STRUCTURAL AND FUNCTIONAL CHANGES OF LEFT VENTRICLE IN DIFFERENT TYPES OF LEFT VENTRICULAR HYPERTROPHY (LVH) IN ESSENTIAL HYPERTENSIVE (EHTN) PATIENTS

ABDUL QAWIR KHAN

Ukrainian Scientific Research Institute of Cardiology, Ukraine.

SUMMARY

Structural and functional changes of left ventricle in different types of left ventricular hypertrophy (LVH) in essential hypertensive (EHTN) patients. 27 Patients with eccentric left ventricular hypertrophy (ELVH), 24 patients with concentric left ventricular hypertrophy (CLVH) and 20 healthy persons as a control group were examined. Radionuclide ventriculography (RVG), echocardiography (Echo) and Exercise Tolerance Test (ETT) were used for the detection of the functional and structural status of the myocardium. The thesis specifies the left ventricular function in dependence of type of LVH. Given new data about the compensation of pumping function of left ventricle in different types of LVH. CLVH is characterized by decrease in volume and early diastolic rate filling along with high pumping function. ELVH is characterized by maintenance of early diastolic filling indicies, which important for the maintenance of left ventricular pumping function through Franik Starling mechanism.

INTRODUCTION

Left ventricular hypertrophy (LVH) defined as an abnormal increase in the left ventricular mass (LVM), is detected by echocardiography (Echo). Its prevalence is strongly associated with age, systolic blood pressure (BPS) and obesity. With the help of Echo we can visualize different forms of left ventricular remodelling in EHTN-eccentric or concentric and symmetric or asymmetric LVH. Increased LVM is now recognised as a powerful, independent risk factor for all cardiovascular diseases. LVH in hypertension is considered as a compensatory mechanism to chronic pressure or volume overload for the maintenance of long-term cardiac output[1].

MATERIAL AND METHODS

Radionuclide ventriculography (RVG) the most sensitive non invasive procedure for assessment of cardiac function, whose indices fully coincides with the results of contrast ventriculography (CVG) and manometric measurements of blood pressure (BP) in the chambers of the heart.[11,12] The procedure was performed in the radioisotope laboratory of the Ukrainian Scientific Research Institute of Cardiology (USRIC). RVG was performed in dynamic variant in gamma camera LFOV-IV on the patients in supine position. Detector of the gamma camera was positioned on the precordium in the left anterior oblique projection (30^0-40^0) with the patients declined 10^0 towards the head. We used Cardiosynchronisor and standard ECG apparatus to monitor the cardiac function during the procedure. Data were registered in the computer RDR II/34a. Patient received infusion of 0.2mg/kg pyrophosphate, after 15 minutes of the infusion patients was given stat indicator

dose of (370-420 MBc), T_c 99^m pertechnatate or pyrophosphate. With the appearance of radioactivity in the right ventricle (RT) which was controlled visually on the screen data measuring started automatically. The data received were stored in the magnetic disc along with the registration of signals of cardiosynchronisor. The data were then calculated according to Vmax programme under care of the supervisor on commercial programme RVI. Total ejection fraction (TEF) and ejection fraction (EF) for the 8 standard zones were detected on the activity-time curve with the formula.

$$EF\% \frac{EDC - ESC}{EDC - BC} \times 100$$

EDC = end diastolic count

ESC = end systolic count

BC = count in background region

On the bases of the results patients with ischaemic heart (IHD) were distinguished i.e. decrease in the EF by 25% or more.[13] End diastolic volumes (EDV) were realized on the bases of planimetric method. EDV and stroke volume (SV) were determined by the formula.

SV = EDV X TEF

ESV = EDV-SV

SI = SV/S

Where

SI = Stroke index and S = surface area of the body in meters.

MV = SV X HR- Where MV = minute volume and HR = heart rate.

CI = MV/S. Where CI = Cardiac index.

TABLE– I

ECHO INDICIES IN EHTN WITH VARIOUS TYPES OF LVH.

Index	ELVH N=27	CLVH N=24	P<
LA cm	3.31±0.11	3.79±0.17	0.05 *
PWTd cm	1.07±0.03	1.33±0.10	0.01 **
PWTs cm	1.65±0.05	1.84±0.06	0.05 *
SWTd cm	0.91±0.02	1.35±0.06	0.001 ***
SWTs cm	1.23±004	1.78±0.07	0.001 ***
BPs mm Hg	152±7	155±6	NS
BPd mm Hg	95±3	100±6	NS
DS (FS)	31.1±1.1	34.5±1.8	NS
LVM GM	254±10	371±40	005 *
MMI gm/m^2	134±5	185±16	0.01 **
EST 10^3DYN/CM^2	88.0±6.2	63.8±4.6	0.001 ***
LA/EDD	0.57±0.03	0.71±0.05	0.05 *
DP	0.34±0.01	0.51±0.02	0.001 ***

* = P< 0.05 NS = Not significant.

** = P< 0.01

*** = P< 0.001

TABLE – II

FUNCTIONAL INDICIES OF LV IN EHTN PATIENTS WITH VARIOUS TYPES OF LVH.

Index	ELVH N=27	CLVH N=24	P<
TEF%	53.6±2.3	57.5±4.4	NS
EDV cm	127±6	106±7	0.05 *
ESV cm	58.6±5.0	45.0±3.3	0.05 *
SV cm	68.586.5±1.8	61.0±3.2	0.05 *
R-R ms	813±37	832±29	0.05 *
ET ms	302±20	287±29	NS
MNER	1.77±0.23	2.00±0.16	NS
PER ml/s	5.49±0.62	6.49±0.71	NS
PFR ml/s	3.03±0.43	1.89±0.32	0.05 *
TPFR ms	115±12	217±41	0.05 *
TER ms	145±16	115±14	NS
FR/PER	0.55±0.07	0.29±0.09	0.01 **

* P = <0.05 NS = Not significant ET = Ejection time FR = filling rate.

** P = <0.01

$$SVR = \frac{BP_m}{MV} \times 80$$

Where

SVR = systemic vascular resistance & BP_m=mean blood pressure.

$$MNER = \frac{SV}{EX \times EDV}$$

Where

MNER= mean normalized ejection rate and ET = ejection time.

Peak ejection rate (PER), peak filling rate (PER), time to pead fillin rate (TPFR) and PER/TPER were also calculated.

Echocardiography (Echo): It is one of the most informative methods for the evaluation of the functions of myocordium and its hypertrophy.[14,15] M-mode Echo. Was performed as commonly used[16] on the apparatus echoline 20 A and "BIOMEDICA". The following indicies were measured. End diastolic diamension (EDD) at the level of "Q" wave of ECG.

End systolic diamension (EDD) in cm was calculated at the point of closest approximation of the left ventricular posterior wall (LVPW) and septum.

Posterior wall thickness (PWT) and septal wall thickness (SWT) in systole and diastole in cm were also calculated. With the help of above echo-data we calculated the left ventricular myocardial mass (LVM) according to the recommendations of Penn convention (Devereu x formula 1993).

LVM = 1.04 x $\{(SWTd + EDD + PWTd)^3$-$(EDD)\}^3$- 13.6.d =in diastole. Left ventricular mass index (LVMI) were calculate by dividing LVMM by surface are of the body i.e. LV MI = LVM/S.

TABLE – III

INDICIES OF STRUCTURE OF FUNCTIONAL STATE OF LEFT VENTRICLE WITH EHTN WITH CHVH AND ELVH WITH THE SAME VALUES OF LVM.

Index	ELVH N=12	CHVH N=20	P<
LA cm	3.52±0.34	3.36±0.25	NS
PWTd cm^2	1.06±0.04	1.16±0.04	0.01
SWTd cm	0.95±0.05	1.17±0.03	0.001
EDD cm	5.78±0.16	5.1±0.09	0.001
ESD cm	4.05±0.18	3.36±0.12	0.001
BPs mmHg	149±6	158±5	NS
BPd mm Hg	98±4	105±3	0.02
DS (FS)%	30.1±2.3	33.6±1.7	NS
LVM gm	281±16	274±16	NS
LVMI gm/m^2	134±7	138±7	NS
EST 10^3 dyn cm^2	92.3±5	70.7±4	0.01
LA/EDD	0.61±0.04	0.69±0.03	NS
DP	0.34±0.01	0.45±0.01	0.001

NS = Not significant.

Relative wall thickness (DP) were calculated with the formula (Lutas 1985).

DP = 2PWTd/EDD.

Fraction shortning (DS) with the formula.

$$DS = \frac{(ED - ESD)}{EDD} \times 100\%$$

EST. According to Reicheck (1982)

$$EST = \frac{0.334 \times ESD \times BPs}{SWTs \times (1 + PWTs / ESD)}$$

$10.^3$ dynes/cm^2

Where

BPs = systolic BP

PWTs = Posterior wall thickness in systole.

Exercise tolerance test (ETT). Stress test was performed in horizontal position of the patients. Stress power was 50.V for 5 minutes. RVG were performed at rest and at last minute of the stress test. Statistical calculation of the materials were done with the help of EVM-PR-AT-286 with the use of statistical variation methods by special calculated programme.

Clinical Characteristics of the patients. 84 Patients with EHTN (II stage WHO 1978) and 20 health persons with (average age) of 46.8± 0.3 years were examined. The duration of disease was 2-24 years. 75 patients were male and 9 were female. The patients were examined in the USRIC Ukraine and symptomatic hypertensive patients were excluded with the help of specific tests. Two steped system of investigation devised by Supreme Scientific

TABLE – IV

CONSTANTS (COEFFICIENTS) OF CORRELATION BETWEEN INDICIES OF FUNCTIONAL STATE OF MYOCARDIAL AND LVH.

Index	MMI	P<	DP	P<	EST	P<
ESD	0.469	0.001	0.506	0.001	0.806	0.001
DS	No	—	0.301	0.05	0.745	0.001
TEF	0.306	0.05	No	—	No	—
MNER	0493	0.001	0.427	0.01	No	—
PER	0.423	0.02	No	—	No	—
TPER	No	—	No	—	No	—
PFR	No	—	No	—	0.421	0.01
TPER	No	—	No	—	0.321	0.05
EST	0.321	—	0.533	0001	—	—
LA	No	—	No	—	No	—
LA	No	—	No	—	No	—
LA/EDD	No	—	0443	0.01	No	—

Council USSR (S.S.C.-U.S.S.R). 1978 for differential diagnosis was used.

Symptoms in these patients were vertigo, headache mainly localized in the occipital region and were related to high BP. in 21% of the cases headache was of shooting character radiating to the temporal region. 64% of patients had complains of chest pain of stabbing and pressing character of various duration. In 40% of patients high BP was associated with the appearance of chest pain. Moreover these patients presented with general weakness, apathy, decrease in working capacity, tiredness and insomnia. Some patients had epistaxis. 48% of patients had family history of EHTN. All the patients had thorough clinical examination including inspection, palpation, percussion nd auscultation. 64% of the patients had displacement of the apex beat 1-2cm towards the left. On auscultation decrease of the lungs or any signs of cardiac failure. All the patients had fundoscopic examination. There were segmental or diffused changes in the fundi i.e. construction of the arteries and arterioles thickening in their walls, dilation and tortuosity of the veins. In 57% of patients phenomenon of arteriovenous nipping Salus symptoms I-III, in 13% Gvist's symptom: Patients with IHD were excluded on the bases of stress test. The patients with renal hypertension were excluded with the help of excretory urogram. The patients with pheochromo-cytoma were excluded with the help of 24 hours testing for vanillymandelic acid V/MA.

RESULTS

The patients were divided into two groups. The patients with CLVH=24 and the patients with ELVH=27 pts. Criteria for differentiation was DP. In patients with DP CLVH/ 0.47 and ELVH D $\leq$ 0.36. The following table shows structural and haemodynamic indicies of the LV in these two types of LVH. (Table No1).

In patients with CLVH there was significant increase in PWT as well as in

SWT during systole and diastole. In contrary to ELVH LVD at the end of diastole was significantly low. It was according to the criteria evaluation of the groups on DP.ESD was also low in the patients with CLVH.

BPd and BPs in these two types were not significantly different i.e. 95±3 mm Hg BPd in CLVH and 100±4 mm Hg BP in ELVH.LVM in CLVH was 371±40 gm and in ELVH it was 254±10 gm ($p< 0.05$). The EST measurement in CLVH was 88.0±4.6 10^3 dyn. Cm^2 and it was 63.8±4.6 10^3 dyn. Cm^2 in ELVH ($P< 0.001$). This difference in EST is according to the physiological principals that with the increase in arterial hypertension due to increase in SVR, LVH is the compensatory process to over come the increase in systolic tension on the LV.

According to this thesis very low values of EST were observed in CLVH group is a process of adaptation of myocardium to pressure over load in contrast to the group of patients with ELVH which is due to the volume over load. The following table shows the indicies of systolic and diastolic function in various types of LVH. (Table No 2)

In the patients with CLVH EDV was low than in the patients with ELVH i.e. 106±7 ml aND 127 ±3.3 ml, respectively ($P<0.05$) ESV in CLVH in contrast to ELVH was also low i.e. 45.01±3.0 ml and 58.6±6.5 ml respectively ($P<0.05$). SV and MY in patients with CLVH in contrast with ELVH were also significantly low Cardiac Index CI in CLVH was 2.2±0-l/min/m^2 in contrast to ELVH where it was 2.5 ±0.43 l/min/m^2 ($P<0.05$). TEF, MNER and PER were not significantly differentiated. We observed significant difference in the indicies of diastolic filling in these two types of LVH. PFR ml/s in CLVH was low i.e. 1.89±0.32 ml/s than in ELVH which was 3.03±0.43 ml/s ($P<0.05$). at the same time TPFR in CLVH was significantly greater in contrast with ELVH i.e. 217±14 ms and 115±12 ms respectively ($P<0.05$). This

TABLE – V

CONSTANTS/ COEFFICIENTS/ CORRELATION BETWEEN INDICIES OF SYSTOLIC AND DIASTOLIC FUNCTIONS OF MYOCARDIUM.

Index	PFR	P<	TPER	P<
TEF	0.336	0.05	No	—
MNER	0.418	0.01	No	—
PER	0.354	0.02	No	—
TPER	No	—	No	—
PFR	—	—	0.712	0.001
TPFR	0.712	–.001	—	—
BPs	0.347	0.02	No	—
BPd	0.453	0.01	No	—
Ds	0.402	0.02	No	—
ESD	0.366	0.05	No	—
EST	0.421	0.01	0.327	005

shows significant decrease in the early diastolic filling of LV in patients with CLVH. The ratio PFR/PER in CLVH was twicely low than in patients with ELVH due to significant decrease in LV filling rate as compared to the ejection rate (ER). There was also other signs of deterioration of LV function in CLVH as compared to ELVH i.e. high value of left atrial (LA) diameter ($P<0.05$), low values of EDD and EDV ($P<0.05$) increase in the ratio LA/EDD i.e. 0.69 ± 0.03 in CLVH in contrast with 0.61 ± 0.04 in ELVH.

According to some researchers[14] systolic dysfunction occurs due to LV dialation in EHTN pts. We compared the indicies of ejection phase PER, MNER, TEE and DS in these two types of LVH. These indicies were somewhat lower in ELVH, but not significantly. Index of after load -EST was significantly high in ELVH I.e. 88.0 ± 6.2 and 63.8 ± 4.6 in ELVH and CLVH respectively. ($P<0.001$), which shows elevation of tension on permyocardial cell at the end of systole. These indicies showed that in EHTN patients with ELVH, LV pumping function and cardiac output remains in normal limits despite of high LV. EST along with low availability of energy of myocardium. One of the factors for the normal pumping function of LV is the preservation of high indicies of diastolic filling due to the compensatory Frank-Starling law.

In the above two types of LVH, LVM was greatly different from each other i.e. in CLVH 371 ± 4gm and in ELVH 274 ± 10gm. Therefore we also compared some indicies of structural and functional status of myocardium in these two types with the same value of LVM. For this purpose patients selected with LVMI from 131-150g/m^2 in both of these groups. (Table No 3).

These patients showed different values of PWT and SWT and LVDD and LVSD and EST it is obious that the difference was the same as was in the previous two types of LVH with different LVM. Pumping function DS in these two types had no significant difference which coincides with our previous results. This shows the importance of the type of LVH not of LVM for the structural and functional status of the myocardium. For the evaluation of the inter relationship between the indicies, which characterize the LV functional state and the grade of its hypertrophy we also correlated these results. (Table No 4).

It is clear that LVMI was directly proportional to the ejection phase, MNER and PER. Coefficients of correlation between MNER and MMI was 0.493 ($P<0.001$) and between PER and MMI was 0.306 ($P<0.05$). DP was directly proportional to systolic function MNER =0.427 ($P<0.01$) and DS =0.301 ($P<0.05$). This verify the results we obtained while interpreting the indicies of ejection phase in groups of patients with various degrees of LVH. Increase in LVM is followed by increase in its systolic function. This fact is proved by increase in PER with high grade LVH and interrelations among LVH and other indicies of systolic function i.e. MNER, TEF, DS. Early diastolic filling indicies do not correlate with MMI and DP. There was significant correlation between DP and LA/EDD =0.443($P<0.01$). This shows diastolic dysfunction due to increase in LV wall thickness which give rise to increase in LA diamension. It shows date rioration LVED filling with the increase in LVM and decrease in diastolic function of LV in CLVH as compared to ELVH. Similarly we did not observe correlation between indicies of LVH and diastolic filling. Obviously LVH induces deterioration of LV filling function not directly through increase in LVM, but indirectly through biochemical processes influencing LV relaxation, deterioration in its blood perfusion, change in the conditions of pre and after load.

For the purpose of assessing the interrelation between LV diastolic function

and degree of after load and systolic properties of LV, We performed comparative analysis between PFR and TPFR from one side indicies of systolic function and stage of BP and EST from another side. (Table No 5).

PFR was directly proportional to incidices of ejection phases i.e. MNER =0.418 (P<0.01) and to PER =0.354 (P<0.02) also to TEF =0.336 (P<0.05) and to DS =0.402 (P<0.02). There was weak but significant correlation between PFR and ESD =0.336 (P<0.05), TPER and PFR =0.712 (P<0.001). PFR was correlated with EST of LV wall thickness, which characterise after load. PFR correlated with EST =0.421 (P<0.01) for TPFR and EST =0.327 (P<0.05). Systolic and diastolic BP were also interrelated with PFR =0.347 (P<0.02) and =0.453 (P<0.01) respectively. Indirect proportion with between PFR and BP and EST shows that increase in the after load decreases the left ventricular relaxation and decreases the earlier phase of LV diastolic filling. As a whole according to the data we obtained shows that patients with EHTN systolic properties of LV and degree of LV after load are the important determinants of the earlier LV diastolic filling rate.

DISCUSSION

In arterial hypertension increase in the afterload leads to increase in the end systolic tension (EST), on the left ventricular wall and give rise to concentric left ventricular hypertrophy (CLVH), which is characterised by parallel deposition of sarcomeres in cardiomycytes and increase in the LVD[2,3]. This increase in the tension on the LV wall (systolic or diastolic) stimulates biochemical and ultra structural changes in the myocardium and induces acceleration in the synthesis of myocardial protein. This leads to the increase in the size of cardiomyocytes both longitudinally and transversely. Fibroblasts, fibrillar collagen and vascular smooth muscles are also involved in this process of hypertrophy[4,5,6]. Proliferation of the noncardiomyocytes induce interstitial remodelling and is thought to be the important determinant of the pathological hypertrophy. Increase in the collegen content of the myocardium leads to the development of myocardial fibrosis. This decreases the passive elastic properties of myocardium, in rigidity and decrease in the diastolic extensibility.

CLVH develops as a result of increase in the systolic tension (afterload) and ELVH develops as a result of increase in the diastolic tension (preload)[7,8,9]. In patients with low stress hypertrophy the development of LVH is not due to stress on LV wall but due to hormonal factors.

ELVH is characterised by increase in the LV dimensions due to dilatation, it is thought to develop in the late stages of EHTN, and is characterised by deterioration in the pumping function of the LV[10,11]. CLVH is characterised by increase in the thickness of LV wall with normal or decrease in LV diamension, with the deterioration in the diastolic filling.

In essential hypertensive patients (EHTN) systemic vascular resistance (SVR) is directly proportional to the relative wall thickness of the left ventricle in diastole i.e. systemic vascular resistance is the most important haemodynamic determinant for the development of concentric left ventricular hypertrophy (CLVH).

Increase in the left ventricular end systolic tension (EST) in essential hypertensive (EHTN) patients leads to reduced left ventricular pumping function which is proven with the indirect proportion between end systolic tension (EST) and fraction shortening (DS). Increase in the relative wall thickness of left ventricle leads to decreased left ventricular end dystolic tension.

Essential hypertensive patients with concentric left ventricular hypertrophy and

with no signs of congestive heart failure are characterised by normal indicies of systolic function with mild to moderate left ventricular mass. Early diastolic fulling indicies of left ventricle in concentric left ventricular hypertrophy significantly decrease.

Essential hypertensive patients with eccentric left ventricular hypertrophy are characterised by maintaining of left ventricular early diastolic fulling indicies which is important for the maintenance of the normal left ventricular pumping function through Frank-Starling mechanism.

While treating patients with essential hypertension it is important to keep in mind the various ways of compensation of left ventricular function in concentric and eccentric left ventricular hypertrophy.

While treating essential hypertensive patients with eccentric left ventricular hypertrophy (which are characterised by deterioration in left ventricular diastolic function) it is important to avoid medicines which decrease left ventricular diastolic volume e.g. diuretics and vasodilators.

REFERENCES

1. Meerson FZ. Myocardium in hyperfunctio, hypertrophy and heart failure M: Medicine, 1965.
2. Alpert NR, Hasenfuss G, Mulieri LA, etal. The reorganisation of the human and rabbit heart in response to haemodynamic overload/Europ Heart J-1992; 13: 9.
3. Korecky B, Masika M. Direct effect of increased haemodynamic load on cardiac mass/circulat Res 1991; 68: 1174.
4. Brilla CG, Maisch B, Weber KT. Myocardial collegen matrix remodelling in arterial hypertensio9n/Europ. Heart J. 1992; 13: 24.
5. Schwart Skopff B, Motz W, Knauer S, et al. Morphometric investigation of intramyocardial arterioles in right septal endomyocardial biopsy of patients with ventricular hypertrophy/J. Cardiovase Phormacol 1992; 20: 12.
6. Weber Kt, Brillac G. Patholocial hypertrophy and cardiac interstitation and renin angiotension system/circulation 1991; 83: 1849.
7. Reichek N, Wilson J, Suuton MSJ, et al. Non invasive determination of left ventricular end systolic stress. Validation of the method and initial application/ circulation 1982; 65: 99.