*Original Article***Anthropometric and Clinical Findings in Obese Japanese: The Saku Control Obesity Program (SCOP)**

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Abstract

BACKGROUND: Japan has entered the epidemic of obesity. To clarify the contributing factors to the development of metabolic syndrome triggered by visceral fat obesity and to investigate the effectiveness of a weight-loss program, we launched a new intervention program for obese people.

METHODS: Japanese subjects with high body mass index (BMI > 28.3 kg/m²) were selected for a weight-loss program from those who had undergone a medical checkup at the Saku Central Hospital. The baseline anthropometric and clinical findings of the participants were analyzed.

RESULTS: At baseline, 235 subjects (116 men and 119 women) participated in this program. The mean weight, waist circumference, and visceral fat area were 86.4 ± 11.8 kg, 101.5 ± 8.7 cm, and 159.0 ± 54.1 cm² in men and 75.2 ± 9.5 kg, 103.7 ± 8.3 cm, and 129.8 ± 47.0 cm² in women, respectively. Using the Japanese diagnostic criteria, the prevalence of metabolic syndrome was 62.9% in men and 51.3% in women. Leptin, c-peptide, and insulin levels tended to increase with increasing numbers of metabolic risk factors in men. In women, c-peptide and free fatty acid levels tended to increase with increasing numbers of these factors, but adiponectin decreased dose-dependently with increasing numbers of factors.

CONCLUSIONS: More than half the subjects were founded to meet the criteria for metabolic syndrome. Immediate intervention to lose weight and to improve other risk factors of metabolic syndrome is necessary in such seriously obese people.

KEY WORDS: obesity, metabolic syndrome, visceral fat area, adipocytokine

Introduction

Japan has entered the escalating epidemic of obesity.¹⁾ Obesity may trigger many serious illnesses, including type 2 diabetes and cardiovascular diseases. In particular, visceral fat obesity is thought to be associated with many metabolic disorders.

The metabolic syndrome is an important cluster of metabolic abnormalities linked with insulin resistance and cardiovascular diseases.^{2,3)} Insulin resistance had long been considered to have a central role in the development of metabolic disorders⁴⁾; however, several clinical studies have demonstrated intra-abdominal visceral fat accumulation to have a crucial, direct role in this development.^{5,6)} According to the new definition released by the Japanese examination committee for the criteria of metabolic syndrome, the presence of abdominal obesity is necessary for the diagnosis.⁷⁾

Recently, it has been shown that adipocytes secrete several proteins called adipocytokines, including adiponectin, leptin, and tumor necrosis factor- α (TNF- α); these may be related to the development of obesity-mediated adverse effects in glucose and lipid metabolism.⁸⁾ Thus, along with weight reduction in obese patients, changes in the concentrations of biochemical

parameters including these adipocytokines should be surveyed.

To prevent the development of metabolic syndrome, weight reduction in obese patients is clearly necessary.⁹⁾ However, it is not well understood how much reduction is appropriate and which method of weight control is the most effective for prevention of metabolic syndrome. In addition, it is unclear whether visceral fat can be reduced effectively by modification of diet and exercise habits.

To clarify the contributing factors to the development of metabolic and cardiovascular disorders and to investigate the effectiveness of a weight-loss program, we launched a new intervention program for obese people.¹⁰⁾ In this report, we present anthropometric and biochemical data, as well as major clinical findings, of all subjects at baseline.

Methods

Japanese obese subjects were selected from people who had undergone a medical checkup in the Saku Central Hospital. They were aged 40–64 years with a body mass index (BMI: kg/m²) greater than 28.3 (the upper 5 percentile of all examinees) and had come for medical checkup since 2000. They were asked to participate in an intervention program for weight loss, the Saku Control Obesity Program (SCOP). The details of the subjects and methods of this program are presented the previous report.¹⁰⁾ The participants had an anthropometric and clinical examination (height, weight, body fat percentage, waist circumference, visceral fat area, and biochemical markers of blood and urine) and were assessed for present illness, physical activity level, and dietary habits at the start of this program.

The height (cm) and weight (kg) of the subjects were measured with an automatic scale (Tanita, BF-220, Tokyo, Japan). Percentage body fat was evaluated by the bioelectric impedance method with the same scale. The BMI was calculated as the weight (kg) divided by the squared height (m²). Visceral and subcutaneous fat areas were assessed by a computed tomography scan at the level of the umbilicus, with the subjects in the supine position, and calculated using commercially available software (Fat Scan; N2 System Corp., Osaka, Japan).

Adipocytokines (i.e., leptin, TNF- α , adiponectin, and free fatty acid), c-peptide, and insulin levels were examined using the laboratory testing services provided by SRL Inc. (Tokyo, Japan). Leptin (ng/mL) was measured by a radioimmunoassay (Human Leptin RIA Kit, LINCO Research, St. Charles, MO, USA) with a sensitivity of 0.5 ng/mL. TNF- α (pg/mL) was measured by an enzyme-linked immunoassay (ELISA; Quantikine TNF- α HS Immunoassay Kit, R&D Systems Inc., Minneapolis, MN, USA) with a sensitivity of 0.12 pg/mL. High-molecular-weight form adiponectin (μ g/mL) was determined using ELISA (Fujirebio Inc., Tokyo, Japan) with a detection limit of 0.18 μ g/mL. Free fatty acid (mEq/L) was determined using an enzymatic assay (NEFA-SS 'Eiken', Eiken Chemical Co. Ltd., Tokyo, Japan) with a sensitivity of 0.005 mEq/L. C-peptide (ng/mL) was measured by a chemiluminescent enzyme immunoassay (CLEIA) (Lumipulse Presto C-peptide, Fujirebio Inc.) with a minimal detection limit of 0.1 ng/mL. Insulin (μ IU/mL) was measured using CLEIA (Lumipulse Presto Insulin, Fujirebio Inc.) with a minimal detection limit of 0.3 μ IU/mL. Other biochemical markers were examined in the clinical laboratory of the Saku Central Hospital.

Comparisons of the mean values of anthropometric and biochemical markers between sexes and between the groups stratified by the number of metabolic risk factors were tested using Student's *t*-test and analysis of variance (ANOVA), respectively. The associations of adipocytokines and insulin resistance markers with anthropometric and other biochemical markers for metabolic syndrome were examined using Pearson's correlation. Statistical significance was set at $p < 0.05$ for all analyses. All statistical analyses were performed using the SPSS® system for personal computers (Release 14.0.1, SPSS Japan, Inc., Tokyo, Japan).

Results

Among the 917 people with BMI > 28.3 kg/m², 235 subjects (116 men and 119 women) participated in this program. **Table 1** shows the basic characteristics of the subjects grouped by sex at baseline. Men were taller, heavier, and had greater visceral fat area than women, but women had significantly greater waist circumferences than men. In terms of clinical and biochemical markers, men showed significantly higher triglyceride and uric acid levels than women. In contrast, total cholesterol, HDL cholesterol, and LDL cholesterol were higher in women than in men.

Table 1 Basic Characteristics of the Subjects

	Men (n = 116)	Women (n = 119)
Age (years)	52.9 $\pm$ 6.6	54.4 $\pm$ 6.5
Height (cm)	168.4 $\pm$ 5.8	155.4 $\pm$ 5.5 *
Weight (kg)	86.4 $\pm$ 11.8	75.2 $\pm$ 9.5 *
BMI (kg/m ²)	30.4 $\pm$ 3.5	31.1 $\pm$ 3.1
Waist circumference (cm)	101.5 $\pm$ 8.7	103.7 $\pm$ 8.3 *
Visceral fat area (cm ²)	159.0 $\pm$ 54.1	129.8 $\pm$ 47.0 *
Systolic blood pressure (mmHg)	132 $\pm$ 15	136 $\pm$ 18
Diastolic blood pressure (mmHg)	82 $\pm$ 13	83 $\pm$ 12
Total cholesterol (mg/dL)	204 $\pm$ 28	216 $\pm$ 39 *
HDL cholesterol (mg/dL)	50 $\pm$ 10	56 $\pm$ 12 *
LDL cholesterol (mg/dL)	122 $\pm$ 27	131 $\pm$ 34 *
Triglyceride (mg/dL)	175 $\pm$ 120	148 $\pm$ 78 *
Fasting glucose (mg/dL)	112 $\pm$ 25	112 $\pm$ 26
HbA1c (%)	5.9 $\pm$ 1.1	5.9 $\pm$ 1.1
Uric acid (mg/dL)	6.6 $\pm$ 1.3	5.3 $\pm$ 1.0 *
C-reactive protein (mg/dL)	0.17 $\pm$ 0.28	0.18 $\pm$ 0.17
Free fatty acid (mEq/L)	0.51 $\pm$ 0.19	0.57 $\pm$ 0.21 *
Leptin (ng/mL)	8.2 $\pm$ 5.6	21.3 $\pm$ 11.2 *
Tumor necrosis factor- α (pg/mL)	1.6 $\pm$ 2.9	1.2 $\pm$ 0.4
Adiponectin (μ g/mL)	2.8 $\pm$ 1.8	5.5 $\pm$ 3.1 *
C-peptide (ng/mL)	2.86 $\pm$ 1.25	2.54 $\pm$ 0.92 *
Insulin (μ IU/mL)	12.11 $\pm$ 9.97	11.11 $\pm$ 5.91

Values are means $\pm$ SD.

*: Significant difference between men and women ($p < 0.05$).

Figure 1 shows the distribution of visceral fat area stratified for BMI and sex. Despite the fact that we selected subjects with BMI > 28.3 at the last medical checkup, 53 subjects (22.6%) had BMIs ≤ 28.3 . However, all subjects were classified as obese (BMI > 25). In terms of the waist circumference, all subjects (except four women) met the criteria of the central obesity defined in the Japanese diagnostic criteria of metabolic syndrome (men: ≥ 85 cm, women: ≥ 90 cm). The prevalence of subjects with visceral fat area less than 100 cm² was 19.1% (men: 8.6%, women: 29.4%). One-fifth of the women with a BMI ≥ 30 had a visceral fat area less than 100.

Using the Japanese diagnostic criteria, the prevalence of metabolic syndrome in men and women was 62.9% and 51.3%, respectively (**Figure 2**). **Figure 2** also presents the prevalence of subjects with high blood pressure, dyslipidemia, and high blood glucose using the cut-off points defined in the Japanese diagnostic criteria of metabolic syndrome. Less than 30% of male and female subjects were diagnosed with diabetes mellitus, based on the Japan Diabetes Society criteria.

Among the adipocytokines, leptin levels exhibited a significantly positive correlation with anthropometric obesity parameters in both men and women (**Table 2**). In women, adiponectin levels were significantly correlated with four components of the metabolic syndrome criteria. In men, however,

Fig. 1. Distribution of all subjects classified according to BMI and visceral fat area.
All men had a waist circumference ≥ 85 cm; with the exception of four subjects (left), all women had waist circumference ≥ 90 cm.

Fig. 2. Prevalence of metabolic syndrome and each metabolic abnormality. The cut-off values defining metabolic abnormalities were established at 130/85 mmHg for high blood pressure; ≥ 150 mg/dL triglyceride and/or < 40 mg/dL HDL cholesterol for dyslipidemia; and 110 mg/dL for high blood glucose; or patients being treated for hypertension, dyslipidemia, and/or diabetes, all according to Japanese diagnostic criteria for metabolic syndrome. A 75-g oral glucose tolerance test was used to calculate the prevalence of diabetes mellitus based on 1999 Japan Diabetes Society criteria.

Table 2 *Pearson's correlations between components of metabolic syndrome and adipocytokines and other plasma biochemical markers in relation to metabolic disorder*

	C-reactive protein	Free fatty acid	Leptin	Tumor necrosis factor- α	Adiponectin	C-peptide	Insulin
Men (n=116)							
Weight	0.381 *	0.082	0.646 *	-0.064	-0.043	0.193 *	0.165
BMI	0.402 *	0.114	0.740 *	-0.041	-0.060	0.285 *	0.247 *
Waist circumference	0.389 *	0.120	0.763 *	-0.094	-0.022	0.186 *	0.123
Visceral fat area	0.088	0.058	0.511 *	-0.092	-0.020	0.228 *	0.164
Systolic blood pressure	0.126	0.071	0.070	-0.124	-0.096	0.039	0.050
Diastolic blood pressure	0.016	0.163	0.062	-0.166	-0.006	-0.031	-0.053
HDL cholesterol	-0.061	0.142	0.033	-0.044	0.132	-0.117	-0.122
Triglyceride	-0.077	0.334 *	0.026	-0.049	-0.198 *	0.186 *	0.078
Fasting glucose	0.012	0.153	0.120	-0.095	-0.133	0.078	0.115
Women (n=118)							
Weight	0.104	-0.068	0.488 *	0.000	-0.007	0.492 *	0.474 *
BMI	0.062	0.139	0.549 *	0.079	0.068	0.447 *	0.478 *
Waist circumference	0.151	-0.074	0.468 *	0.062	0.082	0.416 *	0.366 *
Visceral fat area	0.167	0.158	0.286 *	0.293 *	-0.053	0.325 *	0.341 *
Systolic blood pressure	0.052	0.100	0.061	0.075	-0.134	0.046	0.080
Diastolic blood pressure	0.048	0.056	0.109	-0.065	-0.232 *	0.253 *	0.285 *
HDL cholesterol	-0.056	0.015	0.051	-0.153	0.352 *	-0.208 *	-0.133
Triglyceride	0.129	0.051	0.051	0.172	-0.288 *	0.359 *	0.315 *
Fasting glucose	0.176	0.293 *	0.102	0.184 *	-0.225 *	0.088	0.074

*: Significant correlation ($p < 0.05$)

Fig. 3. Association between adipocytokines and the number of the risk factors: high blood pressure ($\geq 130/85$ mmHg); high triglyceride (≥ 150 mg/dL) and/or low HDL cholesterol (< 40 mg/dL); high blood glucose (≥ 110 mg/dL); or under treatment for hypertension, dyslipidemia, and/or diabetes, according to metabolic syndrome criteria. FFA, free fatty acid.

* Significant difference in the number of the risk factors among groups (analysis of variance [ANOVA], $p < 0.05$).

a significant but smaller correlation was seen only for triglyceride level. C-peptide level in both men and women and insulin level in women was significantly correlated with most parameters of metabolic syndrome.

Figure 3 illustrates the association of adipocytokines and markers of insulin resistance with the number of risk factors comprising metabolic syndrome criteria. In men, leptin, c-peptide, and insulin levels tended to show a graded increase with increasing numbers of the risk factors. In women, c-peptide and free fatty acid levels tended to increase with increasing numbers of the risk factors, but adiponectin decreased dose-dependently with increasing numbers of these factors.

Discussion

In our obese subjects, the prevalence of metabolic syndrome using the Japanese criteria was 62.9% in men and 51.3% in women. These values are notably lower in both men and women compared to the prevalence calculated using the International Diabetes Federation definition⁽¹¹⁾ based on waist circumference for Japanese (men: 77.6%, women: 72.3%), whereas only the values for women are lower using the American Heart Association/National Heart, Lung, and Blood Institute definition (men: 51.7%, women: 72.3%).⁽¹²⁾ When using the visceral fat area for the criteria of central obesity, the prevalence of metabolic syndrome was lower than that using the waist circumference. Based on these results, the cut-off value of waist circumference, which was equivalent to 100 cm² of the visceral fat area, was estimated to be greater than 90 cm. However, the cut-off values of waist circumference in women are lower than those in men for all the criteria of metabolic syndrome in Caucasians and Asians, except for the Japanese criteria. In addition, some studies reported the optimal cut-off point of waist circumference to predict the risk of metabolic syndrome for Japanese women to be less than 85 cm.^(13,14) Considering that women tend to accumulate more subcutaneous fat than visceral fat,⁽¹⁵⁾ other predictors that may play a key role in the development of metabolic disorders in obese women must be determined.

The prevalence of metabolic syndrome defined by Japanese criteria in our obese subjects was much higher than the estimated prevalence in the general population according to the National Health and Nutrition Survey.⁽¹⁾ Our subjects had more risk factors than those who had the same waist circumference in the general population.⁽¹⁾ People with serious obesity, such as our subjects, are a high-risk population in which intervention is necessary to prevent the development of metabolic syndrome.

Adipocytes are present within fat tissues and are capable of releasing numerous vasoactive factors leading to cardiovascular morbidity in obese individuals.⁽¹⁶⁾ It is well known that leptin levels are strongly correlated with fat mass and decrease with weight reduction, and we found significant correlations between leptin levels and anthropometric obesity markers. Adiponectin usually decreases with greater insulin resistance and is lower in people with coronary heart disease than those without this disease. In our study, adiponectin was associated with the risk of metabolic syndrome only in women. The reason for this difference between men and women was unclear, although the balance of the risk for insulin resistance and cardiovascular diseases that our subjects had might be different between men and women.

In conclusion, more than half of our subjects with very high BMI met the criteria for metabolic syndrome. Immediate intervention to encourage weight loss and to improve other risk factors of metabolic syndrome is necessary for these seriously obese people.

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