ORIGINAL RESEARCH—ERECTILE DYSFUNCTION

Uric Acid Level and Erectile Dysfunction in Patients with Coronary Artery Disease

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ABSTRACT

Introduction. Erectile dysfunction (ED) is a frequent complaint of elderly subjects and is closely associated with endothelial dysfunction and cardiovascular disease (CVD). Uric acid is also associated with endothelial dysfunction, oxidative stress, and CVD, raising the hypothesis that an increased serum uric acid might predict ED in patients who are at risk for coronary artery disease (CAD).

Aim. This study aims to evaluate the association of serum uric acid levels with presence and severity of ED in patients presenting with chest pain of presumed cardiac origin.

Methods. This is a cross-sectional study of 312 adult male patients with suspected CAD who underwent exercise stress test (EST) for workup of chest pain and completed a sexual health inventory for men survey form to determine the presence and severity of ED. Routine serum biochemistry (and uric acid levels) were measured. Logistic regression analysis was used to assess risk factors for ED.

Main Outcome Measures. The short version of the International Index of Erectile Function questionnaire diagnosed ED (cutoff score ≤ 21). Serum uric acid levels were determined. Patients with chest pain of suspected cardiac origin underwent an EST.

Results. One hundred forty-nine of 312 (47.7%) male subjects had ED by survey criteria. Patients with ED were older and had more frequent CAD, hypertension, diabetes and impaired renal function, and also had significantly higher levels of uric acid, fibrinogen, glucose, C-reactive protein, triglycerides compared with patients without ED. Uric acid levels were associated with ED by univariate analysis (odds ratio = 1.36, $P = 0.002$); however, this association was not observed in multivariate analysis adjusted for estimated glomerular filtration rate.

Conclusion. Subjects presenting with chest pain of presumed cardiac origin are more likely to have ED if they have elevated uric acid levels. **Solak Y, Akilli H, Kayrak M, Aribas A, Gaipov A, Turk S, Perez-Pozo SE, Covic A, McFann K, Johnson RJ, and Kanbay M. Uric Acid level and erectile dysfunction in patients with coronary artery disease. J Sex Med 2014;11:165–172.**

Key Words. Uric Acid; Erectile Dysfunction; Coronary Artery Disease; Endothelial Dysfunction

Introduction

Erectile dysfunction (ED) is fairly common, especially among elderly men, and is associated with coronary artery disease (CAD) [1–4]. The association of ED has been attributed to the presence of common risk factors such as obesity, hypertension, diabetes, and smoking. Not surprisingly, prospective observational studies have reported that subjects with ED are at risk for future cardiovascular (CV) events [5]. A recent meta-analysis also reported that ED significantly increases the risk of cardiovascular disease (CVD), CAD, stroke, and all-cause mortality. Moreover, the increase was independent of conventional cardiovascular risk factors [6].

ED is strongly associated with the presence of small vessel disease and endothelial dysfunction [7,8]. Subjects with long-standing hypertension, who develop small vessel disease (arteriolosclerosis), are also susceptible to developing ED independent of specific antihypertensive agents [9]. In this regard, uric acid becomes an interesting potential risk factor for ED, as it is strongly linked with endothelial dysfunction [10–12], microvascular disease [13], and hypertension [14,15]. Experimental studies show that uric acid can reduce endothelial nitric oxide bioavailability via multiple mechanisms, including scavenging by uric acid-induced oxidative stress, the stimulation of arginase, and direct scavenging [16–19]. Uric acid can also induce vascular smooth muscle cell proliferation in vitro and induce microvascular disease in vivo, and studies in humans have linked uric acid with microvascular disease [20–24]. An elevated uric acid is also emerging as an independent predictor of hypertension, and pilot clinical studies suggest lowering uric acid can improve endothelial function and lower blood pressure in hypertensive subjects [25–27]. Despite these associations, to date no studies have examined the relationship of uric acid levels to ED.

Uric acid has also been recognized as a novel risk factor for development of CAD, although meta-analyses are mixed on the independence of this relationship [28–30]. Recently we reported that ED is a risk factor for CV disease in subjects presenting with chest pain. Here we used the same cohort study to address a new question—could uric acid be a predictor for ED? We further hypothesized that increased serum uric acid levels may be one of the missing links between CAD and ED. With this background in mind, we evaluated the association of serum uric acid levels with presence and severity of ED in patients presenting with chest pain of presumed cardiac origin.

Materials and Methods

This was a cross-sectional study, and the participants were recruited from a prospectively maintained cohort. Previously we reported that reduced estimated glomerular filtration rate (eGFR), and presence and severity of ED were associated with severity of CAD in this cohort [31]. We included 312 consecutive adult male patients who for the first time presenting with chest pain to our cardiology outpatient clinic. Only married men with a permanent sexual partner were included. Exclusion criteria were as follows: previous evaluation for CAD by coronary angiography, history of established CAD (previous myocardial infarction, coronary artery bypass grafting surgery, heart failure or percutaneous coronary angioplasty), drug therapy for CAD, drug therapy for known ED, liver cirrhosis, gout, chronic obstructive pulmonary disease, depression, cancer and chronic renal replacement therapy. We also excluded subjects if they were taking allopurinol. After detailed medical history and thorough physical examination, patients with chest pain of suspected cardiac origin underwent an exercise stress test (EST). Patients who were deemed to have noncardiac chest pain or required no further testing were excluded from the study. Final participants were subjects who had chest pain of suspected cardiac origin as determined by the clinical exam and EST.

The study was approved by Local Ethics Committee, and all the participants signed written informed consent forms before recruitment. Patients were examined with good medical and laboratory practice according to the recommendations set forth by the Declaration of Helsinki on biomedical research involving human subjects.

Included patients were instructed to complete the sexual health inventory for men (SHIM) survey form. SHIM, also known as International Index of Erectile Function is an established, valid, and reliable questionnaire for determining the presence and severity of ED [32]. Patients with SHIM scores ≤21 were diagnosed with ED.

Based on the definitions of the Framingham Heart Study, patients who were smoking > 10 cigarettes/day were accepted as smokers, and patients who ceased smoking more than 2 years ago were accepted as nonsmokers. Hypertension and diabetes mellitus were described according to the Seventh Report of the Joint National Commit-