Original Article

Obesity as a Risk Factor for Coronary Events in Japanese Patients with Hypercholesterolemia on Low-Dose Simvastatin Therapy

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***Aim*: We previously reported that obesity (defined as a body mass index (BMI) ≥25 kg/m^2) was not an independent risk factor for coronary heart disease (CHD) in hypercholesterolemic patients without a history of CHD from the Japan Lipid Intervention Trial (J-LIT). In this study, the obese J-LIT subgroup was further analyzed to assess CHD risk.**

***Methods*: In the J-LIT study, patients received simvastatin treatment (usually at 5 mg/day) for 6 years. A total of 38,385 patients (mean age: 57.7±7.9, 12,111 men) without prior CHD and/or stroke were analyzed.**

***Results*: In this cohort, 181 CHD (acute myocardial infarction or sudden cardiac death) were observed. Obesity (n=12,929) was not an independent risk factor for CHD (relative risk; 1.18, 95% confidence interval; 0.87–1.59) after adjustment for the major risk known factors, such as age, sex, hypertension, diabetes mellitus (DM), and smoking. However, blood pressure, triglycerides, and fasting plasma glucose all increased, while high-density lipoprotein-cholesterol decreased, with increased BMI. The percentage of patients having two or three risk factors (such as dyslipidemia, hypertension, and DM) also increased with increased BMI.**

***Conclusions*: Obesity was not an independent risk factor for CHD in hypercholesterolemic patients on statin therapy; however, it is important to control obesity, a condition in which CHD risks accumulate, in order to improve associated risk factors along with the treatment of each risk factor, thus further reducing the risk of CHD.**

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Key words; Obesity, Body mass index, Risk factors for coronary events, Simvastatin

Introduction

According to the World Health Organization (WHO)[1], the prevalence of both overweight (body mass index (BMI) ≥25 kg/m^2) and obesity (BMI ≥30 kg/m^2) is increasing worldwide at an alarming rate in both developing and developed countries. The United States national survey showed that adults who were overweight or obese increased from 56% to 66% between 1988–94 and 2003–4[2, 3]. Almost 108 million adults in the USA are either overweight or obese and their weight increases the risk of various major

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diseases, including hypertension[4], dyslipidemia[5], diabetes mellitus (DM)[6, 7], coronary heart disease (CHD)[8], stroke[9], and cancer[10]. It is now generally accepted that obesity should not be classified as a 'disease', but rather as a 'risk factor' in the cluster of factors for atherosclerotic disease[8, 11, 12]. Thus, obesity is often associated with a combination of cardiovascular and metabolic risk factors known as metabolic syndrome. This syndrome is typically characterized by abdominal obesity, dyslipidemia, hypertension, and a raised fasting plasma glucose (FPG) level[13]. In 2005, metabolic syndrome and its diagnostic criteria were also defined in Japan[14].

The prevalence of obesity in Japan is still relatively low compared with in Western countries, but eating a Westernized high-fat, high-energy diet and living a sedentary lifestyle have increased the number of obese people[1]. According to the 2004 National Health and Nutrition Survey, 30.9% of Japanese men and 22.7% of women were obese (≥25 kg/m^2). As observed in Western countries, obesity and its associated diseases have increased, and consequently national healthcare costs have also increased. Recently, the Japanese Health, Labour and Welfare Ministry emphasized the importance of preventing obesity and its associated diseases (or lifestyle-related diseases), especially metabolic syndrome.

The Japan Lipid Intervention Trial (J-LIT) was a prospective nationwide cohort study of a large number of patients with hypercholesterolemia who received open-label treatment with simvastatin (5 to 10 mg/day). The study was carried out for 6 years by physicians managing their patients in daily practice to evaluate the relationship between cardiovascular disease and serum lipid levels[15, 16]. Analysis of the data in this study has already shown that dyslipidemia, DM, and hypertension are significant risk factors for CHD, but has failed to demonstrate that obesity is an independent risk factor for Japanese patients who have hypercholesterolemia with or without a history of CHD. Thus, the risk related to obesity may disappear after adjusting for confounding factors, such as DM and hypertension.

In the present sub-analysis of the J-LIT study population, we examined the CHD risk of obesity in a different subgroup from that previously analyzed, after excluding all high risk patients with a history of CHD or stroke.

Methods

Study Design

The design of J-LIT has been described in detail elsewhere[17, 18]. Patients were generally treated with 5 mg/day simvastatin in an open-label trial. All patients, including those who discontinued simvastatin for any reason, were monitored for 6 years. Serum lipid levels were determined in the laboratories of the participating institutions. Dietary and exercise therapy for dyslipidemia were selected by the investigators and there were no restrictions on medical treatment for complications. The serum low-density lipoprotein cholesterol (LDL-C) level was calculated by Friedewald's formula.

Body weight, blood pressure (BP), FPG, and serum lipids were measured every 6 months after enrollment, and patients were asked about compliance with treatment, cigarette smoking, alcohol consumption, and exercise. Each patient was informed of the purpose of the study, the effects of simvastatin, and the need for long-term treatment. Only verbal informed consent was obtained from the patients, because a commercially available drug preparation was used in the study.

Subjects

The J-LIT study enrolled 52,421 patients, including men aged 35–70 years and post-menopausal women aged ≤70 years, with a serum total cholesterol (TC) level ≥220 mg/dL. Exclusion criteria were uncontrolled DM, serious concomitant hepatic or renal disease, secondary hypercholesterolemia, and malignancy or any other illness with a poor prognosis. Patients with a history of CHD/stroke were excluded from this sub-analysis to simplify the assessment of the risk of obesity itself. A total of 38,385 patients who had hypercholesterolemia and no prior CHD/stroke were analyzed. The follow-up period was 6 years.

Endpoint and Definitions of Major Risk Factors

The primary endpoint was coronary events (acute myocardial infarction or sudden cardiac death). The first event that occurred during the study period was counted once in each patient. All coronary events were reviewed and determined by the Endpoint Classification Committee.

Hypertension was defined as present if diagnosed by the investigators or if the patient was on antihypertensive therapy or had a systolic BP/diastolic BP ≥140/90 mmHg. High BP was defined as a diagnosis of hypertension or a systolic/diastolic BP ≥130/85 mmHg according to the diagnostic criteria of metabolic syndrome in Japan[14]. DM was defined as present if diagnosed by an investigator or if the patient was on drug treatment for DM or had an FPG ≥126 mg/dL. High FPG was defined as DM or an FPG

Table 1. Patient Characteristics and Lipid Profile at Baseline

	Total	Obesity (+)	Obesity (−)	*p*-value
Number of patients	38,385	12,929	25,456	
Male (%)	31.6	34.6	30.0	<0.001
Age (years)	57.7 ± 7.9	56.9 ± 8.2	58.1 ± 7.7	<0.001
Hypertension (%)	45.8	55.6	40.8	<0.001
High Blood Pressure (%)	78.5	85.7	74.8	<0.001
Diabetes mellitus (%)	15.8	18.6	14.3	<0.001
FPG ≥110 mg/dL (%)	2.7	3.3	2.4	<0.001
ECG abnormality (%)	12.8	14.3	12.1	<0.001
Family history of CHD (%)	4.9	5.0	4.8	0.355
Smoking habit (%)	16.7	19.2	15.5	<0.001
Alcohol consumption (%)	29.2	32.8	27.4	<0.001
Serum lipid levels at baseline				
TC (mg/dL)	269.9 ± 34.6	269.3 ± 38.0	270.3 ± 32.7	<0.001
LDL-C (mg/dL)	182.5 ± 33.5	181.1 ± 32.7	183.2 ± 33.8	<0.001
TG (mg/dL)	156 (109–228)	180 (126–259)	145 (102–211)	<0.001
HDL-C (mg/dL)	53.0 ± 15.1	49.8 ± 13.5	54.6 ± 15.6	<0.001
Serum lipid levels during treatment				
TC (mg/dL)	220.4 ± 29.5	220.5 ± 30.1	220.3 ± 29.1	0.491
LDL-C (mg/dL)	133.7 ± 29.0	133.5 ± 29.2	133.8 ± 28.9	0.394
TG (mg/dL)	142 (107–191)	158 (121–211)	134 (102–179)	<0.001
HDL-C (mg/dL)	55.3 ± 13.7	52.3 ± 12.1	56.9 ± 14.2	<0.001

Obesity, body mass index ≥25 kg/m^2.
FPG, fasting plasma glucose; ECG, electrocardiogram; CHD, coronary heart disease; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol.
TC, LDL-C and HDL-C were expressed as mean ± standard deviation, TG is presented as median (interquartile range)
p-value, obesity (+) vs. obesity (−)

≥110 mg/dL. Dyslipidemia was defined as a triglyceride (TG) level ≥150 mg/dL and/or high-density lipoprotein-cholesterol (HDL-C) level <40 mg/dL. Obesity was defined as BMI ≥25 kg/m^2 at baseline, which is the usual criterion for Japanese subjects[19].

Statistical Analysis

All data, including the findings obtained after the termination of simvastatin therapy, were assessed by survival analysis. We calculated the relative risk and 95% confidence interval for the endpoint in each subgroup relative to the reference category by using the Cox proportional-hazards model with adjustment for gender, age at baseline (as a continuous variable), BMI, increased FPG, hypertension, cigarette smoking, alcohol consumption, and physical activity. The mean lipid levels were calculated from the data obtained throughout the treatment period. Mean values for serum lipid levels and age were tested with unpaired *t* test, and the prevalence of baseline characteristics were tested with the chi-square test to compare obesity (+) and obesity (−) groups. For analysis of continuous variables, groups divided by BMI were assessed using analysis of covariance (ANCOVA) with adjustment for gender and age. Results are expressed as the mean ± SD or median (interquartile range). For all statistical analyses, $p<0.05$ was considered significant. All calculations were performed using SAS software (version 8.02; SAS Institute, Inc., Cary, NC, USA).

Results

Follow-Up and Treatment

The mean follow-up period was 5.4 years. Most patients were treated with 5 mg/day simvastatin throughout the study period.

Patient Profile

The baseline characteristics of the patients are shown in **Table 1**. Men accounted for 31.6% and the mean age was 57.7 ± 7.9 years. Almost half of the patients had hypertension and 15.8% had DM. According to the above-mentioned definition of obesity, 12,929 patients were obese and the other 25,456

Table 2. Relative Risk of Coronary Events

	Coronary events (181/38,385)		
	Relative risk	95% confidence interval	*p*-value
Obesity (BMI ≥25 kg/m^2)	1.18	(0.87–1.59)	0.288
Dyslipidemia	1.28	(0.93–1.76)	0.127
TG ≥150 mg/dL	1.23	(0.90–1.67)	0.195
HDL-C <40 mg/dL	1.60	(1.16–2.22)	0.004
Hypertension	2.14	(1.57–2.91)	<0.001
High blood pressure	2.31	(1.41–3.76)	0.001
High FPG	2.25	(1.66–3.06)	<0.001
FPG ≥110 mg/dL	2.35	(1.23–4.48)	0.010
Diabetes mellitus	2.24	(1.62–3.09)	<0.001

BMI, body mass index; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; FPG, fasting plasma glucose.
Dyslipidemia, TG ≥150 mg/dL and/or HDL-C <40 mg/dL; Hypertension, systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg or physician's diagnosis or antihypertensive medications
High blood pressure, systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥85 mmHg or physician's diagnosis or antihypertensive medications; High FPG, diabetes mellitus or FPG ≥110 mg/dL.
Adjusted for age, sex, and smoking.

were not. The rates of hypertension (55.6%) and DM (18.6%) in the obese group were higher than in the non-obese group (40.8 and 14.3%, respectively). The median TG level of the obese group (180 mg/dL at baseline and 158 mg/dL during treatment) was higher than that of the non-obese group (145 mg/dL and 134 mg/dL, respectively), while the HDL-C level of the obese group at baseline and during treatment (49.8 mg/dL and 52.3 mg/dL, respectively) was lower than that of the non-obese group (54.6 mg/dL and 56.9 mg/dL, respectively). The mean serum TC and LDL-C levels were similar in obese and non-obese groups.

Risk Factors for Coronary Events

During the treatment period, coronary events occurred in 181 (113 in non-obese patients and 68 in obese patients) of the 38,385 patients analyzed (**Table 2**). Obesity (defined as BMI ≥25 kg/m^2) was not an independent risk factor for coronary events in this cohort after adjustment for other risk factors, as reported previously[15]. A high TG level (≥150 mg/dL) was also not a risk factor for coronary events, but a low HDL-C level (<40 mg/dL) was a risk factor. High BP (≥130 mmHg systolic and/or ≥85 mmHg diastolic, or diagnosed hypertension) and increased FPG (≥110 mg/dL or diagnosed DM) were also significant risk factors for coronary events.

Influence of Obesity on Blood Pressure, Serum Lipids, and Fasting Plasma Glucose

Patients were stratified into 5 groups according to their BMI values, and the effect of an increase in BMI on the systolic BP, diastolic BP, serum lipids, and FPG was assessed (**Table 3**). The systolic BP, diastolic BP, TG, and FPG all gradually increased, while HDL-C decreased, with an increment of BMI. The mean systolic/diastolic BP was 133.2/77.6 mmHg, median TG was 119 mg/dL, and mean FPG was 107.0 mg/dL in patients with a BMI <20.0 kg/m^2, while these values respectively increased to 145.1/86.1 mmHg, 185 mg/dL, and 116.0 mg/dL in patients with BMI ≥27.5 kg/m^2. Serum HDL-C decreased from 60.4 at a BMI <20.0 kg/m^2 to 49.0 mg/dL at BMI ≥27.5 kg/m^2; however, a small correlation between serum TC or LDL-C levels and the BMI was observed. The influence was similar in men and women (**Table 4**).

Increased Risk of Coronary Events with Clustering of Risk Factors

The risk of coronary events adjusted for age, sex, and cigarette smoking increased significantly along with the increased number of risk factors, such as dyslipidemia (TG ≥150 mg/dL and/or HDL-C <40 mg/dL), hypertension, DM, and obesity (BMI ≥25 kg/m^2). In patients with all four risk factors, the risk of coronary events was 3.3-fold higher than in patients with no or one risk factor (**Fig. 1**).

Discussion

Overweight and obesity are of particular concern for several reasons. Both conditions substantially increase the risk of morbidity and mortality due to hypertension, dyslipidemia, diabetes, CHD, and

Table 3. Influence of an Increased Body Mass Index on Baseline Blood Pressure, Lipids, and Fasting Plasma Glucose

BMI (kg/m^2)	Patients (*n*)	Coronary events (*n*)	Age (years)	SBP (mmHg)	DBP (mmHg)	TC (mg/dL)	LDL-C (mg/dL)	TG (mg/dL)	HDL-C (mg/dL)	FPG (mg/dL)
<20.0	3,133	9	59.4±7.3	133.2±18.9	77.6±11.0	270.2±34.1	182.2±36.4	119 (85-172)	60.4±18.3	107.0±41.7
20.0-<22.5	9,310	35	58.2±7.6	136.2±18.5	80.0±10.8	270.3±32.0	183.7±33.8	137 (98-197)	55.5±15.6	105.4±38.8
22.5-<25.0	13,013	69	57.7±7.7	139.3±18.4	82.2±11.0	270.3±32.8	183.0±33.2	159 (112-229)	52.5±14.4	108.9±42.2
25.0-<27.5	8,313	49	57.1±8.1	141.7±18.5	83.6±10.9	269.2±41.1	181.1±32.8	177 (124-256)	50.3±13.6	111.0±40.5
≥27.5	4,616	19	56.5±8.3	145.1±19.4	86.1±11.6	269.3±31.7	181.1±32.5	185 (130-265)	49.0±13.3	116.0±42.7
p value			<0.001	<0.001	<0.001	0.027	0.007	<0.001	<0.001	<0.001
All	38,385	181	57.7±7.9	139.3±18.9	82.1±11.2	269.9±34.6	182.5±33.5	156 (109-228)	53.0±15.1	109.2±41.2

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; FPG, fasting plasma glucose.
Mean ± standard deviation, TG is presented as median (interquartile range). *P* value for ANCOVA with adjustment for gender and age

Table 4. Influence of an Increased Body Mass Index on Baseline Blood Pressure, Lipids, and Fasting Plasma Glucose in Each Sex

BMI (kg/m^2)	Patients (*n*)	Coronary events (*n*)	Age (years)	SBP (mmHg)	DBP (mmHg)	TC (mg/dL)	LDL-C (mg/dL)	TG (mg/dL)	HDL-C (mg/dL)	FPG (mg/dL)
Men										
<20.0	625	5	57.0±9.1	133.0±18.2	78.2±11.3	267.1±34.2	179.4±38.6	140 (95-209)	56.6±19.2	117.5±47.0
20.0-<22.5	2,547	12	54.8±9.3	136.3±18.6	81.3±11.3	268.2±36.1	180.2±37.6	166 (114-247)	51.2±15.8	111.0±43.4
22.5-<25.0	4,466	39	54.2±8.9	138.6±18.3	83.5±11.2	268.8±37.0	179.4±33.7	193 (136-278)	49.0±14.1	113.7±49.2
25.0-<27.5	3,091	30	53.1±9.0	140.8±18.2	85.2±11.4	267.3±53.9	176.3±32.4	211 (148-305)	47.3±13.3	113.2±39.6
≥27.5	1,382	9	51.2±9.0	144.0±19.6	88.0±12.6	266.7±32.0	174.7±30.3	234 (166-350)	44.8±12.9	116.1±41.7
p value			<0.001	<0.001	<0.001	0.118	<0.001	<0.001	<0.001	0.995
All	12,111	95	53.8±9.1	139.0±18.7	83.7±11.7	268.0±41.2	178.3±34.3	193 (133-284)	48.9±14.7	113.5±44.8
Women										
<20.0	2,508	4	60.0±6.7	133.2±19.0	77.4±10.9	270.9±34.1	182.8±35.9	116 (82-165)	61.4±17.9	104.1±39.7
20.0-<22.5	6,763	23	59.5±6.5	136.1±18.5	79.6±10.6	271.0±30.3	185.0±32.3	128 (94-182)	57.2±15.3	103.2±36.6
22.5-<25.0	8,547	30	59.5±6.3	139.7±18.4	81.5±10.8	271.1±30.5	184.8±32.7	144 (104-204)	54.3±14.3	106.1±37.3
25.0-<27.5	5,222	19	59.5±6.5	142.1±18.6	82.7±10.6	270.4±31.2	183.6±32.7	158 (114-225)	52.0±13.4	109.6±41.0
≥27.5	3,234	10	58.8±6.8	145.6±19.3	85.3±11.1	270.5±31.5	183.4±32.9	167 (122-235)	50.8±13.1	115.9±43.2
p value			<0.001	<0.001	<0.001	0.180	0.617	<0.001	<0.001	<0.001
All	26,274	86	59.4±6.5	139.4±19.0	81.3±11.0	270.8±31.0	184.2±33.0	142 (102-203)	54.8±14.9	107.1±39.1

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; FPG, fasting plasma glucose.
Mean ± standard deviation, TG is presented as median (interquartile range). *P* value for ANCOVA with adjustment for age.

stroke, as well as being related to sleep apnea and respiratory problems, gallbladder disease, and several cancers, as has been mainly reported in Western countries[4-12]. In particular, abdominal obesity is associated with the cluster of cardiovascular and metabolic risk factors known as metabolic syndrome.

NHANES Ⅲ[20] showed that morbidity due to hypertension and dyslipidemia increased as the BMI increased in both men and women, and morbidity from hypertension was 2-fold higher in patients with BMI ≥30 kg/m^2 than in those with BMI <25 kg/m^2. In addition, the prevalence of a high serum TC and low HDL-C was approximately 1.5-fold and 3-fold higher, respectively, in obese subjects. In the present study, obese patients had similar characteristics, including a higher prevalence of hypertension (55.6

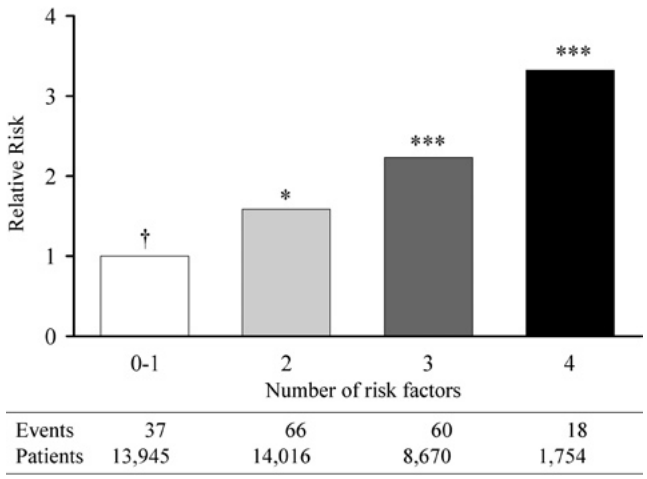

Fig. 1. Relative Risk of Coronary Events and Number of Cardiovascular or Metabolic Risk Factors.

Cardiovascular risk factors are obesity (BMI ≥25 kg/m^2), dyslipidemia, diabetes mellitus, and hypertension. BMI; body mass index, dyslipidemia means; triglycerides ≥150 mg/dL and/or high-density lipoprotein cholesterol <40 mg/dL. The relative risk was adjusted for age, sex, and cigarette smoking.
*p<0.05, ***p<0.001 vs. †Reference category

vs. 40.8% in non-obese patients) and DM (18.6 vs. 14.3%). The mean serum TG level was also higher and the mean HDL-C level was lower in the obese group than in the non-obese group at baseline and during treatment. The mean systolic/diastolic BP gradually increased from 133/78 mmHg to 145/86 mmHg along with an increase of the BMI from <20.0 kg/m^2 to ≥27.5 kg/m^2. In the same manner, serum TG and FPG increased from 119 mg/dL to 185 mg/dL and from 107 mg/dL to 116 mg/dL, respectively, while serum HDL-C decreased from 60 mg/dL to 49 mg/dL. This association of BMI with BP, FPG, and lipid levels suggests that obesity increases the magnitude of the risk associated with each established risk factor. On the basis of these results, we analyzed the risk of coronary events in patients with BMI ≥22.5 kg/m^2 and compared to those with BMI <22.5 kg/m^2; the risk was slight higher (1.42 p=0.04). The risk of coronary events in patients with BMI >27.5 kg/m^2 was not high compared to those with BMI <27.5 kg/m^2.

Obesity is also thought to be a potential risk factor for CHD in Japan, but it is still unclear whether it is an independent risk factor. Some Japanese studies[21, 22] have shown that obesity is an independent risk factor for CHD after adjustment for other risk factors, but this was not confirmed by other case-control studies[23-25]. Shiraishi *et al.*[26] reported that obesity (BMI ≥25 kg/m^2) was an independent risk factor for acute myocardial infarction in young and middle-aged men, but not in women, according to the Kyoto Multi-Center Risk Study. In the present analysis and a previous report[15], however, we did not demonstrate that obesity per se was an independent risk factor for CHD after adjustment for other known risk factors (**Table 2**).

The reasons for this outcome are not clear. Previous Japanese studies have shown both positive and negative results. Obesity seems to be an independent risk factor for men, but not for women, as mentioned above. The J-LIT subjects included a high percentage of women (68.4%) whose cardiovascular risk was significantly lower than that of men. Because of this high proportion of women in this sub-analysis, obesity might not be an independent risk factor for CHD in men and women[27]. Obesity is closely associated with other strong CHD risk factors, such as hypertension, DM, and dyslipidemia, so these may act as confounding factors for obesity, i.e. the risk related to obesity may decrease after adjustment for these confounding factors. Another possibility is related to the lack of measurement of abdominal obesity or waist circumference in this study. Instead, we used a BMI ≥25 kg/m^2 as the criterion for obesity in Japanese subjects according to the Expert Committee on the Criteria for 'Obesity' in Japan[19], although obesity is defined as BMI ≥30 kg/m^2 and overweight means ≥25 kg/m^2 in Western countries[28]. The difference in the definition of obesity between Japan and Western countries may lead to unexpected results in Japanese subjects.

In this observational cohort study, the risk of coronary events increased significantly with an increase in the number of risk factors, including obesity (BMI ≥25 kg/m^2), and obesity was one of the potential risk factors in the daily clinical setting, although hypertension, DM, and dyslipidemia acted as confounders (**Table 2**). In patients having all four of these risk factors, the risk of coronary events was 3.3-fold higher than in patients having no or one risk factor (**Fig. 1**).

There are some limitations of this study. First, this study is a post-hoc non-randomized, observational subanalysis. Second, we could not investigate the characteristics of metabolic syndrome because waist circumference, which is a criterion for metabolic syndrome[14], was not examined in the J-LIT study. Further study will therefore be required to characterize metabolic syndrome.

In conclusion, our data clearly demonstrated that obesity enhances the influence of hypertension, DM, and dyslipidemia, and promotes the accumulation of these risk factors in patients, even though obesity was not an independent risk factor for coronary events in Japanese patients with hypercholesterolemia on statin treatment. In addition, the risk of CHD was increased

in obese patients by comorbidities such as hypercholesterolemia. These results suggest that it is important to manage obesity in order to control associated diseases and modify each risk factor, consequently decreasing the risk of CHD; however, further clinical trials are needed to demonstrate the benefits of weight loss for obese patients.

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