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Smoking as a Risk Factor for Visceral Fat Accumulation in Japanese Men

HIDEAKI KOMIYA,[1,2] YUTAKA MORI,[3] TAKUO YOKOSE[4] and NAOKO TAJIMA[5]

[1] *Department of Exercise Physiology, Utsunomiya University, Utsunomiya, Japan,*
[2] *Department of Public Health, Dokkyo University, School of Medicine, Mibu machi, Japan,*
[3] *Department of Internal Medicine, National Hospital Organization Utsunomiya National Hospital, Kawachi machi, Japan,*
[4] *Matsushita Tokyo Health Care Center, Matsushita Electric Industrial Corporation, Tokyo, Japan, and*
[5] *Division of Diabetes and Endocrinology, Department of Internal Medicine, Jikei University School of Medicine, Tokyo, Japan*

KOMIYA, H., MORI, Y., YOKOSE, T. and TAJIMA, N. *Smoking as a Risk Factor for Visceral Fat Accumulation in Japanese Men*. Tohoku J. Exp. Med., 2006, **208** (2), 123-132 —— Epidemiological and clinical studies on the lifestyle-related obesity have identified smoking, physical activity and alcohol intake as risk factors for obesity. However, no consensus has yet been reached on the effect of smoking on visceral adiposity. This study was designed to assess whether smoking is associated with the accumulation of visceral fat, glucose and lipid metabolism. The subjects were 450 males aged from 24 to 68 years old, who were examined at the health control center in the regular health check conducted by their company. A self-administered questionnaire was used to ascertain smoking status, daily physical activity and alcohol drinking. The number of Brinkman index as an index for smoking status was positively related to being visceral fat area (VFA). In smokers whose Brinkman index was higher, the percent of subjects with abnormal body mass index, VFA, triglyceride, high density lipoprotein-cholesterol, atherosclerotic index, plasma glucose, immunoreactive insulin, or homeostasis model assessment of insulin resistance (HOMA-IR) was higher than that in non-smokers. When evaluated in terms of age-adjusted odds ratios for incidence of a VFA of 100 cm^2 or greater, alcohol drinking was associated with the highest odds ratio. Smoking, physical inactivity and excessive alcohol drinking were associated with visceral adiposity, and smoking affected glucose and lipid metabolism. In conclusions, these findings suggest that smoking is a risk factor for visceral fat accumulation and deterioration of glucose and lipid metabolism. ———— smoking; physical activity; alcohol drinking; visceral fat accumulation

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Correspondence: Hideaki Komiya, Department of Exercise Physiology, Utsunomiya University, 350 Mine machi, Utsunomiya 321-8505, Japan.
e-mail: komiya@cc.utsunomiya-u.ac.jp

Visceral fat accumulation has drawn attention in recent years as a risk factor for the development of lifestyle-related diseases. Included among the factors reported to be involved in this fat accumulation are heredity, aging, hormones, diet and exercise (Reaven 1998). Of note, tumor necrosis factor (TNF)-α, an adipocyte-derived physiologically active substance (Hotamisligil and Spiegelman 1994), has recently been implicated as a factor accounting for the association between visceral fat accumulation and insulin resistance in molecular biological studies. On the other hand, epidemiological studies on lifestyle related diseases have identified lack of physical activity and excessive alcohol intake as risk factors for obesity, visceral fat accumulation particularly (Wannamethee and Shaper 2003). However, no consensus has yet been reached on the effect of smoking on obesity (Seidell et al. 1991; Eisen et al. 1993; Hu et al. 2001; Ichinohe et al. 2005). Nonetheless, smoking is a major risk factor for the development of cardiovascular diseases (Takemura et al. 2000). Additionally, current insights into insulin resistance and hyperinsulinemia as risk factors for arteriosclerosis strongly argue against smoking by patients with obesity or hyperinsulinemia. Meanwhile, a follow-up study of patients who had quit smoking has shown that glucose tolerance deteriorates with increasing body weight (BW) (Williamson et al. 1991), suggesting that diabetic smokers with obesity are less amenable to physician advice against smoking. However, there are as yet no reports that clarify the association between visceral fat accumulation and smoking. In this study, therefore, we investigated the relationship between lifestyle habits such as physical activity, alcohol drinking and smoking, and accumulation of visceral fat associated with aging, and that between these lifestyle habits and glucose and lipid metabolism.

Subjects and Methods

Subjects and questionnaires

The subjects comprised 450 males aged 24 to 68 yr recruited from workers in an electronic company in Tokyo, Japan. They were mainly engaged in clerical, sales, engineering and managerial work. Workers in this company undergo health examinations every year and at this time workers are asked to answer questions about smoking status, alcohol drinking and daily physical activity in self-administered questionnaires for the purpose of this study. The questionnaires consisted of questions on daily cigarette numbers, smoking years, exercise types, exercise duration and frequency of physical activity reported per week, the types and volume of alcohol consumed, as well as the frequency of drinking reported per week.

The questionnaire was distributed to the workers before the day of their medical examination, and was collected on examination day. Questionnaire surveys are naturally conducted with the agreement of all responders. Workers are also allowed to refuse answering.

Before starting our study, all subjects were fully informed of the procedures, risk and discomforts involved in performing the computed tomography (CT) scan of the abdomen and obtained their consent. And the measurements were carried out in accordance with the 1964 Declaration of Helsinki.

Measurement methods

Physical and laboratory examinations included height, BW, body mass index (BMI), blood pressure, plasma glucose (Glu), immunoreactive insulin (IRI), total cholesterol (TC), high density lipoprotein-cholesterol (HDL-C) and triglycerides (TG). Blood sampling and blood pressure measurement were performed early in the morning in fasting conditions. BMI was calculated as weight (kg) divided by the square of height (m). Atherosclerotic index (AI) was calculated using the formula (TC - HDL-C) / HDL-C.

CT images taken at the navel level were used for evaluation of visceral fat area (VFA) and subcutaneous fat area (SFA), and measured according to Tokunaga et al.'s (1983) method, with the VFA-SFA ratio calculated as the V/S ratio. As index for insulin resistance, Homeostatic model assessment-insulin resistance (HOMA-IR: fasting glucose × fasting IRI/405) was calculated using the method of Matthew et al. (1985). Based on a lifestyle habits survey conducted in these subjects, energy expenditure was calculated according to the types and frequency of physical activity per week. Physical activity was assessed through a questionnaire based on their previous daily physical activities using the method of Taylor et al. (1978). Given the high degree of completeness for physical activities, we decided to focus only on physical activity as a sport to the exclusion of

housework and yard work activities. The reported time spent at each activity per week was multiplied by its typical energy expenditure requirements expressed in metabolic equivalents (Mets). One Met, the energy expended sitting quietly, is equivalent to 3.5 ml of oxygen uptake per kilogram of body weight per minute. The energy intake by alcohol drinking was calculated based on the types and volume of alcohol consumed, as well as their customary alcohol drinking frequency reported per week. Alcoholic beverages included beer, sake (rice wine), wine, whiskey and others. Weekly ethanol consumption (g/week) was then estimated from the frequency and volume of each alcohol beverage consumed with the ethanol content of the corresponding beverage. As an index for smoking status, the Brinkman index (Brinkman and Coates 1963) was calculated by multiplying the number of cigarettes smoked per day by the duration of smoking in years. Moreover, the subjects were divided based on their smoking status into three groups: a non-smoking group and two other smoking groups divided using the mean Brinkman index value of 554 as the cutoff point. Similarly, the subjects were divided into three groups based on their exercise habits (a no-exercise group and two other exercise groups divided using 782 kcal/week, the mean energy expended in physical activity, as the cutoff point) as well as their alcohol drinking habits (a non-drinking group and two other drinking groups using the mean alcohol consumption volume of 260 g/week as the cutoff point).

Statistical analysis

The data were expressed as means ± S.D. Statistical analyses were performed using computer software (StatView version 5 for Windows). Age-adjusted covariance and multivariate covariance analyses were performed to test for differences between groups. Multiple logistics analysis was also performed by using VFA as a dependent variable, and smoking, physical activity, alcohol drinking habits as independent variables, for calculation of age-adjusted odds ratios. A p value of less than 0.05 was regarded as being statistically significant.

Results

Classification of glycemic status was done according to the criteria of the Japan Diabetes Society (JDS) with the following modification: normal fasting glucose (NFG), fasting glucose < 110 mg/dl; impaired fasting glucose (IFG), fasting glucose ≧ 110 mg/dl and < 126 mg/dl; diabetes mellitus (DM), fasting glucose ≧ 126 mg/dl. In terms of blood glucose test results, 230 people had NFG, 160 had IFG and 60 had DM. Table 1 compares the age-adjusted mean values or frequencies of possible risk factors for living habits among the three glycemic status groups. Tests for differences in characteristics across the three glycemic level groups were significant except for Brinkman index, Energy expenditure and ethanol consumption. BMI, TC, HDL-C, TG, Glu, IRI, HOMA-IR, AI and VFA showed a linear trend in relation to glycemic status. The percentage of exercise habit was high in NFG as well as the percentage of smoking habit was low in NFG.

With increasing age, slight decreases were seen in BW ($p < 0.05$), BMI and SFA ($p < 0.001$) in these patients, while significant increases were noted in VFA ($p < 0.05$) (Fig. 1).

VFA was compared according to the status of the subjects' smoking, physical activity and alcohol drinking habits. First, with regard to smoking and VFA, the non-smoking group with a Brinkman index value of 0 had a VFA of 85.31 ± 36.36 cm^2; those with a Brinkman index value of less than 554 had a VFA of 83.16 ± 37.31 cm^2; and those with a Brinkman Index value of 554 or greater had a VFA of 97.44 ± 45.31 cm^2. With regard to physical activity, those with a weekly energy consumption of 782 kcal or greater had a VFA of 75.55 ± 36.88 cm^2; those with a weekly energy consumption of less than 782 kcal had a VFA of 87.58 ± 36.89 cm^2; and those with no habit of physical activity had a VFA of 91.38 ± 41.45 cm^2. Lastly, with respect to alcohol drinking and VFA, the non-drinking group with no weekly energy intake from alcohol had a VFA of 76.22 ± 33.18 cm^2; those with a weekly energy intake from alcohol of less than 260 g/week had a VFA of 90.40 ± 39.88 cm^2; and those with a weekly caloric intake from alcohol of 260 g/week or greater had a VFA of 91.35 ± 42.51 cm^2. Thus, the groups with favorable lifestyle habits were associated with low visceral fat areas, and remarkable differences in exercise habit were observed (Table 2). The subjects were then divided into two groups according to the status of their smoking, physical activity and drinking, to inves-

TABLE 1. *Body composition, glycemic parameters, clinical characteristics, Brinkman index, energy expenditure, ethanol consumption, and living habits of subjects*

Items	NFG (230)	IFG (160)	DM (60)
Age (year)	45.9 ± 8.0	48.9 ± 7.4	46.7 ± 7.2 ***
BMI [a]	23.9 ± 2.8	25.0 ± 2.6	25.0 ± 2.9 ***
SBP (mmHg) [a]	127.7 ± 18.4	133.8 ± 17.1	132.4 ± 22.9 *
DBP (mmHg) [a]	77.8 ± 11.3	82.2 ± 11.4	80.3 ± 13.6 **
TC (mg/dl) [a]	209.1 ± 36.1	213.5 ± 30.9	223.5 ± 32.3 *
HDL-C (mg/dl) [a]	54.9 ± 14.3	52.8 ± 13.4	50.1 ± 12.0 *
TG (mg/dl) [a]	138.8 ± 91.1	151.7 ± 85.9	198.3 ±171.5 ***
Glu (mg/dl) [a]	100.0 ± 6.5	116.7 ± 4.4	142.5 ± 23.3 ***
IRI (μU/ml) [a]	7.3 ± 4.6	9.2 ± 4.4	11.9 ± 7.1 ***
HOMA-IR [a]	1.8 ± 1.2	2.7 ± 1.3	4.2 ± 2.7 ***
AI [a]	3.0 ± 1.2	3.3 ± 1.1	3.7 ± 1.3 ***
VFA (cm^2) [a]	79.8 ± 40.1	96.3 ± 38.6	96.4 ± 35.2 *
SFA (cm^2) [a]	118.1 ± 51.4	132.1 ± 47.9	128.5 ± 54.6 **
Brinkman index [a]	520.9 ± 335.0	592.2 ± 329.8	556.5 ± 313.1
Smoking habit	60.4%	65.6%	70.0%
Energy expenditure (kcal/week) [a]	822.8 ± 696.3	780.7 ± 763.1	601.7 ± 288.3
Exercise habit	51.7%	39.4%	38.3%
Ethanol consumption (g/week) [a]	278.7 ± 242.7	248.9 ± 219.5	228.1 ± 191.0
Alcohol drinking habit	77.4%	87.5%	75.0%

[a] Adjustment for age mean ± S.D. (n) * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.
BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure;
TC, total cholesterol; HDL-C, high density lipoprotein-cholesterol; TG, triglycerides;
Glu, plasma glucose; IRI, immunoreactive insulin; HOMA-IR, homeostasis model assessment of insulin resistance; AI, atherosclerotic index; VFA, visceral fat area; SFA, subcutaneous fat area;
NFG, normal fasting glucose; IFG, impaired fasting glucose; DM, diabetes mellitus.

tigate the effects of these habits on VFA. While significant differences were seen between groups who reported physical activity and who reported no physical activity ($p < 0.001$), and between groups who drank and who did not ($p < 0.01$), no significant differences were seen between groups who smoked and who did not, with regard to VFA. These results suggest that, of those who did not physical activity regularly, smokers showed a greater accumulation of visceral fat than non-smokers, regardless of their drinking habits. In addition, the better the subjects' lifestyle habits were, the smaller their VFA tended to be (Fig. 2). When evaluated in terms of age-adjusted odds ratios (95% CI, p values) for incidence of visceral fat-type obesity (defined as a VFA of 100 cm^2 or greater) in these patients, alcohol drinking was associated with the highest odds ratio at 2.969 (95% CI, 1.60 – 5.50; $p = 0.000$) in subjects with an alcohol consumption of less than 260 g/week, and at 3.064 (95% CI, 1.56 – 6.02; $p = 0.000$) in those with an alcohol consumption of 260 g/week or greater. This was followed by physical activity with the odds ratio being 1.499 (95% CI, 0.78 – 2.87; $p = 0.222$) in those with an energy consumption of 782 kcal/week through physical activity, and 1.933 (95% CI, 1.05 – 3.58; $p = 0.034$) in those who did not physical activity regularly. Smoking was not associated with visceral fat-type obesity with the odds ratio being 0.955

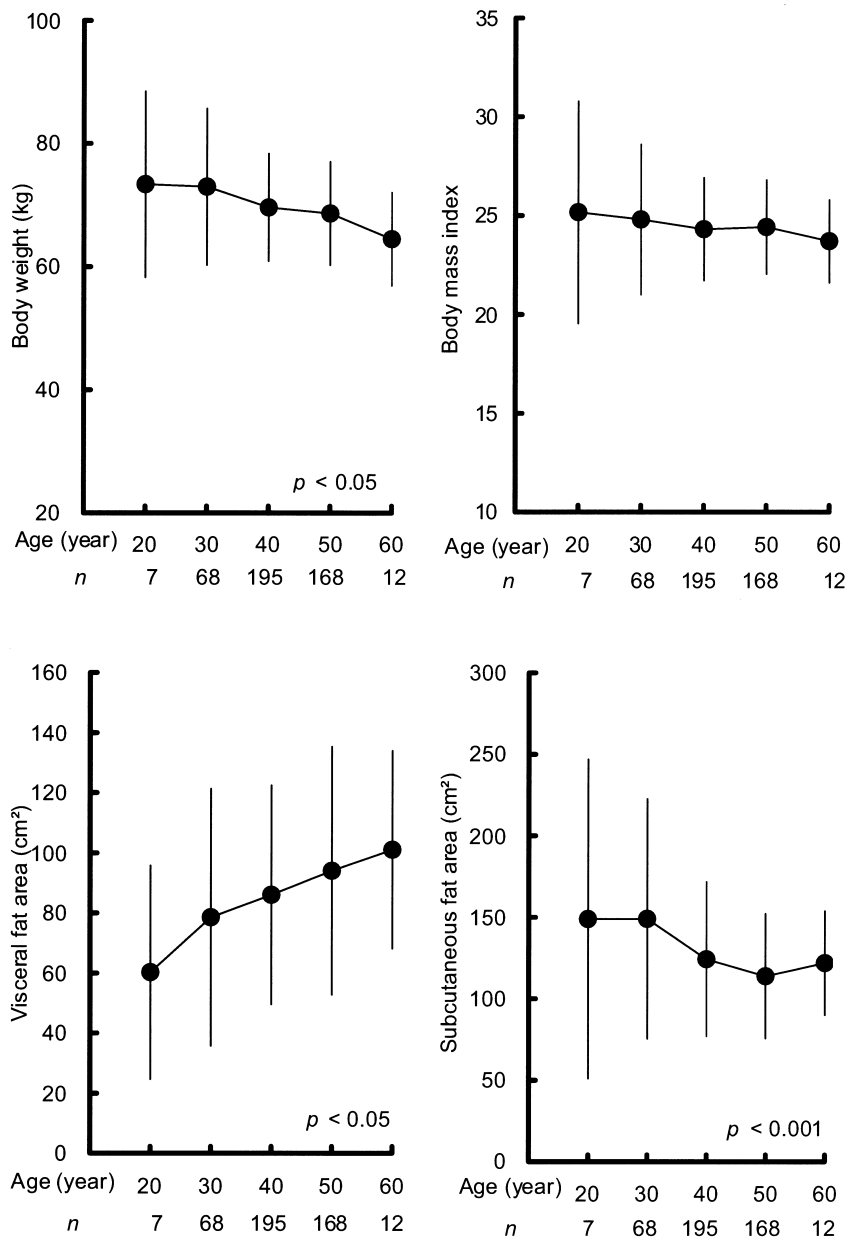

Fig. 1. Changes in body weight, BMI, VFA, and SFA in various age groups (mean ± S.D.). *n*, number of subjects.

(95% CI, 0.60 – 1.53; $p = 0.849$) in subjects with a Brinkman index of less than 554, and 1.526 (95% CI, 0.94 – 2.48; $p = 0.087$) in those with a Brinkman index of 554 or higher (Table 3). With regard to the effect of smoking on glucose and lipid metabolism our study results indicated that the higher the Brinkman index, the more frequent was the incidence of abnormal laboratory findings and that compared to non-smokers, smokers with a Brinkman index value of 554 or greater had a 1.262- to 1.694-fold higher odds ratio for abnormal BMI, VFA, TG, HDL-C, AI, Glu, IRI and HOMA-IR findings (Table 4).

TABLE 2. *The comparison of VFA, SFA and TFA according to the status of the subject' smoking, physical activity, and alcohol drinking habits*

		Number	VFA (cm^2)	SFA (cm^2)	TFA (cm^2)
Smoking habit [a]	0	164	85.31 ± 36.36	124.66 ± 47.87	209.97 ± 71.89
(Brinkman index)	less than 554	162	83.16 ± 37.31	126.51 ± 56.66	209.82 ± 82.31
	554 or greater	124	97.44 ± 45.31	121.50 ± 47.14	218.76 ± 81.70
Exercise habit [a]	782 kcal/week or greater	66	75.55 ± 36.88***	113.16 ± 43.31	188.69 ± 70.92**
(Energy expenditure)	less than 782 kcal/week	139	87.58 ± 36.89	118.20 ± 44.41	205.77 ± 70.95
	0	245	91.38 ± 41.45	131.06 ± 55.36	222.43 ± 82.81
Drinking habit [a]	0	87	76.22 ± 33.18*	124.95 ± 55.49	201.18 ± 77.05
(Ethanol consumption)	less than 260 g/week	247	90.40 ± 39.88	128.39 ± 53.55	218.66 ± 80.85
	260 g/week or greater	116	91.35 ± 42.51	115.71 ± 39.87	207.26 ± 73.39

[a] Adjustment for age. Mean ± S.D. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.
VFA, visceral fat area; SFA, subcutaneous fat area; TFA, total fat area.
Smoking habit (Brinkman index) 0 means non-smoking.
Exercise habit (Energy expenditure) 0 means non-exercise.
Drinking habit (Ethanol consumption) 0 means non-drinking.

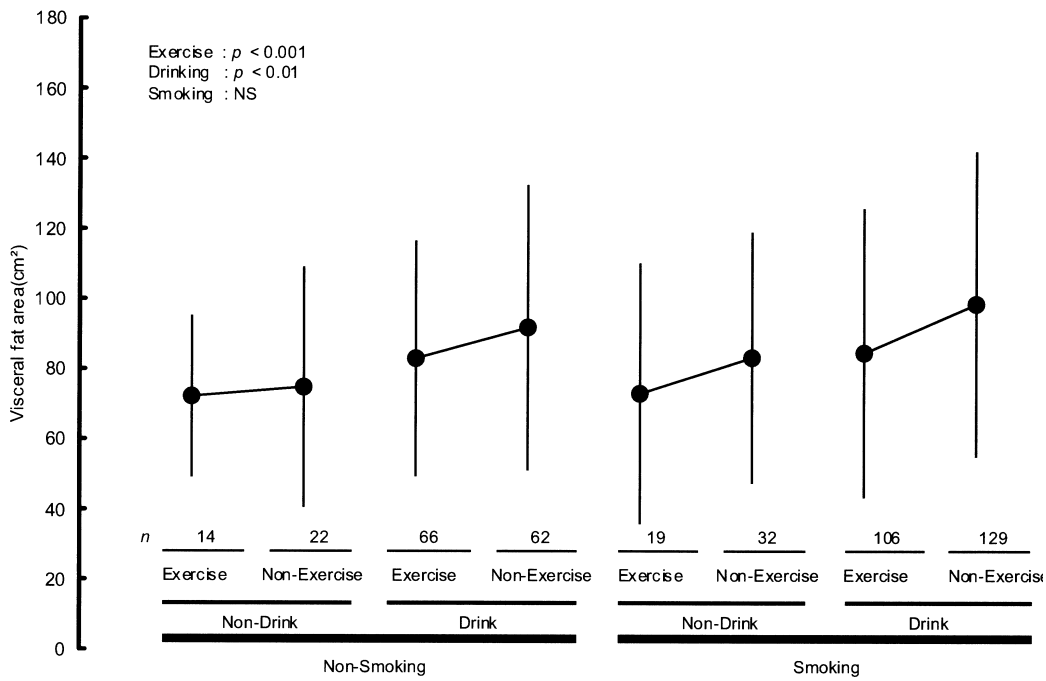

Fig. 2. Comparison of VFA by smoking, physical activity, and alcohol drinking status (mean ± S.D.; all values corrected for age).
n, number of subjects.

TABLE 3. *Crude and age adjusted Odds ratio according to the status of the subject' lifestyle habits*

	Odds ratio (95% CI)	*p* value	adjusted Odds ratio (95% CI)	*p* value*
Smoking habit (Brinkman index)				
0	1		1	
less than 554	0.885 (0.56-1.41)	0.606	0.955 (0.60-1.53)	0.849
554 or greater	1.632 (1.01-2.64)	0.045	1.526 (0.94-2.48)	0.087
Exercise habit (Energy expenditure)				
782 kcal/week or greater	1		1	
less than 782 kcal/week	1.498 (0.79-2.85)	0.218	1.499 (0.78-2.87)	0.222
0	1.632 (0.90-2.97)	0.110	1.933 (1.05-3.58)	0.034
Drinking habit (Ethanol consumption)				
0	1		1	
less than 260 g/week	3.157 (1.71-5.82)	0.000	2.969 (1.60-5.50)	0.000
260 g/week or greater	3.388 (1.74-6.61)	0.000	3.064 (1.56-6.02)	0.000

* Adjustment for age.
Smoking habit (Brinkman index) 0 means non-smoking.
Exercise habit (Energy expenditure) 0 means non-exercise.
Drinking habit (Ethanol consumption) 0 means non-drinking.
95% CI, 95% confidence interval.

DISCUSSION

Our study results showed that while the subjects' BW and SFA were found to decrease slightly with increased age, indicating favorable BW control, VFA was steadily increased in these subjects. So far, increases or decreases in BW have only been addressed in terms of exercise-based energy consumption and diet-based energy intake, where lack of physical activity and excessive caloric intake have been thought to be among the major factors promoting obesity (Hu et al. 2001). Regular physical activity, in particular, has been reported to associate glucose uptake into skeletal muscles via enhanced insulin sensitivity (Miyatake et al. 2002) and through functional improvement of glucose transporter 4 (Perseghin et al. 1996), thereby providing what have come to be termed chronic effects of physical activity against obesity and impaired glucose tolerance. There are also reports that smoking, a major risk factor for cardiovascular disease (Owada et al. 1999), associates obesity, although no consensus on this has been reached (Seidell et al. 1991; Eisen et al. 1993). The considerably higher rate of smoking reported among Japanese adult men compared to that of other industrialized countries, however, raises concern that this may lead to the onset and acceleration of lifestyle-related diseases in these men in whom a healthier lifestyle habits needs yet to be established.

A review of the literature regarding the association between smoking and obesity and/or diabetes suggests that smokers have significantly poorer insulin-secreting capabilities than non-smokers, and that smoking is a risk factor for insulin resistance (Faccini et al. 1992). In a large-scale prospective study involving 100,000 people, Rimm et al. (1993) showed that smoking was an independent risk factor for diabetes, suggesting

TABLE 4. *Effect of smoking on BMI, VFA, glucose and lipid*

Item		Brinkman index less than 554			Brinkman index 554 or greater		
		Odds ratio	95% CI	*p* value	Odds ratio	95% CI	*p* value
BMI	Crude	0.920	0.589-1.437	0.714	1.382	0.863-2.215	0.178
	Adjusted *	0.884	0.563-1.388	0.592	1.440	0.894-2.319	0.134
	Adjusted **	0.905	0.573-1.430	0.669	1.402	0.861-2.283	0.174
VFA	Crude	1.498	0.788-2.850	0.218	1.632	0.895-2.973	0.110
	Adjusted *	0.955	0.595-1.532	0.849	1.526	0.940-2.479	0.087
	Adjusted **	0.955	0.587-1.556	0.855	1.328	0.803-2.195	0.269
TC	Crude	0.947	0.609-1.471	0.807	0.840	0.521-1.354	0.475
	Adjusted *	0.980	0.627-1.530	0.928	0.812	0.502-1.315	0.398
	Adjusted **	0.921	0.584-1.450	0.721	0.756	0.460-1.241	0.268
TG	Crude	0.964	0.608-1.529	0.875	1.580	0.977-2.554	0.062
	Adjusted *	0.921	0.577-1.469	0.729	1.657	1.019-2.696	0.042
	Adjusted **	0.848	0.526-1.367	0.497	1.461	0.885-2.412	0.139
HDL-C	Crude	1.284	0.786-2.099	0.318	1.452	0.864-2.440	0.159
	Adjusted *	1.178	0.715-1.941	0.521	1.610	0.947-2.735	0.784
	Adjusted **	1.183	0.711-1.966	0.518	1.694	0.982-2.921	0.058
AI	Crude	1.422	0.843-2.398	0.187	1.598	0.922-2.769	0.095
	Adjusted *	1.383	0.816-2.344	0.228	1.644	0.943-2.868	0.080
	Adjusted **	1.388	0.813-2.367	0.229	1.687	0.955-2.979	0.072
Glu	Crude	1.275	0.656-2.478	0.474	1.560	0.787-3.093	0.203
	Adjusted *	1.242	0.635-2.429	0.527	1.604	0.803-3.207	0.181
	Adjusted **	1.241	0.630-2.442	0.532	1.621	0.798-3.292	0.182
IRI	Crude	1.590	0.999-2.533	0.051	1.267	0.764-2.102	0.359
	Adjusted *	1.493	0.932-2.391	0.956	1.366	0.817-2.285	0.234
	Adjusted **	1.530	0.948-2.468	0.081	1.397	0.826-2.365	0.213
HOMA-IR	Crude	1.485	0.941-2.343	0.089	1.262	0.771-2.067	0.355
	Adjusted *	1.418	0.894-2.249	0.137	1.328	0.806-2.188	0.266
	Adjusted **	1.472	0.920-2.355	0.107	1.379	0.825-2.305	0.220

* Adjustment for age. ** Adjustment for age, exercise habit and drinking habit.

BMI, body mass index; VFA, visceral fat area; TC, total cholesterol; HDL-C, high density lipoprotein-cholesterol; TG, triglyceride; AI, atherosclerotic index; Glu, plasma glucose; IRI, immunoreactive insulin; HOMA-IR, homeostasis model assessment of insulin resistance.

Normal values indicate below:

BMI under 25 kg/m^2, VFA under 100 cm^2, TC under 220 mg/dl, HDL-C 45 mg/dl or over, TG under 150 mg/dl, AI under 4, Glu under 110 mg/dl, IRI under 10 μU/ml, HOMA-IR under 2.5.

that one of the physiological actions of smoking on the bodily functions may consist in the suppression of early insulin response (Os et al. 2003), in conjunction with the elevation of TG levels in the blood that smoking induces (Freedman et al. 1986).

Likewise, the results of our study show that, in subjects who reported regular physical activity, smoking had few effects on the accumulation of visceral fat, but in those who did not, smoking affected the accumulation of visceral fat, regardless of their alcohol drinking habits. The reason for this may be that smoking leads to less regular physical activity and tends towards less favorable life habits/patterns that are associated with a greater number of risk factors for developing lifestyle-related diseases (Hu et al. 2001). Therefore, as the risk factors for accelerated accumulation of visceral fat interact in a complex manner with hereditary and other lifestyle factors, our study failed to produce results that definitively demonstrated smoking to be a strong and independent risk factor for inducing excessive accumulation of visceral fat to a greater extent than lack of physical activity or heavy alcohol consumption.

When evaluated in terms of the age-adjusted odds ratio for incidence of a visceral fat area of 100 cm^2 or greater according to the status of each lifestyle habit, smoking was not associated with as high an odds ratio as were physical activity or drinking habits. However, a positive correlation was seen between Brinkman index and VFA.

Meanwhile, with respect to the effect of smoking habits on glucose and lipid metabolism, we found that, compared with non-smokers, smokers whose Brinkman index was 554 or greater showed a 1.262- to 1.694-fold greater odds ratio for incidence of abnormal glucose and lipid metabolic findings. While these relative odds ratios were not alarmingly high, they suggest that smoking adversely affects obesity and excessive accumulation of visceral fat, as well as glucose and lipid metabolism, to no small degree.

Our results suggest that, as do physical inactivity and excessive alcohol intake, smoking adversely affects the accumulation of visceral fat, albeit to a smaller degree than does lack of physical activity or alcohol drinking. Therefore, while our findings do not support the view that smoking is a strong independent factor promoting visceral fat accumulation and deterioration of glucose and lipid metabolism, we conclude that smoking, when compounded by other risk factors, such as lack of physical activity and alcohol drinking does associate excessive visceral fat accumulation.

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