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Low Exercise Capacity Is Independent Of LVMI Despite Significant Change In Diastolic Function In Young non complicated Hypertensive Patients

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Abstract:

Systemic hypertension is common disease that affect many organs specially the cardiovascular system. Left ventricle hypertrophy is the main cardiac structural remodeling that occur in response to hypertension, furthermore. The role of LVM in exercise intolerance in young patients with non complicated hypertension receiving antihypertensive drugs is still not well understood.

Aim:

To assess the influence of LVMI on exercise capacity among young non complicated hypertensive patients.

Method:

A total of 80 young age participants involved in this study. They are grouped as group I (control subjects) , n= 40 (female: 17, male: 23) and group II (hypertensive patients), n= 40 (male: 27, female: 13) with different BMI levels. All hypertensive patients are receiving regular antihypertensive medications. Group II further subdivided into group A and B according to their exercise capacity levels. Left ventricle mass (LVM) obtained as LVM=0.8[1.04(IVSd+ PWTd+ LVIDd)^3-(LVIDd)^3] +0.6 then divided by BSA to obtain LVMI. Pulse wave and tissue Doppler analysis are conducted for each participant to get E/e' and PCWP. All individuals subjected to treadmill test using Bruce protocol in order to obtain exercise capacity and to exclude IHD. **Results:** Compared to normal subjects, well-controlled hypertensive patients have significant increase in LVMI (*P value: 0.001*) , E/e' (*P value: 0.00*) and PCWP (*P value: 0.00*). Furthermore, they exhibited significant reduction in exercise capacity (*P value: 0.00*). In hypertensive patients with exercise capacity ≤7 MET versus those with exercise capacity >7 MET, there is significant elevation of E/e' (*P value: 0.01*) and PCWP (*P value: 0.01*) are observed while no significant change of LVMI is observed (*P value: 0.6*). **Conclusion:** LVMI is not correlated to exercise capacity despite significant diastolic function changes in young hypertensive patients who receiving regular antihypertensive treatments, reflecting that medications may modulate structural remodeling but not diastolic function.

Key words: Hypertension, exercise capacity, Left ventricle mass index, pulmonary capillary wedge pressure, E/e', treadmill test.

Abbreviations: LVMI: left ventricle mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, MET: metabolic equivalent of O_2 consumption, BMI: body mass index, PCWP: Pulmonary capillary wedge pressure, IHD: ischemic heart disease. IVSd: interventricular septal thickness at end diastole, PWTd: posterior wall thickness at end diastole, LVIDd: left ventricular internal diameter at end diastole.

Introduction

Remodeling and hypertrophy of LV are commonly reported in patients with hypertension. It occur as a results of complex interaction of numerous hemodynamic and non-hemodynamic factors. Left ventricular mass and geometry is affected by many variables, specially the level of blood pressure which plays major role in LV mass remodeling. Other factors that affect the LV mass and cause structural remodeling other than hypertension are sex, excess salt, ethnicity, obesity and diabetes mellitus, as well as genetic and neurohumoral factors. [(1)]

The most notable symptoms of HTN is the exercise intolerance. For better clarification on how HTN related changes (as LVM and diastolic function changes) can influence functional capacity, numerous recent reports have assessed cardiac structural correlates of decreased exercise capacity with hypertension. [(2)] In contrast, few researchers focused on the effect of LVM related HTN on exercise performance in young well controlled hypertensive patients.[(3)]

The effect of LVM on exercise capacity remains unclear. A greater effort of how LVM changes may participate to exercise intolerance is wanted, since it may represent novel therapeutic targets in the management of exercise intolerance in those patients. [(4)] In our study, we focused on the impact of LVMI in limited exercise capacity in those patients despite optimal medical therapy.

Methods

A total of 80 young age individuals involved in this study. In order to exclude conditions that might affect our outcomes, the following criteria are required:

a) No clinical evidence or previous history of IHD, valvular heart disease, diabetes mellitus, heart failure, respiratory disease and renal failure.

b) Not athletic.

c) Not smoker

All subjects provided information on family history, personal habits (drug ingestion, level and type of physical exercise, known disease condition and alcohol intake).

Those patients who are already diagnosed as having primary non complicated (no end organ damage) hypertension and taking single or combined antihypertensive medications (including ACEI, ARB, beta-blockers or CCB) are included in the study while those who have fluctuations in their blood pressure levels and do not take antihypertensive medications are excluded from patients group to avoid selection bias. The patients were grouped as group I (control subjects) , n= 40 (female: 17, male: 23) and group II (hypertensive patients), n= 40 (male: 27, female: 13) with different BMI levels. In regard to group II, Since exercise capacity less than 7 MET is considered low [(5)], they are subdivided into two subgroups: those with exercise capacity >7 MET (n=22) and those with exercise capacity ≤7 MET (n=18). A complete two dimensional echocardiography is achieved in all patients, using a commercially available ultrasound transducer and equipment (M5sc probe, GE, Vivid E9, 2015, USA). All acquisitions were performed by the same operator with the patients in the left lateral position. According to the American society of echocardiography (ASE) recommendations, M-mode measures of the LV are done at end-diastole.[(6)] It is anatomically validated, recommended and legitimized by ASE.[(7)] The preference of M-mode estimation of LV mass, come from most studies use this way in assessing LVM as well as its technical feasibility and accessibility. Nevertheless, despite good correlation with two-dimensional values [(8)], M-mode has been proposed to

underestimate LV mass. [9] Devereux and colleagues suggested a new modified equation, which is validated on necropsy. [10]

LVM=0.8[1.04(IVSd+ PWTd+ LVIDd)^3-(LVIDd)^3] +0.6. Devereux formula.

Measurement of pulsed-wave Doppler of the early (E), late (A) of mitral inflow velocities as well as deceleration time of early filling phase of left ventricle are carried out. Using tissue Doppler in the 4-chamber view, the peak early diastolic velocity of the lateral and medial mitral annulus (e′) are measured to obtain average E/e'.

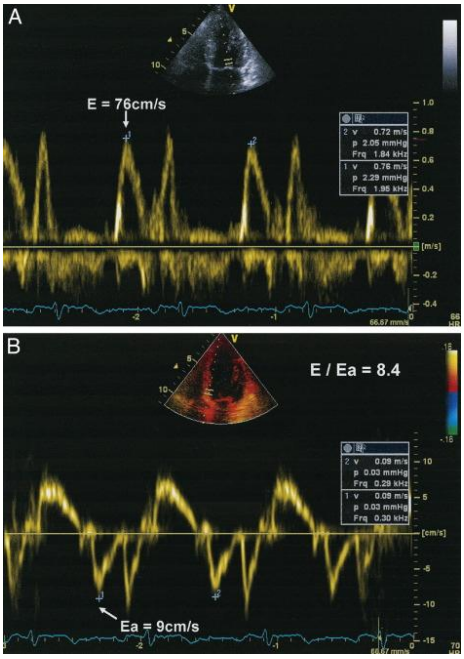

Figure 1: Calculation of E/e' ratio

Pulmonary capillary wedge pressure (PCWP) is measured in an attempt to compare our results with hemodynamic impact of diastolic dysfunction resulting from hypertension

PCWP= (E/e´ x 1.25) + 1.9 or simply 4+ E/e' (Nagueh Formula). [11]

Results:

The values of LVMI, E/e, PCWP and exercise capacity according to study groups at different BMI

Data (M±SD)	**Group I N=40 (male:23, female: 17) Age (23-37yr) BMI (20.8-28.7)**	**Group II N=40 (male:27,female: 13) Age (20-40yr) BMI (22.9-37)**	**P value**
LVMI (g/m^2)	67.8±13.7	89.2±23.4	0.001
E/e	4.3±1.01	7.71±2.31	0.000
PCWP (mmHg)	8.3±1.02	11.4±2.84	0.000
Exercise capacity (MET)	10.45±0.63	8.2±1.9	0.000

Values presented as M±SD. LVMI: left ventricle mass index, MET: metabolic equivalent, PCWP: pulmonary capillary wedge pressure

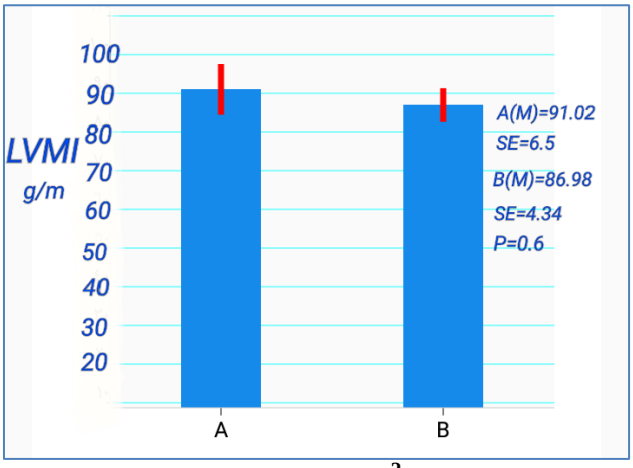

Figure 2: Left ventricle mass index (LVMI), (g/m^2) in group A (exercise capacity >7 MET, n:22) and group B (exercise capacity ≤7 MET, n:18)

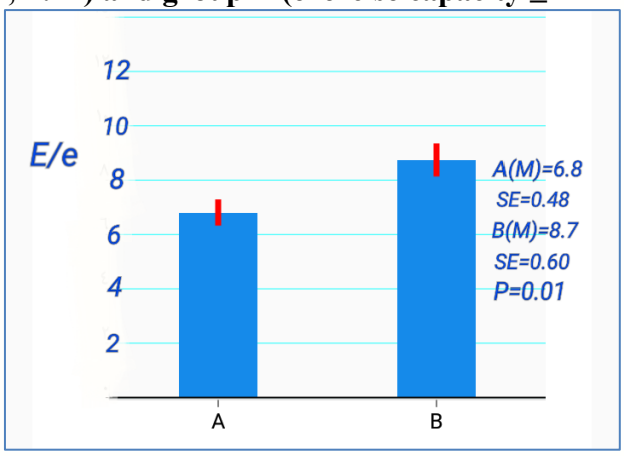

Figure 3: E/e' ratio in group A (exercise capacity >7 MET, n:22) and group B (exercise capacity ≤7 MET, n:18)

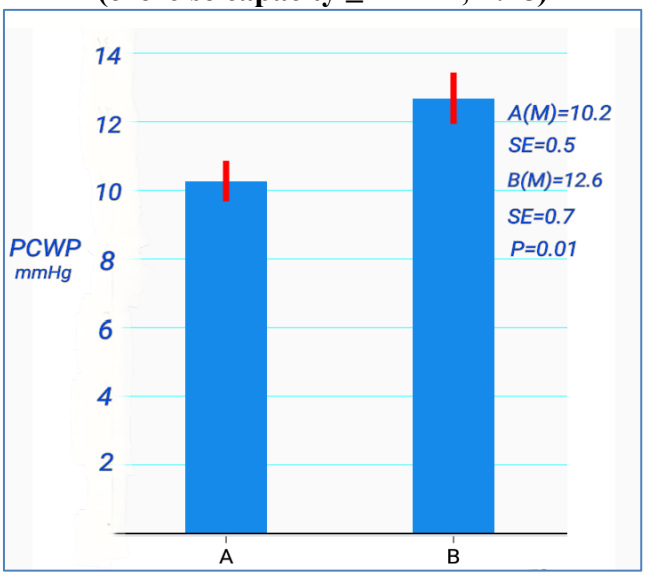

Figure 4: Pulmonary capillary wedge pressure (PCWP), (mmHg) in group A (exercise capacity >7 MET, n:22) and group B (exercise capacity ≤7 MET, n:18)

Discussion:

Blood pressure was 137.7±15.5/86±13.4 mm Hg in non-complicated hypertensive patients (all of them are receiving antihypertensive medications) and

119.3±18.5/75±11.4 mm Hg in normotensive control subjects. Body mass index is more in patients group (30.5±4.01kg/m2) compared to normotensive (24.9±2.2kg/m2) individuals. we demonstrated that there is significantly higher LVMI in hypertensive patient as well as significantly higher E/e and PCWP compared with normotensive individuals. Diastolic dysfunction is the main component of LV function that has been affected by systemic hypertension and it is independent of LV systolic function, namely you may found abnormal diastolic parameters with normal or supra-normal systolic function. [(12)] A study by Jasmine G. *et al*, 2009 [(13)]supported our results in which, diastolic dysfunction is found to be a potent reflector of reduced exercise capacity in hypertensive patients. Diastolic function is important factor in maintaining normal exercise capacity since it plays a major role in generating a maximal cardiac output. Throughout the exercise, the preservation of adequate left ventricular filling to safeguard a normal cardiac output comprises the capability to attain diastolic filling rates larger than the ejection rates during systole. Though majority of our patients are using regular antihypertensive medications with blood pressure level of (137.7±15.5/86±13.4 mmHg), but their exercise capacities are still limited and well correlated with diastolic indices changes. Little W. *et al*, 2006 reported poor improvement in diastolic function in hypertensive subjects despite the use of effective anti-hypertensive drugs.[(14)] No significant increase in LVMI is notable among hypertensive patients with low exercise capacity versus higher one, indicated that an effective treatment may limit structural left ventricle remodeling but not influence exercise capacity, perhaps due to poor affection on diastolic function.

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