Relationship between Metabolic Syndrome and Proteinuria
in the Japanese Population

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Abstract

Objective We investigated the link between metabolic syndrome and proteinuria in Japanese.
Methods A total of 12,023 Japanese subjects, aged 20-79 years, were recruited in a cross-sectional clinical investigation study. From this group, we used data of 2,121 subjects for further investigation. Proteinuria was measured by using urine strip devices. The diagnosis of metabolic syndrome was based on the new criterion in Japan.
Results In the first analysis, 224 men (6.0%) and 359 women (4.3%) were diagnosed as trace positive (±) and 155 men (4.1%) and 147 women (1.8%) were diagnosed as positive (+) with proteinuria. In the second analysis, 264 men (29.7%) and 45 women (3.7%) were diagnosed as metabolic syndrome. Prevalence of proteinuria in subjects with metabolic syndrome was significantly higher than that in subjects with non-metabolic syndrome in both sexes. In addition, the atherogenic index was significantly higher in subjects with metabolic syndrome than in subjects with non-metabolic syndrome.
Conclusion The present study indicated that metabolic syndrome might be an important factor in the etiology of proteinuria in Japanese.

Key words: metabolic syndrome, proteinuria, waist circumference, prevalence

(Introduction)

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Subjects and Methods

Subjects

In the first analysis, we used all data of 12,023 Japanese (3,744 men and 8,279 women) aged 20-79 years, who underwent urine examination and anthropometric measure-
ments from June 1997 to May 2005 at Okayama Southern Institute of Health with informed consent (Table 1).

In the second analysis, among 12,023 subjects, we used data of 2,121 subjects (888 men and 1,233 women) who undertook blood examination and blood pressure measurements in addition to urine examination and anthropometric measurements for further analysis (Table 2).

Urine examination

Urine samples were collected from the second-morning urine (before 10 a.m.) and subjected to the examination within 1 hour. The urine examination was performed using urine strip tests (BAYER, Tokyo, Japan). The reagent strip was dipped directly into the urine sample. Just after dipping, the sample is graded as -: negative, ±: trace positive, + : positive (30 mg/dl), 2+: positive (100 mg/dl), 3+: positive (300 mg/dl) or 4+: positive (1000 mg/dl) by comparison with a standard color chart found on the container’s label (7).

Anthropometric measurements

The anthropometric parameters were evaluated by using the following respective parameters such as height, body weight, body mass index (BMI), waist circumference, hip circumference. BMI was calculated by weight/height$^2$ (kg/m$^2$). The waist circumference was measured at the umbilical level and the hip was measured at the widest circumference over the trochanter in standing subjects after normal expiration over (8).

Blood pressure measurements

Blood pressure of each participant was measured after resting at least 15 minutes in the sitting position.

Blood sampling and assays

We measured overnight fasting serum levels of high-density lipoprotein (HDL) cholesterol, triglycerides (L Type Wako Triglyceride-H, Wako Chemical, Osaka) and plasma glucose. The atherogenic index was calculated as follows: (total cholesterol-HDL cholesterol)/HDL cholesterol.

Diagnosis of metabolic syndrome

The syndrome was defined (3), among men with a waist circumference in excess of 85 cm and women with a waist circumference in excess of 90 cm (9), as having 2 or more components from among the following: 1) Dyslipidemia: triglyceride$\geq$150 mg/dl and/or HDL cholesterol$<40$ mg/dl, 2) Hypertension: blood pressure$\geq$130/85 mmHg, 3) Impaired glucose tolerance: fasting plasma glucose$\geq$110 mg/dl.

Statistical analysis

Data are expressed as mean ± standard deviation (SD) values. Relationship between metabolic syndrome and proteinuria was tested using a $\chi^2$-test: p<0.05 was considered to be statistically significant.

Results

In the first analysis, 224 men (6.0%) and 359 women (4.3%) were diagnosed as ±, and 155 men (4.1%) and 147 women (1.8%) were diagnosed as + in proteinuria (Table 3). Prevalence of proteinuria gradually increased with age in men, but not in women.

In the second analysis, 72 men (8.1%) and 65 women (5.3%) were also diagnosed as ±, and 38 men (4.3%) and 23 women (1.9%) were also diagnosed as + in proteinuria (Table 4).

We clarified the prevalence of metabolic syndrome (Table 5). Among 2,121 Japanese subjects, 461 men (51.9%) had a waist circumference in excess of 85 cm and 73 women (5.9%) had a waist circumference exceeding 90 cm. In addition, the prevalence of metabolic syndrome gradually increased with age under the age of 70 and 264 men (29.7%) were diagnosed as having metabolic syndrome. In turn, the prevalence of metabolic syndrome in women gradually increased with age, especially over the age of 50, and only 45 women (3.7%) were diagnosed with metabolic syndrome.

We evaluated the relationship between the sub criterion of metabolic syndrome and proteinuria, also between metabolic syndrome and proteinuria (Table 6). The prevalence of proteinuria was closely linked to hypertension and impaired glucose tolerance in men. It was also closely linked to waist circumference, hypertension and impaired glucose tolerance in women. The prevalence of proteinuria in subjects with metabolic syndrome (men 15.1%, women 17.8%) was significantly higher than that in subjects with non-metabolic syndrome in both sexes, and the average of age in subjects with metabolic syndrome (49.1±10.9 years) was similar to
that in subjects with non-metabolic syndrome (45.7±12.7 years) in men. As a result, 224 men (28.8%) and 37 women (3.2%) with proteinuria were diagnosed as having metabolic syndrome. In turn, 22 men (30.6%) and 4 women (6.2%) with proteinuria ± 18 men (47.4%) and 4 women (17.4%) with proteinuria + were diagnosed as having metabolic syndrome.

To investigate the effect of overt type 2 diabetes mellitus (fasting plasma glucose ≥126 mg/dl and/or receiving medications for type 2 diabetes mellitus) and overt hypertension (blood pressure ≥140/90 mmHg and/or receiving medications for hypertension) on proteinuria, we excluded the subjects with type 2 diabetes mellitus and hypertension and re-evaluated the relationship between metabolic syndrome and proteinuria (Table 6). As a result, 58 men (among 463 men) and 7 women (among 871 women) were diagnosed as having metabolic syndrome. Only 6 men and 2 women with metabolic syndrome had proteinuria. Finally, the atherogenic index in subjects with metabolic syndrome (men 3.7±1.1, women 3.1±1.1) was also significantly higher than that in subjects with non-metabolic syndrome in both sexes (men 2.8±1.1, women 2.4±1.0).

### Discussion

Our study is the first report on the relationship between metabolic syndrome, defined by the new criterion of metabolic syndrome in Japan, and proteinuria. Metabolic syndrome has important clinical and public health implications because it is a common disorder in Japan (4). Previous studies have documented that metabolic syndrome is an important risk factor for diabetes, coronary heart disease and
The prevalence of proteinuria in Japanese was reported to be 3.5% in men and 1.8% in women by the Japanese Society of Nephrology (13) and our results were similar to those of a previous study (13). However, the prevalence of proteinuria (+/−: 4.1%) was higher than that in women (+/−: 1.8%) in our study. Therefore, the prevalence of proteinuria may have statistically increased with age in men, but not in women.

Several studies have documented the relationship between sub-components of metabolic syndrome and chronic kidney disease. In a cohort study of 101,516 Japanese men and women, BMI was inversely related to risk for end-stage renal disease in women, but not in men (14). In a cross-sectional study, body fat percentage and BMI were positively correlated with the glomerular filtration rate in patients with renal disease (15). Epidemiologic studies have reported that diabetes, hypertension and dyslipidemia are the major risk factors for the development and progression of chronic kidney disease and microproteinuria (16-19). In addition, in some reports in the literature, metabolic syndrome is noted as a critical factor in the development of chronic kidney disease (20-22). In the present study, the results showed that the metabolic syndrome and some sub-criterion of metabolic syndrome using the new criterion in Japan were associated with proteinuria. After excluding subjects with type 2 diabetes mellitus and hypertension, only 6 men and 2 women had proteinuria among the subjects with metabolic syndrome. The finding may stress the clinical significance of type 2 diabetes mellitus and hypertension on proteinuria in subjects with metabolic syndrome. In addition, the atherogenic index in subjects with metabolic syndrome was significantly higher than that in subjects with non-metabolic syndrome. Atherosclerosis induced by metabolic syndrome is thought to play a central role in proteinuria in subjects with metabolic syndrome.

Potential limitations still remain in our study. In men, the

(1) percentage of subjects as classified into age group
age-related change in the prevalence of metabolic syndrome and proteinuria were noted and we could not avoid the influence of age on the relationship between metabolic syndrome and proteinuria. The cross-sectional study design in our study makes it difficult to infer causality between metabolic syndrome and proteinuria. Therefore, our findings are applicable to clinical and public health practice settings. In conclusion, metabolic syndrome is closely linked to proteinuria in the Japanese population. Further intervention studies are necessary to test the effect of prevention and treatment of metabolic syndrome on the risk for proteinuria.

References


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