ventricular systolic dysfunction is a potent and early marker of evolution toward severe CHF requiring hospitalization in subjects with essential hypertension (3). Many hypertensive subjects without symptoms or physical signs of CCF should thus be considered for screening of ALVSD, an argument that raises cost-effectiveness considerations (9). However, important aspects including prevalence, determinants, and prognostic value of ALVSD in the specific setting of essential hypertension are poorly known, because most available studies have been performed in the general population (4–9). The mechanisms of cardiovascular damage in hypertension are still partially unclear; in particular, it is not known, what role the metabolic changes frequently associated with high blood pressure (ie, insulin resistance, dyslipidemia, glucose intolerance, and ectopic fat accumulation) may play. Mild increases in blood pressure are recognized as a risk factor for myocardial infarction and coronary artery disease (10). For this reason, in 2003, the Joint National Committee on High Blood Pressure identified “prehypertension” as a new category of blood pressure in adults (11): prehypertensive (pre-HT) individuals carry a higher risk (3-fold) of developing hypertension and cardiovascular disease in comparison with normotensive (NT) subjects (12). Higher blood pressure is associated with decreased regional left ventricular function in asymptomatic individuals (13).

Left ventricular (LV) functions are routinely assessed by echocardiography method in clinical setup (14). The determinant of LV functions i.e. preload, after load, contractile state of LV can also be assessed by echocardiography (14). The important and reliable parameters of determinant of LV functions can be measured safely, noninvasively, quickly, without any radiological or any other hazards with the help of echocardiography (15). These parameters can be used for the early detection of LV dysfunction, progress of LV dysfunction, and effect of therapeutic intervention i.e. pharmacological and/or non-pharmacological method on LV functions. Left ventricular hypertrophy (LVH) and geometry pattern is associated with important clinical and prognostic implications, probably due to several biological and pathophysiological differences between various forms of LV adaptation to hypertension, including differences in haemodynamic profiles and LV systolic and diastolic function (16). We hypothesized that the metabolic abnormalities of asymptomatic essential hypertension may be linked with altered regional left ventricular (LV) function by affecting mechanisms involved in sustaining normal cardiac function. Right and left ventricular performance are altered more in hypertensives with Obstructive sleep apnea syndrome compared to individuals with hypertension alone(17).Thus, we set forth to investigate the early changes in cardiac morphology and dynamics in asymptomatic untreated essential hypertensive subjects.

MATERIALS AND METHODS

The study was conducted at Govt. Medical College and New Civil Hospital, Surat, on 127 asymptomatic hypertensive and 80 healthy normotensive subjects. The study was approved by the ethical committee of Govt. Medical College and New Civil Hospital, Surat and written informed consent

was obtained from all the participants. Inclusion criteria were as follows: no previous diagnosis of hypertension; no previous treatment with antihypertensive or antidiabetic drugs or any other drug known to affect glucose and lipid metabolism; absence of diabetes ie, a fasting plasma glucose <7.0 mmol/L and a 2-hour plasma glucose concentration <11.1 mmol/L on a 75 g oral glucose tolerance test (OGTT) and no history of chest pain or previous cardiovascular disease. After a 30-minute acclimation period, BP was measured 3 times to the nearest 2 mm Hg in the sitting position using a mercury sphygmomanometer and appropriately sized cuffs. The average of 3 measurements was used to calculate systolic and diastolic BPs; mean BP was calculated as the diastolic value plus one third of the pulse pressure value. Echocardiograms were recorded using MEGAS CVX and MEGAS GPX equipped with ADV4 software from ESAOTE s.p.a. Firenze, Italy. For Doppler echocardiography the frequency used was 3.5 MHz. Echocardigraphic variables were calculated according to the American society of echocardiography (ASE) guidelines (17). Left ventricular internal dimensions at systole and diastole (LVIDs and LVIDd), interventricular septal dimension (IVSd) and posterior wall thickness (PWT) were measured. Stroke volume (SV), cardiac output (CO), percentage ejection fraction (EF %), percentage fraction shortening (FS %) and total peripheral resistance (TPR) were calculated from the measured dimension by the following formula of ASE convention (17):

$$S.V. = (LVIDd)^3 - (LVIDs)^3$$

CO (L/min) = stroke volume (SV) × heart rate (HR)

Cardiac index (C.I.) = Cardiac output/ Body surface area

$$EF\% = \frac{(LVIDd)^3 - (LVIDs)^3}{(LVIDd)^3} \times 100$$

$$FS\ (\%) = [(LVIDd - LVIDs)/LVIDd] \times 100$$

The indices of after load (ESS, EISS and TPR) were derived from the formula:

End-systolic meridional wall stress (ESS):

$$ESS\ (10^3\ dyn/cm^2) = 0.334 \times SBP \times LVIDs/PWTs \times (1 + PWTs/LVIDs).$$

End-isovolumetric Systolic Stress (EISS):

$$EISS\ (10^3\ dyn/cm^2) = 0.334 \times DBP \times LVIDs/PWTs \times (1 + PWTs/LVIDs).$$

Total peripheral resistance:

$$TPR\ (dyne \times sec \times cm^{-5}) = (mean\ BP \times 80)/CO.$$

Left ventricular mass (LVM) were measured using ASE measurements by the following equation (17):

$$LV\ M\ (ASE) = 0.8[1.04(IVS + LVIDd + PWT)^3 - (LVIDd)^3] + 0.6\ g$$

LVMI (ASE) = LVM/Body surface area

The transmitral peak velocity of early (E) and late filling (A) were measured and the E to A ratio calculated (17, 36).

Statistical analysis was performed using the EpiInfo 6 and SPSS package (version13). Data were expressed as Mean±Standard

Deviation. Statistical analysis was performed applying unpaired Student's 't' test to the data of independent samples for equality of means and Levene's test for equality of variances. The probability value P<0.05 was considered statistically significant as this could be interpreted that the factor is less likely to occur due to chance, while a probability value P>0.05 was considered statistically not significant because such a difference could commonly occur due to chance and the factor under study may have no influence on the variables.

RESULTS

There was no significant difference in the demographic characteristic of the study population (hypertensives and normotensives; Table I). SBP, DBP, PP and MAP were significantly higher (P<0.001, Table I) in the hypertensive individuals compare to normotensives. Except IVST, all the parameters of left ventricular structure (LVIDd, LVIDs, PWT, LVM, LVMI and RWT) were significantly higher amongst hypertensives compare to normotensives (Table II). Stroke volume, cardiac output and cardiac index were significantly higher amongst hypertensives compare to normotensives (P<0.05, Table III). However indices of contractility function (EF%, FS%) were significantly higher amongst normotensives compare to hypertensives (P<0.005, Table III). Amongst the indices of after load (ESS, EISS and TPR), ESS and EISS were significantly higher in hypertensive individuals compare to normotensive (P<0.05 Table III). TPR was within normal limit in both the group, however it was higher amongst hypertensive compare to normotensive, but it was not significant (P>0.05 Table III). Amongst the indices of diastolic performance (E, A and

TABLE I: Demographic characteristic and blood pressure pulse profile in the study population.

Variables	*Hypertensives (n=127) (Mean±SD)*	*Normotensives (n=80) (Mean±SD)*	*P value*
Age (years)	54.6±10.07	49.8±8.46	>0.05
Height (m)	1.58±0.07	1.59±0.09	>0.05
Weight (kg)	64.6±11.9	59.2±8.6	>0.05
Body mass index (kg/m^2)	25.8±4.5	23.6±2.6	>0.05
Waist circum-ference (cm)	94.7±13.06	88.8±7.4	>0.05
Hip circum-ference (cm)	94.2±10.4	96.18±6.7	>0.05
Waist-hip ratio	1.005±0.12	0.92±0.15	>0.05
Body surface area (m^2)	1.6±0.15	1.58±0.12	>0.05
Pulse/min.	79.05±7.10	78.16±5.9	>0.05
SBP (mm Hg)	158.4±19.19	118±9.04	<0.001
DBP (mm Hg)	95.6±6.7	78.5±5.4	<0.001
PP (mm Hg)	62.8±18.1	44.08±8.9	<0.001
MAP (mm Hg)	116.6±8.96	92.4±5.4	<0.001

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, PP: pulse pressure, MAP: Mean arterial pressure.

TABLE II: Left ventricular structure in the study population.

Variables	*Hypertensives (n=127) (Mean±SD)*	*Normotensives (n=80) (Mean±SD)*	*P value*
LVIDd (cm)	3.33±0.43	2.60±0.41	<0.0001
LVIDs (cm)	4.70±0.36	4.24±0.32	<0.05
PWT (cm)	1.21±0.15	0.99±0.14	<0.005
IVST (cm)	0.95±0.13	0.96±0.18	>0.05
LVM (gm)	191.9±44.46	139.9±37.03	<0.001
LVMI (gm/m^2) AE	117.2±29.62	87.72±23.39	<0.001
RWT	0.51±0.07	0.47±0.07	<0.05

LVIDd: left ventricular internal dimension at diastole, LVIDs: Left ventricular internal dimension at systole, PWT: Posterior wall thickness, IVST: Inter-ventricular septal thickness, LVM: Left ventricular mass, LVMI: Left ventricular mass index as per American society of echocardiography, RWT : Relative wall thickness.

E/A ratio), there was no significant difference observed in early filling (E velocity), however late filling (A velocity) was significantly higher in hypertensive groups (Table III). E/A ratio were significantly lower in hypertensive individuals because of augmented late filling (Table III).

TABLE III: Left Ventricular cardiac performance in the study popultion.

Variables	*Hypertensives (n=127) (Mean±SD)*	*Normotensives (n=80) (Mean±SD)*	*P value*
SV (ml)	67.35±15.6	58.62±14.7	<0.05
CO (L/min)	5.32±1.34	4.56±1.05	<0.05
CI (L/m^2)	3.26±0.92	2.84±063	<0.05
EF%	64.06±8.25	75.95±7.74	<0.005
FS%	29.33±5.64	38.45±6.34	<0.005
ESS ($X10^3$ $dyne/cm^2$)	201.02±38.08	149.32±24.48	<0.05
EISS ($X10^3$ $dyne/cm^2$)	157.87±20.22	140.15±21.12	<0.05
TPR ($dyne \times sec \times cm^{-5}$)	1852.86±464.8	1760.36±460.2	<0.05
E (cm/sec)	70.07±10.56	71.72±6.29	>0.05
A (cm/sec)	66.55±11.58	51.05±7.98	<0.005
E/A ratio	1.05±0.12	1.40±0.32	<0.005

SV: Stroke volume, CO: cardiac output, CI: cardiac index, EF% : percentage ejection fraction, FS%: percentage fractional shortening, ESS: end systolic stress, EISS: end isovolumetric systolic stress, E: early filling velocity, A: late filling velocity, E/A: ratio of early and late filling velocity.

DISCUSSION

An increasing interest in the pathophysiological differences between patients with various patterns of left ventricular hypertrophy (LVH) and geometry in hypertension has been observed (20-22). In the early stages of hypertension there occurs elevation of adrenergic tone typically characterized by hyperkinetic status i.e. an increased heart rate, stroke volume, cardiac output, and cardiac index. This is replaced with high total peripheral resistance (23). In permanent hypertension, reduced cardiac output is mainly the result of LV diastolic dysfunction in the course of LVH and decreased beta-receptor reactivity in mode of “down-regulation”. Hypertrophy and remodeling lead to an increase in peripheral resistance (23). In our study, the haemodynamic profile in patients with LVH suggests that increased left ventricular filling which is due to volume overload or elevated venous return, is responsible for the increase of stroke volume and normal systolic function, this is also purported in the report by Ganau et al in 1992 (20). In this study left ventricular contractility was assessed with the use of traditional indices, left ventricular ejection fraction (EF) and fraction shortening (FS), which reflected the dynamics of the left ventricle. In various studies, the midwall fractional fiber shortening (FS) parameters, (more adequate from the physiological point of view,) have been introduced for left ventricular contractility assessment. Shimuzu et al. in 1991 (24), De Simone et al. in 1994 (25), and Aurigemma et al. in 1995 (26) indicated that the left ventricular dynamics and geometry might overestimate the myocardial function. They also proved that the application of FS% in relation to ESS (end systolic stress) allows the significant reduction of the percentage of hypertensives with overestimated left ventricular systolic function, and identification of the subjects with diminished left ventricular contractile performance and left ventricular hypertrophy, associated with the high cardiovascular morbidity and mortality. Similarly, in our study population with left ventricular hypertrophy, the ejection fraction and fractional shortening values were diminished, indicating the left

ventricular systolic dysfunction. When we compare the data of study groups based on Left Ventricular mass index we found the high total peripheral resistance (TPR), end systolic stress and (ESS) and end isovolumetric stress (EISS) in the hypertensive groups compared to normotensive. Increased values of stroke volume (SV), stroke volume index (SVI), cardiac output (CO) and cardiac index (CI), which we interpret as the inability to compensate pressure overload by a reduction in the volume load. These data can also be explained by compensatory mechanism i.e. increased sympathetic activity (nor epinephrine release) and Renin-Angitensin-Aldosterone system (23). Balci B, Yilmaz et al. in 2002 (27) observed the similar results regarding systolic function in essential hypertension. However, de Simone et al in 1999 (28) showed in their study the values of cardiac output diminished in patients with hypertensive left ventricular hypertrophy.

Evaluations of alterations in diastolic function in the hypertensive population showed that alterations are prevalent and changed in regard to normotensive patients and, as found in other studies, were influenced mainly by age (29). On evaluating patients according to age range and cardiac geometry, we observed that in the elderly group, most of the patients had inversion of the E/A ratio, indicating a more permanent diastolic dysfunction, partly independent of alterations in cardiac geometry, in contrast to that of the lower age range (Table III).

On evaluating diastolic function in the hypertensive study population with or without normal left ventricular mass index, significant incipient structural alterations were observed as compared with the normotensive group (Table III). Zabalgoitia M, et al 1997(30) already emphasized the presence of diastolic dysfunction, even in the absence of hypertrophy.

Giorgi D, et al. 2002 (31) in their work “Ultrasonic tissue characterization and Doppler tissue imaging in the analysis of left ventricular function in essential arterial hypertension” reported that early diastolic myocardial velocity (E-wave velocity) of the lateral wall and of the septum were significantly lower, while the late diastolic myocardial velocity (A-wave velocity) was significantly higher in hypertensives compared to athletes. In our study too the E/A ratio at the septum level was significantly lower in hypertensives compared to controls.

Study by Balci B, et al. 2002 (27) observed that in essential hypertension, especially with concentric hypertrophy, global diastolic function is impaired.

In the natural history of left ventricular hypertrophy, compliance disturbances may appear with more and more intense accumulation of collagen or ischemic/fibrosis process. The relaxation abnormalities which were more pronounced in our patients with left ventricular hypertrophy are difficult to interpret as it may be anticipated that this phenomenon is also present in subjects with less favorable concentric hypertrophy. However, the relationship between Left Ventricular diastolic dysfunction and adverse prognosis has not yet been proved. In another study by Kosmala PM, et al in 2006 (33) demonstrated that in hypertensive patients there was increase in LV circumferential systolic and decreased

diastolic function. The former may be a compensatory response to the impairment in LV longitudinal systolic performance. Moreover, determination of left ventricular diastolic function abnormalities is multifactorial and amongst the factors that affect the mitral flow in essential hypertension, are the LV mass, preload, afterload, blood pressure parameters, changes in coronary microcirculation and adrenergic activity (34). The pathophysiological differences in hypertensive patients with various types of LVH and geometry help to explain the results of prognostic studies from Balci B et al (27). These studies showed the highest mortality in patients with concentric hypertrophy, lower but still significantly increased mortality in subjects with eccentric hypertrophy, and slightly increased mortality in patients with concentric remodeling, compared with subjects with normal LV geometry. Among the reasons for prognostic differences in hypertensive patients with various types of LVH and geometry, differences in haemodynamic, left ventricular systolic and diastolic dysfunction have to be considered.

In the presence of unnaturally increased arterial Blood pressure, due to any cause, the heart must maintain a normal cardiac output to preserve the consistence of the milieu interior or Claude Bernard-the composition of extra cellular fluid in which the cellular functions depend (34). The heart can accomplish this augmented workload only by expenditure of energy accompanied by physiological stretching of cardiac muscle fibres, which ultimately undergo hypertrophy i.e. left ventricular hypertrophy (35). The present study documented the fact that the resting systolic LV function parameters i.e. stroke volume; cardiac output and cardiac index were normal or even better than normal amongst asymptomatic hypertensive subjects. These data can be explained by compensatory mechanism i.e. increased sympathetic activity, Renin-Angiotensin-Aldosterone System (23). The wall force/after load during ejection of LV influences the quantity of blood ejected by ventricle, i.e. abrupt increase or decrease in impedance of LV ejection inversely alter the stroke volume and do so when end diastolic volume is independently controlled (15). It should be emphasized here further, that after load is never constant during ventricular ejection, but continuously decline as the left ventricular volume and midwall radius decrease as predicted by Laplace relation ($T = PxR/2h$ where T = wall stress/tension, P = pressure, R = radius of L.V. and h = thickness of L.V. wal). Increasing after load (ESS, EISS) causes immediate negative changes in myocardial wall shortening and contractile state (25). The significantly increased wall stress is due to altered structure and geometry of LV i.e. left ventricular hypertrophy which can be of concentric or eccentric type (20, 28). An increase arterial blood pressure augments after-load and LV stress by negative feedback mechanism. This depresses the myocardial fibre shortening. This further decreases the myocardial performance and the viscous cycle is once on lead to progressive impairment of myocardial performance. In this context, it is worth to consider the Framingham-study which has stated that the most important means of preventing the cardio-vascular complication is to identify and treat hypertension before complication develop (22). In this context, epidemiological approach by detecting the hypertension in early phase

is the final reply for the prevention of hypertensive heart disease process (22). With the same objective, the study was carried out amongst the newly asymptomatic hypertensive subjects to assess the LV functions by using the echocardiography.

Conclusion

The overall left ventricular systolic functions were normal amongst the asymptomatic essential hypertensive subjects. However contractility function were impaired in hypertensive individuals compared to normotensive. After-load was significantly increased amongst hypertensive. Ejection fraction and fractional shortening are hallmark of LV pump functioning. More public awareness programs are to be set up to educate the society about the early detection and benefit of control of blood pressure by various means for improvement of cardiac physiology even when the hypertension is in asymptomatic stage.

Limitations

The study population size was small, however it was bigger then many studies. Follow-up was incomplete, but this is common in such type of studies because of drop out and the study participants came from a small city and mobile, migrant population. Unavailability of better instrumentation and technique. Further studies with a large population size and better instrumentation i.e. Tissue Doppler Imaging (TDI) and cardiac MRI are required to assess the cardiac performance in asymptomatic essential hypertension.

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