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Original Article

Obesity and the Risk of Diabetes Mellitus in Middle-aged Japanese Men

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The morbidity of diabetes mellitus is increasing gradually in Japanese populations. It is important to clarify the risk factors of diabetes in Japanese populations in order to take adequate measures against the increasing morbidity of diabetes. In order to evaluate the link between past and concurrent obesity and diabetes in middle-aged Japanese men, we conducted a worksite-based historical cohort study in Okayama, Japan in 1999. Annual health examination data of middle-aged male workers in a worksite were collected. The relative risks of past and concurrent obesity for developing diabetes were calculated. Subjects with a past history of obesity at between 40 and 50 years of age had a significantly higher risk of developing diabetes by age 55 than did subjects in the normal weight group. These results suggest that, in order to prevent diabetes in middle-aged Japanese men, health guidance for normal weight maintenance should be provided not only for middle-aged men, but also for men under age 40.

Key words: obesity, body mass index, diabetes mellitus, cohort study

Diabetes mellitus is a common disease. As of 1999, there were 2.1 million diabetic patients in Japan [1]. A study conducted by the Japanese Ministry of Health and Welfare estimated that there were 6.9 million people diagnosed with, or highly suspected of having, diabetes in Japan [2]. The number of patients has been increasing gradually, and it has been estimated that the number of patients diagnosed with or highly suspected of having diabetes will reach more than 10 million within 10 years [3].

The most common form of diabetes mellitus in the Japanese population is type 2 diabetes. It is well known that this type of diabetes has several risk factors, such as a family history of the disease, male sex, advancing age, and some environmental- and lifestyle-related factors [2, 4-10]. The main reasons for the increasing incidence of diabetes in the Japanese population are considered to be environmental and lifestyle changes [3].

Among the lifestyle-related factors, obesity is reported to be one of the strongest risk factors for developing type 2 diabetes [10-15]. It is also reported that type 2 diabetes is more strongly associated with past than with concurrent obesity [14-16]. However, most of these reports are from North America or Europe. And while it is reported that different ethnic groups share similar risk factors for diabetes, the impact of these factors differs between ethnic groups [4, 5]. To reduce the increasing prevalence of diabetes in Japan, it is therefore important

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to evaluate the risk factors for diabetes in the Japanese population. Despite this fact, there have been only a few cohort studies concerning diabetes and obesity in the Japanese population [7, 17].

In this study, we evaluated the risk of obesity for diabetes in middle-aged Japanese men by means of an historical cohort study with a 15-year follow-up period.

Materials and Methods

We conducted a worksite-based study in Okayama, Japan in 1999. The study population consisted of Japanese male workers in the information industry in Okayama, Japan. In Japan, employers are required to conduct annual employee health examinations, and to give adequate health guidance according to the results of these examinations. It is required that the health examinations data be kept at the worksite for at least 5 years, and in the case of the present worksite, the data was kept for more than 20 years. We used the data between 1975 and 1998 for evaluation of the association between obesity and diabetes.

Before data collection, guidelines for handling health examination data for this analysis were established. Only the health care staff from the worksite handled and transcribed the original data, and all personal information was omitted. Non-staff investigators had access to the transcribed data only. Consent to collect data using these guidelines was obtained from the employer prior to the start of the study.

Male workers who were between 30 and 40 years of age in 1975 were enlisted as study subjects. The health examination data of these subjects at 40, 45, 50 and 55 years of age were collected. For subjects who did not undergo health examinations at the specified ages, available data at 40 ± 2, 45 ± 2, 50 ± 2 or 55 ± 2 years of age was used. The data collected included body weight, height and fasting plasma glucose level (FPG) at each age. Whether or not a subject had been diagnosed as diabetic before the examination at each age was part of the routine health questionnaire given at each examination and was incorporated into the study data. At each age, subjects whose FPG value was 126 mg/dl or higher [18, 19] or who had already been diagnosed as diabetic were judged to be patients with diabetes in this analysis. Body mass index (BMI) was calculated as weight in kg divided by the square of height in m. We categorized subjects into 4 groups according to their BMI value at each age, *i.e.*, BMI less than 18.5 (underweight), between 18.5 and 22.9 (normal weight), between 23.0 and 24.9 (overweight), and 25.0 or more (obese) [4, 20].

In the historical cohort examination, we excluded those subjects whose health examination data were not available for all ages (*i.e.*, 40, 45, 50 and 55 years). We also excluded those subjects who had been diagnosed with diabetes before 40 years of age, or whose FPG value at 40 years of age was 126 mg/dl or higher.

Changes in BMI, FPG and diabetes-related morbidity were calculated, following the analysis of the risks of past and concurrent obesity for diabetes. Changes in BMI from 40 to 55 years of age were classified into three categories: decrease in BMI, increase in BMI of less than 1.5, and increase in BMI of 1.5 or more. We evaluated the relationship between changes in BMI and the risk of developing diabetes by the age of 55.

Statistical analyses were conducted by SPSS 8.0J. For analyses of ratios, Mann-Whitney's U test or Spearman's correlation coefficient by rank test were used. Repeated measures of ANOVA were performed for analyzing the difference between variables at each age. The risk of obesity for diabetes was compared with the normal weight group and calculated as a relative risk with 95% confidence intervals. A P-value less than 0.05 was considered to indicate statistical significance.

Results

As potential subjects, 280 male workers were enlisted. There were 127 subjects for whom health examination data was available at each of the ages given above, and who were considered to be non-diabetic at 40 years of age. These 127 subjects were analyzed in this study.

Characteristics of the subjects at each age are summarized in Table 1. No significant differences were observed between the characteristics of the study group and those of the group of potential subjects excluded from the study. Subject body weight, BMI and FPG value increased with increasing age. Diabetes-related morbidity also increased with increasing age. The rate of obesity at 40 years of age was 14.2%, and by age 55 it increased to 23.6%. Less than 1.0% of subjects at each age had a BMI equal to or greater than 30.0. Diabetes-related morbidity at 55 years of age was 19.7%, and this value was significantly greater than those at 40, 45 or 50 years of age.

Table 2 shows the relationship between concurrent and past BMI category and diabetes-related morbidity at 55 years of age. Statistical significance was observed between the BMI category at each age and diabetes-related morbidity at 55 years of age. Incidence of diabetes from 40 to 55 years of age was calculated to be 31.40 per 1,000 person-years.

The relative risks for diabetes at age 55 due to concurrent and past history of being obese or overweight are shown in Table 3. Subjects who were obese in the past showed a 3 times greater likelihood of becoming diabetic by 55 years of age than did subjects of the normal weight group ($P < 0.05$). Concurrently obese subjects at 55 years of age showed a higher risk of diabetes than normal-weight subjects, although the difference was not statistically significant. Those who were overweight in the

Table 1 Characteristics of subjects (n = 127) at each age[a]

Age at examination	40	45	50	55
Body weight (kg)[b]	61.6 ± 8.1	62.8 ± 8.3	63.2 ± 8.1	63.5 ± 8.7
	(53.0–74.0)	(52.8–75.0)	(53.0–75.0)	(52.2–74.5)
BMI (kg/m²)[b]	22.3 ± 2.6	22.7 ± 2.8	22.8 ± 2.8	23.0 ± 3.0
	(19.0–25.7)	(19.0–25.9)	(19.5–26.3)	(19.3–26.8)
BMI category[c]				
< 18.5	5.5%	5.5%	4.7%	7.1%
18.5–22.9	58.3%	48.0%	50.4%	40.9%
23.0–24.9	22.0%	27.6%	22.8%	28.3%
≥ 25.0	14.2%	18.9%	22.0%	23.6%
FPG (mg/dl)[b]	83.6 ± 7.3	95.5 ± 13.0	100.3 ± 12.6	105.1 ± 19.6
	(75.0–93.0)	(81.8–109.0)	(87.0–116.2)	(88.0–126.0)
Diabetes-related morbidity[d]	0.0%	1.6%	4.7%	19.7%

[a], Values are expressed as the mean ± standard deviation with 10 percentile and 90 percentile values given in parentheses for variables or percentage for ratios; [b], $P < 0.001$ (repeated measures ANOVA); [c], $P < 0.05$ (Spearman's correlation coefficient by rank test); [d], $P < 0.001$ (Mann-Whitney's U test).

Table 2 Relationship between diabetes-related morbidity at age 55 and past and concurrent BMI[a]

BMI	at age: 40[b]	45[c]	50[c]	55[b]
< 18.5	0.0 (0/ 7)	0.0 (0/ 7)	0.0 (0/ 6)	11.1 (1/ 9)
18.5–22.9	13.5 (10/74)	14.8 (9/61)	10.9 (7/64)	13.5 (7/52)
23.0–24.9	28.6 (8/28)	20.0 (7/35)	27.6 (8/29)	22.2 (8/36)
≥ 25.0	38.9 (7/18)	37.5 (9/24)	35.7 (10/28)	30.0 (9/30)

[a], Values are expressed as diabetes-related morbidity (%) and number of subjects with diabetes at age 55/total number of subjects in parentheses; [b], $P < 0.05$ (Mann-Whitney's U test); [c], $P < 0.01$ (Mann-Whitney's U test).

Table 3 Relative risks and 95% confidence intervals of concurrent and past obesity for diabetes at age 55 with normal weight group (BMI between 18.5 and 22.9) as reference[a]

BMI	at age: 40	45	50	55
23.0–24.9	2.11 (0.93–4.81)	1.36 (0.55–3.32)	2.52 (1.01–6.30)	1.65 (0.66–4.15)
≥ 25.0	2.88 (1.27–6.51)	2.52 (1.15–5.62)	3.27 (1.38–7.70)	2.23 (0.92–5.37)

[a], Values are expressed as relative risks and 95% confidence intervals in parentheses. Numbers of subjects are same as the number displayed in Table 2.

past or at present also represented high relative risks for diabetes at 55 years of age; however, significance was observed in only the overweight group at 50 years of age.

The BMI of two-thirds of the subjects increased from 40 to 55 years of age. There was no significant correlation between BMI change and diabetes-related morbidity at 55 years of age. When subjects were subdivided by BMI category at 40 years of age, though the sample size became rather small, diabetes-related morbidity at 55 years of age was not related to the BMI change (Table 4).

Discussion

In this study, we analyzed the incidence of diabetes mellitus in middle-aged Japanese men, paying special attention to the relationship between diabetes mellitus and obesity. It is well known that the risks for diseases and the rate of obesity are different among different ethnic groups [4, 5]. Therefore, to consider measures against the increasing prevalence of diabetes among the Japanese population, it is important to grasp the current status and risk factors of diabetes in the Japanese population.

The WHO defines individuals with a BMI of 30 or higher as obese [21]. In this study, however, the percentage of middle-aged men who were judged to be obese by the WHO criteria was less than 1%. The rate of obesity in the Japanese population is far less than that in American populations [4, 20, 22]. Therefore, the Japan Society for the Study of Obesity defines obesity in Japan as a BMI of 25 or more [20]. The WHO Western Pacific Region of the International Association for the Study of Obesity also defines obesity in Asians using the same criteria, and defines being overweight as having a BMI between 23.0 and 24.9 [4]. We categorized subjects in the present study according to the latter 2 criteria. Based on these criteria, 15% to 25% of our subjects were obese.

We observed that subjects who were obese at 40, 45 and/or 50 years of age had an almost three times greater risk of developing diabetes by age 55 compared to subjects in the normal weight group. Being overweight at 50 years of age also represented a 2.5 times higher risk of diabetes at 55 years of age. However, subjects currently obese at 55 years of age showed no significant risk for diabetes. In this study, there is a possibility that the past and concurrent risks of diabetes were underestimated. This is because those who were judged as diabetic at 55 years of age might already have been diagnosed with and treated for diabetes before 55 years of age, and thus might have taken steps to control their body weight. We therefore should not conclude that concurrent obesity was not a risk for diabetes, since the underestimation of risk was more likely to occur in patients with concurrent than in those with past obesity. Nonetheless, a past history of obesity was shown to be a risk factor for diabetes in Japanese middle-aged men in this study.

In previous studies from the United States and the European countries [11, 12, 14–16], past obesity was also reported as one of the risks for diabetes. As mentioned above, however, the criteria of obesity differ between Japanese and Europeans. Our results show that all Japanese men with a BMI of 25 or more—all of whom were classified as obese according to the Japanese criteria, but many of whom would have been classified as overweight by the criteria for Europeans—were at risk for diabetes. This finding suggests that plans for prevention of diabetes in the Japanese should be designed not using the WHO criteria, but using the Japanese criteria for obesity.

There have been relatively few cohort studies on the

Table 4 Relationship between diabetes-related morbidity at age 55 and BMI change from 40 to 55 years of age[a]

BMI at 40 years of age	BMI change from 40 to 55 years of age		
	BMI change < 0	0 ≤ BMI change < 1.5	BMI change ≥ 1.5
< 18.5	0.0 (0/ 3)	0.0 (0/ 1)	0.0 (0/ 3)
18.5–22.9	18.2 (4/22)	8.0 (2/25)	14.8 (4/27)
23.0–24.9	10.0 (1/10)	36.4 (4/11)	42.9 (3/ 7)
≥ 25.0	37.5 (3/ 8)	50.0 (2/ 4)	33.3 (2/ 6)
Total	18.6 (8/43)	19.5 (8/41)	20.9 (9/43)

[a], Values are expressed as diabetes-related morbidity (%) and number of subjects with diabetes at age 55/ total number of subjects in parentheses.

Japanese population concerning the relationship between past obesity and diabetes [7, 17]. Those studies that have been made indicate that obesity is a risk for diabetes. Therefore, to prevent diabetes, health guidance for normal body-weight maintenance is considered to be desirable [3]. It should be noted, however, that the above studies were based on 8 or fewer years of observation. To date, we have found no reports observing the relation of past obesity and diabetes for a longer period. Thus it has been unclear which generation should be targeted for optimal health guidance. Our data showed that being obese at 40 years of age already presented a risk for developing diabetes by age 55. This result suggests that it is better to give necessary health guidance to people under 40, in order to prevent their being obese at age 40 or later. In the present study, the risk ratios of obese subjects were higher than those of normal-weight subjects at both 45 and 50 years of age. Therefore, health guidance for people in their forties would also seem highly important.

Before closing, we should mention the limitations of our study. For judgment of diabetes, we used only FPG values. That is, neither the glucose tolerance test nor HbA1c values were used. In general, FPG and plasma glucose 2 h after 75 g glucose load (2hPG) are used for diagnosis of diabetes mellitus [18, 19, 23]. However, for epidemiological purposes, the American Diabetes Association (ADA) has recommended the use of FPG $\geq$ 126 mg/dl alone [19]. In the recommendations of the Japan Diabetes Society, it was stated that 2hPG $\geq$ 200 mg/dl alone could be used for epidemiological studies. But in cases in which this proves difficult, use of the FPG value alone is also permitted [18]. These simplifications of the diagnostic criteria for epidemiological studies were made to facilitate fieldwork. In the health examination data we used, FPG values were available, but 2hPG values were not. We therefore used the FPG values alone for judgment of whether subjects were diabetic. However, some patients with diabetes diagnosed by the combined use of the FPG and 2hPG would be judged not diabetic by the simplified criteria [18, 24]. Thus it has been reported that patients with diabetes who showed elevated 2hPG values as a prodrome outnumbered those who showed elevated FPG values as a prodrome in the Japanese population [18]. From this point of view, some of the slightly diabetic patients might have been misclassified as not diabetic in this study, and the prevalence of diabetes might have been estimated as slightly lower than it would have been using a combination of the FPG and 2hPG.

In addition to the subjects with FPG $\geq$ 126 mg/dl, we classified subjects with previously known diabetes as diabetic. This was to avoid misclassifying those subjects who were treated as diabetic and whose hyperglycemia was improved. Whether or not subjects had been previously diagnosed as diabetic was determined by questionnaire at the health examination. It was suspected that not only definite diabetic subjects but also borderline subjects might have reported being diagnosed as diabetic, and therefore might have been classified as diabetic in this study. From this point of view, the estimated prevalence of diabetes might have been slightly higher than the prevalence of definitive diabetic cases.

Over the 15 years for which data were collected, the number of tests at the annual health examination was increased. With an increasing number of examinations comes an increase in abnormal findings and an increase in diagnosis or suspected diagnosis of diabetes. Thus the prevalence of diabetes at elder age would be slightly lower if the number of examinations was not changed for the 15 years. The prevalence rate of diabetes in this study rose significantly between 50 and 55 years of age. And while the aging of subjects would be one obvious reason for this increase, we cannot rule out the possibility that the increased variety of tests also played a role.

Even for epidemiological purposes, it might be desirable to use the same diagnostic criteria as used clinically. However, this may sometimes be difficult in fieldwork because of several obstructions, such as difficulty in obtaining the cooperation of subjects or an overly long period for completion of studies. To best clarify the risk of past obesity for diabetes, a prospective cohort study would probably be ideal, but such a study would take more than 20 years to complete. In the present study we used an historical cohort method to determine the risk of past obesity, although the criteria for judgment of diabetes was not ideal. In the future, we consider that it would be preferable to analyze the relationship between obesity and diabetes using a prospective method.

There was a further limitation with respect to the indices we used. We did not analyze family history or dietary, exercise or life habits of subjects, although all these parameters are known to relate to the development of diabetes [6–9]. We used only BMI as an index of obesity, and did not use waist circumference, waist-to-hip ratio or abdominal visceral adipose tissue accumulation.

Some reports have suggested that fat distribution, which is related to the latter 3 indices, is more closely related to the risk of developing diabetes than is BMI [13, 21]. Further studies on the risks of diabetes that involve these indices as factors, in addition to a more conclusive method of confirming diabetes, are required.

Although our present study had its limitations, it is one of the first steps in considering what measures could be taken against the increasing prevalence of diabetes among the Japanese population. Further studies in this area are required.

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