

The effect of Valsalva maneuver on diastolic filling indices in patients with essential hypertension.

Salam A. Mahdi*

Najeeb H. Mohammed**

Hilal B. AL-Saffar***

MBChB

MBChB, MSc, DM, PhD.

MBChB, CABP, FRCP.

Summary:

Background: Left ventricular hypertrophy and diastolic dysfunction are considered to be an important risk factor for cardiovascular morbidity and mortality in asymptomatic hypertensive patients. At the bedside, left ventricular geometric remodeling and diastolic dysfunction in hypertension can not be diagnosed without echocardiography which is a useful adjunct to the medical history, physical examination, ECG, and chest radiography. Hence, it provides an opportunity for good management and prognosis of what appears to be preclinical hypertensive complication.

Subjects and Methods: 127 subjects with essential hypertension of either sex attending echo unit were subjected to medical history, clinical examination, physical measurements, ECG, M-mode and Doppler echocardiography. They were classified as 46 treated hypertensives where they were on regular antihypertensive medication, and 81 untreated hypertensive patients. In addition, they were sex and age matched to 39 healthy subjects who served as control group.

Results: The results of this study revealed that hypertensive patients especially those with stage II hypertension were prone to develop left ventricular hypertrophy (LVH) of concentric geometric pattern and diastolic dysfunction. However, small percentage of those patients found to have diastolic dysfunction despite they were without LVH. In addition, Doppler echocardiography clarify that hypertensives with abnormal transmitral inflow profile; of left ventricular impaired relaxation pattern suffered left ventricular systolic dysfunction. Moreover, in this study there was no evidence of pseudonormal transmitral inflow filling pattern which is excluded after Valsalva maneuver.

Conclusion: There is a strong association between left ventricular hypertrophy and diastolic dysfunction which was more common in patients with stage II hypertension. However, left ventricular diastolic dysfunction is usually follows left ventricular hypertrophy, but it still may proceed especially in those patients with left ventricular hypertrophy (LVH) of concentric geometric pattern. In addition, left ventricle diastolic dysfunction is not necessary coincide with the development of systolic dysfunction, namely normal ejection fraction and fractional shortening.

Keywords: Hypertension, Left Ventricular Hypertrophy (LVH), Diastolic dysfunction, Valsalva maneuver.

Fac Med Baghdad
2010, Vol. 52, No.1
Received: Apr. 2009
Accepted: May. 2009

Introduction:

Since normal systole is important for pumping blood from left ventricle to the body, the normal diastole is also essential for filling the left ventricle. Diastole represents the capacity of the left ventricle to receive a volume of blood that guarantee an adequate stroke volume at a low-pressure regimen with normal pulmonary venous pressure (1). For descriptive purposes, left ventricular diastole can be divided into four phases: isovolumic relaxation, rapid early filling, slow late filling, and atrial systole (2). Normal diastolic function is evaluated by adequate ventricular filling at rest and with exercise without an abnormal increase in diastolic filling pressures. Accordingly, diastolic dysfunction is characterized

by: an increased intraventricular diastolic pressure, Delayed relaxation, increased stiffness with Prolonged time for returning to presystolic length and force (3). In hypertension, diastolic dysfunction is usually present as asymptomatic finding on non-invasive testing, or as dyspnea and pulmonary edema despite their left ventricular systolic function is normal (4). The pathophysiology of the abnormalities in diastolic function of the left ventricle can be divided into structural and functional processes in the cardiomyocyte or within the extracellular matrix (3). Patients with proven left ventricle diastolic dysfunction had been shown to demonstrate characteristic abnormalities in the Doppler echocardiographic spectral of transmitral inflow profile which includes four patterns (5): (1) Normal transmitral inflow pattern; where E/A ratio > 1- 1.5, IVRT is between 70- 95 msec and DT is ranged from 165 to 210 msec., with no

*Ministry of Health.

**Dept. of Physiology, College of Medicine, University of Baghdad.

***Dept. of Medicine, College of Medicine, University of Baghdad.

reversal of E/A ratio during performing Valsalva maneuver (6). (2) Impaired relaxation pattern; where E/A ratio will be reversed or less than 1 and IVRT and DT are more than 100 msec. and 220 msec. respectively (7). (3) Pseudonormal filling pattern; in which all parameters were within normal, but it can be unmasked by performing Valsalva maneuver for altering the left ventricle loading condition by increasing intrathoracic pressure which will decrease left ventricle preload transiently. In normal subjects, Valsalva maneuver lead to an equal decline in E-peak and A-peak velocities, hence, E/A ratio remained over 1.0. While in patients with pseudonormal filling pattern, it will convert to impaired relaxation pattern and the E/A ratio will be reduced below one (8). (4) Restrictive filling pattern; when E/A ratio > 2, IVRT < 60 msec. and DT < 150 msec.

Subjects and methods:

One hundred and sixty six (166) subjects of either sex were involved in this study. They were classified as 46 regularly treated hypertensive patients (Group T), 23 men and 23 women with a mean age of 51 ± 7 years, 81 untreated hypertensive patients (Group U), 27 male and 54 female with a mean age of 53 ± 9 year, and 39 healthy non-hypertensive subjects served as control (Group C); 17 men and 22 women with mean age 51 ± 10 years. Each subject was submitted for medical history, clinical examination, physical measurements (height, weight, body surface area and body mass index), blood pressure measurement, M-mode and Doppler echocardiography (using Philips EnVisor / 2005 2B with 2.5-3.5 MHz transducer), in addition to an ECG and chest X-ray. This study was conducted in the echocardiographic units of both Baghdad-Medical City Teaching Hospital and The Iraqi Centre for Heart Diseases / the Specialist Surgical Hospital in the period between March and September 2008. While, the average of three measurements of blood pressure using mercury sphygmomanometer, the first and fifth Korotkoff's sounds (disappearance of sound) were considered to identify systolic and diastolic blood pressure values respectively. Stage I hypertension was considered if the systolic blood pressure is between 140-150 mmHg and or diastolic blood pressure is between 90-99 mmHg while in Stage II hypertension the systolic blood pressure is equal or more than 160 mmHg and or diastolic blood pressure is equal or more than 100 mmHg (JNC/6, 2003). Body surface area (BSA) and body mass index (BMI) were calculated according to the following equations:

$$BSA (m^2) = [Wt (kg) \times Ht (cm)] \times 0.007184. (RRRRR)$$

$$BMI = Wt(kg) / Ht(m)^2.$$

The echocardiographic examination was performed in a dimly light room while the subject was at rest and in sinus rhythm with partial left lateral decubitus position. The following measurements were recorded according to the standards recommended by the American Society of Echocardiography (RRRRRRR): Left ventricular internal dimensions at end systole (LVIDs) and end diastole (LVIDd). Interventricular septal thickness (IVST) and LV posterior wall thickness (PWT) at end of diastole.

Left ventricular ejection fraction (EF %) and fractional shortening (FS %). These parameters reflect systolic function.

1. Peak E-wave velocity, peak A-wave velocity, E/A ratio, E-wave deceleration time (DT) and isovolumetric relaxation time (IVRT) using Doppler echocardiography.

2. Left ventricular mass, left ventricular mass index (LVMI) and left ventricular relative wall thickness (RWT). These parameters determine different left ventricular geometric patterns.

Accordingly, left ventricular geometric patterns (Figure 1) can be classified as: normal geometry when LV mass index and relative wall thickness are normal, concentric remodeling with normal LV mass index and high relative wall thickness, eccentric hypertrophy with elevated LV mass index and normal relative wall thickness, and finally concentric hypertrophy, if both LV mass index and relative wall thickness are elevated.

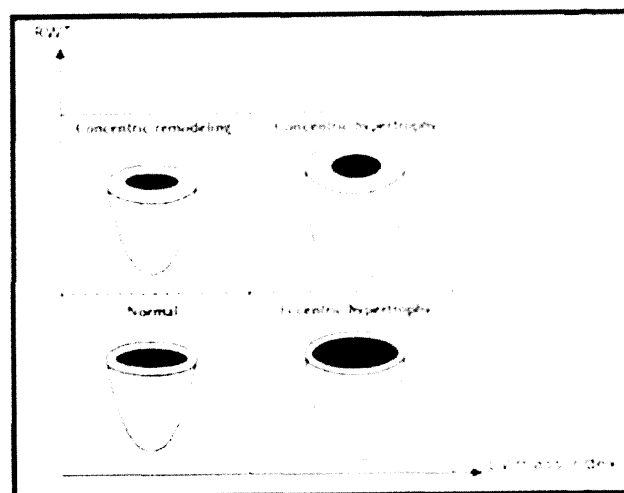


Figure 1: Normal and abnormal LV geometric patterns, RWT: relative wall thickness (Devereux et al., 1993).

Results:

Firstly, all subjects involved in this study were sex and age matched and they are non obese neither overweight ($BMI < 27.5 \text{ kg/m}^2$). As shown in Table 1, The parameters that reflect diastolic function were significantly higher in untreated hypertensives when compared with that of treated hypertensives and control ($p < 0.05$). These parameters include left ventricular posterior wall thicknesses (PWT), interventricular septal wall thicknesses (IVST), left ventricular mass, left ventricular mass index (LVMI) and left ventricular relative wall thickness (RWT). While, Doppler transmitral inflow parameters again of untreated hypertensives revealed significantly lower values of E/A ratio with an increased values of deceleration time (DT) and isovolumetric relaxation time (IVRT).

While the results obtained from table 2 showed that left ventricular hypertrophy (LVH) was present in 42% of untreated hypertensive patients when compared with 20% of treated hypertensives.

Moreover, what is concerned with geometric remodeling patterns; table 2 illustrate that concentric remodeling was found in 30% of untreated hypertensives, 27% with eccentric hypertrophy, and 15% with concentric hypertrophy, however these percentages were significantly higher when compared with those of treated hypertensives. In addition, 31 out of 81 untreated hypertensive patients (38%) developed diastolic dysfunction of an impaired relaxation pattern versus 8 out of 46 treated hypertensives (17%). Furthermore, when patients with normal transmitral inflow pattern had further undergone Doppler-Echocardiographic examination while performing Valsalva maneuver to unmask the pseudonormal pattern of diastolic dysfunction, none of those patients converted to impaired relaxation pattern of diastolic dysfunction, which means that there were no patients with pseudonormal pattern of diastolic dysfunction come across in this study.

Table 3 showed that higher percentages of untreated hypertensives with LVH (68%) developed diastolic dysfunction of impaired relaxation pattern versus 17% without LVH. While the severity of hypertension has its own impact on the development of LVH and thus diastolic dysfunction, 66% of patients with Stage II hypertension developed LVH when compared with 14% of those with Stage I hypertension. What was noticed from Table 4, untreated hypertensive patients with diastolic dysfunction of left ventricular impaired relaxation pattern showed significantly slight elevation in ejection fraction and fractional shortening (69.9 ± 3.2 and 33.0 ± 2.4 vs. 68.6 ± 2.6 and 31.8 ± 2.0 of those with normal pattern), this means that they have relatively enhanced LV systolic function despite they have LV diastolic dysfunction.

Table 1: Demographic, Anthropometric, M-mode and Doppler echocardiographic parameters of hypertensive and control groups.

Variable	Group T n = 46	Group U n = 81	Group C n = 39	T vs. C P-value	U vs. C P-value	T vs. U P-value
Age (year)	51 \pm 7	53 \pm 9	51 \pm 10	0.974	0.315	0.198
Height (cm)	165.8 \pm 7.3	165 \pm 9.6	166.8 \pm 5.1	0.671	0.637	0.938
Weight (kg)	74.9 \pm 5.5	74.7 \pm 6.5	73.4 \pm 4.6	0.173	0.246	0.874
BMI (kg/m ²)	27.5 \pm 1.2	27.4 \pm 1.4	26.7 \pm 1.8	0.031	0.022	0.912
BSA (m ²)	1.86 \pm 0.10	1.85 \pm 0.12	1.83 \pm 0.07	0.4261	0.542	0.888
PWT (cm)	0.88 \pm 0.15	1.0 \pm 0.14	0.88 \pm 0.10	0.546	0.0001	0.0001
IVST (cm)	0.92 \pm 0.15	1.1 \pm 0.18	0.92 \pm 0.11	0.118	0.0001	0.0001
LV mass (g)	176.3 \pm 45.8	225.9 \pm 42.0	158.1 \pm 59.9	0.115	0.0001	0.0001
LVMI (g/m ²)	95.9 \pm 26.0	122.9 \pm 23.6	86.0 \pm 32.0	0.136	0.0001	0.0001
RWT	0.41 \pm 0.08	0.46 \pm 0.05	0.40 \pm 0.04	0.251	0.0001	0.0001
E/A ratio	1.18 \pm 0.18	1.03 \pm 0.19	1.19 \pm 0.13	0.097	0.0001	0.008
DT (msec)	199 \pm 18	220 \pm 31	192 \pm 17	0.071	0.0001	0.0001
IVRT (msec)	93 \pm 9	97 \pm 14	91 \pm 5	0.342	0.016	0.045

- Values were expressed as mean \pm SD.
- P-values less than 0.05 were considered as statistically significant.
- Group T= Treated hypertensives, Group U= Untreated hypertensives, Group C= Control group, PWT= Left ventricular posterior wall thickness, IVST= Interventricular septum thickness, LV mass= Left ventricle mass, LVMI= Left Ventricle Mass Index, RWT= Left Ventricle

Table 2: Distribution of left ventricular hypertrophy, geometric patterns and diastolic dysfunction in treated and untreated hypertensives groups.

Variable	Group T n = 46	Group U n = 81	T vs. U P-value
Without LVH	37 (80%)	47 (58%)	0.010
Normal Geometry Concentric Remodeling	35 (76%) 2 (4%)	23 (28%) 24 (30%)	0.0001
With LVH	9 (20%)	34 (42%)	0.010
Eccentric Hypertrophy Concentric Hypertrophy	6 (13%) 3 (7 %)	22 (27%) 12 (15%)	0.0001
Impaired relaxation	8 (17%)	31 (38%)	0.014

Group T= Treated hypertensives, Group U= Untreated hypertensives and LVH= Left Ventricle Hypertrophy.

Table 3: Distribution of left ventricular diastolic dysfunction and hypertension stages in untreated hypertensive groups with LVH and without LVH.

Variable	Untreated Hypertensives		P-value
	Without LVH n = 47	With LVH n = 34	
Impaired Relaxation	8 (17%)	23 (68%)	0.0001
Hypertension Stage I	32 (86%)	5 (14%)	0.0001
Hypertension Stage II	15 (34%)	29 (66%)	

Table 4: Comparison of left ventricular systolic function between untreated hypertensives with and without diastolic dysfunction.

Variable	Untreated Hypertensives		P-value
	Normal Pattern n= 50	Impaired Relaxation n= 31	
EF (%)	68.6 ± 2.6	69.9 ± 3.2	0.012
FS (%)	31.8 ± 2.0	33.0 ± 2.4	0.014

Discussion:

M-mode and Doppler echocardiography are known to be very important for providing indices regarding left ventricular mass, systolic and diastolic performance, while it remains reasonably cheap, available, and wholly noninvasive (9). These measurements are proved to be better for predicting the evolutionary process of hypertension as compared with other variables, such as systolic, diastolic blood pressure, and hypertension staging (10). In this study, since that all subjects involved were sex, age, and BMI matched (Table 1), thus it is possible to exclude the apparent effect of these parameters on the result. Specifically, the BMI of all subjects was less than 27.5 (kg/m²), where BMI of 30 kg/m² is used as a cutoff for obesity with its risk for the development of hypertension (RRR). As it was noticed again from (Table 1), in untreated hypertensive group, the significant higher values of left ventricular posterior wall and interventricular septal wall thicknesses, which are roughly considered as an indicator for LVH (11), LV mass and LV mass index came in parallel with the results of Ghanem, et al. (12). Mechanism While, the significant increment of the relative wall thickness in both hypertensive patients comparing with the control is similar to the study by Gaasch who had showed the relative wall thickness increases in direct proportion to elevations in systolic blood pressure (13). In addition, the expanded percentage of patients with LVH within the untreated group (Table 1) is due to the uncontrolled hypertension which is the fundamental trigger to the sequence of biologic events that lead to the increment in the LV mass as supported by several meta-analyses studies which have been demonstrating the reversal and regression of LVH depending on the using various antihypertensive drugs, the baseline LV mass and the degree of blood pressure reduction. (14) The analyzing of left ventricular geometry (Table 2) detect that untreated

hypertensives have a higher percentage of eccentric and concentric LVH due to uncontrolled blood pressure as proposed early by Kannel and Bertoli, et al. (15, 16) In addition, those authors had mentioned that LVH is a strong indicator of bad prognosis in hypertensive individuals and in the general population. Other contributing factors for LVH include the stage of hypertension as had been proposed by Rizzoni, et al. which supports the finding in this study (Table 3) where a larger percent of the untreated hypertensives with LVH were significantly categorized as Stage II hypertension. (17) Doppler echocardiography has emerged as an important noninvasive diagnostic tool, providing reliable data in staging the diastolic dysfunction, where the abnormality in left ventricular relaxation and compliance alters the onset, rate, and extent of left ventricular pressure decline and filling during diastole. This elevation in filling pressures may results in exertional dyspnea and fatigue especially during exercise. (18) It's obvious from the examination of pulsed wave Doppler parameters (Table 1), that the untreated hypertensives revealed the lower values of E/A ratio with the enhanced values of DT and IVRT hence there are a larger percentage of LV diastolic dysfunction as impaired relaxation pattern (Table 2). This diastolic dysfunction is due to progressive increase in A-wave and decrease in E-wave, caused by a low pressure gradient between left atrium and left ventricular. This finding go in parallel with the study of Avdi?, et al., who mentioned that over 40% of patients with essential hypertension developed diastolic dysfunction and it is necessary to detect LV diastolic dysfunction and it's prevention with improved essential hypertension monitoring. (19) Furthermore, the diastolic dysfunction can be detected even before demonstrable LVH (Table 3) which alert for monitoring these patients as reported by Galderisi, et al. (20) this finding suggests that in asymptomatic hypertensive subjects, the exclusion of LVH does not rule out LV diastolic dysfunction if present, it's most likely mild. However, the explanation of this result may be viewed as; although those patients have normal LV mass, they still have abnormality in the geometric pattern, named "concentric remodeling". Identically, it was obvious in this study (Table 4) those patient with impaired LV relaxation, showed a significantly slight elevation in ejection fraction and fractional shortening which mean a larger number of patients with relative enhanced LV systolic function despite they have LV diastolic function. The effect of nonuniform wall thickening is greatest with increased relative wall thickness and thus leads to overestimation of myocardial performance between those individuals. Therefore, it's important to look for other parameters for assessment LV systolic function especially in hypertensive patients with a high prevalence of concentric LV geometry. Hence, shifting to measuring of other parameters such as "LV midwall shortening" substantially reduced the number of hypertensive patients with supranormal LV function and identified low left ventricular systolic performance.

Conclusion:

The results of this study provided evidences about a strong association of left ventricular remodeling and hypertrophy with diastolic dysfunction using M-mode and Doppler echocardiographic parameters. These functional and structural abnormalities were more common in untreated hypertensives with Stage II hypertension. However, left ventricular diastolic dysfunction is usually follows the left ventricular hypertrophy, but it still may precede especially in patients with concentric geometric remodeling. In addition, left ventricle diastolic dysfunction showed no relation with systolic dysfunction?namely ejection fraction and fractional shortening especially in untreated hypertensives with high incidence of concentric left ventricle geometry.

References:

- 1) Solomon S., Nikolic S., Fraser R., Yellin E. *Contraction-relaxation coupling: determination of the onset of diastole.* Am. J. Physiol., 1999; 277: H23-H27.
- 2) Opie L. H.: *The Heart: Physiology, From Cell to Circulation.* Philadelphia, Pa: Lippincott Williams & Wilkins; 1998.
- 3) Zile M., Brutsaert D. *New concepts in diastolic dysfunction and diastolic heart failurePart II: causal mechanisms and treatment.* Circulation, 2002; 105: 1503-1508
- 4) Phillips R. A. Diamond J. A.: *Diastolic function in hypertension.* Curr. cardiol., 2001; 3(6): 485-97.
- 5) Erbel R., Neumann T., Zeidan Z., Bartel T., Buck T.: *[Echocardiography diagnosis of diastolic heart failure]* Herz., 2002 Mar; 27(2): 99-106.
- 6) Mottram Philip M., Marwick Thomas H.: *Assessment of diastolic function: what the general cardiologist needs to know,* Heart, 2005; 91: 681-695.
- 7) Redfield M. M., Jacobsen S. J., Burnett J. C. Jr. *Burden of systolic and diastolic ventricular dysfunction in the community: appreciating the scope of the heart failure epidemic.* JAMA 2003; 289: 194-202.
- 8) Ural D., Ural E., Kahraman G., Caymaz O., Aktulun C., Komsuolu B.: *Effect of the Valsalva manoeuver on diastolic filling indices in patients with essential hypertension.* J. Hum. Hypertens., 2001 Sep; 15(9): 607-12.
- 9) Krumholz H. M., Larson M., Levy D.: *Prognosis of left ventricular geometric patterns in the Framingham Heart Study.* J. Am. Coll. Cardiol., 1995; 25: 879-884.
- 10) Ganau A., Devereux R., Roman M.: *Patterns of left ventricular hypertrophy and geometric remodeling in essential hypertension.* J. Am. Coll. Cardiol. 1992; 19: 1550-1560.
- 11) Devereux R. *Does increased blood pressure cause LVH or vice versa?* Ann. Intern. Med., 2000; 112: 57-8.
- 12) Ghanem Wisam M., Murin J., Bulas J., Kozlikova K., Jaber J., Radman A.: *[Left ventricular hypertrophy in hypertension]* Bratisl Lek Listy., 2000; 101(8): 455-9.
- 13) Gaasch W.: *LV radius to wall thickness ratio.* Am. J. Cardiol., 1979; 43: 1189-1194.
- 14) Klingbeil A., Schneider M., Martus P., Messerli F., Schmieder R.: *A meta-analysis of the effects of treatment on*

left ventricular mass in essential hypertension. *Am. J. Med.*, 2003; 115: 41-46.

15) Kannel W. B. Prevalence and natural history of electrocardiography LVH. *Am. J. Med.*, 1983; 75: 4-8.

16) Bertoli d., Bacano L., Carrantino L., Caudullo M., Pettacchi R., Filorizzo G. Prevalence of echocardiographic patterns of left ventricular geometry in hypertensive patients. *Proceedings of xx 1st congress of the European society of cardiology* 1998, August 22-26, Vienna, Austria. P. 2278.

17) Rizzoni D., Muiesan M., Montani G., Zulli R., Calebich S., Agabiti-Rosei E.: Relationship between initial cardiovascular structural changes and daytime and nighttime blood pressure monitoring. *Am. J. Hypertens.*, 1992; 5: 180-186

18) Aurigemma G. P., Gottdiener J. S., Shemanski L., Gardin, Kitzman. Predictive value of systolic and diastolic function for incident congestive heart failure in the elderly: the cardiovascular health study. *J. Am. Coll. Cardiol.*, 2001; 37: 1042-8.

19) Avdi? S., Mujcinovi? Z., As?eri? M., Nuki? S., Kusljugi? Z., Smaji? E., Arapci? S. Left ventricular diastolic dysfunction in essential hypertension *Bosn. J. Basic Med. Sci.*, 2007; Feb; 7(1): 15-20.

20) Galderisi M., Petrocelli A., Alfieri A., Garofalo M., de Divitiis O. Impact of ambulatory blood pressure on left ventricular diastolic dysfunction in uncomplicated arterial systemic hypertension. *Am. J. Cardiol.*, 1996; 77: 597-601.