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Hypertension, and not sex hormones or insulin resistance affects left ventricular mass in aging men

Epidemiological studies indicate that left ventricular hypertrophy (LVH) is an independent risk factor for cardiovascular morbidity and mortality. Therefore, of special interest are factors that may lead to LVH. Among well-established factors, affecting left ventricular mass (LVM) are age, male gender, obesity and hypertension (8). There are also data which indicate that anabolic steroids may be associated with LVH as well as sudden cardiac death (13). Some authors suggest that insulin resistance and hyperinsulinemia may be other causative factors accounting for LVH (12).

In this study, we attempted to answer the question if there is any association between left ventricular mass in aging males and concentrations of testosterone (T), estradiol (E_2), sex hormone binding globulin (SHBG) and insulin resistance (IR).

MATERIAL AND METHODS

We evaluated 107 men older than 50 years of age, mean 60.1 ± 7.0 years. Stable coronary artery disease (CAD) was diagnosed in 42 subjects according to the presence of exertional angina, history of myocardial infarction (32 subjects) and typical ECG abnormalities in resting 12-lead ECG and/or during exercise treadmill testing. Thirty-two (32) individuals had arterial hypertension. Obesity, defined as body mass index (BMI) exceeding 30 kg/m^2, was established in 18 subjects. None of the patients demonstrated hyperglycemia as defined by fasting plasma glucose above 7.0 mmol/l. No acute infection was diagnosed during the clinical assessment of the patients. Exclusion criteria were as follows: congestive heart failure, tumors, autoimmune and inflammatory diseases, renal and hepatic disorders, endocrine pathology as well as drug and/or alcohol abuse.

Blood samples were taken from antecubital vein at 8 in the morning. Blood glucose was measured by enzymatic method (P.Z. Cormay, Lublin, Poland). Total T and E_2 concentrations were assessed by RIA, using a commercially available kits from Immunotech (Marseilles, France). The level of SHBG was determined by ELISA assay from DPC. Fasting plasma insulin level was measured by RIA kit (Medgenix, Fleures, Belgium). IR was determined from fasting plasma insulin and glucose using the "Homeostasis Model Assessment (HOMA)" (15).

Transthoracic echocardiography was performed using a Hitachi EUB-450 ultrasonograph with 3.5 MHz transducer. In M-mode presentation of parasternal long-axis view, left ventricular end-diastolic diameter (LVEDD), interventricular septum (IVS) and left ventricular posterior wall (LVPW) were measured. Left ventricular mass (LVM) was calculated according to the Devereux formula (3): LVM (g) = 1.04*[(LVEDD + IVS + LVPW)^3 – (LVEDD)^3] – 14. LVM was indexed by the body surface area (LVMI, g/m^2).

The study protocol was approved by the University Ethics Committee and written informed consent was obtained from each person before enrollment.

Data were presented as Mean ± SD for all continuous variables. The differences between subgroups were assessed by Student's unpaired *t* test. Associations among variables were evaluated by Pearson's rank correlation test. To investigate independent relationship between LVM, LVMI and other variables, we used multiple regression analysis. Dummy variables were used for CAD (0 = absent, 1 = present) and arterial hypertension (0 = absent, 1 = present). $P < 0.05$ was considered significant in the whole analysis.

RESULTS

Table 1. Correlation coefficients between left ventricular mass (LVM)/ left ventricular mass index (LVMI) and age, weight, BMI, hypertension, sex hormones and insulin/insulin resistance

	LVM		LVMI	
	r	p	r	p
Age	0.04	0.698	0.09	0.352
Weight	0.38	0.000	0.15	0.115
BMI	0.37	0.000	0.21	0.034
Hypertension	0.23	0.015	0.23	0.019
T	-0.16	0.100	-0.13	0.180
T/SHBG	-0.08	0.445	-0.11	0.244
E_2	0.10	0.303	0.10	0.291
Insulin	0.09	0.359	0.05	0.598
HOMA-IR	0.09	0.366	0.05	0.601

Table 1 shows correlation coefficients between parameters of left ventricle mass (LVM, LVMI) and the rest of assessed variables. LVM and LVMI were positively correlated with BMI ($r = 0.37$; $p < 0.001$ and $r = 0.21$; $p = 0.034$ respectively) and the presence of hypertension ($r = 0.23$; $p = 0.015$

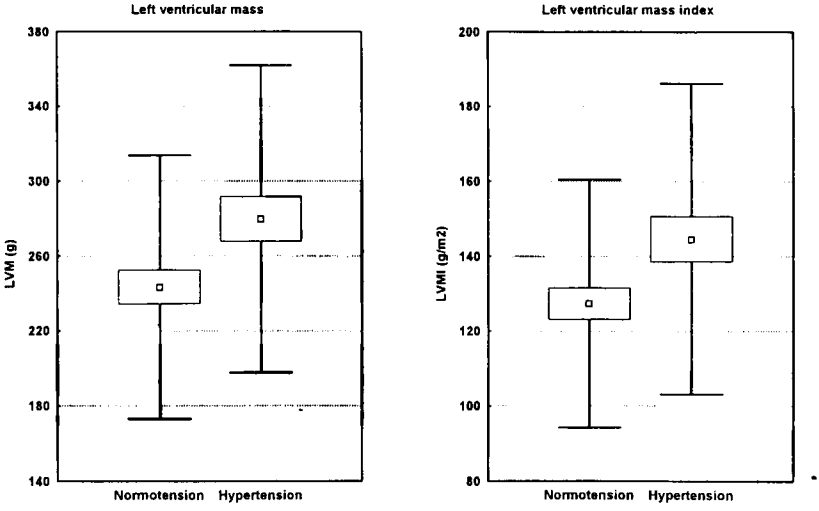

Fig. 1. Left ventricular mass (LVM) and left ventricular mass index (LVMI) in normotensive and hypertensive men

and r = 0.23; p = 0.019 respectively). Additionally, LVM correlated with body weight (r = 0.38; p < 0.001). None of sex hormones were significantly related to LVM or LVMI. There were no associations between the parameters of left ventricular mass and insulin or insulin resistance. LVM and LVMI were higher in hypertensive than in normotensive men (279.9 ± 82.2 g vs. 243.4 ± 70.3 g, p = 0.015 and 144.6 ± 41.5 g/m^2 vs. 127.4 ± 33.1 g/m^2, p = 0.019, respectively; Fig.1). Multiple regression analysis showed that LVM was related to body weight and presence of hypertension. The latter factor was also significantly associated with LVMI (Table 2).

Table 2. Multiple regression analysis between left ventricular mass (LVM)/ left ventricular mass index (LVMI) and examined parameters

Independent values	LVM	
	β	p
Weight	0.339	0.0003
Hypertension (absent – 0, present – 1)	0.178	0.048
CAD (absent – 0, present – 1)	0.154	0.086
	$R^2 = 0.198$	p = 0.00004
	LVMI	
	β	p
Hypertension (absent – 0, present – 1)	0.192	0.045
BMI	0.173	0.073
CAD (absent – 0, present – 1)	0.153	0.106
Age	0.098	0.299
	$R^2 = 0.116$	p = 0.013

DISCUSSION

Our study indicates that LVM and LVMI are mainly related to hypertension in the group of aging males. Body weight also seems to affect heart muscle, being positively associated with LVM. However, in multiple regression analysis the indices of body mass and left ventricle mass (BMI and LVMI) have not been significantly associated.

Epidemiological studies proved that left ventricular hypertrophy (LVH) is an independent risk factor for morbidity and mortality of cardiovascular diseases (9, 10). However, the mechanisms of this phenomenon still remain to be elucidated. For many years the research interests have been focused on androgens, whose receptors have been found in cardiomyocytes of men and women of any age (6, 14). Androgen receptors are present in cytosol and nucleus of cardiac myocytes (11). Since childhood left ventricular mass increases at much greater rate in boys than in girls (5), even after adjustment for weight. The Framingham Study revealed that left ventricular mass increased with age in women, whereas it remained constant in men (2). Interestingly, autopsy study demonstrated a decrease in LV mass with age in males (16). This may be related to decline of T level observed in aging males by many researches (1, 4). In our study T level did not correlate with LVM and LVMI, most probably due to specific selection criteria of the study group. We included subjects with conditions known to induce LVH such as hypertension and prior myocardial infarction, which could attenuate the possible correlation between T and parameters of left ventricle mass.

Many researches focused on the role of insulin and insulin resistance in left ventricular remodeling. Lind et al. found that insulin resistance is the only independent factor predicting LVH (12). In the other study, analysis of effects of hypertension treatment revealed that decrease of LVM was observed only in a subgroup of patients without increase of insulin resistance in the course of treatment (7). The relationship between LVM and IR was markedly weakened after adjustment for the presence of obesity (7). Since obesity is associated with both hypertension and IR, it seems reasonable to believe that a culprit factor is obesity and LVH is primary an adaptive response to increased hemodynamic load of heart due to elevated blood pressure. This hypothesis is consistent with findings of our study, where no significant association between LVM and insulin or insulin resistance has been found, and the only factor affecting LVM is hypertension.

CONCLUSIONS

1. Systemic hypertension is the main factor affecting left ventricular mass.
2. No relationships between left ventricular mass and levels of total testosterone, estradiol, sex hormone binding globulin and insulin resistance have been found.

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SUMMARY

Left ventricular hypertrophy (LVH) is an independent risk factor for cardiovascular morbidity and mortality. The aim of the study was to find which factors influence left ventricular mass (LVM) and whether relationships exist between sex hormones: testosterone (T), estradiol (E_2), sex hormone binding globulin (SHBG) and insulin resistance (HOMA-IR) and LVM. The study group consisted of 107 males at the age of over 50 years (mean 60.1±7.0). Positive significant correlations between LVM or left ventricle mass index (LVMI) and hypertension (0.23; $p = 0.015$ and 0.23; $p = 0.019$ respectively) as well as between LVM and body weight (0.38; $p < 0.001$) were observed. LVM and LVMI were higher in hypertensive than in normotensive men (279.9 ± 82.2 vs. 243.4 ± 70.3 g, $p = 0.015$ and 144.6 ± 41.5 vs. 127.4 ± 33.1 g/m^2, $p = 0.019$ respectively). Multiple regression analysis showed LVM to be independently associated with hypertension and body weight. For LVMI such correlation was found only with hypertension. No relationships were observed between LVM/LVMI and insulin/insulin resistance.

Nadciśnienie, a nie hormony płciowe czy insulinooporność, wpływa na zwiększenie masy lewej komory serca u starzejących się mężczyzn

Przerost lewej komory (LVH) jest niezależnym czynnikiem, który wpływa na zwiększoną zachorowalność i śmiertelność z powodu chorób układu krążenia. Celem pracy była ocena, jakie czynniki wpływają na zwiększenie masy lewej komory (LVM) serca oraz czy istnieje zależność pomiędzy poziomem hormonów płciowych: testosteronem (T), estradiolem (E_2), globuliną wiążącą hormony płciowe (SHBG) oraz insulinoopornością (HOMA-IR) a LVM. Badaniem objęto 107 mężczyzn w wieku powyżej 50 lat (średnio 60,1±7,0). Stwierdzono dodatnią korelację pomiędzy LVM i wskaźnikiem masy lewej komory (LVMI) a występowaniem nadciśnienia tętniczego (odpowiednio 0,23; $p = 0,015$ i 0,23; $p = 0,019$) oraz pomiędzy LVM a ciężarem ciała badanych (0,38; $p < 0,001$). LVM i LVMI wyższe były u mężczyzn z nadciśnieniem tętniczym w porównaniu z mężczyznami bez nadciśnienia (odpowiednio 279,9 ± 82,2 vs. 243,4 ± 70,3 g, $p = 0,015$ i 144,6 ± 41,5 vs. 127,4 ± 33,1 g/m^2, $p = 0,019$). Również analiza regresji wielokrotnej potwierdziła, że LVM wykazywała zależność od nadciśnienia tętniczego i ciężaru ciała, podczas gdy LVMI zależał jedynie od nadciśnienia. Nie obserwowano natomiast żadnej zależności pomiędzy LVM/LVMI a stężeniem hormonów płciowych oraz insuliną/insulinoopornością.