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Abstract

We compared the levels of hepatic enzymes in 220 Japanese men with metabolic syndrome with those in age and sex-matched subjects without the syndrome. Metabolic syndrome was defi ned by the new criteria published in Japan, and hepatic enzymes, i.e., aspartate aminotransferase (AST), alanine aminotransferase (ALT) and γ-glutamyl transpeptidase (γGTP), were measured. AST, ALT and γGTP in subjects with metabolic syndrome were signifi cantly higher than those in subjects without the syndrome, and metabolic syndrome was closely aociated with hepatic enzymes in this cohort of Japanese men.

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Short Communication

Comparison of Hepatic Enzymes between Japanese Men with and without Metabolic Syndrome

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We compared the levels of hepatic enzymes in 220 Japanese men with metabolic syndrome with those in age and sex-matched subjects without the syndrome. Metabolic syndrome was defined by the new criteria published in Japan, and hepatic enzymes, *i.e.*, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and γ-glutamyl transpeptidase (γGTP), were measured. AST, ALT and γGTP in subjects with metabolic syndrome were significantly higher than those in subjects without the syndrome, and metabolic syndrome was closely associated with hepatic enzymes in this cohort of Japanese men.

Key words: metabolic syndrome, hepatic enzymes

The metabolic syndrome, which is characterized by abdominal obesity, dyslipidemia, and elevation of blood pressure and fasting plasma glucose levels, is a common disorder in Japan [1, 2]. For example, in a previous cohort, 30.7% of men and 3.6 % of women were diagnosed as having the metabolic syndrome using the new criteria in Japan [1]. The metabolic syndrome has been associated with an increased risk for cardiovascular disease. However, the link between metabolic syndrome as defined using the new criteria in Japan and hepatic enzymes still remains to be investigated. In the present study, therefore, we compared the levels of hepatic enzymes in subjects with metabolic syndrome with those in age and sex-matched subjects without the syndrome.

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Subjects and Methods

Subjects. We used the data of 220 Japanese men with metabolic syndrome and 263 Japanese men without metabolic syndrome, aged 23-77 years, who met all of the following criteria: (1) Received an annual health checkup each year from June 1997 to May 2005 at Okayama Southern Institute of Health; (2) Received fasting blood examination and a cardiopulmonary exercise test as part of the annual health checkup; (3) Provided written informed consent; (4) Had no history of hepatitis virus infection, hepatitis B antigen (HBsAg) or antibodies against hepatitis C viruses (Table 1).

Anthropometric measurements and blood examination. Anthropometric parameters, *i.e.*, height, weight, and waist circumference, were mea-

sured. Body mass index (BMI) was calculated as weight/[height]^2 (kg/m^2). The waist circumference was measured at the umbilical level. Blood examinations, *i.e.*, aspartate aminotransferase (AST) by the Wroblewski-Karmen method, alanine aminotransferase (ALT) by the Wroblewski-Karmen method, and γ-glutamyl transpeptidase (γGTP) by the L-γ-glutamyl-3-carboxy-4-nitroanilide method, were also measured. The institutional normal upper limit of AST was 35 IU/l, that of ALT was 35 IU/l, and that of γGTP was 55 IU/l.

Diagnosis of metabolic syndrome. The metabolic syndrome was defined, among men with a waist circumference in excess of 85 cm and women with a waist circumference in excess of 90 cm, as having 2 or more of following components: 1) Dyslipidemia: triglycerides $\geqq$ 150 mg/dl and/or HDL cholesterol $<$ 40 mg/dl; 2) High blood pressure: blood pressure $\geqq$ 130/85 mmHg; 3) Impaired glucose tolerance: fasting plasma glucose $\geqq$ 110 mg/dl [2].

Table 1 Comparison of parameters using the criteria and subcriteria of metabolic syndrome in Japanese men

Metabolic syndrome	(+)	(−)	*p* Value
Number of Subjects	220	263	
Age	48.9 ± 10.5	49.3 ± 11.1	0.6937
Height (cm)	168.6 ± 5.7	168.3 ± 5.7	0.5336
Body weight (kg)	81.4 ± 12.8	71.9 ± 12.1	< 0.0001
Body mass index (kg/m^2)	28.6 ± 3.8	25.3 ± 2.5	< 0.0001
AST (IU/L)	29.6 ± 12.9	24.7 ± 9.7	< 0.0001
ALT (IU/L)	43.9 ± 28.3	32.4 ± 22.8	< 0.0001
γGTP (IU/L)	63.6 ± 51.2	46.2 ± 41.9	< 0.0001
Waist Circumference	(+)	(−)	
Number of Subjects	351	132	
Age	47.6 ± 10.5	53.1 ± 10.7	< 0.0001
AST (IU/L)	28.2 ± 11.8	23.5 ± 10.2	< 0.0001
ALT (IU/L)	42.4 ± 27.7	24.9 ± 15.4	< 0.0001
γGTP (IU/L)	58.3 ± 47.9	43.1 ± 43.5	0.0015
Dyslipidemia	(+)	(−)	
Number of Subjects	270	213	
Age	49.0 ± 10.8	49.2 ± 10.9	0.8311
AST (IU/L)	29.0 ± 12.8	24.2 ± 9.0	< 0.0001
ALT (IU/L)	41.9 ± 28.5	32.2 ± 21.5	< 0.0001
γGTP (IU/L)	61.8 ± 52.3	44.4 ± 37.6	< 0.0001
High blood pressure	(+)	(−)	
Number of Subjects	361	122	
Age	49.7 ± 10.9	47.5 ± 10.6	0.0528
AST (IU/L)	27.8 ± 12.2	24.2 ± 9.0	0.0031
ALT (IU/L)	38.6 ± 26.6	34.8 ± 24.4	0.1635
γGTP (IU/L)	59.2 ± 50.7	39.3 ± 30.1	< 0.0001
Impared glucose tolerance	(+)	(−)	
Number of Subjects	185	298	
Age	52.5 ± 9.2	47.0 ± 11.2	< 0.0001
AST (IU/L)	26.5 ± 13.6	27.2 ± 10.1	0.5213
ALT (IU/L)	37.2 ± 29.6	37.8 ± 23.7	0.7987
γGTP (IU/L)	58.4 ± 54.4	51.5 ± 41.8	0.1222
Metabolic syndrome (Non drinkers)	(+)	(−)	
Number of Subjects	47	56	
Age	46.5 ± 12.0	48.2 ± 12.1	0.4765
AST (IU/L)	32.2 ± 17.3	23.3 ± 9.7	0.0014
ALT (IU/L)	52.7 ± 36.3	32.7 ± 22.2	0.0009
γGTP (IU/L)	47.6 ± 30.9	31.7 ± 21.0	0.0026

Alcohol consumption habits. The data on alcohol consumption habits were obtained at interviews by well-trained staff in a structured way. The subjects were asked if they currently drank alcohol on a regular basis. Subjects answering "yes" were classified as current drinkers. Those answering "no" were further asked whether they had ever drunk alcohol on a regular basis. Those answering "no" were classified as nondrinker and those answering "yes" were classified as previous drinkers.

Statistical analysis. Data are expressed as the mean ± standard deviation (SD). The relationship between metabolic syndrome and drinking habits was tested using an χ^2 test and parameters were compared between groups using an unpaired-t test. Values of $p < 0.05$ were considered to be statistically significant.

Results

Table 1 and 2 compare the results between subjects with and those without metabolic syndrome. There were no significant differences in age or drinking habits between the 2 groups. Body weight and BMI in the subjects with metabolic syndrome were significantly higher than those in the controls. The levels of AST, ALT and γGTP were also significantly higher in the subjects with metabolic syndrome. We also compared the levels of hepatic enzymes between subjects with and without each component of the definition of metabolic syndrome. By this analysis, there was no significant difference of age between subjects with or without dyslipidemia or high blood pressure. However, there was a significant difference of age between the sub-groups with or without abdominal obesity and impaired glucose tolerance. The levels of AST, ALT and γGTP in subjects with abdominal obesity or dyslipidemia were significantly higher than those in subjects without these components of the metabolic syndrome. AST and γGTP in subjects with elevated blood pressure were also significantly higher than those in subjects with normal blood pressure.

To strictly avoid the influence of alcohol consumption habits, we paerformed a separate analysis using only data of nondrinkers and compared the hepatic enzyme levels between subjects with and those without metabolic syndrome. As in the overall analsysis, the AST, ALT and γGTP levels in subjects with metabolic syndrome were significantly higher than those in the subjects without the syndrome.

Table 2 Relationship between metabolic syndrome and drinking habits

	MS (+)	MS (−)
Current drinker	168	193
Non drinker	47	56
Previous drinker	5	14

Not significant ($p = 0.2258$) by χ^2 test
MS: Metabolic syndrome

Discussion

We compared the hepatic enzyme levels in subjects with metabolic syndrome with those in age and sex-matched controls without metabolic syndrome subjects as defined using the criteria in Japan.

Nonalcoholic steatohepatitis represents an advanced stage of fatty liver disease developed in the absence of alcohol abuse and is frequently associated with the metabolic syndrome and type 2 diabetes. The actual prevalence of nonalcoholic steatohepatitis in type 2 diabetes and obesity is unknown. It is estimated that 75% of type 2 diatetic patients present some form of non alcoholic fatty liver of different degrees. Several genetic and acquired factors are involved in its pathogenesis [3]. Wannamethee *et al.* reported that elevated levels of ALT and γGTP within the normal range are independent predictors of type 2 diabetes in older men [4]. Nannipieri *et al.* also reported that mild elevation in hepatic enzymes is associated with features of the metabolic syndrome by follow-up study [5].

The metabolic syndrome is now considered to reflect a failure of normal partitioning of surplus fat exclusively into adipose tissue [6, 7]. The failure leads to fat storage in the liver, muscle and pancreatic β cells, which causes hepatic steatosis, dyslipidemia, hepatic and peripheral insulin resistance, and insulin secretory failure. Adipocytokines such as leptin and adiponectin are proposed to play a critical role in preventing accumulation of lipids [7]. In this regard, it is interesting that hypoadiponectinemia has been seen in patients with nonalcoholic steato-

hepatitis [8]. In addition, administration of adiponectin has been shown to alleviate nonalcoholic fatty liver disease in mice [9]. In this study, hepatic enzyme levels in subjects with metabolic syndrome were significantly higher than those in subjects without the syndrome, even after strictly controlling for alcohol consumption. In addition, a contribution of waist circumference and dyslipidemia to the development of liver functional abnormality was noted.

Potential limitations still remain in our study. First, the cross-sectional study design in our study makes it difficult to infer causality between metabolic syndrome and hepatic enzymes. Second, we were not able to evaluate hepatic fat accumulation by using ultrasound systems. Therefore, our findings are not fully applicable to clinical and public health practice settings. In conclusion, metabolic syndrome was found to be closely linked to hepatic enzymes in a large cohort of Japanese men. Further intervention studies are necessary to test the effect of prevention and treatment of metabolic syndrome on hepatic enzymes.

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