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Absence of an independent association between serum uric acid and left ventricular mass in Caucasian hypertensive women and men

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Abstract *Background and aim:* Experimentally uric acid may induce cardiomyocyte growth and interstitial fibrosis of the heart. However, clinical studies exploring the relationship between serum uric acid (SUA) and left ventricular (LV) mass yielded conflicting results.

The aim of our study was to evaluate the relationships between SUA and LV mass in a large group of Caucasian essential hypertensive subjects.

Methods and results: We enrolled 534 hypertensive patients free of cardiovascular complications and without severe renal insufficiency. In all subjects routine blood chemistry, including SUA determination, echocardiographic examination and 24 h ambulatory blood pressure (BP) monitoring were obtained.

In the overall population we observed no significant correlation of SUA with LV mass indexed for height$^{2.7}$ (LVMH$^{2.7}$) ($r = 0.074$). When the same relationship was analysed separately in men and women, we found a statistically significant correlation in female gender ($r = 0.27$; $p < 0.001$), but not in males ($r = -0.042$; $p =$ NS). When we grouped the study population in sex-specific tertiles of SUA, an increase in LVMH$^{2.7}$ was observed in the highest tertiles in women (44.5 ± 15.6 vs 47.5 ± 16 vs 55.9 ± 22.2 g/m$^{2.7}$; $p < 0.001$), but not in men.

The association between SUA and LVMH$^{2.7}$ in women lost statistical significance in multiple regression analyses, after adjustment for age, 24 h systolic BP, body mass index, serum creatinine and other potential confounders.

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Conclusions: Our findings do not support an independent association between SUA and LV mass in Caucasian men and women with arterial hypertension.

Introduction

Hyperuricemia is particularly common in hypertensive patients, especially in those with metabolic syndrome (MetS) [1—4], where may be a marker of hyperinsulinemia [5] and insulin resistance [5], as well as of renal dysfunction [1,3,6,7] and diuretic use [1,3]. In some, but not in all, studies [1,2,8] performed in hypertensive subjects, the association between serum uric acid (SUA) and cardiovascular (CV) events remained significant after adjustment for potential confounding factors.

The development of left ventricular hypertrophy (LVH), in hypertensive patients with high concentration of SUA may potentially explain, at least in part, the enhanced CV risk observed in these subjects, because LVH is a strong predictor of CV events [9]. Indeed, uric acid is thought to induce experimentally cardiomyocyte growth and interstitial fibrosis of the heart, in part via activation of the renin—angiotensin system (RAS) [10,11] and in part by inducing endothelin-1 gene expression in cardiac fibroblasts [12].

However, clinical studies exploring the relationship between SUA and left ventricular (LV) mass yielded conflicting results [8,13—22]. Moreover, in some studies a significant effect of SUA on LV mass (LVM) was observed only in women [14,16], while others described the opposite [15].

The aim of our study was to evaluate in a large group of Caucasian essential hypertensive subjects the relationship between SUA and LVM and to assess the influence of gender, if any, on this relationship.

Methods

The population of this cross-sectional study was selected from 646 hypertensive Caucasian patients consecutively attending our Hypertension Unit.

The exclusion criteria were: secondary or malignant hypertension, heart failure, positive history or clinical signs of ischemic heart disease, cerebrovascular disease, severe renal function impairment, defined by an estimated glomerular filtration rate (GFR) <30 ml/min/1.73 m^2, gout, treatment with SUA-lowering medication (with the exception of losartan) in the last year, dyslipidemia requiring pharmacological treatment, type 1 diabetes or type 2 diabetes requiring insulin therapy, major non cardiovascular diseases.

Fifty-two subjects met these criteria and therefore were not enrolled.

Of the remaining individuals 60 were also excluded, because suboptimal echocardiographic tracings or fewer than 80% valid ambulatory blood pressure monitoring (ABPM) readings were obtained. Hence, the final statistical analysis involved 534 patients.

Before entering the study, 311 hypertensive subjects had been pharmacologically treated. These patients were studied at least 2 weeks after the discontinuation of all antihypertensive drugs.

All the participants to this study may be considered as sedentary subjects.

Persons who reported smoking cigarettes regularly during the past year were considered current smokers.

Informed consent was obtained from each patient. The study protocol was approved by the local review board.

Study design

After the period of pharmacological washout, clinic blood pressure (BP) was recorded by a doctor, in the non-dominant arm using the auscultatory method with a mercury sphygmomanometer and appropriated cuff for arm diameter, following the 2007 guidelines of the European Society of Hypertension (ESH) [23]. Three consecutive measurements were taken at 2 min intervals and averaged.

The following morning, after an overnight fast of at least 12 h, blood samples were drawn to perform routine blood chemistry.

Furthermore, 24 h ABPM and echocardiographic study were carried out.

Measurements

Determination of routine biochemical parameters was performed with standard techniques by using an autoanalyser (ILab 300+, Instrumentation Laboratory, Milan, Italy).

Serum uric acid was measured using an uricase/peroxidase method implemented in the above mentioned autoanalyser.

Estimated GFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [24].

Low-density lipoprotein cholesterol (LDL) was calculated by the Friedwald formula.

The presence of type 2 diabetes was defined as fasting plasma glucose of 126 mg/dl or higher or use of oral hypoglycemic agents.

The diagnosis of the MetS was based on the joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity [25].

A portable, non-invasive SpaceLabs 90207 recorder (Redmond, Washington, USA) performed the 24 h ABPM.

M-mode measurements were taken with the American Society of Echocardiography (ASE) recommendations [26]. LVM was determined using the ASE corrected cube-formula [27]. It was indexed by both body surface area (LVMI) and by height elevated by a power of 2.7 ($LVMH^{2.7}$), in order to provide a more stringent allowance for obesity [28].

A cut-off point of 51 g/$m^{2.7}$ in either gender was set to separate normal from LVH [29].