Significance of the Presence of Metabolic Syndrome in Patients with Asymptomatic Arteriosclerosis Affecting the Aorta and the Cerebral, Extra-cranial Carotid and Coronary Arteries

Tomohide Ohnuki1, Wakoh Takahashi1, Youichi Ohnuki1, Shiaki Kawada2 and Shunya Takizawa1

Abstract

Objective  The presence of metabolic syndrome (MetS) is strongly associated with stroke and cardiovascular diseases. However, the relationship between MetS and the localization of atherosclerosis at various sites remains uncertain. In this study, in order to reveal the relevance of MetS to atherosclerosis at several sites, we investigated the relationships among vascular risk factors, asymptomatic cerebral infarction and atherosclerosis in the aorta and carotid and coronary arteries in adults without overtly symptomatic cerebrovascular or cardiovascular disease.

Methods  The subjects in this study included 2,759 Japanese participants (1,845 men and 914 women, mean age: 52 years) with no history of stroke or cardiovascular events. The diagnosis of MetS was made based on modifications to criteria obtained from the National Cholesterol Education Program Adult Treatment Panel. In all subjects, the presence of cerebral infarction in the extra-cranial carotid, coronary and aortic arteries was investigated using MRI, B-mode ultrasonography and CT.

Results  Of the 2,759 subjects, 796 (28.9%) fulfilled the criteria for MetS. The presence of MetS increased the odds ratio (OR) to 1.89 (95% confidence interval (CI): 1.35-2.65, p-value <0.0001) for asymptomatic cerebral infarction, 1.70 (95% CI: 1.37-2.10, p-value <0.0001) for carotid arteriosclerosis, 2.07 (95% CI: 1.62-2.27, p-value <0.0001) for coronary calcification and 1.67 (95% CI: 1.33-2.09, p-value<0.0001) for aortic calcification.

Conclusion  The presence of MetS was found to be significantly correlated with arteriosclerosis in all regions, including the cerebral small-vessels, extra-cranial carotid arteries, coronary arteries and abdominal aorta. MetS might be a predictor for small and large vessel disease throughout the body.

Key words: metabolic syndrome, cerebral small-vessel disease, atherosclerosis, healthy subject, primary prevention

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Introduction

The concept of metabolic syndrome (MetS) is based on a syndrome of multiple risk factors proposed in the 1980s. Reaven (1) suggested that the combination of lifestyle-related diseases, including hypertension and glucose and lipid metabolism disorders, referred to as “Syndrome X” might be a significant risk factor for stroke and ischemic heart disease. In 1989, Kaplan (2) described the “deadly quartet” of obesity, hypertension, diabetes mellitus and dyslipidemia and attached importance to the combination of these risk factors as a predictor of atherothrombosis. Recently, several studies have suggested that a similar cluster
of several risk factors, so-called “metabolic syndrome,” might be strongly associated with strokes and other cardiovascular diseases (3-8). Nevertheless, the significance of multiple risk factors as predictors of atherosclerosis has so far been examined predominantly at limited sites such as the extra-cranial carotid arteries or other vascular territories (9-11). Therefore, it remains to be clarified whether multiple risk factors are predictive of atherosclerosis at several sites within the vascular tree.

In this study, in order to reveal the relevance of the presence of MetS to atherosclerosis at several sites, we investigated the relationships among vascular risk factors, asymptomatic cerebral infarction and atherosclerosis in the aorta and carotid and coronary arteries in adults without overtly symptomatic cerebrovascular or other cardiovascular disease.

### Materials and Methods

The subjects in this study included 2,759 participants (1,845 men and 914 women, mean age: 52 years) who underwent medical check-ups at the HIMEDIC Imaging Center at Lake Yamanaka between January 1996 and December 2002. All subjects were Japanese and resided in large cities, including Tokyo, Osaka and Nagoya. Most of the subjects were managers or office workers, and they and their family members belonged to a relatively wealthy group within the general population of Japan, as previously described (11). Subjects with a history of stroke or cardiovascular events such as ischemic heart disease were excluded from this study.

The diagnosis of MetS was made based on modifications to criteria obtained from the National Cholesterol Education Program Adult Treatment Panel (NCEP-ATPIII) (12, 13). The criteria were as follows: (1) body mass index (BMI, body weight (kg)/height (m$^2$)) ≥25 kg/m$^2$, (2) triglycerides ≥150 mg/dL or on medications for hypertriglyceridemia, (3) high density lipoprotein (HDL) cholesterol ≤40 mg/dL (for men) or ≤50 mg/dL (for women) or on medications for hypercholesterolemia, (4) systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg or on medications for hypertension and (5) fasting plasma glucose ≥110 mg/dL. In this study, obesity was defined as a BMI ≥25 kg/m$^2$, instead of using waist girth. Blood pressure was measured three times at rest, and the average of the second and third measurements was used in this study.

MRI studies were conducted using T1-weighted, T2-weighted and fluid attenuated inversion recovery (FLAIR) images. Any lesion measuring 3 mm in maximum diameter that showed high intensity on T2-weighted images and low intensity on T1-weighted images was diagnosed as a cerebral infarction. The extra-cranial carotid arteries were evaluated using B-mode ultrasonography with a 7.5-MHz probe (SSA-250A, Toshiba, Tochigi). The scanning range included the distal common carotid arteries and carotid bifurcations and the proximal segments of the internal carotid arteries. Atherosclerosis was defined as the presence of nodular or calcified lesions or an IMT (intimal plus medial complex thickness) exceeding 1.0 mm.

The aorta and coronary arteries were evaluated based on the presence of calcified lesions in the vessel walls detected on helical computed tomography (Superhelix 900S, Toshiba, Tochigi). In the coronary arteries, any hyperdense lesion in the left main, left anterior descending, circumflex or right coronary artery was diagnosed as calcification. Atherosclerosis of the aorta was defined as the presence of high-density lesions in the vessel walls from the ascending aorta to the bifurcation of the common iliac arteries, according to previous criteria.

The data in this study were statistically analyzed using SPSS Statistics 19 (IBM, New York). A multiple logistic regression analysis was used to calculate the odds ratio (OR) of MetS and each vascular risk factor for arteriosclerosis at each site.

### Results

Of the 2,759 subjects, 837 (30%) had a BMI ≥25, 1,004 (36%) had a triglyceride level ≥150 mg/dL, 569 (20.6%) had an HDL cholesterol level <40 or 50 mg/dL, 1,385 (50%) had hypertension and 1,055 (38%) had hyperglycemia. Of the total number of subjects, 796 (28.9%) met the criteria for MetS (Tables 1, 2).

Of the 796 subjects with MetS, carotid atherosclerosis was seen on ultrasonography in 222 (28%) patients and asymptomatic cerebral infarction was observed on MRI in 73 (9%) patients. Aortic and coronary artery calcifications were detected on CT in 203 (26%) subjects and 176 (22%) subjects, respectively. The prevalence of carotid atherosclerosis, asymptomatic cerebral infarction on MRI and aortic and coronary artery calcification was significantly greater in the

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subjects with MetS than in those without MetS (Table 3).

In the presence of MetS, the ORs increased to 1.89 for asymptomatic cerebral infarction (95% confidence interval (CI): 1.35-2.65, p-value <0.0001), 1.70 for carotid atherosclerosis (95% CI: 1.37-2.10, p-value <0.0001), 2.07 for coronary calcification (95% CI: 1.62-2.27, p-value <0.0001) and 1.67 for aortic calcification (95% CI: 1.33-2.09, p-value <0.0001), as shown in Table 4. The relative risk that each component of MetS confers for asymptomatic cerebral infarction, carotid atherosclerosis and coronary and aortic calcification is shown in Table 5. The presence of hypertension increased the OR for asymptomatic cerebral infarction significantly (2.54, 95% CI: 1.64-3.92, p-value<0.0001), followed by hypertension (2.4, 95% CI: 1.09-5.29, p-value <0.01) and BMI (1.33, 95% CI: 1.03-1.71, p-value <0.03; Table 4). Hypertension also increased the likelihood of aortic calcification (1.51, 95% CI: 1.19-1.92, p-value <0.01), as did low HDL cholesterol (1.46, 95% CI: 1.12-1.91, p-value <0.005) and high triglycerides (1.31, 95% CI: 1.03-1.67, p-value <0.03; Table 5).

The association between each component of MetS and the risk of multiple arteriosclerotic lesions was determined. Of all the components of MetS, high fasting plasma glucose levels were found to be significantly associated with the risk of multiple arteriosclerotic lesions (OR=1.552, 95% CI: 1.24-1.94, p-value <0.0001).
The authors state that they have no Conflict of Interest (COI).

References


http://www.naika.or.jp/imonline/index.html

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