# URIC ACID : A Risk Factor for Renal and Cardiovascular Disease

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There is a growing body of evidence which indicates an elevated serum uric acid (SUA) level is associated with a poor prognosis in hypertension, heart failure, renal and cardiovascular disease. Interestingly, the association of elevated serum uric acid and cardiovascular disease (CVD) has been recognized for more than a century. In spite of the long standing awareness of this association, little attention has been paid to its potential significance.

We examined the association between SUA and coronary heart disease (CHD) events in treated hypertensive patients. Pretreatment and annual uric acid was measured in 7906 participants in a protocol-directed, systematic, hypertension treatment program. CHD events (100 fatal and 117 non-fatal MI and 49 revascularizations) as well as 116 non-CVD deaths were recorded during 6.7 years of follow-up. In multivariate Cox regression models SUA was directly associated with CHD events independent of age, gender, race, history of CVD or diabetes, smoking, blood pressure, body mass index, left ventricular hypertrophy, cholesterol, glucose, and serum creatinine. In these treated hypertensive patients the use of diuretics was directly related to an elevated SUA. After adjusting for the diuretic induced increase in SUA the expected benefit on mortality from diuretic therapy was increased approximately 23%. Additionally when compared to other risk factors for CVD the increased risk associated with an increase of one standard deviation of SUA was similar to that seen for serum cholesterol and systolic blood pressure.

Uric acid has also been shown to be an independent predictor of impaired prognosis in patients with chronic heart failure. Anker et al. examined the relationship of elevated SUA to survival in 112 patients with heart failure. In Cox-proportional hazard analysis, low peak VO2 ($p=0.001$), low LVEF ($p=0.0004$), and elevated SUA ($p=0.0001$) predicted poor prognosis. SUA emerged as the most powerful predictor of adverse outcomes in these patients.

To determine the association of SUA with all-cause and cardiovascular mortality by gender and race, Alderman et al. analyzed data from the First National Health and Nutrition Examination Survey (NHANES I) Epidemiologic Follow-up Study. The study group contained 6009 subjects with an average of 16.4 years of follow-up. During that time 1657 deaths occurred. In this analysis SUA had a continuous, independent and significant positive relation to cardiovascular mortality in both men and women, blacks and whites.

Therefore, several investigators have demonstrated a specific, continuous, and significant independent association of SUA to CVD events. It is especially interesting to note that this association persists, and in fact is even more robust, in well treated hypertensive patients. What remains to be determined is whether this cardiovascular risk factor (SUA) is causative, and whether a reduction of SUA would contribute to cardiovascular prevention and protection beyond that produced by successful control of blood pressure.