Characteristics of Metabolic and Lifestyle Risk Factors in Young Japanese Patients With Coronary Heart Disease

A Comparison With Older Patients

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SUMMARY

Coronary heart disease (CHD) is recognized as a lifestyle-related disease and is the second leading cause of death in Japan. However, the cardiac risk factor profile of young patients with CHD has not been clarified in suburban areas of Japan. Our study aimed to determine metabolic and lifestyle risk factors in young patients and compare them with older patients living in suburban areas of Nagano Prefecture.

A multicenter study was conducted in 86 young (aged less than 40 years) and 91 older (aged 50 years and over) patients diagnosed with CHD from 1992 to 2002. There was a strong association between obesity and the occurrence of CHD events in young patients (odds ratio = 3.61, $P = 0.006$). Lifestyle in the young patients was characterized by a lack of physical activity and regular physical activity was found to decrease the risk of the CHD events in these patients (odds ratio = 0.31, $P = 0.030$). In older patients, hypertension was identified as an independent risk factor for CHD events.

The results of the present study have demonstrated that obesity and a lack of regular physical exercise are independent risk factors for CHD events in younger patients. Thus, the data may be useful for the effective screening of high-risk individuals and the development of educational programs for the prevention of CHD, especially in younger Japanese. (Int Heart J 2006; 47: 343-350)

Key words: Acute myocardial infarction, Angina pectoris, Young patients, Obesity, Physical activity

CORONARY heart disease (CHD) is recognized as a lifestyle-related disease and was the second leading cause of death in Japan in 2004.¹⁾ In general, the risk of a CHD event increases with age and the number of deaths/100,000 people

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among Japanese males over 55 years old was 10-fold higher than in males less than 40 years old.²⁾ Although the risk factor profile for CHD is different between younger and older patients,³⁾ the profile of younger adults with CHD has not been fully examined in Japan, most likely due to limited sample size. According to epidemiological data published in the 1990s in the United States, the incidence of myocardial infarction in patients under the age of 45 years accounted for approximately 4-10% of all myocardial infarctions.⁴⁾ However, more recent studies have indicated that the incidence of CHD events in men less than 40 years old was increasing.^{4,5)} Moreover, in our previous study that examined temporal trends in young Japanese patients with CHD over the last 20 years, we found that the number of young patients with CHD caused by multiple risk factors was increasing.⁶⁾

A previous study has pointed out that a westernized lifestyle is strongly correlated to the increased prevalence of atherosclerotic CHD among young Japanese.⁵⁾ Although lifestyle risk factors such as diet, a lack of physical activity, and smoking may be closely related to the development of CHD in young patients,⁷⁾ most studies have focused attention on only metabolic risk factors, including hypertension, dyslipidemia, diabetes, and obesity. Thus, the aims of the present study were to characterize the distribution of both metabolic and lifestyle risk factors and to analyze the contributory risk factors for CHD events in young patients living in Nagano Prefecture.

METHODS

Subjects: Of the 117 general medical hospitals with over 100 beds in Nagano, 20 from various regions of the prefecture were selected and asked to participate in the study. Eligible young subjects aged less than 40 years were admitted to one of these 20 hospitals and diagnosed with CHD between 1992 and 2002. The number of young patients treated in each hospital ranged from 1 to 8, and the total number of young patients was 91. After excluding 3 subjects who died and 2 subjects who did not consent to participate in this study, 86 patients were enrolled (participation rate, 95%). According to statistics published by the National Cardiovascular Center of Japan between 1977 and 1996, acute myocardial infarction (AMI) events reached a peak in men in their 60s and in women in their 70s, and the population from 50 to 79 years accounted for over 80% of the AMI patients.⁸⁾ Therefore, older subjects who were at least 50 years old and diagnosed with CHD from 1992 to 2002 were eligible to participate in the study. Ninety-one of the 107 older patients consented to participate in the study (participation rate, 85%).

Definition of CHD events: The definition of CHD in this study included AMI and angina pectoris. The diagnosis of AMI was defined based on symptoms, an electrocardiogram, and enzyme criteria according to the ACC/AHA guideline.⁹⁾

Although some of the study subjects had experienced CHD events more than twice, only data from first-time CHD events were collected.

Data collection: After written informed consent was obtained, the medical records of eligible patients were reviewed and biochemical data and the presence of metabolic disorders, including obesity, hypertension, dyslipidemia, and diabetes, were noted according to the following definitions: Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m^2), and overweight ($30.0 > \text{BMI} \geq 25.0$) and obese ($\text{BMI} \geq 30.0$)¹⁰⁾ patients were defined as obesity in this study. Hypertension was defined as systolic blood pressure ≥ 140 mmHg and/or diastolic pressure ≥ 90 mmHg¹¹⁾ or as the use of antihypertensive medication. Dyslipidemia was defined as a history of receiving antidyslipidemia agents or as satisfying the following criteria on admission: serum total cholesterol (TC) ≥ 220 mg/dL, triglycerides (TG) ≥ 150 mg/dL, high-density lipoprotein cholesterol (HDL-C) < 40 mg/dL, and/or low-density lipoprotein cholesterol (LDL-C) ≥ 140 mg/dL.¹²⁾ Diabetes was defined as a history of treatment with either insulin or oral hypoglycemic medication, and additional criteria were fasting plasma glucose ≥ 126 mg/dL or casual plasma glucose > 200 mg/dL.¹³⁾ To be considered eligible, data had to be measured within the first 72 hours following the CHD event. Final diagnoses, confirmed by hospital discharge records, were also taken into account. Patients were considered to have multiple risk factors when they had 3 or more metabolic risk factors, as previously described.⁶⁾

Lifestyle risk factors were determined by the mailed self-administered questionnaire. Fifty-five (64%) of the 86 younger patients and 64 (70%) of the 91 older patients sent back the questionnaire. Participants were asked to report on their cigarette smoking, physical activity, and alcohol consumption prior to the initial hospital admission. A current smoker was defined as a person who continued smoking after the CHD event. Physical activity was considered only leisure-time activity and assessed with respect to intensity, duration, and frequency. Regular physical activity was defined as activity of moderate intensity performed for over 30 minutes at least twice a week. Habitual alcohol drinking was defined as consumption at least 20 g of alcoholic beverage more than 3 times a week.

All data were collected from May 2001 to December 2003.

Statistical analysis: The significance of continuous variables, such as coronary lesions, BMI, and biochemical parameters, were calculated using the 2-tailed Student *t*-test, and the differences in nominal variables were analyzed using the chi-square test or Fisher's exact 2-tailed test. Univariate logistic regression analysis was carried out to estimate the association between the onset of a CHD event and established coronary risk factors, including obesity, history of hypertension, dyslipidemia, diabetes, and smoking history, a lack of habitual physical activity, and

habitual alcohol consumption in the younger patients. Only the significant risk factors were further analyzed using stepwise multiple logistic regression analysis to identify the independent contributory factors for CHD events in these patients. All analyses were performed with SPSS software (version 11) and a *P* value of less than 0.05 was considered statistically significant.

RESULTS

Gender and disease classifications were significantly different between the younger and older patients. The percentage of younger female patients was significantly less than that of the older female patients. The prevalence of AMI was significantly greater and the number of coronary lesions was less in the younger patient group than in the older patient group (Table I).

In the younger patients, the prevalence of obesity was significantly increased, and therefore, the calculated BMI was significantly greater compared with the older patients. Although the difference was not statistically significant (*P* = 0.183), the younger patients tended to report awareness of being overweight earlier in life (less than 18 years) than did the older patients. The older patients had a significantly higher prevalence of hypertension than the younger patients. Serum TC, LDL cholesterol, and TG levels were significantly elevated in the younger patients compared with the older patients. In contrast, serum HDL-C level, history of dyslipidemia or diabetes, fasting plasma glucose level, and the prevalence of multiple risk factors did not differ between the 2 age groups (Table II).

The incidences of smoking history and current smoker were significantly higher in the younger group than in the older group, while regular physical activity was significantly more prevalent in the older patients. There was no difference in habitual alcohol consumption between the 2 groups (Table II).

Table I. Clinical Characteristics

		Younger patients (<i>n</i> = 86)	Older patients (<i>n</i> = 91)	<i>P</i> value
Age (years)		34.8 ± 4.1	61.9 ± 7.7	
	(Range)	20-39	50-83	
Gender	Male	82 (95%)	74 (81%)	0.002
	Female	4 (5%)	17 (19%)	
Diagnosis of CHD	AMI	62 (72%)	44 (48%)	0.001
	AP	24 (28%)	47 (52%)	
Number of coronary lesions		1.1 ± 0.8	1.7 ± 0.9	< 0.001

Data are presented as mean ± SD.

AMI indicates acute myocardial infarction and AP, angina pectoris.

Table II. Cardiac Risk Factor Profile

Risk factors	<i>n</i>	Younger patients	<i>n</i>	Older patients	<i>P</i> value
Obesity (BMI $\geq$ 25)	75	43 (57%)	86	32 (37%)	0.011
BMI (kg/m ²)	75	25.7 $\pm$ 3.8	85	24.2 $\pm$ 3.6	0.010
History of hypertension	86	27 (31%)	83	50 (60%)	< 0.001
Diagnosis of FH	85	9 (10%)	81	3 (3%)	
History of dyslipidemia	85	48 (56%)	81	41 (51%)	NS
Serum total cholesterol (mg/dL)	78	224.0 $\pm$ 60.0	79	198.4 $\pm$ 41.5	0.002
Serum triglycerides (mg/dL)	78	210.7 $\pm$ 198.0	78	137.7 $\pm$ 92.0	0.004
Serum HDL-cholesterol (mg/dL)	70	47.5 $\pm$ 18.3	53	48.0 $\pm$ 13.9	NS
Serum LDL-cholesterol (mg/dL)	70	132.9 $\pm$ 53.9	54	116.5 $\pm$ 36.1	0.044
History of diabetes	84	19 (23%)	83	29 (35%)	NS
Fasting plasma glucose (mg/dL)	63	130.5 $\pm$ 71.0	60	123.8 $\pm$ 42.4	NS
Number of patients with MRFs	85	20 (24%)	81	20 (25%)	NS
Smoking history	61	49 (80%)	88	56 (64%)	0.028
Current smoker		16 (26%)		7 (8%)	0.002
Regular physical activity	55	8 (15%)	67	20 (30%)	0.045
Habitual alcohol consumption	53	9 (17%)	71	12 (17%)	NS

BMI indicates body mass index; FH, familial hypercholesterolemia; HDL, high-density lipoprotein; LDL, low-density lipoprotein and MRFs, multiple risk factors. Current smoker is defined as continued cigarette smoking after a CHD event. Regular physical activity is defined as leisure-time activity of moderate intensity performed for over 30 minutes at least twice a week. Habitual alcohol consumption is defined as consumption of at least 20 g of alcohol beverages more than 3 times a week.

Table III. Results of Univariate and Multivariate Logistic Regression Analysis of Risk Factors for CHD Events in Younger Patients

	Crude Odds Ratio	95% CI	<i>P</i> value	Adjusted Odds Ratio	95% CI	<i>P</i> value
AMI	2.61	1.40-4.85	0.003			
Multivessel disease	0.21	0.10-0.41	< 0.001			
Obesity (BMI $\geq$ 25)	2.27	1.20-4.27	0.011	3.61	1.43-9.11	0.006
History of hypertension	0.30	0.16-0.57	< 0.001	0.20	0.08-0.52	0.001
History of dyslipidemia	1.27	0.69-2.33	NS			
History of diabetes	0.54	0.28-1.08	NS			
Smoking history	2.33	1.08-5.02	0.030	1.61	0.62-4.19	0.329
Regular physical activity	0.40	0.16-1.00	0.049	0.31	0.11-0.89	0.030
Habitual alcohol consumption	0.98	0.38-2.54	NS			

Multivessel disease is defined as having 2 or 3 coronary lesions. CI indicates confidence interval.

Multivariate logistic regression analysis demonstrated a strong association between obesity and CHD events in the younger patients (odds ratio = 3.61, *P* = 0.006). Also, regular physical activity was found to decrease the risk of a CHD event in these patients (odds ratio = 0.31, *P* = 0.030) (Table III). Conversely,

hypertension was an independent risk factor for a CHD event in the older patients.

DISCUSSION

The findings of the present study indicate that the important contributory factors for a CHD event in the younger patients were obesity and physical inactivity. In contrast, hypertension was found to an independent risk factor for a CHD event in the older patients.

In the present study, the prevalence of obesity in the younger patient group was significantly greater than that of the older patients (57% versus 37%, $P = 0.011$) and much greater than that of healthy control subjects in their 20s (18.1% in men and 7.4% in women) and in 30s (29.3% in men and 14.3% in women) reported by The National Nutrition Survey in Japan, 2001.¹⁴⁾ According to previous Japanese case-control studies, the prevalence of obesity in young male patients with CHD aged 20 to 39 years old was 15-35%.¹⁵⁾ Thus, the younger patients in our study had a considerably higher prevalence of obesity. It is generally recognized that obesity, per se, is an independent risk factor for CHD in western countries.¹⁶⁾ The Pathobiological Determinants of Atherosclerosis in Youth (PDAY) study autopsied a large sample of American youth, aged 15 to 34 years, and reported a strong association between BMI and the development of atherosclerotic lesions in coronary arteries, especially in men.¹⁷⁾ Obesity is also associated with additional unfavorable effects, including dyslipidemia,¹⁸⁾ elevated systolic blood pressure,¹⁹⁾ increased insulin resistance,¹⁹⁾ and proinflammatory state,^{20,21)} all of which may enhance the risk of CHD.

Although the difference was not statistically significant, the younger patients in the present study tended to be obese by about age 18 or earlier. Recently, some investigators have proposed the idea that cardiovascular disease may have its origin in childhood. Japanese cohort studies revealed that the incidence of childhood obesity that continued into adulthood ranged from 32.2% to 58.5% in men and from 41.0% to 48.0% in women.^{22,23)} In addition, the published cohort studies which investigated obese adults for more than 10 years suggested that past obesity, especially obesity lasting over 10 years, might cause an approximately 2-fold increase in the risk of CHD.²⁴⁾ Our data show that obesity is the most important independent metabolic risk factor for a CHD event in the younger Japanese subjects. Thus, intensive community-based intervention for primary prevention of obesity should be carried out, especially in childhood.

In the present study, a lack of physical activity was identified as another independent risk factor accounting for CHD events in the younger patients and regular physical activity was found to decrease the risk of CHD events in these

patients. The Japanese National Health Promotion Movement, known as “Health Japan 21”, recommends engaging in moderate physical activity over 30 minutes at least twice a week.¹⁴⁾ The National Nutritional Survey in Japan found that out of 15,000 subjects queried, 29.7% of men and 27.1% of women engaged in the recommended amount of physical activity for at least a 1-year period.¹⁴⁾ In our study, however, only 15% of the younger patients achieved the recommended physical activity level, whereas 30% of the older patients did so. In order to prevent obesity, moderate physical activity is an important factor and is accompanied by a low risk for CHD.

Study limitations and implications: There were limitations in this study. Aging itself influences dietary habits and the extent of physical activity. Furthermore, atherosclerosis develops gradually and the CHD risk is dependent on the sum of long-term exposure to a variety of coronary risk factors. Thus, the current questionnaire data may reflect the age-related changes in lifestyle, especially in the older patients.

Further, a well-designed, nation-wide, prospective study will be required to determine whether or not (1) our findings are representative of the younger patients with CHD in both the urban and rural areas of Japan, (2) childhood obesity accounts for the increased rate of mortality and morbidity due to CHD in adulthood, and (3) direct clinical interventions at an early age can reduce CHD events in adults. In the near future, special attention should be focused on those young subjects who are more susceptible to CHD in Japan.

Conclusions: The results of the present study have demonstrated that obesity and a lack of regular physical exercise are independent risk factors for CHD events in younger patients. Thus, the data may be useful for the effective screening of high-risk individuals and the development of educational programs for the prevention of CHD, especially in younger Japanese.

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