Is the Metabolic Syndrome a Risk Factor in Japanese CKD Population?

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Metabolic syndrome recently attracts a considerable attention not only from medical professionals but from the general public. Metabolic syndrome, whose concept is basically the same as syndrome X, a deadly quartet, insulin-resistance and visceral fat syndrome, is characterized by complex metabolic derangements in association with prothrombotic and proinflammatory state which accelerates arteriosclerosis. Metabolic syndrome increases risk of developing cardiovascular diseases including angina pectoris, myocardial infarction, heart failure and stroke. Obesity is the phenotypic hallmark of the metabolic syndrome, and derangement of adipocytokines is viewed as the essential common denominator, regardless of cause.

Diagnostic criteria of metabolic syndrome of the National Cholesterol Education Program (NCEP)-Adult Treatment Panel III (ATPIII) is defined by the presence of any of 3 abnormalities out of 5 criteria as follows; waist circumference, triglyceride, HDL-cholesterol, blood pressure, and fasting glucose level. The definition of metabolic syndrome of Japanese Society of Internal Medicine is different from the NCEP-ATP III and the WHO criteria. Japanese criteria apparently put stress on the obesity defined by more than 100 cm² of visceral fat mass, which is easy to be estimated by measuring waist circumferences, that is the essential factor for the definition of metabolic syndrome. In case of men, more than 85 cm of waist circumference counts a risk factor for metabolic syndrome. In contrast, 90 cm of that is a risk factor in the case of women. Microalbuminuria is involved in the WHO criteria but not in the NCEP-ATP III nor in the Japanese diagnostic criteria.

Prevalence of metabolic syndrome defined by NCEP-ATP III with BMI >25 kg/m² is 11.2-20% from the community-based screening program in Japan. Miyatake et al (1), however, reported that the prevalence of metabolic syndrome defined by the Japanese definition, was 30.7% and 3.6% in men and women in Okayama Prefecture, respectively. Takeuchi et al reported the prevalence of metabolic syndrome in men in the towns of Tanno and Sobetsu in Hokkaido was 25.3% (2). In the Hisayama study, the prevalence of metabolic syndrome was 21.1% in men and 8.2% in women in Japanese criteria, while 16.6% of men and 22.0% of women were diagnosed as metabolic syndrome by NCEP-ATP III definition. The Japanese definition of metabolic syndrome may be harsh for middle-aged men because of 85 cm of abdominal circumference. The prevalence seems change significantly by use of different criteria and the validation of the definitions of metabolic syndrome needs to be done in the line of cardiovascular as well as renal risk reduction of the patients. Metabolic syndrome may be a risk of chronic kidney disease as well.

The relationship between metabolic syndrome and chronic kidney disease (CKD) or proteinuria has recently been paid attention. Tanaka et al (3) assessed the prevalence of metabolic syndrome and renal disease from a hospital-based screening program including 6,980 participants. They found that 12.4% of general population had metabolic syndrome and among them 11% had proteinuria, which is a significantly higher prevalence of proteinuria compared to those without metabolic syndrome, 3.0%. of whom have proteinuria. When CKD is defined as GFR<60 ml/min/1.73 m², the prevalence of CKD was 16% in a population of metabolic syndrome, while it was 12% in cases without metabolic syndrome (3). In this issue of Internal Medicine, Miyatake et al (4) report the association of proteinuria with metabolic syndrome. They studied 2,121 Japanese subjects who underwent an annual health examination program in Okayama. The prevalence of proteinuria was 15.1% of men and 17.8% of women with metabolic syndrome. The prevalence of proteinuria in metabolic syndrome was significantly higher than those of general population (3.5% in men and 1.8% in women). The report raises an important issue about the association of metabolic syndrome with proteinuria.

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Microalbuminuria, detected by a method which is 10-fold
more sensitive than the measurement of proteinuria, is an independent and strong predictor of cardiovascular risk and an early sign of endothelial damage. Nakamura et al (5) assessed the prevalence of microalbuminuria and analyzed the association with obesity in Iwate Prefecture. They found that obesity was independently associated with the presence of microalbuminuria. Interestingly, microalbuminuria is evident in subjects with central obesity without an apparent relationship to hypertension and diabetes. In the United States, the prevalence of metabolic syndrome defined by NCEP-ATPIII is 24.7% from the data of NHANES III (6). Microalbuminuria was present in 7.8% in men and 5.0% in women (7). 34% of women and 42% of men with microalbuminuria had metabolic syndrome. In the subjects with metabolic syndrome the comorbidity of CKD and microalbuminuria was 6.0% and 12.3%, respectively, while the prevalence of CKD (1.2%) and microalbuminuria (4.7%) was significantly lower in participants without metabolic syndrome (6).

Why is the metabolic syndrome highly associated with proteinuria reflecting glomerular abnormality? As mentioned above, complex metabolic derangements in association with prothrombotic and proinflammatory state may evoke the glomerular lesions, and hypertension and hyperlipidemia are the risk factors for CKD. It was reported that insulin resistance and hyperinsulinemia causes glomerular hypertrophy independent of hyperglycemia (8). Obese people often have hyperphagia, which is associated with an excess excretory load to the kidney. Chagnac et al (9) reported that renal plasma flow and glomerular filtration rate were 51% and 31% increased in obese subjects. These overloads to glomeruli may cause endothelial injury and eventually glomerulosclerosis. Obesity-associated nephropathy was reported in US and Japan. The pathological characteristics of the obesity-associated nephropathy is glomerulomegaly and focal segmental glomerulosclerosis (FSGS) (10). The clinical manifestation of the obesity-associated FSGS differs from the classic idiopathic FSGS and characterized by less proteinuria and more indolent progression.

In conclusion, risk of proteinuria and microalbuminuria in association with metabolic syndrome needs to be evaluated and should be paid more attention from the viewpoint of developing cardiovascular diseases and progression of chronic kidney disease. Microalbuminuria, in particular is an early marker of the endothelial dysfunction and glomerular lesion. Measuring the microalbuminuria and proteinuria, which is often slighted in daily practice, should be encouraged by medical professionals to accurately evaluate the status of the metabolic syndrome.

References


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