

Uric Acid: An Additional Component of Metabolic Syndrome?

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The significance of metabolic syndrome in association with cardiovascular diseases has triggered extensive debate,^{1,2} and the number of medical reports in this area is increasing exponentially. One of several controversial points is whether the 5 components (elevated glucose, higher triglyceride, lowered high-density lipoprotein [HDL] cholesterol, central obesity, and hypertension) of metabolic syndrome, as proposed by the Adult Treatment Panel III (ATP III) of the National Cholesterol Education Program (NCEP),³ are equally important. This debate has even been challenged by a new definition from the International Diabetes Federation (IDF), which singled out central obesity as the central core of metabolic syndrome.⁴ Another interesting point is whether these 5 components adequately cover the whole spectrum of this syndrome. For example, vascular inflammation markers such as highly sensitive C-reactive protein (CRP) have been proposed as additional components of metabolic syndrome.⁵

Metabolic syndrome is a group of risk factors that predispose to cardiovascular disease. Many studies have confirmed a positive association between hyperuricemia and cardiovascular disease.⁶⁻⁸ As a matter of fact, hyperuricemia was reported as one independent predictor of future cardiovascular events in an 11-year follow-up study from Taiwan.⁹ The link between insulin resistance, the major abnormality of metabolic syndrome, and hyperuricemia was elucidated by Facchini et al,¹⁰ who reported that urinary uric acid clearance decreased in proportion to increases in insulin resistance in normal volunteers. They attributed that to compensatory hyperinsulinemia in subjects with

insulin resistance possibly causing decreased renal excretion of uric acid in association with increased sodium reabsorption. Very recently, it was reported that uric acid reduced endothelial nitric oxide (NO) bioavailability,¹¹ which is essential for insulin-stimulated glucose uptake in skeletal muscle through the NO-dependent pathway.¹² All these observations led to the frequently asked question of whether uric acid should be listed as one component of metabolic syndrome.

Liou et al¹³ report in an article in this issue that factor analysis showed serum uric acid concentrations contributed little as an additional component of metabolic syndrome. Specifically, they found that a model loaded without uric acid explained a very similar proportion of the total variance (62.5%), as did the model loaded with uric acid (56.9%). It has to be pointed out that the study population in this study was specific for relatively healthy middle-aged men (mean age 52 years old). Subjects with diabetes and hypertension under medications were excluded from analysis. Therefore, the findings from this study cannot be generalized to other populations, such as women, the elderly, or individuals with diabetes or hypertension who take medications. In fact, Lee et al¹⁴ demonstrated that women might have a higher prevalence of hyperuricemia among elderly Taiwanese. A larger study involving different aspects of populations is needed. In addition, therapeutic investigations using uric acid-lowering medications in order to further explore the integrated and complex associations of uric acid and other metabolic components are clearly warranted.

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