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ORIGINAL ARTICLE

Relationship between serum uric acid, metabolic syndrome and resting heart rate in Chinese elderly

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KEYWORDS
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Summary
Objective: Both serum uric acid (SUA) and resting heart rate (RHR) are positively associated with metabolic syndrome (MetS). However, little is known regarding the relationship between SUA and RHR. We aimed to investigate the relationship between SUA and RHR in the elderly with MetS.
Methods: With a retrospective observational analysis, 867 Chinese elderly subjects (437 males and 430 females) were divided into 4 groups according to SUA quartiles. We first investigated the relationship between SUA and MetS. Then we evaluated whether there is an independent association of SUA with RHR in these subjects.
Results: There were significant differences of MetS incidence in groups of Quartile 1—4 in male and female (all $P < 0.01$). Female had higher MtS incidence than male (53.49% versus 43.24%; $P = 0.003$). After adjusting age, sex and diuretics usage, SUA levels intimately correlate with RHR, creatinine, waist-to-height ratio, waist circumference, high-sensitivity C-reactive protein (hsCRP) and white blood cells (all $r > 0.30$, $P < 0.05$). When RHR exceeded 86 bpm, after adjusting for various known risk factors, Odds ratios of concomitant SUA level were 1.243, 1.908, and 2.194 in the second, third, and fourth urate quartile respectively compared to the first quartile. ROC curve analysis demonstrated statistically significant value of RHR for hyperuricemia diagnosis (area under the curve was 0.702 with 95% CI of 0.605—0.791, $P = 0.000$).

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blockers; BMI, body mass index; BP, blood pressure; CCB, calcium channel blocker; hsCRP, high-sensitivity C-reactive protein; HbA1C, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; IDF, International Diabetes Federation; LDL-C, low density lipoprotein cholesterol; MtS, metabolic syndrome; RHR, resting heart rate; ROC, receiver—operating characteristic; SUA, serum uric acid; TG, triglyceride; TIA, transient ischemia attack; WBC, white blood (cell) count; WC, waist circumference; WHpR, waist-to-hip ratio; WHtR, waist-to-height ratio.

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Conclusion: The SUA has significant correlation with RHR in MetS. RHR appears to be a potentially detective marker to predict the elevated SUA and cardio-metabolic risk in Chinese elderly.

Introduction

Uric acid (urate) is a by-product of purine catabolism catalyzed by the activation of xanthine oxidase [1,2]. Historically, urate was just considered as a risk for the development of gout and kidney stones [3]. Since the 1900s, however, multiple pieces of evidences, based mainly on epidemiological studies, have linked serum urate levels to metabolic syndrome, chronic kidney disease, and cardio-cerebrovascular events [4—6]. Recent studies suggest that urate may be not only a risk factor of metabolic syndrome but also an independent predictor of cardio-metabolic diseases and mortality [1,3]. Moreover, in animal models, decreasing urate levels can prevent or reverse features of the metabolic syndrome [6].

Although urate can also function as an antioxidant, it might be an inexpensive marker of the effects of oxidative stress on the heart because its antioxidant activity can be overcome by the pro-oxidant and pro-inflammatory effects on cells [1,6]. In experiments with cultured vascular cells, urate induces cellular proliferation, inflammation, oxidative stress, and the activation of local renin—angiotensin system [6]. Oxidative stress in the human heart alter the myofibrillar energetic supply, electrophysiological and structural remodeling [2,4]. Although hyperuricemia could be associated with AF [4], it is uncertain if increased urate is related to elevated resting heart rate (RHR). So we have reasons to presume that SUA may be associated with RHR.

RHR is determined by sinus node activity, considered as a marker of autonomic nervous system activity, and largely influenced by the interaction of sympathetic and vagal activity [7]. An elevated heart rate implies sympathetic hyperactivity and/or reduced parasympathetic tensity [8]. Epidemiological evidence also suggests that a high RHR is connected with increased cardiovascular morbidity and mortality independent of conventional risk factors in general populations [9]. RHR is positively associated with sub-clinical inflammation and increased RHR may also be a sign of sub-clinical heart disease [9]. It is reported that insulin resistance and elevated sympathetic nerve activity are closely linked with each other [10]. Acute reflex activation of the sympathetic nerve system could induce acute insulin resistance in humans [10]. Moreover, chronically increased sympathetic nerve activity can precede the development of insulin resistance and obesity [10,11].

As described above, both hyperuricemia and increased RHR are the risk makers and predictors of cardio-metabolic diseases, correlates with inflammation course and similarly share some pathological process. However, data remains very limited on the association between SUA and RHR. To address this issue, the present study aimed to investigate the relationship between them.

Study population

This study was designed as a retrospective observational study performed in the Department of Cardiology, the Second Hospital of Shandong University, in China. In the study, 867 elderly subjects (437 males and 430 non-pregnant females) aged 60—91 years were recruited through a random selection from September 17, 2010 to November 29, 2012. Each subject undergoes a thorough medical history evaluation and a complete physical examination, together with a series of blood and urine tests, chest X-ray and electrocardiogram. During this period, determination of SUA levels was a routine part of the initial biochemical examination. The physical examination was performed on all subjects by a qualified doctor or nurse per established standard methods [12]. Patients with severe cardio-renal or nutritional disorders that would affect blood pressure, lipid, glucose and uric acid metabolism were excluded. Thus, those with a cardiac ejection fraction <50% and/or a creatinine level of $\geq$132.6 μmol/L were excluded in the current study. Patients with terminal malignant diseases and those not independent in daily activities were also not included. This research was conducted in accordance with the ethical principles stated in the ''Declaration of Helsinki''. All procedures were approved by the Ethics Committee of the Second Hospital of Shandong University.