THE EFFECTS OF LEFT VENTRICULAR GEOMETRY AND HYPERTROPHY ON THE DIASTOLIC FILLING INDICES IN HYPERTENSION

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Abstracts
Objectives:

The aim of this study is to show the effects of left ventricular hypertrophy and geometric patterns on the left ventricular diastolic function in patients with essential hypertension. In addition, it's aimed to identify whether the diastolic dysfunction is associated with systolic dysfunction. Finally, to determine the occurrence of the diastolic dysfunction in hypertensive patients with normal left ventricular mass.

Patients and Methods:

135 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 43 treated hypertensives, and 92 untreated hypertensive patients. In addition to 32 healthy subjects served as control group.

Results:

The results of this study showed that untreated stage II hypertensive patients have more changes in left ventricular mass and geometry and, hence, a higher percentage of diastolic dysfunction. There was a small percentage of patients having diastolic dysfunction despite they were without LVH. In addition, Doppler echocardiographic examination showed that hypertensive patients with left ventricular diastolic dysfunction were having a normal left ventricular systolic function.

Conclusion:

Left ventricular hypertrophy and geometric changes have an obvious effects on the Left ventricular diastolic function especially in untreated stage II hypertensive patients.

Keywords: Hypertension, LVH and Diastolic dysfunction.

Introduction

Left ventricular hypertrophy and diastolic dysfunction are considered to be an important risk factor for cardiovascular morbidity and mortality in asymptomatic hypertensive patients [1]. In the last two decades, M-mode and Doppler echocardiography played a very crucial role in a lot of reports, clinical research and early diagnosis of abnormalities in left ventricular mass and diastolic function [2]. 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 [3]. Diastole represents the capacity of the left ventricle to receive a volume of blood that guarantees an adequate stroke volume at a low-pressure regimen with normal pulmonary venous pressure [4]. From the physiological point of view, left ventricular diastole can be divided into four phases: isovolumic relaxation, rapid early filling, slow late filling, and atrial systole [5]. 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 [6].

In hypertension, the left ventricle adapts to sustained pressure overload through alteration in geometry and diastolic function. Diastolic dysfunction in general hypertensive populations may imply a higher prevalence of coronary disease and that may indicate a worse prognosis and demands a more detailed evaluation of the hypertensive patient. It's usually present as asymptomatic finding on non-invasive testing, or as dyspnea and pulmonary edema despite their left ventricular systolic function is normal [7]. 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 [8]. 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 reversal of E/A ratio during performing Valsalva maneuver.

(2) Impaired relaxation pattern; where E/A ratio will be less than 1 (reversed) and IVRT and DT are more than 100 msec. and 220 msec. respectively.

(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. In normal subject, it leads 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.

(4) Restrictive filling pattern; when E/A ratio > 2, IVRT < 60 msec. and DT < 150 msec.

Patients and Methods

One hundred sixty seven (167) non obese subjects of either sex were involved in this study. They were classified as 43 regularly treated and well controlled hypertensive patients (THR G), 22 men and 21 women with a mean age of 50 ± 6 years, 92 untreated hypertensive patients (UTHR G), 30 male and 62 female with a mean age of 53 ± 7 year, and 32 healthy non-hypertensive subjects served as control (C G); 15 men and 17 women with mean age 51 ± 10 years. Patients with ischemic heart disease, valvular

heart disease, cardiomyopathy, thyrotoxicosis, and patients with structural heart dieses were excluded from the study. All patients with normal systolic function on echo study. The patients were submitted for medical history and clinical examination. While all subjects underwent physical measurements (height, weight, body surface area and body mass index), blood pressure measurement, M-mode and Doppler echocardiography in the echocardiographic units of both Baghdad/Medical City Teaching Hospital in the period between September 2008 and March 2009. Using a mercury sphygmomanometer, blood pressure was determined by the average of three measurements, while the first and fifth Korotkoff sounds 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 [9]. Body surface area (BSA) and body mass index (BMI) were calculated according to the following equations [10]:

$$BSA(m^2) = \sqrt{\frac{Height\,(cm) \times weight\,(kg)}{3600}}$$

$$BMI = \frac{Weight\,(kg)}{Height^2\,(m)}$$

The following M-mode echocardiographic measurements were considered while the subject was at rest and in sinus rhythm with partial left lateral decubitus position. The measurements were according to the standards recommended by the American Society of Echocardiography [11]:

1. Left ventricular internal dimensions at end systole (LVIDs) and end diastole (LVIDd).
2. Interventricular septal thickness (IVST) and LV posterior wall thickness (PWT) at end of diastole.
3. Left ventricular ejection fraction (EF %) and fractional shortening (FS %).
4. Left ventricular mass and left ventricular mass index (LVMI), normally <134 g/m^2 in men and <110 g/m^2 in women.
5. Left ventricular relative wall thickness (RWT) with partition value of <0.45 was considering normal.
6. According to LVMI and RWT, left ventricular geometric patterns 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 [12].

Doppler echocardiographic application was used to measure Peak E-wave velocity, peak A-wave velocity, E/A ratio, E-wave deceleration time (DT) and isovolumetric relaxation time (IVRT) [2].

Results

Table 1 shows the demographic, anthropometric and clinical characteristics of all subjects involved in this study which were age matched and they are non obese (BMI < 27.5 kg/m^2). The untreated hypertensive patients have a significant elevation in SBP and DBP when compared with the treated hypertensive patients and control.

M-mode echocardiographic parameters of hypertensives and control groups where shown in table 2. It's obvious that untreated hypertensive patients demonstrate higher values regarding LV internal dimension, posterior wall thickness, interventricular thickness and LV mass (p<0.05). Hence the derived parameters, LVMI and RWT, were elevated in untreated hypertensives. Furthermore they have a higher value regarding EF%, FS% and left atrial dimension.

Table 1: Demographic, Anthropometric and clinical characteristics.

Variable	THR G n = 43	UTHR G n = 92	C G n = 32	THR G vs. C G *P*-value	UTHR G vs. C G *P*-value
Age (year)	50 ± 6	53 ± 7	51 ± 10	0.71	0.30
BMI (kg/m^2)	27.4 ± 1.2	27.5 ± 1.4	26.5 ± 1.8	0.015	0.002
BSA (m^2)	1.9 ± 0.10	1.85 ± 0.12	1.83 ± 0.08	0.324	0.625
SBP	130.8 ± 5.4	156.4 ± 10.4	128.6 ± 5.1	0.503	0.0001
DBP	82 ± 3.5	95 ± 5.5	81 ± 6	0.090	0.0001

- Values were expressed as mean ± SD.
- P-values less than 0.05 were considered as statistically significant.
- THR G= Treated Hypertensive Group, UTHR G= Untreated Hypertensive Group, C G= Control Group, SBP=Systolic Blood Pressure, DBP=Diastolic Blood Pressure.

Table 2: M-mode echocardiographic parameters of hypertensives and control groups.

Variable	THR G n = 43	UTHR G n = 92	C G n = 32	THR G vs. C G P-value	UTHR G vs. C G P-value
LVIDd (cm)	4.6 ± 0.2	4.8 ± 0.3	4.5 ± 0.6	0.091	0.008
LVIDs (cm)	3.2 ± 0.1	3.4 ± 0.2	3.1 ± 0.5	0.059	0.044
PWT (cm)	0.96 ± 0.15	1.06 ± 0.13	0.90 ± 0.09	0.182	0.0001
IVST (cm)	0.97 ± 0.14	1.12 ± 0.13	0.95 ± 0.10	0.011	0.0001
LV mass (g)	175.1 ± 45.6	226.8 ± 41.1	167.8 ± 57.1	0.539	0.0001
LVMI (g/m^2)	94.6 ± 25.7	123.1 ± 23.0	91.3 ± 30.7	0.614	0.0001
RWT	0.44 ± 0.05	0.45 ± 0.04	0.40 ± 0.04	0.0001	0.0001
EF%	69.5 ± 2.6	69.0 ± 2.9	65.7 ± 4.4	0.0001	0.0001
FS %	32.8 ± 1.9	32.4 ± 2.2	30.1 ± 2.9	0.0001	0.0001
LAD (cm)	2.95 ± 0.53	3.45 ± 0.61	2.59 ± 0.46	0.004	0.0001

- LVIDd= Left ventricular internal dimensions at end diastole, LVIDs= Left ventricular internal dimensions at end systole, PWT= Left ventricular posterior wall thickness, IVST= Interventricular septum thickness, LV mass= Left ventricle mass, LV MI= Left Ventricle Mass Index, RWT= Left Ventricle Relative Wall Thickness, EF= Left ventricular ejection fraction and FS= fractional shortening.

Depending on LV mass and LVMI, figure 1 shows that left ventricular hypertrophy (LVH) was present in 46% of untreated hypertensive patients when compared with 20% of treated hypertensives (p=0.002). Moreover, what is concerned with geometric remodeling patterns; figure 2 illustrate that concentric remodeling was found in 26% of untreated hypertensives, 29% with eccentric hypertrophy, and 16% with concentric hypertrophy; however these percentages were significantly higher when compared with those of treated hypertensives. Moreover, the severity of hypertension has its own impact on the development of LVH and thus diastolic dysfunction, where, 88% of patients with Stage II hypertension developed LVH when compared with 12% of those with Stage I hypertension as demonstrated in figure 3.
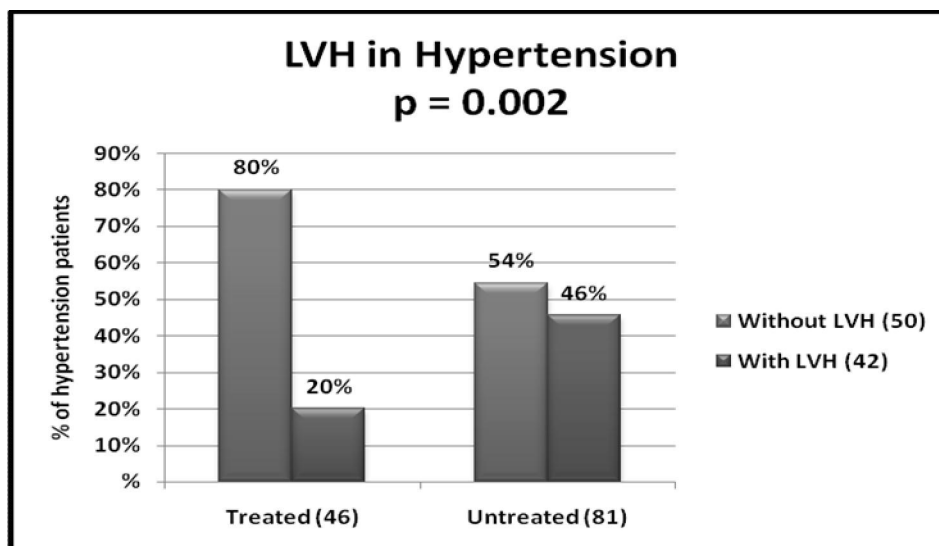
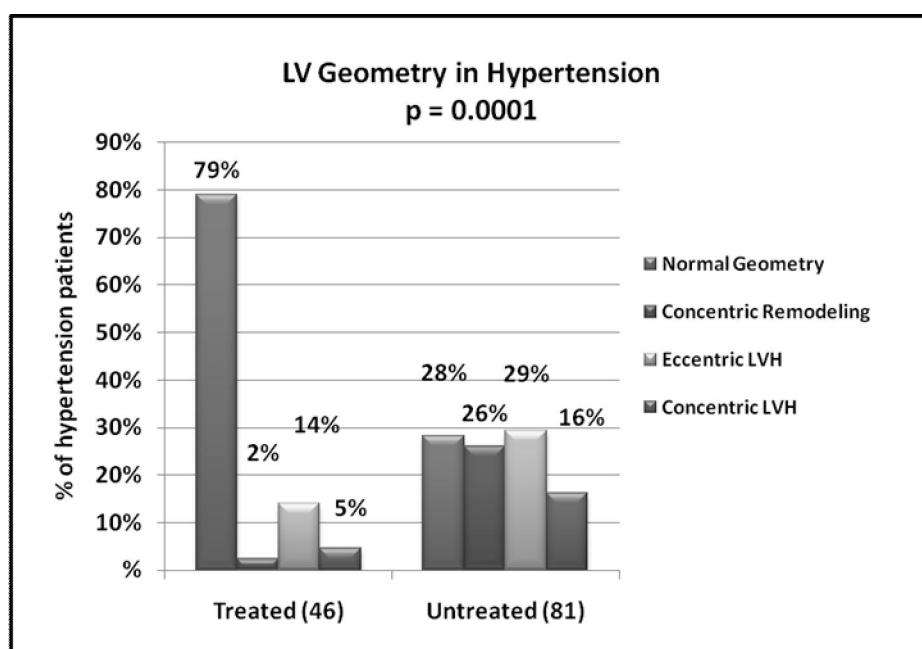*Figure 1: Distribution of LVH in treated and untreated hypertensives groups.*

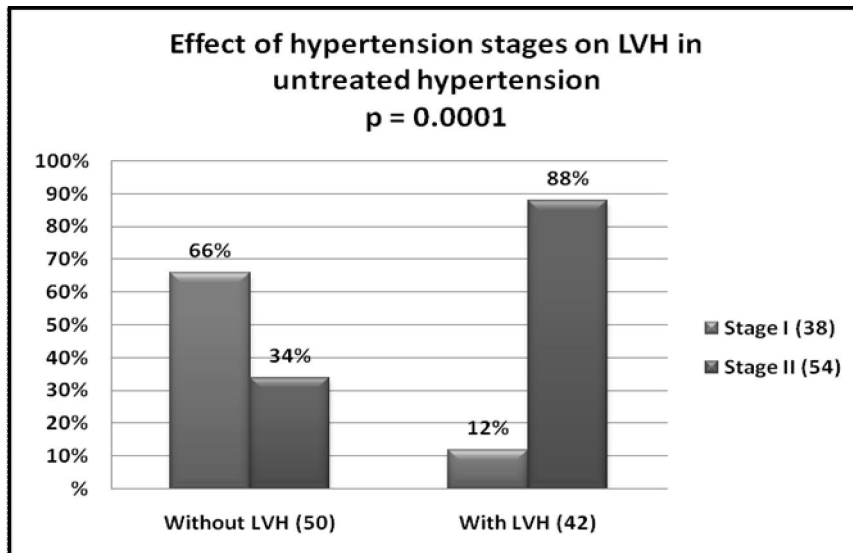*Figure 2: Distribution of left ventricular geometric patterns in hypertension.*

Figure 3: the Effect of hypertension stages on LVH in untreated hypertension.

Table 3 shows the Doppler echocardiographic parameters of hypertensives and control groups. The transmitral inflow pattern; E/A ratio, deceleration time (DT) and isovolumetric relaxation time (IVRT) were with higher values in untreated hypertensive group when compared with control ($p<0.05$). In addition, 41% of 92 untreated hypertensive patients developed diastolic dysfunction of an impaired relaxation pattern versus 16% of 43 treated hypertensives as shown in figure 4. Furthermore, figure 5 showed that higher percentages of untreated hypertensives with LVH (71%) developed diastolic dysfunction of impaired relaxation pattern versus 16% without LVH ($P<0.05$).

Table 3: Doppler echocardiographic parameters of hypertensives and control groups.

Variable	THR G n = 43	UTHR G n = 92	C G n = 32	THR G vs. C G *P*-value	UTHR G vs. C G *P*-value
E/A ratio	1.13 ± 0.17	1.02 ± 0.18	1.18 ± 0.13	0.175	0.0001
DT (msec)	200.1 ± 18.5	220.5 ± 30.2	193.7 ± 17.3	0.132	0.0001
IVRT (msec)	93.0 ± 9.0	97.7 ± 14.1	91.6 ± 5.2	0.454	0.018

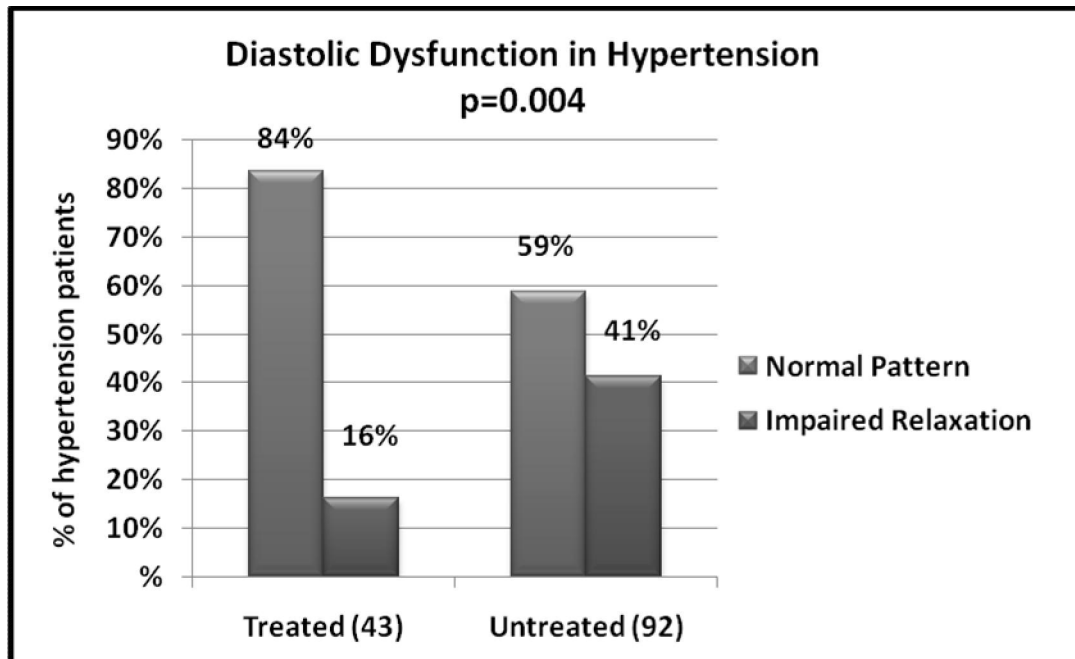- DT= E-wave Deceleration Time and IVRT= Isovolumetric Relaxation Time.

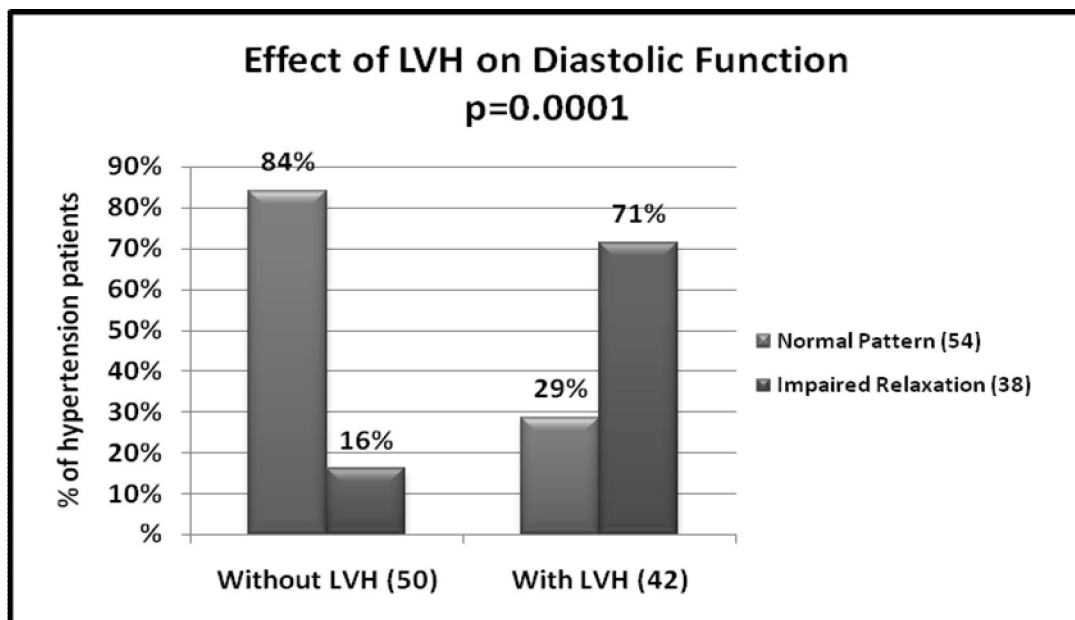*Figure 4: Distribution of diastolic dysfunction in hypertension.*

Figure 5: Distribution of diastolic dysfunction in untreated hypertensive patients with LVH and without LVH.

Regarding LV systolic function, untreated hypertensive patients with diastolic dysfunction showed significantly slight elevation in ejection fraction and fractional shortening compared with those with normal pattern (70.6 ± 3.0 and 33.2 ± 2.3 vs. 68.2 ± 2.5 and 31.8 ± 1.9). In addition, SBP and DBP showed a higher readings in those with LV diastolic dysfunction (table 4).

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

Variable	Untreated Hypertensives n= 92		P-value
	Normal Pattern n= 54	Impaired Relaxation n= 38	
EF (%)	68.2 ± 2.5	70.6 ± 3.0	0.001
FS (%)	31.8 ± 1.9	33.2 ± 2.3	0.002
SBP (mmHg)	153.3 ± 9.7	160.7 ± 9.8	0.001
DBP (mmHg)	93.4 ± 4.8	97.5 ± 5.8	0.0001

Discussion

The M-mode and Doppler echocardiography measurements are proved to be better for predicting the evolutional process of hypertension as compared with other variables, such as systolic, diastolic blood pressure, and hypertension staging [13]. In this study all subjects involved were non-obese with BMI less than 30kg/m^2 to exclude the apparent effect of the obesity on the result due to specific biologic mechanisms including alterations in insulin resistance, the renin-angiotensin-aldosterone system, and sympathetic tone. [14]. In addition, both hypertensive groups showed a significant variation regarding BMI which lay in the overweight rang when compared with the control. This finding may prove that not only the obesity rang of BMI, but also the overweight rang are consider as a primary risk factor in the development of hypertension, Pascual M., et al[15]. Furthermore, the untreated hypertensives showed a significant elevation in SBP and DBP which reflect the roll of the antihypertensive medication in control blood pressure [16]. As apart of the pathophysiology of the elevation in the left ventricle after load, is the wall hypertrophy and changes in the geometry. These changes were obvious from Table 2 which demonstrates that untreated hypertensive group, have a higher left ventricular internal dimension and more posterior wall and interventricular septal wall thicknesses. This finding came in parallel with the results of Ghanem [17]. 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 [18]. Several meta-analyses studies have been demonstrating the reversal and regression of LVH depending on the using various antihypertensive drugs that affect collagen synthesis by alteration; preload, afterload, and renin-angiotensin-aldosterone system [19]. Analyzing left ventricular geometry (figure 2) detect that untreated hypertensives have a higher percentage of eccentric and concentric LVH. In this study, since coronary disease was an exclusion factor for the analysis of patients, and thus the initial alterations present in left ventricular geometry were subsequent to the hypertensive disease itself. This finding go with Kannel and Bertoli, et al. and other authors who had also added that LVH is a strong indicator of bad prognosis in hypertensive individuals and in the general population [20] [21]. Other contributing factors for LVH include the stage of hypertension as had been proposed by Galderisi, et al. which supports the finding in this study (figure 3) where a larger percent

of the untreated hypertensives with LVH were significantly categorized as Stage II hypertension [22].

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 and filling during diastole. This elevation in filling pressures may results in exertional dyspnea and fatigue especially during exercise [23]. It's obvious from the examination of pulsed wave Doppler parameters (Table 3), 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 (Figure 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 also proved that the left ventricular geometric change, contribute to the deterioration of cardiac diastolic function during the development of hypertrophy. This finding go in parallel with the study of Avdic, 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 [25]. Furthermore, despite the diastolic dysfunction showed a strong relation with LVH, but it can be detected even before development of LVH as noticed from (figure 3) which showed that 16% of the untreated hypertensive patients without LVH had developed diastolic dysfunction. So this study demonstrated that left ventricular diastolic function could be deteriorated in the early stage of hypertension which agrees with Galderisi [22]. In addition those patients have an obvious geometric changes evolved the left atrium (table 2) and that means the cardiac geometrical changes is not limited to the left ventricle but may extend to the left atrium especially with presence of the diastolic dysfunction [24]. These findings prove that in asymptomatic hypertensive subjects, the exclusion of LVH does not rule out LV diastolic dysfunction but 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" which is in agreement with Abhayaratna, 2006 [23].

Finally, it was obvious from Tables 2 and 4 that those patient with impaired LV relaxation, showed a significantly elevation in SBP,DBP, 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 [26]. 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.

Conclusion

Left ventricular diastolic dysfunction has a strong association with Left ventricular remodeling and hypertrophy in untreated Stage II hypertension. However, left ventricular diastolic dysfunction is usually follows the left ventricular hypertrophy, but it may occur in initial stages of hypertension especially in patients with concentric geometric remodeling. In addition, left ventricular diastolic dysfunction has no affect on the systolic function–namely ejection fraction and fractional shortening especially in untreated hypertensives with high incidence of concentric left ventricle geometry.

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