ORIGINAL ARTICLE

Left ventricular hypertrophy and coronary heart disease in patients with metabolic syndrome and arterial hypertension

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Background: Metabolic syndrome is considered as a situation associated with cardiovascular complications, obesity, hypertension and diabetes. Aim of the present study was the investigation of the prevalence of cardiac complications in patients suffering from metabolic syndrome (MS) and hypertension.

Methods: Patients with a follow up in our Hypertension Unit, with hypertension and fulfilling at least 3 of the 5 risk criteria of NCEP / ATP-III, namely: abdominal obesity (waist circumference of > 102 cm for men, and > 88 cm in women), triglycerides > 150 mg/dl, HDL-C < 40 mg/dl for men and < 50 mg/dl in women, blood pressure > 130/85 mmHg, and fasting glucose >110 mg/dl, were included in the study. All patients were evaluated by recording past history for coronary heart disease (CHD), office and home blood pressure as well as 24-h-ABPM, ECG, M-Mode echocardiography and fasting plasma glucose to insulin ratio (FPG/FPI). No one patient was under antihypertensive or antilipidemic therapy. As left ventricular hyperrophy (LVH) characterized a left ventricular mass index (LVMI) of > 125 gm/m^2 for men and > 110 gm/m^2 for women, using the criteria of Penn convention.

Results: From the 143 studied patients (82 M/ 61 F, aged 17-81 years), 11 patients (5%) had CHD and 65 (45.5%) LVH. The left ventricular wall thickness (LVWT) was found to be significantly related to pulse pressure ($p<0.003$) and significantly inversely related to FPG/FPI ratio (insulin sensitivity index). Multiple regression analysis with these relationships together and confounding factors age, sex, BMI waist, and duration of hypertension as independent variables showed FPI to be the only significant variable explaining 41% of the variation in LVWT, while duration of hypertension was the main determinant for the presence of CHD ($p= 0.0044$).

Conclusions: We conclude that LVH was present in about 46% of hypertensives with metabolic syndrome and the main determinant was the fasting plasma glucose to insulin ratio, while duration of hypertension was also a significant factor for the development of CHD.

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The clustering of impaired glucose metabolism (with insulin-resistance and hyperinsulinemia) and elevated triglycerides, low HDL-cholesterol, hypertension and abdominal obesity is known as the metabolic syndrome (MS)[1]. Criteria to identify MS were recently standardized by the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III[2] (Table 1); individuals with MS suffer an excess of cardiovascular disease (CVD) and especially coronary artery disease and atherosclerosis[3,4]. Left ventricular hypertrophy (LVH) is frequently found in hypertensive subjects[5] and is considered to be a consequence of the pressure load imposed on the left ventricle. However the degree of blood pressure elevation explained only about 50% of the variation of left ventricular mass. Thus, other factors may be involved in the development of LVH in hypertension. Recently, LVH has been associated with insulin resistance and hyperinsulinemia in MS[5-7].

Aim of the present study was the investigation of the prevalence of cardiac complications in patients suffering from MS and hypertension and also whether LVH and CAD are associated with the insulin – resistance /hyperinsulinemia.

Patients and Methods

One hundred forty three patients (82M/61F, aged 17-81 years) with a follow up in our Hypertension Unit suffering from essential hypertension and fulfilling at least 3 of the 5 NCEP (ATP-III) criteria for the diagnosis of metabolic syndrome (Table 1) were included in the study. All previous antihypertensive and antilipidemic medication was discontinued for at least 4-5 weeks and the patients received placebo. The wash-out period was considered necessary in order to clarify the metabolic parameters and blood pressure. All patients were evaluated by recording past history for coronary heart disease (including previous MI, office and home blood pressure, as well as 24h-ABPM, and ECG).

A comprenhesive two dimentional and Doppler echocardiography was performed by a single investigator who was unaware of the results of the other investigations. Left ventricular wall thickness was measured using the M-mode echocardiography.

The metabolic investigations, blood pressure measurements and echocardiographic evaluation were performed at the end of the placebo period; the metabolic

Table 1: *Characteristics of patients*

Variables	M±SD
Age (y)	56.7±11.5
Males, (%)	57.3
BMI (Kg/m2)	30.7±4.1
Waist (cm)	107.5±8.7
Blood Pressure (mmHg)	
Office supine systolic	162±19.7
>> >> diastolic	91.5±8.7
Home systolic	155.2±21.2
Home diastolic	88.9±11.6
24h ambulatory systolic	153.2±20.8
24h ambulatory diastolic	85.7±18.9
Fasting plasma insulin, FPG (mU/l)	14.1±8.85
Fasting plasma glucose, FPI (mg/dl)	112±34.1
FPG/FPI ratio	11.6±9.27
Total cholesterol (mg/dl)	240.2±44.6
Triglycerides (mg/dl)	203±81.9
HDL-cholesterol (mg/dl)	41±9.7
LDL-cholesterol (mg/dl)	158±40.4
Serum uric acid (mg/dl)	5.6±1.6
LVMI (gm/m2)	124.7±34.7
Intraventricular septum thickness, (cm)	1.1±0.17
Left ventricular wall thickness, LVWT (cm)	2.2±0.31
Duration of hypertension, months	11.6±22

studies were performed after the patients were fasted overnight. Insulin sensitivity was evaluated by the fasting plasma glucose to insulin ratio (FPG / FPI). Insulin was measured using a commercial radioimmunoassay kit.

As left ventricular hypertrophy (LVH) was characterized a Left Ventricular Mass Index (LVMI) of > 125 gm/m^2 for men and >110 gm/m^2 for women, using the criteria of Penn convention[8,9]

Statistics

Relationships between myocardial characteristics and the other variables (metabolic and others) were evaluated by means of Pearson's correlation coefficients. Multiple regression analysis was used to assess the influences of potential confounding factors, such as age, sex, obesity, and blood pressure. Two-tailed significance values are given, and p<0.05 was considered statistically significant.

Results

The mean values of the variables studied are given in Table 2.

Age and sex, as well as office SBP, house SBP , home DBP fasting insulin plasma levels and the FPG / FPI ratio were significantly related to left ventricular wall thickness (Table 3). Insulin sensitivity as was evaluated by the fasting glucose to fasting plasma insulin ratio was inversely correlated to left ventricular wall thickness (Figure 1) , while LVWT was also positively related to pulse pressure (Figure 2). Duration of hypertension was

Table 2: *Relationships between the studied variables and Left ventricular wall thickness, LVWT.*

	r	P
Age	0.21	<0.007
Blood Pressure (mmHg)		
Office systolic	0.28	<0.000
Office diastolic	0.09	NS
Home systolic	0.29	<0.000
Home diastolic	0.25	<0.001
24h –systolic	0.31	<0.000
24h-diastolic	0.28	<0.000
Fasting plasma insulin (mU/l)	0.33	<0.008
>> >> glucose (mg/dl)	0.25	<0.002
FPG/FPI	-0.33	<0.008
Waist (cm)	0.03	NS

found to be significantly related for the presence of CHD.

Multiple regression analysis was performed to evaluate the above relationships and the effects of confounding factors such as age, sex, BMI and waist, and duration of hypertension as independent variables were also taken into account. From this analysis LVWT was significatly and inversely related only to insulin sensitivity (p< 0.008), which was the only variable explaining 41% of the variation in LVWT, while duration of hypertension was the main determinant for the presence of CHD (slope =0.49, p=0.004).

Discussion

From the results of the present study is clearly shown that left ventricular hypertrophy is closely related to the degree of insulin resistance in untreated hypertensive patients with metabolic syndrome.

Peripheral insulin resistance (and hyperinsulinemia) is governed mainly by the rate of glucose disposal in skeletal muscles[10]. Insulin- mediated glucose disposal by muscle varies about 10-fold in healthy nondiabetic, normotensive individuals. The more insulin sensitive the

Figure 1: *The relationship between left ventricular wall thickness (LVWT) and insulin sensitivity as evaluated by fasting plasma glucose to insulin ratio (FPG/FPI) (r=-0.33, P<0.008)*