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POST-PRANDIAL GLYCEMIA DOES NOT INFLUENCE LEFT VENTRICULAR MORPHOLOGY AND FUNCTION IN NON-DIABETIC ESSENTIAL HYPERTENSIVES

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Using digitized M-mode echocardiograms and 75-mg oral glucose tolerance test (OGTT), we evaluated the possible influence of post-prandial glycemia on left ventricular (LV) morphology and function in never-treated, non-obese, non-diabetic hypertensives. We enrolled 89 subjects (49 men, age 45±11 years) with never-treated hypertension (24h BP > 135 and/or 85 mmHg), body mass index < 30 Kg/m2, glycemia at fast < 110 mg/dl and at 120 min during OGTT < 140 mg/dl. We measured glucose and insulin at fast, 30,60,90 and 120 min during OGTT, and metabolic clearance rate of glucose,an index of insulin sensitivity. With regard to the LV we evaluated: LV end-diastolic diameter, septal and posterior wall thickness, LV mass index, peak shortening and peak lengthening rate of LV diameter, peak thinning rate of LV posterior wall. Out of the 89 subjects, 31 had LV hypertrophy (LVMi > 134 g/m2 in men, > 110 g/m2 in women); LV systolic function was normal (peak shortening rate of LV diameter > 1.9 sec-1) in all the patients; 25 patients had preclinical LV diastolic dysfunction (peak lengthening rate of LV diameter < 3.6 sec-1 and/or peak thinning rate of LV posterior wall < 8.4 cm/sec). The metabolic parameters did not correlate with LV morphologic characteristics, nor with LV systolic function. With regard to diastolic function, peak thinning rate of LV posterior wall was inversely related to glycemia at 120 min ($r = -0,20$, $p<0.05$) and to glucose MCR ($r=-0.25$, $p<0.01$). From stepwise multiple regression analysis the main independent determinants of peak thinning rate of LV posterior wall (multiple $R = 0.31$, $p=0.0092$) were glucose MCR (beta = 0.23, $p=0.02$) and LVMi (beta = - 0.20, $p=0.04$), whereas post-prandial glycemia did not enter the equation.

In conclusion, in never-treated, non-obese, non-diabetic essential hypertensives, post-prandial glycemia is not related to LV remodeling. With regard to LV diastolic function, the influence of post-prandial glycemia is outweighted by insulin sensitivity, that appears to be an independent determinant of LV diastolic function.

Key Words: Insulin Resistance, Post-Prandial Glycemia, Left Ventricular Diastolic Function

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RHO KINASE ASSOCIATES WITH INSULIN RECEPTOR SUBSTRATE-1 AND MODULATES INSULIN SIGNALING IN VASCULAR SMOOTH MUSCLE CELLS

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Recent studies from our laboratory have shown that insulin stimulates myosin-bound phosphatase (MBP) in vascular smooth muscle cells (VSMCs) by decreasing site-specific phosphorylation of the myosin-bound subunit (MBS) of MBP via nitric oxide/cGMP mediated Rho/Rho kinase inactivation. Because insulin-stimulated vasodilatory effects are known to be mediated via the IRS-1/PI3-kinase pathway. In the present study, we tested potential interactions between Rho kinase and insulin signaling pathways in primary VSMC cultures. In control VSMCs, insulin inactivates ROK-*alpha*, the major Rho kinase isoform in VSMCs and inhibits thrombin-induced increase in ROK-*alpha* association with the insulin receptor substrate-1 (IRS-1). Hypertension (in spontaneous hypertensive rats) or expression of an active $RhoA^{V14}$ upregulate Rho kinase activity and increase ROK-*alpha*/IRS-1 association resulting in IRS-1 serine phosphorylation which leads to inhibition of both insulin-induced IRS-1 tyrosine phosphorylation and PI3-kinase activation. In contrast, expression of dominant negative RhoA or cGMP dependent protein kinase type I*alpha* (cGK I*alpha*) inactivates Rho kinase, abolishes ROK-*alpha*/IRS-1 association, and potentiates insulin-induced tyrosine phosphorylation, PI3-kinase activation, Akt phosphorylation leading to decreased MBS^{Thr695} phosphorylation and decreased MBP inhibition. Collectively, these results suggest a novel function for ROK-*alpha*in insulin signal transduction at the level of IRS-1 and potential cross-talk between cGK I*alpha*, Rho/Rho kinase signaling, and insulin signaling at the level of IRS-1/PI3-kinase.

Key Words: Rho Kinase, Insulin Signaling, IRS-1/PI3-Kinase

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RELATIONSHIP BETWEEN OBESITY DECREASE AND REGRESSION OF HYPERTENSIVE LEFT VENTRICULAR HYPERTROPHY

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There is a well-known relationship between obesity and hypertensive left ventricular hypertrophy. However, less is known about the relationship between obesity decrease and regression of hypertensive left ventricular hypertrophy.

Aim of the study is assessment of relationships between obesity decrease and regression of hypertensive left ventricular hypertrophy.

Number of 73 patients with II-III stage hypertension (43 male), average age 55.9 ± 8 and LVH determinated by echocardiography (average left ventricular mass (LVM) index: 164 ± 32 g/m2; Penn convention) have been treated (by medication and by diet) for a year. Each subject underwent two-dimensional and Doppler echocardiography,12-lead ECG, exercise stress testing (Bruce - protocol), 24-h ambulatory monitoring blood pressure, 24-h Holter monitoring with Lown classification of ventricular arrhythmia's and heart rate variability. Mean body mass index (BMI) was 28.7 ± 3.6 kg/m^2 (23 to 39), and 28 (39%) patients were obese (BMI > 30 kg/m^2) (OH group).

After one year systolic BP (SBP) was reduced on average 168 ± 26 to 158.2 ± 21 mmHg, diastolic BP (DBP) from 102 ± 12.7 to 97 ± 11 mmHg. LV mass index was reduced from 163 ± 32 to 150.2 ± 27 g/m2 (all $p<0.001$). 22 patents (30.1%) lost weight more than 5%. These patients significantly decreased LV mass 309 ± 79 vs 278.4 ± 61 g; $t=3.22$ $p<0.004$), LV mass index (161 ± 35 vs 148 ± 29 kg/m^2; $t=2.68$; $p<0.02$), LV diastolic dimension (52.3 ± 4.7 vs 50.5 ± 4.4 mm; $t=2.95$, $p<0.008$), Cornell's index (1.55 ± 0.4 vs 1.41 ± 0.4, $p<0.02$), peak double product (DP) (27.3 ± 5 vs 24.4 ± 5, $t=2.8$, $p<0.02$), DP/METTs (2.48 ± 1 vs 1.84 ± 1, t=2,15; $p< 0.05$), mean 24h systolic BP (SBP) (144.1 ± 17 vs 138.6 ± 16 mmHg, $t=2.2$ $p<0.04$), mean 24h diastolic BP (DBP) (89.5 ± 11 vs 85.7 ± 12 mmHg, $t=2.2$, $p<0.04$), mean SBP per day (148.2 ± 18 vs 141 ± 16 mmHg, $t=2.6$, $p<0.02$), mean DBP per day (92.7 ± 11 vs 88 ± 13 mmHg, $t=2.6$, $p < 0.02$) and increase of mean 24h RR intervals per night (938.2 vs 999 ms; $t=3$, $p<0,007$).

Patients (51.70%) who didn't achieve significant loss of weight significantly decreased LV mass index (163 ± 30 vs 152 ± 25 kg/m^2; $t=2.1$; $p<0.05$), office SBP (170.3 ± 27 vs 158.9 ± 19, $t=2.2$, $p<0.03$), grades of ventricular arrhythmias (2.73 vs 1.95, $t=2.1$, $p < 0.04$), and mean VES/24h (66.6 vs 20, $t=2.22$, $p<0.04$).

Hypertensive patients with LVH with significant loss of weight after one year, achieved higher grade of LVH regression, lower DP at exercise, lower values of BP during 24-hour monitoring and improvement of heart rate variability, than patients without significant loss of weight.

Key Words: Obesity, Left Ventricular Hypertrophy, Hypertension