

# The Relation of Left Ventricular Diastolic Dysfunction and Increased Left Ventricular Mass with Blood Pressure Variability in Non-Established Hypertensive Patients

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## ABSTRACT

**Background:** long term high blood pressure is a major risk factor for coronary artery disease, stroke, heart failure, peripheral vascular disease, vision loss and chronic kidney disease. **Objective:** the aim of this study is to demonstrate the relation between left ventricular diastolic dysfunction, increased left ventricular mass and ambulatory blood pressure recording in subjects not known to be hypertensive.

**Patients and Methods:** this study is cross sectional study that was carried out on (100) normotensive patients in Cardiology Department Clinic at Matrouh Specialized Cardiothoracic and Interventional Catheterization Center from October, 2017 to January 2019. **Results:** significantly marked difference in left ventricular (LV) mass between two groups (normal blood pressure and latent hypertension) and significantly marked difference in diastolic dysfunction. According to (normal circadian and impaired circadian) there is significant difference between the two major groups in sex where male >female and marked difference in LV mass between the two groups (normal circadian and impaired circadian) and in smoking.

**Conclusion:** ambulatory blood pressure (AMBP) plays an important role as a predictor to estimate prevalence of hypertension based on diastolic dysfunction and increased left ventricular mass in persons with normal blood pressure measures at office specially masked hypertension in white coat hypertensive patients.

**Keywords:** Left ventricular diastolic, Blood pressure variability.

## INTRODUCTION

Hypertension determines an increased risk of cardiovascular events which may be predicted by the occurrence of target-organ damage (TOD) <sup>(1)</sup>. In addition to elevated mean levels of blood pressure (BP), short-term daytime or 24-h BP variability (BPV) was shown to carry an independent prognostic value in hypertensive patients and is directly related to TOD <sup>(2)</sup>. Moreover, whenever present, left ventricular dysfunction in hypertension, even if asymptomatic, is a potent predictor of adverse cardiovascular events <sup>(3)</sup>.

With the growing acknowledgement of the importance of BPV, in its different components, as a possible new cardiovascular risk factor in hypertensive patients, BPV hypothesized its role in predicting subclinical left ventricular systolic dysfunction in newly diagnosed, never treated hypertensive patients, by focusing in our study on short-term BP variations occurring over a 24-h period or selectively only during the daytime subperiod <sup>(4)</sup>.

Ambulatory BP becomes important tools for diagnosis of hypertension in pre hypertensive stage and white-coat or isolated clinic hypertension, which currently defines individuals whose blood pressure (BP) is elevated in the medical setting, but normal when assessed away from the medical environment, such as by 24-h ambulatory BP recording and/or home BP measurement <sup>(5)</sup>.

High normal blood pressure is defined as systolic blood pressure (SBP) 140 mm Hg or higher and/or diastolic blood pressure (DBP) 90 mm Hg or higher <sup>(6)</sup>.

## AIM OF THE WORK

The aim of this study is to demonstrate the relation between left ventricular diastolic dysfunction, increased left ventricular mass and ambulatory blood pressure recording in subjects not known to be hypertensive.

## PATIENTS AND METHODS

This study is cross sectional study that was carried out on (100) normotensive patients in Cardiology Department Clinic at Matrouh Specialized Cardiothoracic and Interventional Catheterization Center from October, 2017 to January 2019.

**The ethics committee of Al AZHAR University of Medical Sciences approved the study, and written informed consent was obtained from each patient after thorough explanation of the study to patients before enrollment.**

## Inclusion criteria

1. Age:  $\geq 18$  years.
2. Sex: both sexes.
3. High normal blood pressure and left ventricular diastolic dysfunction and increased left ventricular mass according to hypertension guidelines.

## Exclusion criterions were:

1. Any patient with blood pressure  $>140/90$  mm Hg.
2. Patients on current antihypertensive medication.
3. Patients with diabetes.

4. Renal dysfunction (serum creatinine  $\geq 2$  mg/dl or macro albuminuria  $\geq 300$  mg/24 h).
5. Significant valvular or pericardial disease.
6. Heart failure.
7. Coronary heart disease.
8. Previous stroke.
9. Rhythm disturbances interfere with assessment of echocardiographic finding (e.g. right or left bundle-branch block and atrial fibrillation)
10. Patients with night-time working habits.
11. Patients with already depressed left ventricular ejection fraction (LVEF) ( $<55\%$ ).

**Each included patient was subjected to**

1. Full history taking about the presence of traditional risk factors, including a family history of hypertension, tobacco smoking, coffee or alcohol consumption, and lack of physical activity (defined as aerobic exercise on a regular basis three to four times per week). Thorough clinical examination: general and systematic examination.
2. Routine 12 leads ECG to diagnose any arrhythmia, IHD and evidence of chamber enlargement.
3. Chest X ray: to exclude cardiomegaly
4. Routine laboratory tests.
5. Echocardiography with assessment according to recommendations of the American Society of echocardiography (ASE) to measure:
  - Left ventricular internal dimensions
  - Left ventricular mass
  - Left ventricular ejection fraction by two-dimensional echocardiography.
  - Diastolic function indices include: E/A, Em, E/Em, LA volume, pulmonary artery pressure estimated by measurement of peak velocity of TR.
6. Twenty-four-hour ambulatory BP monitoring (ABPM).
7. AMBPM parameters : provides a more reliable measure of a patient’s BP than isolated clinic measures and is not subject to the ‘white-coat effect’ which can overestimate BP, particularly in susceptible patients.

**All patients' had conventional office blood pressure measurement:**

All patients were seated comfortably in a quiet environment for 5 min before beginning BP measurements, three BP measurements should be recorded, 1–2 min apart, and additional measurements only if the first two readings differ by  $>10$  mmHg. BP is recorded as the average of the last two BP readings, with using a standard bladder cuff (12–13 cm wide and 35 cm long) for most patients, but have larger and smaller cuffs available for larger (arm circumference  $>32$  cm) and thinner arms, respectively, and the cuff was positioned at the level of the heart, with the back and arm supported to avoid muscle contraction and isometric exercise-dependent increases in BP, with using phase I and V (sudden reduction/disappearance)

Korotkoff sounds to identify SBP and DBP respectively.

Measuring BP in both arms at the first visit to detect possible between-arm differences.

Patients underwent a 24 h ABPM and a transthoracic echocardiogram. Based on the ABPMs (TONOPORT V, GE Medical Systems) a portable blood pressure measuring device, we analyzed average 24 h systolic and diastolic blood pressure (BP), average daytime (6 a.m.-10 p.m.) and nighttime (10 p.m.-6 a.m.) systolic and diastolic BP and the number of dipper or non-dipper patients according to the recommendations of ESC guidelines.

Transthoracic echocardiography was done using a commercially available echocardiographic instrument (Vivid S5, Vivid S6, GE Medical Systems) according to the recommendations of the American Society of echocardiography.

**Statistical analysis**

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean  $\pm$  standard deviation (SD). Qualitative data were expressed as frequency and percentage.

**The following tests were done:**

- Independent-samples t-test of significance was used when comparing between two means.
- Chi-square ( $\chi^2$ ) test of significance was used in order to compare proportions between two qualitative parameters.
- The confidence interval was set to 95% and the margin of error accepted was set to 5%. The p-value was considered significant as the following:
- Probability (P-value)
  - P-value  $<0.05$  was considered significant.
  - P-value  $<0.001$  was considered as highly significant.
  - P-value  $>0.05$  was considered insignificant.

**RESULTS**

We enrolled a consecutive subset of 100 patients. See tables 1-3 for their demographic, heart rate, and blood pressure data.

**Table (1): Distribution of the studied cases according to demographics data (n = 100)**

		No.	%
Gender	Male	66	66
	Female	34	34
Age (years)	$\leq 40$	46	46
	$>40$	54	54
Age (years)	Min. – Max.	18.0 – 61.0	
	Mean $\pm$ SD.	41.74 $\pm$ 10.77	
	Median	41.5	

**Table (2): Descriptive analysis of the studied cases according to height, weight, BMI, heart rate and blood pressure (n = 100)**

	Min. – Max.	Mean ± SD.	Median
Height (cm)	159.0 – 190.0	170.9 ± 7.13	170.0
Weight (kg)	69.0 – 115.0	86.36 ± 9.11	86.0
BMI (kg/m <sup>2</sup> )	23.30 – 35.50	29.55 ± 2.55	29.50
Heart Rate	52.0 – 105.0	76.45 ± 10.07	76.0
Systolic	100.0 – 139.0	119.6 ± 10.38	120.0
Diastolic	70.0 – 89.0	77.08 ± 6.35	78.0

**Table (3): Distribution of the studied cases according to normality of blood analysis and chest X ray (n = 100)**

	No.	%
Blood glucose / HA1C	100	100.0
Lipid profile	100	100.0
Chest X ray	100	100.0

**Table (4): Descriptive analysis of the studied cases according to different echo parameters (n = 100)**

Echo	Min. – Max.	Mean ± SD.	Median
LV Mass (gm)	120.0 – 440.0	194.4 ± 73.39	166.9
LVIDD (mm)	34.0 – 59.0	47.24 ± 6.0	46
E/A (m/sec)	0.61 – 2.20	1.01 ± 0.31	1
Estimated PASP (mmHg)	15.0 – 44.0	24.22 ± 5.84	23
L.A. volume E/e'	4.67 – 17.70	8.53 ± 2.50	8.12

In present study age, sex and smoking were significantly different between the two major groups (normal blood pressure and latent hypertension, table 6).

On comparing the two groups according the circadian rhythm there was significant difference only in ambulatory results (Tables 5-6).

**Table (5): Comparison between normal and latent groups according to ambulatory result (n = 100)**

		Ambulatory result				Test of Sig.	p
		Normal (n = 54)		Latent (n = 46)			
		No.	%	No.	%		
Gender	Male	26	48.1	40	87	$\chi^2 = 16.672^*$	<0.001*
	Female	28	51.9	6	13		
Age	Min. – Max.	18.0 – 61.0		32.0 – 58.0		t=3.633*	<0.001*
	Mean ± SD	38.41 ± 11.51		45.65 ± 8.37			
	Median	37		45			
Smoking	Non smoker	42	77.8	20	43.5	$\chi^2 = 12.404^*$	<0.001*
	Smoker	12	22.2	26	56.5		
Diastolic Dysfunction	Absent	32	59.3	23	50	$\chi^2 = 0.860$	0.354
	Present	22	40.7	23	50		
	Grade I	16	72.7	13	56.5	$\chi^2 = 1.289$	0.256
	Grade II	6	27.3	10	43.5		
LV Mass (gm)	Min. – Max.	121.4 – 362.9		120.0 – 440.0		U=1182.0	0.678
	Mean ± SD	191.7 ± 64.09		197.5 ± 83.62			
	Median	172.2		164.8			
Circadian rhythm	Normal	34	63	15	32.6	$\chi^2 = 9.159^*$	<0.003*
	Impaired circadian rhythm	20	37	31	67.4		

$\chi^2$ : Chi square test

t: Student t-test

U: Mann Whitney test

**Table (6): Comparison between normal and impaired circadian groups (n = 100)**

	Circadian rhythm				Test of Sig.	p
	Normal (n = 49)		Impaired circadian rhythm (n = 51)			
	No.	%	No.	%		
<b>Gender</b>						
Male	29	59.2	37	72.5	$\chi^2=1.989$	0.158
Female	20	40.8	14	27.5		
<b>Age</b>					t=0.199	0.843
Min. – Max.	18.0 – 58.0		25.0 – 61.0			
Mean ± SD	41.96 ± 10.88		41.53 ± 10.76			
Median	42.0		41.0			
<b>Smoking</b>					$\chi^2=2.226$	0.136
Non smoker	34	69.4	28	54.9		
Smoker	15	30.6	23	45.1		
<b>Diastolic Dysfunction</b>					$\chi^2=0.146$	0.702
Absent	26	53.1	29	56.9		
Present	23	46.9	22	43.1		
Grade I	17	73.9	12	54.5		
Grade II	6	26.1	10	45.5	$\chi^2=1.841$	0.175
<b>LV Mass (gm)</b>					U=1140.0	0.450
Min. – Max.	122.1 – 362.9		120.0 – 440.0			
Mean ± SD	191.8 ± 61.06		196.8 ± 84.09			
Median	185.8		157.1			
<b>Ambulatory result</b>					$\chi^2=9.159$	<0.003*
Normal	34	69.4	20	39.2		
Latent	15	30.6	31	60.8		

□<sup>2</sup>: Chi square test

t: Student t-test

U: Mann Whitney test

**DISCUSSION**

Hypertension (HTN), is a long term medical condition in which the blood pressure in the arteries is persistently elevated (7). Long term high blood pressure, however, is a major risk factor for coronary artery disease, stroke, heart failure, peripheral vascular disease, vision loss and chronic kidney disease (8).

We worked in this study to assess the prevalence of blood pressure variability in patients with diastolic dysfunction and increased left ventricular mass. We also aimed to clarify ambulatory predictors and to estimate prevalence of hypertension based on diastolic dysfunction and increased left ventricular mass.

Our study groups were classified as;

According to the level of ambulatory BP result into: those had normal blood pressure (54%) and those had latent hypertension (46%).

According to the circadian rhythm into those had normal circadian rhythm (49%) and those had impaired circadian rhythm (51%).

Our results were in agreement with **Feola et al.** (9). They studied 52 subjects and the clinical history showed at least one BP measurement > 140/90 mmHg in the year prior to observation. The

average age was 48 ± 11, without any significant correlation to LVMI (r = 0.13). Their results showed LVMI had a significant correlation with systolic BP at ABPM (24 h systolic BP r = 0.34; daytime systolic BP r = 0.35; nighttime systolic BP r = 0.28; 6-12 systolic BP r = 0.29) but not with diastolic BP.

This was not matching with current study in diastolic BP. This discrepancy between results is partly attributed to the large number of current study ethnical, regional, lifestyle pattern differences and difference of subset inclusion criteria. Dipper patients represented 76.3% of the population, without any difference in LVMI between dippers and non-dippers (p = 0.09). Dipper patients had a higher prevalence of normal left ventricles as compared with non-dippers (p < 0.0001).

Our study also was in agreement with **Ito et al.** (10). They studied 36 untreated hypertensive non-diabetic patients (16 males and 20 females) whose casual systolic blood pressure (CSBP) and/or diastolic blood pressure (CDBP) were higher than 140 mmHg and 90 mmHg, respectively. All patients were less than 65 years of age without organic heart disease. Their results showed

significant positive correlations between the LVMI and ASBP ( $r = 0.51$ ,  $p < 0.005$ ), the SHI ( $r = 0.49$ ,  $p < 0.005$ ), CSBP ( $r = 0.47$ ,  $p < 0.01$ ) and RSBP ( $r = 0.41$ ,  $p < 0.05$ ), however, there were no significant correlations between the LVMI and ADBP. This was not matching with current study in ADBP. This discrepancy between results is partly attributed to the large number of current study ethnical, regional, lifestyle pattern differences and difference of subset inclusion criteria.

Our results were also in agreement with Müller-Brunotte *et al.* <sup>(11)</sup>. Their results showed that hypertension is associated with LV diastolic dysfunction, and diastolic function is further impaired in the presence of hypertensive LV hypertrophy. Indeed, LV diastolic dysfunction is considered to be an early sign of hypertensive heart disease.

According to (normal circadian and impaired circadian) there was insignificant difference between the two major groups in sex where male >female ( $p$  value =0.158) and LV mass where ( $p$ -value, <0.450) and smoking ( $p$ -value, <0.136). There was significant difference in ambulatory result ( $p$ -value, <0.003) that was in agreement with Verdecchia *et al.* <sup>(12)</sup> except in gender where female in this study >male. This discrepancy between results is partly attributed to ethnical, regional, lifestyle pattern differences.

## CONCLUSION

Hypertension determines an increased risk of cardiovascular events which may be predicted by the occurrence of target-organ damage (TOD). In addition to elevated mean levels of blood pressure (BP), short- term daytime or 24-h BP variability (BPV) has been shown to carry an independent prognostic value in hypertensive patients and is directly related to TOD. Whenever present, left ventricular diastolic dysfunction in hypertension, even if asymptomatic, is a potent predictor of adverse cardiovascular events. Ambulatory blood pressure (AMBp) plays an important role as a predictor to estimate prevalence of hypertension based on diastolic dysfunction and increased left ventricular mass in persons with normal blood pressure measures at office specially masked hypertension in white coat hypertensive patients.

## RECOMMENDATION

1. Multiple cardiology centers sharing in large study.
2. Including patients with renal dysfunction

(serum creatinine  $\geq 2$  mg/dl or macro albuminuria  $\geq 300$  mg /24 h.

3. Including diabetic patients.
4. Survey of all family members who were diagnosed as hypertensive patient.

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