

THE RELATION OF LEFT VENTRICULAR DIASTOLIC DYSFUNCTION AND INCREASED LEFT VENTRICULAR MASS WITH BLOOD PRESSURE VARIABILITY IN NON-ESTABLISHED HYPERTENSIVE PATIENTS

By

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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: 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 was a cross sectional study that 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: there was a 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 was a 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 (ABMP) played 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 hypertension mediated -organ damage (HMOD) (*Sadurska et al., 2012*).

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 HMOD (*Park et al., 2020*).

Moreover, whenever present, left ventricular dysfunction in hypertension, even if asymptomatic is a potent predictor of adverse cardiovascular events (*De Simone et al., 2010*).

With the growing acknowledgement of the importance of BPV, in its different components, as a possible new cardiovascular risk factor in hypertensive patients, we 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 sub period (*Webb et al., 2010*).

Ambulatory BP become important tools for diagnosis of hypertension in pre hypertensive stage, white-coat or isolated clinic hypertension 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 (*Parati et al., 2020*).

High normal blood pressure is defined as systolic blood pressure 130–139 mmHg and/or diastolic blood pressure 80–89 mmHg. (*Mancia et al., 2013*).

The aim of this study was 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 was a cross sectional study that 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: ≥ 18 years.
2. Sex: both sexes.
3. High normal blood pressure where systolic Bp 130–139 mmHg and/or diastolic BP 85–89 mmHg by conventional blood pressure and left ventricular diastolic dysfunction and increased left ventricular mass.

Exclusion criteria:

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 ≥ 2 mg/dl or macro albuminuria ≥ 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:

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 an All of participants had normal blood.

1. Glucose, chest X ray and Lipid profile as regard in **table (3)**. Regular basis three to four times per week and thorough clinical examination: general and systematic examination and had Conventional office blood pressure measurement.
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. Body mass index was calculated according to formula $BMI = \frac{\text{weight (kg)}}{\text{height (m)}^2}$.
6. Trans thoracic echocardiography (TTE): Using a commercially available echo-cardio graphic instrument (Vivid S5, Vivid S6, GE Medical Systems) according to the recommendations of the American Society of

echocardiography ASE (*Armstrong et al., 2012*) to measure:

- Left ventricular internal dimensions (LVID).
 - Left ventricular ejection fraction by two dimensional echocardiographs (LVEF).
 - Diastolic function indices (DFI) including: pulsed wave at mitral valve leaflets, (E/A), tissue Doppler at base of septal mitral leaflet, Em, E/Em and LA diameter.
 - Left ventricular mass(LVM): Original calculations from Troy and coworkers were the first to be recommended as standard to estimate LV mass from M-mode Measurements, Formula was used according to *Foppa et al . (2005)*.
7. Twenty-four-hour ambulatory BP monitoring (ABPM). A 24 h ABPM. 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, AMBPM parameters.

Statistical analysis:

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution

Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. Significance of the obtained results was judged at the 5% level. Chicago, Illinois, USA).

The following tests were done:

- Independent-samples t-test of significance was used when comparing between two means.

- Chi-square (x2) test of significance was used in order to compare proportions between two qualitative parameters.
- Mann Whitney-U test
- 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:

RESULTS

We enrolled a consecutive subset of 100 patients.

According to demographic distribution we enrolled consecutive subset of 100 patients (66 male, 66% and 34 female, 34%), with a mean age of 41.74 ± 10.77 years.

Their height ranged from 159-190 cm, with mean of 170.9 ± 7.13 cm and weight

of (969-115kg) with mean of 86.36 ± 9.11 kg, body mass index BMI ranged from (23.30 – 35.50 kg\ m² with mean of 29.55 ± 2.5 kg\ m²).

All of participants had normal blood Glucose, chest x ray and Lipid profile (Table 1).

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

	Mean ± SD.	Mean ± SD.
Height (cm)	170.9 ± 7.13	
Weight (kg)	86.36 ± 9.11	
BMI (kg/m²)	29.55 ± 2.55	
	No.	%
Blood glucose / HA1C	100	100.0
Lipid profile	100	100.0
Chest X ray	100	100.0
	No	%
Gender	Male	66
Age (years)	Female	34
	≤40	46
	>40	54
Age (years)	Min. – Max.	18.0 – 61.0
	Median	41.50

According to their Echocardiographic data their left ventricular masses were between 120.0 – 440 gm with a mean of 194.4 ± 73 gm. Left ventricular internal diastolic dimension (LVIDD) ranged from 34.0 – 59 mm with a mean of 47.24 ± 6 g.

E/A (m/sec): (0.61 – 2.20) with mean (1.01 ± 0.31), Estimated PASP: (mmHg) 15.0 – 44 with mean (24.22 ± 5) and Left atrial L.A diameter ranged from (23-43mm) with a mean of (32.95 ± 4.87) and (E/e'): (4.67 – 17.70) with mean (8.53 ± 2.50), (Table 2).

Table (2): Descriptive analysis of the studied cases according to different echo parameters (n = 100)

Echo	Mean ± SD.
LV Mass(gm)	194.4 ± 73.39
LVIDD(mm)	47.24 ± 6.0
E/A (m/sec)	1.01 ± 0.31
Estimated PASP (mmHg)	24.22 ± 5.84
E/e'	8.53 ± 2.50
LA diameter \mm	32.95 ± 4.87

In present study age, sex and smoking were significantly different between the two major groups (normal blood pressure and latent hypertension, (Table 3).

On comparing the two groups according the circadian rhythm, there was a significant difference only in ambulatory results (Table 4).

Table (3): Comparison between normal and latent groups according to ambulatory result (n = 100)

Ambulatory result \ Parameter	Normal (n = 54)		Latent (n = 46)		p
	No.	%	No.	%	
Gender					
Male	26	48.1	40	87.0	<0.001
Female	28	51.9	6	13.0	
Age					
Min. – Max.	18.0 – 61.0		32.0 – 58.0		<0.001
Mean ± SD	38.41 ± 11.51		45.65 ± 8.37		
Median	37.0		45.0		
Smoking					
Non smoker	43	79.6	19	41.3	<0.001
Smoker	11	20.4	27	58.7	
Diastolic Dysfunction					
Grade I	40	74.1	18	39.1	<0.001
Grade II	14	25.9	28	60.9	
BMI					
Min. – Max.	23.30 – 32.60		26.90 – 35.50		0.005
Mean ± SD	28.90 ± 2.55		30.32 ± 2.35		
Median	29.50		29.50		
LV Mass (gm)					
Min. – Max.	119.97 – 439.96		126.78 – 439.96		0.042
Mean ± SD	188.25 ± 78.14		201.51 ± 67.53		
Median	157.11		197.54		
L.A volume E[e`					
Min. – Max.	4.64 – 17.70		5.11 – 14.60		0.961
Mean ± SD	8.60 ± 2.78		8.44 ± 2.15		
Median	8.12		8.0		
LA diameter \mm					
Min. – Max.	23.0 – 40.0		25.0 – 43.0		0.094
Mean ± SD	32.19 ± 4.42		33.85 ± 5.27		
Median	33.0		35.0		
Circadian rhythm					
Normal	24	63.0	15	32.6	0.002
Impaired circadian rhythm	20	37.0	31	67.4	

χ^2 : Chi square test, t: Student t-test, U: Mann Whitney test, p: p value for comparing between normal and latent

Table (4): Comparison between normal and impaired circadian groups (n = 100)

Circadian rhythm parameter	Normal (n = 49)		Impaired circadian rhythm (n = 51)		P
	No.	%	No.	%	
Gender			bmm		
Male	29	59.2	37	72.5	0.158
Female	20	40.8	14	27.5	
Age					
Min. – Max.	18.0 – 58.0		25.0 – 61.0		0.843
Mean ± SD	41.96 ± 10.88		41.53 ± 10.76		
Median	42.0		41.0		
Smoking					
Non smoker	36	73.5	26	51.0	0.021
Smoker	13	26.5	25	49.0	
Diastolic Dysfunction					
Grade I	34	69.4	24	47.1	0.024
Grade II	15	30.6	27	52.9	
BMI					
Min. – Max.	24.70 – 34.10		23.30 – 35.50		0.003
Mean ± SD	28.80 ± 2.13		30.28 ± 2.73		
Median	29.10		30.10		
LA diameter (mm)					
Min. – Max.	25.0 – 40.0		23.0 – 43.0		0.697
Mean ± SD	32.76 ± 4.50		33.14 ± 5.25		
Median	33.0		33.0		
LV Mass (gm)					
Min. – Max.	119.97 – 384.48		121.39 – 439.96		<0.001
Mean ± SD	172.93 ± 63.69		214.93 ± 76.73		
Median	149.72		200.26		
L.A volume E\`e`					
Min. – Max.	4.67 – 17.70		5.11 – 14.60		0.446
Mean ± SD	8.72 ± 2.79		8.34 ± 2.20		
Median	8.83		8.0		
Ambulatory result					
Normal	34	69.4	20	39.2	0.002
Latent	15	30.6	31	60.8	

χ²: Chi square test, t: Student t-test, p: p value for comparing between normal and impaired circadian rhythm

DISCUSSION

Hypertension (HTN), is a long term medical condition in which the blood pressure in the arteries is persistently elevated (Naish and court 2014). 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 (Lackland et al., 2015).

It can be modified if early diagnosed and if diet and therapy are prescribed. Ambulatory blood pressure monitoring (ABPM) provides important benefits in the management of hypertensive patients as the large number of readings during

24h offer a clearer assessment than a single measurement and provides a more reliable measure of a patient's BP than isolated clinic measures and is not subjected to the white-coat effect' which can overestimate BP, particularly in susceptible patients.

Average blood pressure (BP) value for 24 hours and average values during day and night time correlated more strongly to cardiovascular morbidity than single office values. Different summary measures of BP from ABPM have been described and all have evidence of prognostic significance for cardiovascular morbidity beyond average value (*Grossman et al., 2013*).

We assessed 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, this study conducted on 100 normotensive Patients with diastolic dysfunction and increased left ventricular mass).

In our study, we enrolled a consecutive subset of 100 patients (66 male, 66% and 44female, 44%), their body mass index BMI ranged from (23.30 to 35.50) their Heart rate ranged from (52.0 to 105.)), systolic blood pressure ranged from (100.0 to 139.0), diastolic blood pressure ranged from (70.0 to 89.0) with mean (77.08 ± 6.35) and LV Mass (gm.) ranged from (120.0 to 440).

Our study group consisted were classified as:

According to the level of average 24h 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 were 49% and those had impaired circadian rhythm been 51%.

In the present study, LA diameter, diastolic function E/e had no difference between the two major groups (normal blood pressure and latent hypertension).

There were marked differences between two groups according to age, gender (sex), smoking and in circadian rhythm there was a marked difference in LV mass between two groups and diastolic dysfunction that was in agreement with *De Simone et al. (2011)* who 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. Their results showed LVMI had a significant correlation with systolic BP at ABPM but not with diastolic BP.

Muller et al. (2017) 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 that 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. Dipper patients had a higher prevalence of normal left ventricles as compared with non-dippers.

There was a significant correlation between LV mass and BMI that was in agreement with *Rashid et al. (2014)* their results showed that there was linear correlation between BMI and LV mass.

According to circadian rhythm, there was no significant difference between the two major groups in age, sex, LA diameter but there was a significant difference between two groups in LV mass where significant and that was in agreement with *Mustafa et al. (2016)*. They found that Nocturnal diastolic BP variability estimated as SD had significantly higher values in patients with LVH, night time had higher values in patients with LVH vs. those with normal LV mass, but disagreement with our study that we studied normotensive patients.

Smoking, diastolic dysfunction and ambulatory result were marked significant between two groups and that was in agreement with *Zhang et al. (2015)* except in gender where female in this study >male this discrepancy between results is partly attributed to ethnical, regional, lifestyle pattern differences.

Quinaglia et al. (2011) showed significant correlation between diastolic dysfunction and dipping of blood pressure.

Normal ambulatory results and circadian rhythm rather than increased LV mass and diastolic dysfunction may be due to some of participants were athletic,

hard worker, obese and majority age above age of 40.

CONCLUSION

Left ventricular diastolic dysfunction and increased left ventricular mass is 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 ≥ 2 mg/dl or macro albuminuria ≥ 300 mg /24 h.
3. Including diabetic patients.
4. Survey of all family members who were diagnosed as hypertensive patient.
5. Survey for all persons with increased body mass index (BMI).
6. Survey for all smoker persons.

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العلاقة بين إعتلال عضلة القلب الانبساطية وزيادة الكتلة الوظيفية للبطين الأيسر وتغير مستوى ضغط الدم في المرضى الذين لا يعانون من ارتفاع ضغط الدم

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خلفية البحث: يعتبر مرض ارتفاع ضغط الدم الشرياني من أكثر عوامل الخطورة لبعض الأمراض مثل قصور الشرايين التاجية وجلطات المخ وفشل عضلة القلب وفقدان البصر وتصلب الشرايين الطرفية والفشل الكلوى الحاد أو المزمن.

الهدف من البحث: لاكتشاف العلاقة بين اعتلال عضلة القلب الانبساطية وزيادة الكتلة الوظيفية للبطين الأيسر وتسجيل ضغط الدم عبر جهاز ضغط الدم المحمول في المرضى الذين لا يعانون من ارتفاع ضغط الدم.

المرضى و طرق البحث: هذه الدراسة اشتملت على تحديد نسبة ارتفاع ضغط الدم الشرياني على ١٠٠ مريض تم تردهم على ضغط الدم المحمول العيادات الخارجية بالمركز التخصصي لجراحة القلب والقسطرة التداخلية بمطروح من الفترة أكتوبر 2017 ويناير 2019 والذين لديهم اعتلال عضلة القلب الانبساطية وزيادة الكتلة الوظيفية للبطين الأيسر.

نتائج البحث: كان هناك علاقة قوية لزيادة الكتلة الوظيفية للبطين الأيسر واعتلال عضلة القلب الانبساطية بين المجموعتين (الضغط الطبيعي والضغط الكامن) وبالنسبة للإيقاع اليومي للضغط كان هناك اختلاف واضح بين المجموعتين طبقاً للجنس حيث كان الرجال أكثر من النساء وكذلك فى التدخين وزيادة الكتلة الوظيفية للبطين الأيسر.

الاستنتاج: جهاز ضغط الدم الشرياني المحمول يمثل أهمية كبيرة فى تشخيص واكتشاف مرضى ارتفاع ضغط الدم خاصة الذين يعانون من متلازمة المعطف الأبيض وحالات الضغط المقنعة.