

Abnormality of risk factors for atherosclerotic disease among young Japanese aged 19–39 years old: an evaluation of health checkup data

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Abstract

Objectives Japanese public health policies on the prevention of atherosclerotic diseases have focused on controlling obesity. The aim of this study was to assess the prevalence of abnormality in risk factors for atherosclerotic disease among young Japanese classified according to body mass index (BMI).

Methods Data were obtained from 359 men (mean age 32 ± 5 years) and 1,108 women (mean age 33 ± 4 years) between 2005 and 2010. Abnormal levels of aspartate aminotransferase, alanine aminotransferase, and/or gamma-glutamyltranspeptidase were considered to indicate liver dysfunction, and abnormal levels of low-density lipoprotein-cholesterol, high-density lipoprotein-cholesterol, and/or triglycerides were considered to indicate dyslipidemia. The cutoff points for high blood pressure (HBP) and hyperglycemia were set as a reference in the high-normal range.

Results No significant difference was observed in both sexes in all items among each year. In men, HBP (12.9 %), liver dysfunction (33.9 %), dyslipidemia (29.9 %), and hyperglycemia (2.7 %) were observed in the normal BMI group ($18.5 < \text{BMI} \leq 25 \text{ kg/m}^2$). In women, these abnormalities were observed in both the normal BMI group and lean group.

Conclusions Asymptomatic abnormalities, particularly liver dysfunction and dyslipidemia, were observed in a substantial percentage of subjects without obesity. Therefore, we recommend that the comprehensive public health policy should be directed at all individuals, including the non-obese group, for the early prevention/detection against atherosclerotic diseases.

Keywords Obesity · Dyslipidemia · Liver dysfunction · Atherosclerotic disease · Japanese

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Introduction

Within the context of the need for an anti-obesity initiative, visceral fat has been included as an index in the criteria for metabolic syndrome in the Japanese general population [1]. As such a criterion, visceral fat is defined as an essential factor, which is different from the criteria defined by World Health Organization and American National Cholesterol Education Programs, Adult Treatment Panel III [2, 3]. The concept of a metabolic syndrome has been established. However, an important problem with the Japanese criteria is the possibility of underestimating the risks for atherosclerotic diseases in individuals who are not obese. A number of cohort studies in the Japanese general population have shown that subjects without abdominal obesity are equally at risk for atherosclerotic disease as individuals

with abdominal obesity [4–6]. The data from these epidemiologic studies were informative for developing public health planning policies, but older subjects formed the predominant age group in many of the studies. Data from young subjects are valuable for developing a strategy for preventing atherosclerotic disease at an early stage.

The health checkup system in Japan legally requires employers to implement regular health checkups for employees. However, the frequency at which these health checkups occur decreases with decreasing number of employees [7]. The specific health checkup examination designed to counter metabolic syndrome was implemented in Japan in 2008, but the program has been targeting individuals aged 40 years or more. Overall, some Japanese individuals, especially those under 40 years of age, have no opportunity to undergo a regular checkup. To resolve this issue, some public health centers provide medical checkups and health guidance for the younger segment of the population. In the study reported here, we evaluated data obtained from health checkups conducted by a public health center for Japanese individuals aged younger than 40 years.

Subjects and methods

Subjects

The subjects enrolled in this study included 359 men and 1,108 women (age 19–39 years) living in Sagami-hara City, Kanagawa Prefecture, Japan. The data were collected during health checkups conducted by the Sagami-hara Public Health Center from April 2005 to March 2010. We provided the public with information relating to the implementation of this health checkup service through our public relations magazine or on the Internet. Only one set of data for each individual, that collected at the first visit, was used for analysis to avoid any overlap of data. The study subjects accounted for 66.7 % (1,467/2,201) of all individuals who underwent the health checkups. No subject was pregnant and regularly seeing a doctor for ischemic heart disease, hypertension, liver dysfunction, dyslipidemia, and diabetes mellitus. Sagami-hara City is a typical modern Japanese town and has a population of 700,000, of whom 200,000 are aged between 19 and 39 years.

The data were anonymized without any matching links to personal data. This study was performed in accordance with the recommendations outlined in the Declaration of Helsinki. This research was also in accordance with the ethical guidelines for epidemiological research laid down by the Ministry of Education, Culture, Sports, Science and Technology and by the Ministry of Health, Labor and Welfare. The protocol for this study was approved by the ethics board at Sagami-hara City.

Analysis

Each subject was asked to fast the night preceding the medical checkup, which was performed at the health center between 0900 and 1100 hours. The height and weight of each subject were measured with the subject wearing indoor clothes but no shoes and the body mass index (BMI, kg/m^2) calculated. A physician measure the blood pressure (BP) with a mercury sphygmomanometer on the right arm of seated subjects after a 5-min rest. Systolic BP (SBP) was recorded at the appearance of sounds, and diastolic BP (DBP) was recorded at the disappearance of sounds (V-phase Korotkov). Blood samples were collected for routine laboratory tests, including aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyltranspeptidase (GTP), total cholesterol, high-density lipoprotein-cholesterol (HDL-C), triglycerides (TG), and fasting blood sugar (FBS). Biochemical measurements were performed at the Health Sciences Research Institute (Yokohama, Japan) using routine laboratory methods. Low-density lipoprotein-cholesterol (LDL-C) was calculated by the Friedewald formula according to the recommendation of the Japan Atherosclerosis Society: $\text{LDL-C} = \text{total cholesterol} - \text{HDL-C} - \text{TG} \times 0.2$ [8]. The subjects with a TG level ≥ 400 mg/dL were excluded from the analysis of LDL-C level.

The cutoff points were lean (BMI < 18.5 kg/m^2) versus obese (BMI ≥ 25 kg/m^2); high BP (HBP; SBP ≥ 130 mmHg and/or DBP ≥ 85 mmHg); liver dysfunction [AST level > 40 IU/L, ALT level > 45 IU/L, and/or GTP level > 50 IU/L (men) and > 32 IU/L (women)]; dyslipidemia (LDL level ≥ 140 mg/dL, HDL level < 40 mg/dL, or TG level ≥ 150 mg/dL); hyperglycemia (FBS level ≥ 100 mg/dL). To assess HBP and hyperglycemia from the prophylactic standpoint, the criteria for these measures were set as a reference in the high-normal range defined by the Japanese Society of Hypertension and Japan Diabetes Society [9, 10].

A subject with abnormal values of AST, ALT, or GTP was defined as having liver dysfunction, and a subject with abnormal values of LDL-C, HDL-C, or TG was defined as having dyslipidemia. The following items were regarded as risks for atherosclerotic disorders (RISK): obesity, HBP, liver dysfunction, dyslipidemia, and hyperglycemia. In comparison, among the groups categorized by BMI, items other than obesity were regarded as RISK.

Statistical analysis

The *t* test or analysis of covariance (ANCOVA) was used to assess the significance of differences as mean values. In ANCOVA, age was used as a covariate, and sequential Bonferroni correction was performed on the result. Logistic

regression was used to examine the relationship among risks, after adjusting for age. The atherosclerotic risks, such as HBP, liver dysfunction, dyslipidemia, and hyperglycemia, were defined as dependent variables, and the groups categorized by BMI were defined as independent variables. Analyses were performed using SPSS statistics ver. 18 (SPSS, Chicago, IL). A *P* value of <0.05 was considered to be significant. In Bonferroni correction for comparison among the three groups, a *P* value of <0.016 (0.05/3) was considered to be significant.

Results and discussion

Although the data were collected during a 5-year period, no significant difference was observed in both men and women in all items within each year. In men, obesity (33.4 %), liver dysfunction (42.6 %), and dyslipidemia (38.4 %) accounted for more than 30 % of all conditions. Fifteen percent of the women were lean (Table 1). The proportion of both obese men and lean women in our study is consistent with that observed in subjects in the same-age groups in a recent national demographic survey [11]. However, some other epidemiologic studies performed in subjects belonging to the same age group as our subjects reported slightly different results [12, 13]; in these two studies, the proportion of men with liver dysfunction observed in workers at a manufacturing company was lower than that in our study. These differences can be explained, at least partly, as being due to socioeconomic factors, including the type of work; in our study, 75.0 % of the male workers belonged to the service sector.

Approximately 65 % of men and 25 % of women had more than one RISK factor. In both men and women, all items showed greater exacerbation in the obesity group than in the normal group (Table 2). When adjusted for difference in age, the obesity group had a significantly higher risk of abnormality in all items involved in atherosclerotic disorders than normal group (Table 3). It is clear that not only obesity but also dyslipidemia and liver dysfunction account for the development of atherosclerosis and other metabolic disorders [4–6, 14]. These results imply that one of the main target groups of the disciplinary health educational program “*Hokenshido*”, which was established to achieve behavior modification, should be young obese Japanese to prevent atherosclerotic disorders.

Some subjects in the non-obese group had RISK factors other than overweight. Liver dysfunction and/or dyslipidemia was diagnosed in 30 % of men with normal BMI,

Table 1 Descriptive statistics of variables associated with the risk for atherosclerotic disorders

Descriptive variables	Men (<i>n</i> = 359)	Women (<i>n</i> = 1,108)
Age (years)	32 ± 5	33 ± 4
BMI (kg/m ²)	23.9 ± 4.1	21.3 ± 3.3
≥25 kg/m ²	120 (33.4)	127 (11.5)
<18.5 kg/m ²	15 (4.2)	168 (15.2)
SBP (mmHg)	114 ± 13	105 ± 11
DBP (mmHg)	74 ± 11	67 ± 9
SBP ≥130 mmHg or DBP ≥85 mmHg	64 (17.8)	52 (4.7)
AST (IU/L)	23 ± 9	18 ± 5
>40 IU/L	17 (4.7)	6 (0.5)
ALT (IU/L)	32 ± 22	15 ± 8
>45 IU/L	65 (18.1)	12 (1.1)
GTP (IU/L)	41 ± 44	19 ± 19
>50 or 32 IU/L	138 (38.4)	70 (6.3)
LDL-C (mg/dL)	114 ± 32	102 ± 26
≥140 mg/dL	70 (19.8)	92 (8.3)
HDL-C (mg/dL)	56 ± 14	71 ± 15
<40 mg/dL	31 (8.6)	10 (0.9)
TG (mg/dL)	122 ± 85	66 ± 36
≥150 mg/dL	92 (25.6)	45 (4.1)
FBS (mg/dL)	90 ± 13	85 ± 7
≥100 mg/dL	23 (6.4)	33 (3.0)
RISK	1.40 ± 1.42	0.33 ± 0.70
0	122 (34.5)	828 (74.8)
1	85 (24.0)	201 (18.2)
2	61 (17.2)	48 (4.3)
≥3	86 (24.3)	30 (2.7)

Values are presented as the mean ± standard deviation (SD), or as the number with the percentage in parenthesis

BMI Body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *GTP* gamma-glutamyltransferase, *LDL-C* low-density lipoprotein cholesterol, *HDL-C* high-density lipoprotein cholesterol, *TG* triglyceride, *FBS* fasting blood sugar, *RISK* risk for atherosclerotic disorders

and in women, these abnormalities were observed not only in the normal BMI group but also in the lean group. When absolute number of subjects was used to evaluate the risk for atherosclerotic disease, in men, those individuals with abnormal HBP, GTP, and LDL-C levels in the normal BMI group were comparable to that in the obese group; in women, these abnormalities were observed most often in the normal BMI group. These results are supported by previous reports that atherosclerotic and metabolic

Table 2 Risk for atherosclerotic disorders in subjects categorized by BMI

Descriptive statistics	Lean	Normal	Obese	P value			
				Normal vs. lean		Normal vs. obese	
				t test	ANCOVA	t test	ANCOVA
Men							
Age (years)	27 ± 5	32 ± 5	32 ± 5	<0.001	–	1.000	–
SBP (mmHg)	110 ± 7	111 ± 12	119 ± 14	1.000	NA	<0.001	NA
DBP (mmHg)	73 ± 8	72 ± 11	78 ± 11	1.000	NA	<0.001	NA
AST (IU/L)	18 ± 5	22 ± 8	27 ± 10	0.147	NA	<0.001	NA
ALT (IU/L)	15 ± 5	26 ± 15	45 ± 27	0.133	NA	<0.001	NA
GTP (IU/L)	17 ± 4	38 ± 44	49 ± 43	0.221	NA	0.078	NA
LDL-C (mg/dL)	90 ± 20	109 ± 32	128 ± 29	0.063	0.566	<0.001	<0.001
HDL-C (mg/dL)	64 ± 12	62 ± 14	49 ± 11	1.000	0.558	<0.001	<0.001
TG (mg/dL)	74 ± 30	105 ± 67	161 ± 105	0.462	NA	<0.001	NA
FBS (mg/dL)	87 ± 8	89 ± 13	92 ± 12	1.000	1.000	0.027	0.031
RISK (No.)	0.07 ± 0.26	0.86 ± 1.04	1.84 ± 1.32	0.026	0.227	<0.001	<0.001
Women							
Age (years)	32 ± 5	33 ± 4	33 ± 4	<0.001	–	1.000	–
SBP (mmHg)	102 ± 10	104 ± 11	113 ± 12	0.010	0.024	<0.001	<0.001
DBP (mmHg)	65 ± 8	67 ± 9	74 ± 10	0.343	0.879	<0.001	<0.001
AST (IU/L)	19 ± 4	18 ± 4	21 ± 8	0.009	NA	<0.001	NA
ALT (IU/L)	15 ± 6	14 ± 6	23 ± 15	0.622	NA	<0.001	NA
GTP (IU/L)	19 ± 11	18 ± 16	30 ± 36	1.000	1.000	<0.001	<0.001
LDL-C (mg/dL)	90 ± 22	101 ± 24	119 ± 28	<0.001	<0.001	<0.001	<0.001
HDL-C (mg/dL)	77 ± 16	71 ± 14	61 ± 16	<0.001	<0.001	<0.001	<0.001
TG (mg/dL)	58 ± 26	63 ± 27	103 ± 66	0.306	NA	<0.001	NA
FBS (mg/dL)	84 ± 7	85 ± 7	90 ± 8	0.031	0.094	<0.001	<0.001
RISK (No.)	0.13 ± 0.37	0.18 ± 0.44	0.79 ± 0.96	0.704	NA	<0.001	NA

P value was calculated by the t test or analysis of covariance, adjusted for age

Values are presented as the mean ± SD

ANCOVA analysis of covariance, NA no available

disorders are found in normal BMI groups [4–6, 15, 16]. Both the Japanese criteria for metabolic syndrome and the public health policy focus on obesity; consequently, there is the possibility that such abnormalities in the non-obese group will be overlooked. The liver dysfunction and dyslipidemia observed in the non-obese group were impossible to miss, thereby illustrating the necessity for countermeasures against health deterioration in such groups.

Our study has a number of limitations. The subjects voluntarily underwent this health checkup service, which may have caused a selection bias. Secondly, this study lacked any consideration of lifestyle. Further studies are required to confirm our results on these factors. We are

currently analyzing the contribution of both lifestyle and family history on RISK factors in young Japanese individuals in a different observation period.

In conclusion, we found that RISK factors were observed in a substantial number of young non-obese Japanese subjects. RISK factors other than overweight cause asymptomatic changes which can lead to the development of severe complications. The Japanese public health policy against metabolic syndrome focuses on anti-obesity measures/education; however, a comprehensive policy directed at all individuals, including those in the non-obese group, is necessary to prevent an increase in atherosclerotic diseases.

Table 3 Associations between obesity and risks for atherosclerotic disorders

Descriptive statistics	Lean [n (%)]	Normal [n (%)]	Obese [n (%)]	Odds ratio ^a			
				Normal vs. lean		Age-adjusted	
				Crude	Age-adjusted		
		Normal vs. obese		Age-adjusted			
		Crude	Age-adjusted				
Men							
High blood pressure	1 (6.7)	29 (12.9)	34 (28.3)	0.48 (0.06–3.79)*	0.76 (0.09–6.30)	2.66 (1.52–4.64)	2.65 (1.51–4.66)
Liver dysfunction	0	76 (33.9)	77 (64.2)	–	–	3.49 (2.19–5.55)	3.53 (2.20–5.65)
AST	0	5 (2.2)	12 (10.0)	–	–	4.87 (1.67–14.2)	5.00 (1.71–14.6)
ALT	0	24 (10.7)	41 (34.2)	–	–	4.32 (2.45–7.63)	4.38 (2.48–7.73)
GTP	0	70 (31.3)	68 (56.7)	–	–	2.88 (1.82–4.55)	2.92 (1.83–4.66)
Dyslipidemia	0	67 (29.9)	71 (59.2)	–	–	3.40 (2.14–5.39)	3.45 (2.15–5.53)
LDL-C	0	35 (15.7)	35 (30.2)	–	–	2.32 (1.36–3.97)	2.34 (1.35–4.06)
HDL-C	0	11 (4.9)	20 (16.7)	–	–	3.87 (1.79–8.39)	3.86 (1.78–8.36)
TG	0	39 (17.4)	53 (44.2)	–	–	3.75 (2.28–6.18)	3.74 (2.27–6.17)
Hyperglycemia	1 (6.7)	6 (2.7)	16 (13.3)	2.60 (0.29–23.3)	5.28 (0.51–55.2)	5.59 (2.13–14.7)	5.53 (2.10–14.6)
Women							
High blood pressure	4 (2.4)	30 (3.7)	18 (14.2)	0.64 (0.22–1.83)	0.74 (0.25–2.13)	4.31 (2.32–7.99)	4.29 (2.30–8.01)
Liver dysfunction	11 (6.5)	38 (4.7)	23 (18.1)	1.43 (0.71–2.86)	1.50 (0.75–3.02)	4.51 (2.58–7.87)	4.49 (2.57–7.84)
AST	0	1 (0.1)	5 (3.9)	–	–	33.3 (3.86–287)	32.8 (3.80–284)
ALT	1 (0.6)	3 (0.4)	8 (6.3)	1.62 (0.17–15.6)	1.30 (0.13–13.1)	18.2 (4.75–69.4)	18.1 (4.73–69.1)
GTP	10 (6.0)	37 (4.6)	23 (18.1)	1.33 (0.65–2.72)	1.44 (0.70–2.98)	4.64 (2.65–8.11)	4.61 (2.63–8.08)
Dyslipidemia	7 (4.2)	76 (9.3)	49 (38.6)	0.42 (0.19–0.93)	0.45 (0.20–0.99)	6.09 (3.97–9.35)	6.11 (3.97–9.40)
LDL-C	5 (3.0)	58 (7.1)	29 (23.0)	0.40 (0.16–1.01)	0.42 (0.17–1.07)	3.89 (2.38–6.37)	3.87 (2.36–6.35)
HDL-C	0	4 (0.5)	6 (4.7)	–	–	10.0 (3.43–29.3)	9.97 (2.77–35.9)
TG	2 (1.2)	16 (2.0)	27 (21.3)	0.60 (0.14–2.63)	0.65 (0.15–2.82)	13.4 (7.00–25.8)	13.4 (6.98–25.8)
Hyperglycemia	2 (1.2)	16 (2.0)	15 (11.8)	0.60 (0.14–2.63)	0.64 (0.15–2.82)	6.67 (3.21–13.9)	6.70 (3.22–13.9)

^a The data in parentheses represent 95 % confidence intervals (CI). Logistic regression was used to adjust for age. The criteria for high blood pressure, liver dysfunction, dyslipidemia, and hyperglycemia are described in the [Subjects and methods](#) section

Conflict of interest None.

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