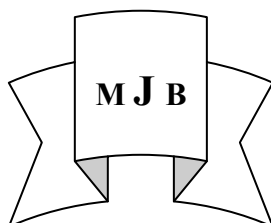


## The Resting Cardiac Index in Different Left Ventricular Geometric Patterns in Essential Hypertensive Patients Not in Heart Failure State.

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### **Abstract**

This study was performed in Baghdad Teaching Hospital during the period from 21/10/2003 to 30/3/2004 on a study sample of 120 untreated non-obese essential hypertensive patients not in a heart failure state, 78 males and 42 females, their age mean  $\pm$  SD is  $53.62 \pm 9.22$  year. They were distributed after performing echocardiographic examination into 14 patients with normal LV geometric pattern (group 1) , 6 males and 8 females, their age mean  $\pm$  SD was  $51.58 \pm 9.43$  year, and 106 patients with abnormal LV geometric pattern (group 2) , 72 males and 34 females, their age mean  $\pm$  SD was  $53.94 \pm 9.63$  years. Patients with signs and symptoms of heart failure and those with cardiac or extracardiac diseases were excluded from the study. The aim of the study was to examine whether there are differences in cardiac index between those with normal and those with abnormal LV geometric patterns, and among the three categories of abnormal LV geometric patterns, namely, concentric remodeling, eccentric hypertrophy, and concentric hypertrophy. It has been concluded that there are no statistically significant differences in cardiac index between those with a normal and those with abnormal LV geometric patterns, and non-significant differences in cardiac index among the three categories of abnormal LV geometric patterns too, as far as all patients were not having any of the signs and symptoms of heart failure. Therefore, there is still a chance of initiating antihypertensive medication in view of controlling elevated blood pressure and keeping a normal Frank-Starling mechanism and a normal cardiac index before decompensation state and developing congestive heart failure.

### **الخلاصة**

أجريت هذه الدراسة في وحدة صدى القلب في مستشفى بغداد التعليمي للفترة من ٢١ / ١٠ / ٢٠٠٣ ولغاية ٣٠ / ٣ / ٢٠٠٤. تناولت الدراسة ١٢٠ مريضاً مصابين بارتفاع ضغط الدم غير المعالج وبدرجات شدة الضغط المختلفة وبفترات مرضية مختلفة أيضاً، ٧٨ من الذكور و ٤٢ من الإناث، متوسط أعمارهم  $53.62 \pm 9.22$  سنة. تم تقسيم المرضى بعد إجراء فحص صدى القلب إلى مجموعتين، المجموعة الأولى ١٤ مريضاً لديهم نمط طبيعي للشكل الهندسي للبطين الأيسر، ٦ من الذكور و ٨ من الإناث، متوسط أعمارهم  $51.58 \pm 9.43$  سنة. والمجموعة الثانية تتكون من ١٠٦ من المرضى الذين لديهم نمط غير طبيعي للشكل الهندسي للبطين الأيسر، ٧٢ من الذكور و ٣٤ من الإناث، متوسط أعمارهم  $53.94 \pm 9.63$  سنة. الغرض من هذه الدراسة هو لمعرفة هل هناك فرق مهم إحصائياً في المؤشر القلبي بين مجموعة المرضى الذين لديهم نمط طبيعي للشكل الهندسي للبطين الأيسر والذين لديهم نمط غير طبيعي للشكل الهندسي للبطين الأيسر وكذلك هل هناك فرق مهم إحصائياً في المؤشر القلبي فيما بين الأنواع الثلاثة للنمط غير الطبيعي للشكل الهندسي للبطين الأيسر. ظهر من نتائج الدراسة بأنه لا توجد فروقات مهمة إحصائياً للمؤشر القلبي بين المجموعتين الأولى والثانية، وكذلك للمؤشر القلبي بين الأنواع الثلاثة للنمط غير الطبيعي للشكل الهندسي للبطين الأيسر طالما أن المرضى غير مصابين بحالة فقدان آلية فرانك-ستارلنك أي أنهم غير مصابين بحالة فشل القلب. أستنتج من هذه الدراسة بأن المرضى المصابين بارتفاع ضغط الدم الذين لديهم نمط طبيعي أو غير طبيعي للشكل الهندسي للبطين الأيسر وبأنواعه الثلاث من الممكن أن تتم

معالجتهم والسيطرة على ارتفاع ضغط الدم لديهم بصورة جيدة بالعقاقير المخفضة للضغط الدموي قبل أن يفقدوا آلية فرانك-ستارلنك أي قبل أن يصلوا إلى حالة فقدان التعويض التي بدورها تؤدي إلى حالة فشل القلب الاحتقاني.

## **Introduction**

Insults to the myocardium as in case of hypertensive impact on the heart is followed by a series of compensatory changes that are beneficial in the short run but have long-term deleterious effects. Structural remodeling and other factors, including left ventricular hypertrophy, myocardial ischemia, increased heart rate, and abnormal calcium flux, can impair the myocardial function and increase the burden on the heart by altering the preload and afterload on the myocardium, thus, affecting the systolic and diastolic functions of the heart[1]. Hypertensive left ventricular hypertrophy differs according to whether there is pressure and/or volume overload, giving rise to different LV geometric patterns, either concentric remodeling, eccentric or concentric LV hypertrophy[2].

The blood pressure is the product of the cardiac output multiplied by the peripheral resistance. The cardiac output changes markedly with body size, it has been important to find some means by which the cardiac outputs of different sized people can be compared with one another. Experiments have shown that the cardiac output increases approximately in proportion to the body surface area. Therefore, it is frequently stated in terms of the cardiac index, which is the cardiac output per square meter of body surface area. The cardiac index, for a normal adult human weighing 70 kilograms with a body surface area of about 1.7 square meters, is about 3 liters/min/m<sup>2</sup>. The normal range of cardiac index, in the basal (resting) state in the supine position is wide, between 2.5 and 4.2 liters/min/m<sup>2</sup> with

an average normal of 3 liter/min/m<sup>2</sup>. This average normal makes it possible for cardiac index to decline by almost 40 per cent and still remain within the normal limits[3,4].

A cardiac index of less than 2.5 liters/min/m<sup>2</sup> usually represents a marked disturbance of cardiovascular performance and is almost always clinically apparent. Although the resting cardiac index is insensitive in detecting mild to moderate cardiac impairment, it provides a valuable measure of the integrated function of the cardiovascular system, especially in critically ill patients[4].

## **Objectives**

To study whether there are differences in the cardiac index in the different LV geometric patterns in untreated hypertensive patients who are not in a heart failure state.

## **Patients And Methods**

### **Study sample**

One hundred twenty untreated essential hypertensive patients not in a heart failure state were enrolled in this study. Their age mean  $\pm$  SD is 53.62  $\pm$  9.22 year, 78 males and 42 females, with stages of hypertension ranging from stage I to stage III, and duration of hypertension from >1 year to >10 years. They were distributed according to the LV geometric pattern as assessed by echocardiographic examination into 14 patients with normal LV geometric pattern (group1), 6 males and 8 females, their age mean  $\pm$  SD was 51.58  $\pm$  9.43 year, and 106 patients with abnormal LV geometric pattern (group 2), 72 males and 34 females, their age mean  $\pm$  SD was 53.94  $\pm$  9.63 years. Patients with

cardiac or extra-cardiac diseases were excluded from the study.

#### **Blood pressure measurement**

Blood pressure (BP) was measured using a standard mercury sphygmomanometer, measurements were obtained while the patient is sitting for at least five minutes with the non-dominant arm at the level of the heart, relaxed and supported. A mean of at least three consecutive readings of systolic (phase I) and diastolic (Phase V) of Korotkoff sounds, at one minute intervals, to identify systolic and diastolic values respectively.

Using systolic blood pressure >140mmHg and/or diastolic blood pressure >90mmHg, the individuals were classified as hypertensive[5].

Clinical assessment for signs and symptoms of heart failure

All hypertensive patients included in this study were assessed clinically for signs and symptoms of heart failure by questioning and physical examination of the cardiovascular system searching for the following signs and symptoms:

1. Exertional dyspnoea
2. Paroxysmal nocturnal dyspnoea
3. Orthopnoea
4. Jugular venous distention
5. Bilateral basal lung crackles
6. Displaced cardiac apical impulse
7. Extra-heart sounds (S3 and S4)[6]

Patients with any of the aforementioned signs and symptoms were excluded from the study.

#### **Echocardiographic methods**

Imaging was obtained for each patient using a commercial instrument with a mechanical transducer of 2.5-3.5 MHz, Voluson 530D type, Austrian made, supplied by Kretz Technik Company. Transthoracic 2-D guided M-mode echocardiograms were recorded according to the American Society of Echocardiography guidelines [7]. Left ventricular internal dimension and interventricular septal and posterior wall thickness were

measured at end-diastole and end-systole on up to 3 cycles.

#### **Calculation of general characteristics**

1.Body surface area was calculated as square root of (product of height in cm x weight in kg) divided by square root of 3600[8].

2.Body mass index (Quetelet index, BMI) was calculated as weight in kg / height<sup>2</sup> in m<sup>2</sup>. All patients with a BMI > 30 were grouped as obese and those < 30 were grouped as non-obese[5].

3.Mean BP was calculated as diastolic BP + 1/3 (systolic BP– diastolic BP) in mmHg[9].

4.Cardiac index was calculated according to the equation: stroke volume in ml x heart rate in beat per minute / body surface area in m<sup>2</sup> / 1000 to get the cardiac index in Liter/minute/m<sup>2</sup>. [3]

#### **Calculation of derived echocardiographic variables**

1. Relative wall thickness was expressed as the ratio of 2x posterior wall thickness / LV end-diastolic diameter[10].

2. LV mass was calculated using the Penn convention [11,12] according to the equation:

LV mass = 1.04[(LV end-diastolic diameter in cm + posterior wall thickness in cm + interventricular septum thickness in cm)<sup>3</sup> – (LV end-diastolic diameter in cm)<sup>3</sup> – 14, measured in gm.

3. LV mass was considered as an unadjusted variable and normalized for the appropriate power of its prognostically validated allometric relation to height (height<sup>2.7</sup>). [13] LV mass / height<sup>2.7</sup> values of 49.2 gm/m<sup>2.7</sup> in men and 46.7gm/m<sup>2.7</sup> in women were used as upper limits of gender-specific normal 95% confidence intervals[10].

4. LV mass was also normalized for body surface area giving LV mass index (LVMI). Normal LVMI in

women is  $< 110 \text{ gm/m}^2$ , while in men LVMI is  $< 134 \text{ gm/m}^2$ . [14]

5. Left ventricular systolic function was assessed by measurement of:

a. LV fractional shortening [(end-diastolic – end-systolic diameter / end-diastolic diameter)  $\times 100$ ], normal value is 30-45%. [15]

b. LV ejection fraction was estimated as [(LV end-diastolic volume in ml – LV end-systolic volume in ml / LV end-diastolic volume in ml)  $\times 100$ ], normal value is 50 - 85%. [8]

#### **Left ventricular geometric patterns**

LV geometry was deduced depending on correlating the relative wall thickness with the LV mass/height<sup>2.7</sup> in  $\text{gm/m}^{2.7}$ . Increased relative wall thickness ( $>0.43$ ) represents the 97.5<sup>th</sup> percentile in previously described normal subjects [2,16]. These geometric patterns are as follow:

a. Normal geometry was present when LV mass /height<sup>2.7</sup> and relative wall thickness were both normal.

b. Concentric remodeling was present when there was normal LV mass/height<sup>2.7</sup> with increased relative wall thickness.

c. Eccentric LV hypertrophy was present when there was high LV mass / height<sup>2.7</sup> with normal relative wall thickness.

d. Concentric LVH was present when there was an increase in both LV mass/height<sup>2.7</sup> and relative wall thickness [17].

#### **Data handling and statistical analyses**

Data were presented as mean  $\pm$  standard deviation (SD) for continuous variables. The unpaired Student's t test was used to compare means of the dependent variables of the two groups of normal and abnormal LV geometric patterns. The analysis of variance (ANOVA) was used to compare means of the three abnormal LV geometric patterns. A 2-

tailed  $p$  value  $< 0.05$  was considered statistically significant [18].

All calculations were performed by software package statistical system (SPSS version 12 for windows, SPSS Inc., Chicago, Illinois).

#### **Results**

Table 1 shows the general and echocardiographic characteristics of the two groups included in the study. Both groups were age matched and body mass index matched. The resting heart rate was higher in group 2 with abnormal LV geometric pattern compared to those in group 1 with normal LV geometric pattern ( $p=0.02$ ). Systolic, diastolic, and mean blood pressure were higher in group 2 compared to group 1 (for all  $p=0.0001$ ). Interventricular septal wall thickness in diastole and in systole, LV posterior wall thickness in diastole and in systole, and LV internal dimension in diastole and in systole were higher in group 2 compared to group 1 (for all  $p=0.0001$ ). LV fractional shortening during systole was higher in group 2 compared to group 1 ( $p=0.03$ ). There was non-significant difference between the two groups in respect to LV ejection fraction ( $p=NS$ ). There was significant difference between the two groups in respect to LV end-diastolic volume which is higher in those with abnormal LV geometric pattern ( $p=0.02$ ), while, non-significant difference between the two groups in respect to LV end-systolic volume and the cardiac index (for both  $p=NS$ ). There were significant differences between the two groups in respect to LV mass index ( $\text{gm/m}^2$ ), LV mass/height<sup>2.7</sup> in  $\text{gm/m}^{2.7}$ , and relative wall thickness of the left ventricle (for all  $p=0.0001$ ).

Table 2 shows the cardiac index in each category of the abnormal LV geometric patterns. On stratification of the three categories of the abnormal

LV geometric patterns in group 2, the cardiac indexes showed non-significant differences among the three categories of LV geometric patterns,

namely, the concentric remodeling, eccentric hypertrophy, and the concentric hypertrophy pattern( $p=NS$ ).

**Table 1** shows the general and echocardiographic characteristics of the two groups included in the study.

| Dependent variable                                   | Independent variable                         |                                                  | <i>P</i> value * |
|------------------------------------------------------|----------------------------------------------|--------------------------------------------------|------------------|
|                                                      | Normal LV geometric pattern(n=14 ) (mean±SD) | Abnormal LV geometric pattern (n=106 ) (mean±SD) |                  |
| Gender(male:female)                                  | 6:8                                          | 72:34                                            | -                |
| Age (year)                                           | 51.57±9.43                                   | 53.94±9.63                                       | NS               |
| Body mass index(kg/m <sup>2</sup> )                  | 27.04±2.37                                   | 28.75±3.28                                       | NS               |
| Resting heart rate (beat/min)                        | 74.57±1.90                                   | 78.30±4.30                                       | 0.02             |
| Systolic BP(mmHg)                                    | 149.28±4.50                                  | 192.83±17.28                                     | 0.0001           |
| Diastolic BP(mmHg)                                   | 94.28±1.89                                   | 116.13±8.86                                      | 0.0001           |
| Mean BP(mmHg)                                        | 118.32±10.40                                 | 141.70±10.96                                     | 0.0001           |
| Interventricular septal thickness in diastole (mm)   | 8.17±0.24                                    | 12.64±1.36                                       | 0.0001           |
| Interventricular septal thickness in systole (mm)    | 11.00                                        | 18.01±2.08                                       | 0.0001           |
| LV posterior wall thickness in diastole(mm)          | 8.3±0.29                                     | 12.84±1.40                                       | 0.0001           |
| LV posterior wall thickness in systole(mm)           | 11.38±0.27                                   | 18.29±2.16                                       | 0.0001           |
| LV internal dimension in diastole(mm)                | 48.23±1.87                                   | 58.74±4.84                                       | 0.0001           |
| LV internal dimension in systole(mm)                 | 28.61±0.96                                   | 34.42±3.00                                       | 0.0001           |
| LV fractional shortening during systole%             | 39.39±1.07%                                  | 41.27±2.26                                       | 0.03             |
| LV ejection fraction %                               | 57.27±2.08%                                  | 57.66±3.45                                       | NS               |
| LV end-diastolic volume (ml)                         | 124.80±4.08                                  | 136.37±13.08                                     | 0.02             |
| LV end-systolic volume (ml)                          | 53.34±4.12                                   | 57.79±8.77                                       | NS               |
| Cardiac index(Liter/min/m <sup>2</sup> )             | 2.84±0.08                                    | 3.12±0.37                                        | NS               |
| LV mass index(gm/m <sup>2</sup> BSA)                 | 80.31±4.54                                   | 205.43±46.00                                     | 0.0001           |
| LV mass/height <sup>2.7</sup> in g/ m <sup>2.7</sup> | 38.32±3.24                                   | 97.20±21.87                                      | 0.0001           |
| Relative wall thickness of LV                        | 0.34±0.02                                    | 0.43±0.04                                        | 0.0001           |

\* Student's t test to compare means of two independent variables.

*P*: probability value

N: number of patients

NS: statistically not significant

LV: left ventricle

Mm:millimeter

Gm:gram

M:meter

**Table 2** shows the cardiac index in each category of the abnormal LV geometric patterns.

| Independent variable<br>Abnormal LV geometric<br>pattern (n=106) | Dependent variable<br>Cardiac index<br>(liter/min/m <sup>2</sup> ) | P value* |
|------------------------------------------------------------------|--------------------------------------------------------------------|----------|
| Concentric<br>remodeling(n=8)                                    | 2.85±0.31                                                          | NS       |
| Eccentric<br>hypertrophy(n=42)                                   | 3.15±0.38                                                          |          |
| Concentric<br>hypertrophy(n=56)                                  | 3.14±0.38                                                          |          |

\*Analysis of variance to compare means of >2 independent variables.

P: probability value

N: number of patients

NS: statistically not significant

### **Discussion**

Hypertension places increased tension on the left ventricular myocardium, causing it to stiffen and hypertrophy. Even before left ventricular hypertrophy (LVH) develops, changes in both systolic and diastolic function may be seen. Those with minimally increased left ventricular muscle mass may have supernormal contractility reflecting an increased inotropic state with a high percentage of fractional shortening and increased wall stress[19], and with increasing hemodynamic load, either systolic or diastolic dysfunction may develop, progressing to different forms of congestive heart failure[20]. But in our study, there are findings different from the aforementioned report. The resting heart rate, the systolic, diastolic, and mean blood pressures were all significantly higher in those with abnormal LV geometric patterns compared to those with normal LV geometric pattern. All structural echocardiographic measurements including the interventricular septal wall thickness and posterior wall thickness and LV

end-diastolic volume were significantly higher in those with abnormal LV geometric pattern compared with those with normal LV geometric pattern. The LV mass index and relative wall thickness were highly significantly higher in those with abnormal LV geometric pattern compared to those with normal LV geometric pattern too. In spite of all these significant differences in the abovementioned parameters, we see the end-systolic volume and the cardiac index showed non-significant differences between the two groups. Both of these two parameters were normal in the two groups, although the end-diastolic volume in those with abnormal LV geometric pattern was higher than that in those with normal LV geometric pattern, we see both groups were having normal end-systolic volume and normal cardiac index and without statistically significant differences. This means that there is still a normal Frank-Starling mechanism and the condition have not reached a state of decompensation that gives the picture of congestive heart failure. Our finding

goes in line with previous reports that mentioned that hypertrophy as a response to the increased afterload of an elevated systemic vascular resistance can be viewed as necessary and protective up to a certain point, namely the Frank-Starling mechanism which states that "within physiological limits, the heart pumps all the blood that comes to it without allowing excessive damming of blood in the veins". Therefore, the significance of this mechanism is that, regardless of the arterial pressure load up to a reasonable limit, the important factor that determines the amount of blood pumped by the heart is still the rate of entry of blood into the heart[3]. Beyond that point, a variety of dysfunctions accompany LVH.[21,22] By the time blood pressure becomes elevated, the initiating hemodynamic changes, that end in a heart failure state, may no longer be apparent, because they may have been "normalized" by multiple compensatory interactions. Nonetheless, when a group of untreated young hypertensive patients was studied initially, cardiac output was normal or slightly increased and peripheral resistance was normal too[23]. Over the next 20 years, cardiac output fell progressively, while peripheral resistance rose. In a much larger study involving over 2600 subjects in Framingham followed for 4 years by echocardiography, an increased cardiac index and end-systolic wall stress were related to the development of hypertension before the decompensation state, i.e., before the failure of the Frank-Starling mechanism.[24]

### **Conclusion**

It has been concluded that there are non-significant differences in cardiac index between those with a normal and those with abnormal LV geometric

patterns, and among the three categories of abnormal LV geometric patterns as far as all patients were not having any of the signs and symptoms of heart failure. Therefore, there is still a chance of initiating antihypertensive medication in view of controlling hypertension and keeping a normal Frank-Starling mechanism and a normal cardiac index before decompensation state and developing congestive heart failure.

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