Dietary glycemic index and risk of type 2 diabetes mellitus in middle-aged Japanese men

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Dietary glycemic index and risk of type 2 diabetes in middle-aged Japanese men

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Abstract

Objective: This cohort study investigated the association between dietary glycemic index (GI), glycemic load (GL), and the incidence of type 2 diabetes in middle-aged Japanese men, and the effect of insulin resistance and pancreatic B-cell function on the association.

Materials/Methods: Participants were 1,995 male employees of a metal products factory in Japan. Dietary GI and GL were assessed using a self-administered diet history questionnaire. The incidence of diabetes was detected in annual medical examinations over a 6-year period. The association between GI and GL and the incidence of diabetes was evaluated using Cox proportional hazards models.

Results: During the study, 133 participants developed diabetes. Age and body mass index (BMI)-adjusted hazard ratios (HRs) across the GI quintiles were 1.00 (reference), 1.62, 1.50, 1.68, 1.80, and those of GL were 1.00 (reference), 1.07, 1.48, 0.95, 0.98. The HR for the highest GI quintile was significantly greater than that for the lowest quintile. The influence of GI was more pronounced in the lowest insulin resistance subgroups. GI and pancreatic B-cell function were independently associated with the incidence of type 2 diabetes; participants with low-B cell function and the highest tertile of GI had the highest risk of diabetes.

Conclusions: Dietary GI is associated with the incidence of diabetes in middle-aged Japanese men. GI and B-cell function were independently associated with incidence of diabetes. GI is higher and B-cell function is lower in Asian people, as compared with Western people, and this

may result in a higher prevalence of diabetes in Asian populations.

Key words

B-cell function, cohort study, incidence, insulin resistance

Abbreviations

BMI, body mass index; GI, glycemic index; GL, glycemic load; HbA1c, glycated hemoglobin; HDL, high density lipoprotein; HOMA-IR, HOMA of insulin resistance; HOMA-B, HOMA of beta-cell function; DHQ, diet history questionnaire; P-Y, person-years.

1. Introduction

The prevalence of type 2 diabetes is similar in Asian and Western countries even though the prevalence of obesity is lower in Asia [1]. The high incidence of diabetes in the relatively lean Asian population may be explained, in part, by the presence of more abdominal fat in Asians, as compared with Caucasians of a similar body mass index (BMI) [2,3]. Furthermore, non-obese Asians who have low pancreatic B-cell function are at high risk for diabetes [4–6].

Dietary factors may also play a role in the high incidence of diabetes in the Asian population. An association between dietary glycemic index (GI), glycemic load (GL), and the incidence of type 2 diabetes has been reported in Western countries [7–9]; however, the association between GI and type 2 diabetes in the Asian population is not clear because high GI rice is a significant part of the Asian diet [10–14], and Asian GI values are higher than those in Western countries [15–19]. At present, the only study examining the relationship between GI and type 2 diabetes in the Asian population was conducted in women [12], and none have investigated the association in Asian men.

A high GI diet is associated with insulin resistance and postprandial hyperglycemia and hyperinsulinemia, which may cause pancreatic B-cell failure and diabetes mellitus [20]. However, no studies evaluating the influence of insulin resistance or B-cell function on the association between GI and the incidence of diabetes have been reported.

In this 6-year prospective study of Japanese men, we investigated the relationship between dietary GI, GL, and the risk of developing type 2 diabetes. The objectives of the study were to investigate whether dietary GI and GL are associated with the risk of diabetes and to examine the effect of insulin resistance and B-cell function on the relationship.

2. Methods

2.1. Participants

The study participants were male employees of a factory that produces zippers and aluminum sashes in Toyama Prefecture, Japan. Detailed information on the study population has been previously reported [6, 13]. The Industrial Safety and Health Law in Japan requires that employers conduct annual health examinations for all employees. A test for diabetes mellitus was conducted during annual medical examinations between 2003 and 2009. In 2003, 2,275 (89%) of 2,543 male employees aged 35–55 years received health examinations and responded to the diet survey. Of these 2,275 potential participants, 280 (12%) were excluded: 139 were diabetic or had high fasting plasma glucose (≥126 mg/dL) at the time of the baseline examination, 70 did not have fasting plasma insulin levels measured at the baseline examination, nine men had a total daily calorie intake below 500 kcal or above 5,000 kcal, and

62 did not participate in consecutive follow-up annual health examinations. Thus, 1,995 participants were included in the present study.

2.2. Data collection

The annual health examination included a medical history, physical examination, anthropometric measurements, and the measurement of fasting plasma glucose, fasting insulin, glycated hemoglobin (HbA1c), and serum lipid levels. Height was measured without shoes to the nearest 0.1 cm using a stadiometer. Weight was measured, with participants wearing only light clothing and no shoes to the nearest 0.1 kg using a standard scale. BMI was calculated as weight/height^2 (kg/m^2). Blood pressure was measured using a mercury sphygmomanometer after the subject rested for 5 min in a seated position. All measurements were taken by trained staff.

Plasma glucose levels were measured enzymatically using an Abbott glucose UV test (Abbott Laboratories, Chicago, IL, USA), and plasma insulin levels were determined using radioimmunoassay (Shionogi Co., Tokyo, Japan). HbA1c was measured by high-velocity liquid chromatography using a fully automated hemoglobin A1c analyzer (Kyoto Daiichi Kagaku, Kyoto, Japan). Total cholesterol and triglycerides were measured using an enzyme assay. High-density lipoprotein (HDL)-cholesterol was measured using direct methods. Insulin resistance was calculated by the homeostasis model assessment (HOMA) method using the formula: HOMA-IR = fasting insulin (μU/mL) × fasting plasma glucose (mg/dL)/405 [21]. The HOMA of beta-cell function (HOMA-B) was calculated using the following formula: HOMA-B = 360 × fasting insulin (μU/mL)/[fasting plasma glucose (mg/dL) - 63] [21].

A questionnaire was used to identify voluntary health-related behaviors such as alcohol consumption, smoking, and habitual exercise. A self-administered questionnaire was also used to collect information about a medical history of hypertension, dyslipidemia, diabetes, the use of antidiabetic medication, and a family history of diabetes. High blood pressure and dyslipidemia were defined using the Japanese criteria for metabolic syndrome [22]: high blood pressure was defined as a systolic blood pressure ≥130 mmHg or a diastolic blood pressure ≥85 mmHg; dyslipidemia was defined as serum triglycerides ≥150 mg/dL or HDL-cholesterol <40 mg/dL.

2.3. Dietary assessment and calculation of dietary GI and GL

Dietary habits during the preceding month were assessed using a self-administered diet history questionnaire (DHQ) [23]. The DHQ was developed to estimate the dietary intakes of macronutrients and micronutrients for epidemiological studies in Japan. A detailed description of the methods used for calculating dietary intakes and the validity of the DHQ have been reported previously [11, 24, 25]. Estimates of dietary intake for 147 food and beverage items, energy, and nutrients were calculated in 2007 using an *ad hoc* computer algorithm developed for the DHQ that was based on the Standard Tables of Food Composition in Japan [26].

Of the 147 food and beverage items included in the DHQ, six (4.1%) were alcoholic beverages, eight (5.4%) contained no available carbohydrate, and 63 (42.9%) contained less than 3.5 g of available carbohydrate per serving. The calculation of dietary GI and GL was thus based on the remaining 70 items. The GI databases used were an international table of GI [27], several publications concerning the GI of Japanese foods [28-30], recent articles on GI values published after the publication of the international GI table [31, 32], and an online database provided by the Sydney University Glycemic Index Research Service [33]. Although concerns have been expressed regarding the utility of GI for mixed meals (overall diet) [34,35], many researchers have shown that the GI of a mixed meal can be consistently predicted as the weighted mean of the GI values of each of the component foods [36, 37]. We calculated dietary GI by multiplying the percentage contribution of each food to the daily carbohydrate intake by the GI value of the food, and then summed these products. GL was calculated by multiplying the dietary GI by the total daily carbohydrate intake and dividing by 100. We used energy-adjusted values by the density method (per 1,000 kcal) for dietary GL [11].

2.4. Diagnosis of diabetes

Fasting plasma glucose and HbA1c were measured during the annual medical examinations. Participants with HbA1c >6.0% were given a 75g oral glucose tolerance test (OGTT). According to the definition of the American Diabetes Association [38] and the Japanese Diabetes Society [39], the diagnosis of diabetes was confirmed by at least one of the following observations: 1) a fasting plasma glucose concentration of ≥126 mg/dL, 2) 2 h glucose level of ≥200 mg/dL in a 75g OGTT, or 3) treatment with insulin or an oral hypoglycemic agent.

2.5. Statistical analysis

We calculated the incidence rates and HRs for diabetes according to the quintile of dietary GI, dietary GL and total energy intake. The Cox proportional hazard model was used to calculate HRs adjusted for multiple variables, including age (<40, 40–44, 45–49, ≥50 years), BMI (<22, 22–25, ≥25 kg/m^2), family history of diabetes (no, yes), alcohol consumption determined by the DHQ (nondrinker, consumed <20 g/day, consumed ≥20 g/day), smoking status (never, ex-smoker, or current smoker), habitual exercise (no, yes), total energy intake (kcal/day, quintile), and dietary total fiber intake (g/1000 kcal, quintile). The HR for diabetes was calculated separately for BMI (<22, 22–25, ≥25 kg/m^2), the HOMA-IR or HOMA-B tertile in each GI tertile, and the joint effects of GI and BMI, HOMA-IR, or HOMA-B by cross-classifying participants by both variables. The statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS version 12.0J; Tokyo, Japan). A *p*-value of < 0.05 was deemed statistically significant.

3. Results

The mean participant age at baseline was 46.0 years and the mean BMI was 23.4 kg/m^2. The mean dietary GI was 69.2 and the mean dietary GL (1,000 kcal) was 87.9. White rice was the largest contributor to dietary GI (61.2%), followed by noodles (5.4%), bread (5.2%), and confectioneries (4.9%).

The participants' baseline characteristics according to the dietary GI and GL quintile are shown in Table 1 (GI) and Table 2 (GL). No association was observed between dietary GI and age, BMI, serum lipid levels, fasting plasma glucose and insulin, blood pressure, prevalence of high blood pressure, or dyslipidemia. The higher GL quintiles were associated with significantly lower HDL-cholesterol, lower fasting plasma glucose, higher fasting insulin, lower systolic/diastolic blood pressure, and a lower prevalence of high blood pressure. Furthermore, high GI and GL were associated with lower dietary energy intake, lower fat intake, lower dietary fiber intake, and higher carbohydrate intake.

During the 6-year follow up (8,988 person-years), we documented 133 cases of diabetes.

Among these, 115 diagnoses were based on high fasting plasma glucose levels, 16 were diagnosed according to a 75g OGTT, and two participants had been treated with hypoglycemic medication.

The crude incidence rates (per 1,000 person-years) across the GI quintiles from lowest to highest were 10.1, 15.7, 13.6, 16.1, and 18.3, respectively (Table 3). The age- and BMI-adjusted HRs (Model 1) across the GI quintiles were 1.00 (reference), 1.62, 1.50, 1.68, and 1.80. The HR of the highest GI quintile was significantly higher than that of the lowest quintile. Further adjustment for family history of diabetes, alcohol intake, smoking, physical activity, the presence of high blood pressure, and dyslipidemia at baseline (Model 2) did not affect the HRs. When we used a model adjusted for the variables used in Model 2 plus dietary factors (Model 3), the HRs across the quintiles were higher than those in Models 1 and 2, and the HRs for the 4th and 5th quintiles were significantly higher than that of the 1st quintile.

The crude incident rates (per 1,000 person-years) across the GL quintiles were 13.3, 15.0, 19.5, 12.4, and 14.0 (Table 3). The age- and BMI-adjusted HRs across the BMI quintiles were 1.00 (reference), 1.07, 1.48, 0.95, and 0.98, and no association was found between GL and the incidence of diabetes. The relationships remained non-significant even after additional adjustments for potential confounders (Models 2, 3).

Because GI was inversely associated with total energy intake and total fiber intake (Table 1) and positively associated with the incidence of diabetes, we further evaluated the association between total energy intake and total fiber intake and the incidence of diabetes (Table 3). There were no associations between the total energy intake, total fiber intake and incidence of diabetes.

We analyzed the association between GI and the incidence of diabetes separately in subgroups based on the degree of BMI, insulin resistance, or pancreatic B-cell function at baseline. There were no differences in the associations between GI and baseline characteristics among the different BMI, insulin-resistance, and B-cell-function subgroups (Supplemental Table 1). High GI was associated with a significantly higher risk of diabetes in participants with a BMI < 22 kg/m^2, but not in the subgroup with a BMI of 22–24.9 kg/m^2, or in participants with a BMI ≥ 25 kg/m^2 (Table 4). Similarly, significant positive associations were observed in participants in the lowest HOMA-IR and HOMA-B tertiles, but not in the other tertiles (Table 4). We examined the joint effects of GI and BMI/HOMA-IR/HOMA-B by cross-classifying participants by both variables (Figure 1). We found a significant interaction between GI and HOMA-IR ($p = 0.005$), and the influence of GI was more pronounced in the lowest HOMA-IR tertile subgroups. On the other hand, participants in the lowest HOMA-B tertile with the highest GI had the highest risk of diabetes (Figure 1-C). We observed no interaction between GI and BMI or HOMA-B.

4. Discussion

This study investigated the association between dietary GI and GL and the incidence of type 2 diabetes in middle-aged Japanese men. The results indicated that GI, but not GL, had a significant positive association with the incidence of diabetes. The analyses of insulin resistance and dietary GI indicated that the association between high dietary GI and type 2 diabetes was stronger in the lowest HOMA-IR subgroup. Furthermore, GI and pancreatic B-cell function were independently associated with incidence of type 2 diabetes, and the participants with low-HOMA-B and the highest GI had the highest risk of diabetes.

The results of previous studies that evaluated the association between dietary GI and incidence of diabetes were controversial [8]. Although some reports showed no association between GI and diabetes, other reports and a recent meta-analysis showed positive associations. Differences in these results are probably due to differences in participant characteristics such as age, gender, ethnicity, and lifestyle. All previous studies of the association between GI and GL and the risk of diabetes have been conducted in Western countries [7–9], with the exception of one Chinese study of women [12]. The present study is the first report on an association between GI and GL and the risk of diabetes in Asian men. We found that the HR for the highest GI quintiles was 1.80 (Model 1) to 1.96 (Model 3); these values are somewhat higher than those reported in previous studies (0.89–1.59 for multivariate adjusted models) [8].

The GL was not associated with the incidence of diabetes in our study, and our findings agree with those of previous studies showing that GI, but not GL, was associated with the incidence of diabetes [15, 19]. Although some studies have reported that dietary GL was associated with the risk of diabetes [12, 16], a meta-analysis comparing the highest and lowest GI and GL quintiles showed that the HR for developing diabetes was more highly associated with GI than GL [8]. Thus, dietary GI is a better predictor of the risk of diabetes than is dietary GL.

High GI foods are thought to increase insulin resistance, impair pancreatic B-cell function, and eventually lead to type 2 diabetes [20]. The adverse effects of a high GI diet have been reported to be more evident in overweight or obese people, who, presumably, were insulin resistant at baseline [17, 40]. However, evidence of an effect of insulin resistance on the association between GI and diabetes is inconsistent. Some studies have shown that high GI was associated with a higher relative risk of diabetes in people who had a high BMI [12, 19], whereas other studies have indicated that high GI was more strongly associated with incidence of diabetes in people with a low BMI [9, 15]. These studies used obesity as a marker of insulin resistance, but in our study, insulin resistance was directly measured by HOMA-IR; thus, we were able to compare the association between GI and the incidence of diabetes according to the degree of insulin resistance. We found a significant interaction between GI and HOMA-IR and also found a significant association between GI and the incidence of diabetes only in participants who were in the lowest tertile of HOMA-IR. Insulin resistance is a strong risk factor for type 2 diabetes, and it may be difficult to detect the effect of other risk factors in participants with higher insulin resistance.

In our study, GI and pancreatic B-cell function were independently associated with the incidence of diabetes, and participants with the lowest pancreatic B-cell function and the highest dietary GI were at the highest risk of diabetes. Dietary GI is higher in Asian populations than in Western populations. For example, the present study showed mean GI values of 69.2, which were similar to those previously reported in Japan [10, 14], and higher than the values (range 48–60) reported in US and European studies [15–19]. Furthermore, both obese and lean Asians who have lower B-cell function are at high risk for developing type 2 diabetes [4–6]. Our study indicates that the high prevalence of type 2 diabetes in Asian populations may be explained by high GI diets in people with lower B-cell function. Thus, an evaluation of the risk of type 2 diabetes in Asian people must consider life style and food intake as well as genetic background.

Individuals at high risk for diabetes are encouraged to increase their dietary fiber intake and to eat foods containing whole grains [41]. The consumption of such foods is associated with decreased dietary GI. However, the use of GI is recommended as an additional method for management of diabetes in an ADA position statement [41] and a recommendation of the American Dietetic Association [42] because the effects of lower-GI diets on glucose metabolism were conflicting [42]. In our study, total fiber intake was not associated with the incidence of diabetes. Furthermore, a higher GI was associated with a higher risk for diabetes, despite a lower total energy intake, and there was no association between total energy intake and the incidence of diabetes. The appropriate energy intake of each person is important for maintaining body weight and preventing obesity and diabetes. However, appropriate energy intake is influenced by many factors, including body composition and physical activity. It is difficult to evaluate the association between total energy intake itself with diabetes, and indices of the quality of food intake such as GI, rather than the quantity of food intake, would be more useful for a population approach.

The strengths of this study include a large sample size, foods contributing to the dietary GI that differed from those in US and European populations, and the fact that it was the first study of the relationship between GI and the incidence of diabetes conducted in Japanese men.

Moreover, several previous cohort studies used information collected from self-administered questionnaires, whereas our conclusions are based on more reliable data, obtained from medical examinations and fasting blood glucose and insulin levels, HOMA-IR, and HOMA-B. Additionally, GI and GL were calculated using responses to a validated questionnaire [11]. A limitation of the present study is that the sample included only people who were employed. Poor health may exclude some individuals from working; thus, the prevalence of obesity may be lower in our sample than in the general Japanese population. Another limitation is that we did not measure waist circumference at baseline, which might have provided more information about abdominal fat accumulation and insulin resistance than measuring BMI did. A further limitation of the present study is that we did not determine whether the diabetes that developed was type 1 or type 2. However, the study participants were middle-aged men and, as the condition was detected in an annual medical check-up, with relatively mild diabetes being found, it is most likely that the cases were type 2 diabetes.

In conclusion, our results indicate that dietary GI is associated with the incidence of diabetes in middle-aged Japanese men. Dietary GI and pancreatic B-cell function were independently associated with the incidence of diabetes. Dietary GI is higher and pancreatic B-cell function is lower in Asian people, as compared with Western people, and this may result in a higher prevalence of diabetes in Asian populations. Our findings suggest that a low GI diet may be beneficial in preventing type 2 diabetes mellitus in Asian people.

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Table 1. Baseline characteristics of study participants according to dietary glycemic index quintiles

	Q1 (lowest)	Q2	Q3	Q4	Q5 (highest)	p[b]
Glycemic index	< 66.2	66.2–68.5	68.6–70.4	70.5–72.6	≥ 72.7	
Age(y)	45.7 ± 6.0	46.2 ± 6.0	45.7 ± 6.2	46.0 ± 6.1	46.3 ± 5.8	0.286
Height (cm)	169.7 ± 6.0	169.7 ± 6.1	170.0 ± 5.9	169.3 ± 5.9	169.1 ± 6.1	0.113
Weight (kg)	68.2 ± 9.6	67.5 ± 9.5	67.0 ± 9.0	67.3 ± 9.5	67.3 ± 9.3	0.178
Body mass index (kg/m^2)	23.6 ± 2.9	23.4 ± 2.9	23.1 ± 2.8	23.4 ± 2.8	23.5 ± 2.9	0.541
Total cholesterol (mg/dL)	207.5 ± 34.0	208.6 ± 33.5	208.4 ± 35.1	210.8 ± 33.8	201.9 ± 31.5	0.101
Triglycerides (mg/dL)[a]	106 (68–157)	103 (69–151)	114 (78–168)	103 (66–156)	97 (67–143)	0.073
HDL cholesterol (mg/dL)	57.9 ± 14.9	57.3 ± 13.2	58.7 ± 15.4	57.9 ± 15.1	58.4 ± 14.6	0.522
Fasting plasma glucose (mg/dL)	92.5 ± 10.1	92.8 ± 9.4	92.5 ± 9.6	93.4 ± 10.4	93.0 ± 9.6	0.300
Fasting insulin (µU/mL)[a]	5.1 (3.0–7.3)	4.9 (3.0–7.0)	4.7 (3.0–7.0)	5.0 (3.0–8.0)	4.7 (3.0–7.0)	0.129
HOMA-IR[a]	1.15 (0.73–1.74)	1.10 (0.70–1.67)	1.06 (0.73–1.62)	1.13 (0.69–1.76)	1.07 (0.68–1.53)	0.212
HOMA-B[a]	66.2 (43.5–94.1)	60.9 (40.0–92.8)	60.6 (40.0–90.0)	61.4 (41.5–93.9)	59.6 (39.8–90.0)	0.026
Glycated hemoglobin A1c (%)	5.0 ± 0.4	5.0 ± 0.4	5.0 ± 0.4	5.0 ± 0.5	5.0 ± 0.4	0.954
Systolic blood pressure (mmHg)	120.5 ± 18.0	119.8 ± 17.4	120.4 ± 15.1	121.9 ± 18.8	120.2 ± 20.9	0.668

Diastolic blood pressure (mmHg)	77.9 ± 12.9	76.9 ± 12.1	78.0 ± 11.1	78.6 ± 13.4	77.6 ± 14.6	0.765
Family history of diabetes (%)	13.9	12.6	14.0	14.7	12.2	0.837
Smoking status						0.001
Non-smoker (%)	33.3	32.1	29.7	30.8	28.2	
Ex-smoker (%)	16.2	15.2	14.5	16.4	11.7	
Current smoker (%)	50.5	52.8	55.9	52.7	60.2	
Alcohol intake						0.333
Non-drinker (%)	21.4	24.5	24.4	27.1	21.6	
Light drinker (<20g/day; %)	36.3	34.6	33.7	32.3	30.7	
Moderate/heavy drinker (≥20g/day; %)	42.3	40.9	41.9	40.5	47.7	
Habitual exercise – Yes (%)	33.6	30.8	25.4	25.9	25.1	0.021
Prevalence of high blood pressure[c] (%)	8.7	8.8	6.3	10.4	7.9	0.302
Prevalence of dyslipidemia[c] (%)	10.2	10.1	9.0	9.0	6.6	0.402
Glycemic index	63.4 ± 2.8	67.5 ± 0.7	69.5 ± 0.5	71.5 ± 0.6	74.2 ± 1.3	<0.001
Glycemic load (/1,000 kcal)	76.0 ± 16.2	85.1 ± 15.0	87.7 ± 17.0	92.9 ± 16.6	97.7 ± 19.9	<0.001
Total energy intake (kcal/day)	2383 ± 695	2270 ± 631	2198 ± 586	2096 ± 518	2044 ± 559	<0.001

Total fiber intake (g/1,000 kcal)	5.7 ± 1.5	5.3 ± 1.3	4.9 ± 1.3	4.7 ± 1.2	4.0 ± 1.2	<0.001
Protein (% energy)	12.5 ± 2.3	12.1 ± 2.2	11.6 ± 2.0	11.6 ± 2.0	10.8 ± 2.1	<0.001
Fat (% energy)	24.1 ± 6.7	22.4 ± 6.1	21.6 ± 6.3	20.8 ± 5.9	18.4 ± 6.3	<0.001
Carbohydrates (% energy)	54.9 ±9.1	57.3 ± 8.0	57.3 ± 8.9	58.9 ± 8.2	59.7 ± 9.2	<0.001

Values are mean ± standard deviation or %.

[a]Values are geometric means (interquartile range).

[b]Linear regression was used for continuous variables based on ordinal variables containing the median value for each quintile, and a chi-squared test was used for categorical variables.

[c]High blood pressure and dyslipidemia were defined using the Japanese criteria for metabolic syndrome.

Table 2. Baseline characteristics of study participants according to dietary glycemic load quintiles

	Q1 (lowest)	Q2	Q3	Q4	Q5 (highest)	p[b]
Glycemic load (/1,000 kcal)	< 72.8	72.8–83.1	83.2–91.5	91.6–103.3	≥103.4	
Age(y)	45.4 ± 6.0	46.5 ± 6.0	45.9 ± 6.2	45.9 ± 5.9	46.2 ± 6.1	0.264
Height (cm)	169.7 ± 5.9	169.9 ± 6.0	169.6 ± 5.8	169.4 ± 5.8	169.2 ± 6.4	0.102
Weight (kg)	67.9 ± 9.4	67.8 ± 9.3	67.3 ± 9.6	66.8 ± 8.6	67.4 ± 9.9	0.178
Body mass index (kg/m^2)	23.5 ± 2.8	23.4 ± 2.8	23.3 ± 2.8	23.2 ± 2.8	23.5 ± 3.1	0.650
Total cholesterol (mg/dL)	206.8 ± 33.4	205.8 ± 34.7	206.4 ± 35.2	208.6 ± 31.6	209.8 ± 33.4	0.101
Triglycerides (mg/dL)[a]	108 (69–161)	100 (66–150)	109 (71–160)	99 (67–147)	106 (71–157)	0.772
HDL cholesterol (mg/dL)	61.5 ± 15.5	58.8 ± 13.7	57.3 ± 15.3	57.7 ± 14.5	54.9 ± 13.4	<0.001
Fasting plasma glucose (mg/dL)	93.6 ± 9.9	93.2 ± 9.6	93.1 ± 10.6	92.3 ± 9.7	92.0 ± 9.3	0.010
Fasting insulin (μU/mL)[a]	4.5 (3.0–7.0)	4.8 (3.0–7.0)	5.0 (3.0–7.3)	4.9 (3.0–7.0)	5.1 (3.0–8.0)	0.003
HOMA-IR[a]	1.03 (0.66–1.64)	1.09 (0.69–1.66)	1.14 (0.75–1.76)	1.11 (0.72–1.60)	1.15 (0.73–1.76)	0.015
HOMA-B[a]	55.3 (37.9–81.3)	59.8 (40.0–83.1)	64.1 (44.7–96.0)	63.7 (41.5–93.9)	66.4 (43.2–102.9)	<0.001
Glycated hemoglobin A1c (%)	5.0 ± 0.4	5.0 ± 0.4	5.0 ± 0.4	5.0 ± 0.4	5.0 ± 0.4	0.747
Systolic blood pressure (mmHg)	123.1 ± 16.7	120.6 ± 18.7	121.1 ± 17.6	119.4 ± 17.1	118.6 ± 20.2	<0.001

Diastolic blood pressure (mmHg)	79.9 ± 12.0	78.4 ± 13.4	78.1 ± 12.2	76.5 ± 12.1	76.1 ± 14.3	<0.001
Family history of diabetes (%)	12.0	13.5	16.1	13.8	12.2	0.451
Smoking status						0.021
Non-smoker (%)	23.0	29.9	30.9	34.3	36.1	
Ex-smoker (%)	17.8	15.5	14.6	16.5	9.6	
Current smoker (%)	59.3	54.6	54.5	49.3	54.3	
Alcohol intake						<0.001
Non-drinker (%)	6.5	12.7	16.3	33.3	50.5	
Light drinker (<20g/day; %)	17.5	29.9	42.5	40.8	37.1	
Moderate/heavy drinker (≥20g/day;%)	76.0	57.4	41.2	26.0	12.4	
Habitual exercise – Yes (%)	28.8	31.7	29.4	29.5	21.5	0.018
Prevalence of high blood pressure[c] (%)	11.8	8.0	8.8	7.0	6.6	0.070
Prevalence of dyslipidemia[c] (%)	8.7	7.8	10.1	9.5	8.9	0.833
Glycemic index	67.1 ± 4.7	68.3 ± 3.7	69.2 ± 3.3	70.0 ± 3.3	71.4 ± 3.0	<0.001
Glycemic load (/1,000 kcal)	62.7 ± 8.8	78.0 ± 3.0	87.2 ± 2.5	97.1 ± 3.3	114.4 ± 9.6	<0.001
Total energy intake (kcal/day)	2394 ± 616	2299 ± 581	2183 ± 578	2104 ± 556	2011 ± 653	<0.001

Total fiber intake (g/1,000 kcal)	4.9 ± 1.6	5.1 ± 1.5	5.0 ± 1.3	4.9 ± 1.4	4.6 ± 1.3	0.001
Protein (% energy)	12.7 ± 2.8	12.3 ± 2.1	11.8 ± 1.9	11.5 ± 1.6	10.3 ± 1.6	<0.001
Fat (% energy)	25.7 ± 7.7	23.7 ± 5.7	22.1 ± 5.3	20.1 ± 4.2	15.7 ± 4.4	<0.001
Carbohydrates (% energy)	46.0 ± 5.6	53.3 ± 3.2	57.5 ± 2.8	62.0 ± 2.9	69.4 ± 4.5	<0.001

Values are mean ± standard deviation or %.

[a]Values are geometric means (interquartile range).

[b]Linear regression was used for continuous variables based on ordinal variables containing the median value for each quintile, and a chi-squared test was used for categorical variables.

[c]High blood pressure and dyslipidemia were defined using the Japanese criteria for metabolic syndrome.

Table 3. Adjusted hazard ratio for type 2 diabetes according to quintiles of glycemic index, glycemic load, total energy intake, and total fiber intake in 1,995 Japanese men

	Q1 (lowest)	Q2	Q3	Q4	Q5 (highest)
Glycemic index					
N	402	396	401	402	394
Total person-years	1786	1778	1766	1796	1862
Incident cases (n)	18	28	24	29	34
Rate per 1,000 person-years	10.1	15.7	13.6	16.1	18.3
Adjusted hazard ratio (95% CI) Model 1	1.00 (reference)	1.62 (0.89–2.93)	1.50 (0.81–2.77)	1.68 (0.93–3.03)	1.80 (1.01–3.18)
Adjusted hazard ratio (95% CI) Model 2	1.00 (reference)	1.68 (0.92–3.04)	1.56 (0.84–2.89)	1.73 (0.96–3.13)	1.88 (1.06–3.35)
Adjusted hazard ratio (95% CI) Model 3	1.00 (reference)	1.71 (0.94–3.10)	1.66 (0.89–3.10)	1.86 (1.01–3.44)	1.96 (1.04–3.67)
Glycemic load					
N	400	401	398	400	396
Total person-years	1733	1735	1739	1856	1924
Incident cases (n)	23	26	34	23	27
Rate per 1,000 person-years	13.3	15.0	19.5	12.4	14.0

Adjusted hazard ratio (95% CI) Model 1	1.00 (reference)	1.07 (0.61–1.88)	1.48 (0.87–2.52)	0.95 (0.53–1.70)	0.98 (0.56–1.72)
Adjusted hazard ratio (95% CI) Model 2	1.00 (reference)	1.14 (0.65–2.02)	1.54 (0.89–2.65)	1.07 (0.58–1.96)	1.23 (0.67–2.28)
Adjusted hazard ratio (95% CI) Model 3	1.00 (reference)	1.16 (0.66–2.06)	1.56 (0.89–2.71)	1.07 (0.57–1.99)	1.24 (0.65–2.34)
Total energy intake (range, kcal/day)	(<1,703)	(1,703–1,971)	(1,972–2,246)	(2,247–2,641)	(>2,641)
N	399	399	399	399	399
Total person-years	1,790	1,776	1,748	1,758	1,917
Incident cases (n)	24	24	32	24	26
Rate per 1,000 person-years	13.4	14.6	18.3	14.2	13.6
Adjusted hazard ratio (95% CI) Model 1	1.00 (reference)	1.13 (0.65–1.96)	1.49 (0.88–2.54)	1.11 (0.63–1.95)	1.00 (0.57–1.74)
Adjusted hazard ratio (95% CI) Model 2	1.00 (reference)	1.10 (0.63–1.92)	1.44 (0.84–2.48)	1.06 (0.60–1.87)	0.97 (0.55–1.71)
Adjusted hazard ratio (95% CI) Model 3	1.00 (reference)	1.12 (0.64–1.97)	1.45 (0.84–2.49)	1.07 (0.60–1.91)	0.97 (0.55–1.72)
Total fiber intake (range, g/1,000kcal)	(<3.7)	(3.8–4.5)	(4.6–5.2)	(5.3–6.0)	(>6.0)
N	400	450	391	370	384
Total person-years	1,938	2,016	1,781	1,590	1,663
Incident cases (n)	35	26	17	23	32
Rate per 1,000 person-years	18.1	12.9	9.5	14.5	19.2

Adjusted hazard ratio (95% CI) Model 1	1.00 (reference)	0.73 (0.44–1.22)	0.56 (0.31–1.01)	0.80 (0.47–1.35)	0.99 (0.61–1.60)
Adjusted hazard ratio (95% CI) Model 2	1.00 (reference)	0.73 (0.44–1.23)	0.59 (0.32–1.05)	0.83 (0.48–1.43)	0.98 (0.59–1.64)
Adjusted hazard ratio (95% CI) Model 3	1.00 (reference)	0.72 (0.43–1.21)	0.59 (0.33–1.06)	0.84 (0.49–1.45)	0.99 (0.59–1.66)

Model 1, adjusted for age and body mass index; Model 2, adjusted for age, body mass index, family history of diabetes, smoking, alcohol intake, habitual exercise, and presence of hypertension and hyperlipidemia at baseline; Model 3, adjusted for variables used in Model 2 and dietary total energy (for the glycemic index, glycemic load, and total fiber intake) and dietary total fiber intake (for the glycemic index, glycemic load, and total energy intake).

Table 4. Incidence and adjusted hazard ratios[a] for type 2 diabetes according to glycemic index tertiles of body mass index, HOMA-IR and HOMA-B in 1,995 Japanese men

	Glycemic index tertiles (range)						
	T1 (< 68.0)		T2 (68.0-71.0)		T3 (≥ 71.1)		p for trend[b]
Body mass index (kg/m^2)							
< 22.0							
Incident cases (n)/N	3/203		11/227		15/206		
Crude rate per 1,000 person-years	3.2		10.4		15.1		
Multivariate-adjusted HR (95% CI)	1.00	(reference)	4.09	(1.13-14.9)	5.78	(1.63-20.5)	0.005
22.0-24.9							
Incident cases (n)/N	14/278		14/257		18/272		
Crude rate per 1,000 person-years	11.5		12.4		14.4		
Multivariate-adjusted HR (95% CI)	1.00	(reference)	1.10	(0.52-2.34)	1.20	(0.59-2.44)	0.608
≥25.0							
Incident cases (n)/N	19/196		20/169		19/187		
Crude rate per 1,000 person-years	21.9		28.8		22.5		
Multivariate-adjusted HR (95% CI)	1.00	(reference)	1.41	(0.75-2.66)	1.11	(0.58-2.11)	0.719
HOMA-IR tertiles							
< 0.85							
Incident cases (n)/N	4/217		8/207		16/219		
Crude rate per 1,000 person-years	4.1		8.5		15.4		
Multivariate-adjusted HR (95% CI)	1.00	(reference)	2.07	(0.61-6.95)	3.67	(1.21-11.2)	0.015
0.85-1.43							
Incident cases (n)/N	10/222		9/232		21/240		

Crude rate per 1,000 person-years		10.2		8.6		18.6	
Multivariate-adjusted HR (95% CI)	1.00	(reference)	0.78	(0.31-1.94)	1.58	(0.73-3.41)	0.221
≥ 1.44							
Incident cases (n)/N		22/238		28/214		15/206	
Crude rate per 1,000 person-years		20.5		31.4		16.3	
Multivariate-adjusted HR (95% CI)	1.00	(reference)	1.73	(0.98-3.05)	0.83	(0.43-1.62)	0.472
HOMA-B tertiles							
< 48.4							
Incident cases (n)/N		16/227		23/230		31/226	
Crude rate per 1,000 person-years		16.1		23.0		30.0	
Multivariate-adjusted HR (95% CI)	1.00	(reference)	1.64	(0.86-3.13)	1.86	(1.01-3.44)	0.049
48.4-79.3							
Incident cases (n)/N		10/218		11/205		12/224	
Crude rate per 1,000 person-years		10.3		11.8		11.5	
Multivariate-adjusted HR (95% CI)	1.00	(reference)	1.34	(0.56-3.20)	1.26	(0.53-3.00)	0.600
≥79.4							
Incident cases (n)/N		10/232		11/218		9/215	
Crude rate per 1,000 person-years		9.4		11.6		8.9	
Multivariate-adjusted HR (95% CI)	1.00	(reference)	1.39	(0.58-3.31)	0.93	(0.37-2.34)	0.922

HR, hazard ratio.

[a]Adjusted for age, body mass index, family history of diabetes, smoking, alcohol intake, habitual exercise, and presence of hypertension and hyperlipidemia at baseline.

[b]Linear regression was used for continuous variables based on ordinal variables containing the median value for each glycemic index tertile.

Figure legends

Figure 1. Adjusted hazard ratios for type 2 diabetes by different levels of glycemic index and body mass index (A), HOMA-IR (B), and HOMA-B (C) in 1,995 Japanese men

HRs were adjusted for age, body mass index, family history of diabetes, smoking, alcohol intake, habitual exercise, and presence of hypertension and hyperlipidemia at baseline.

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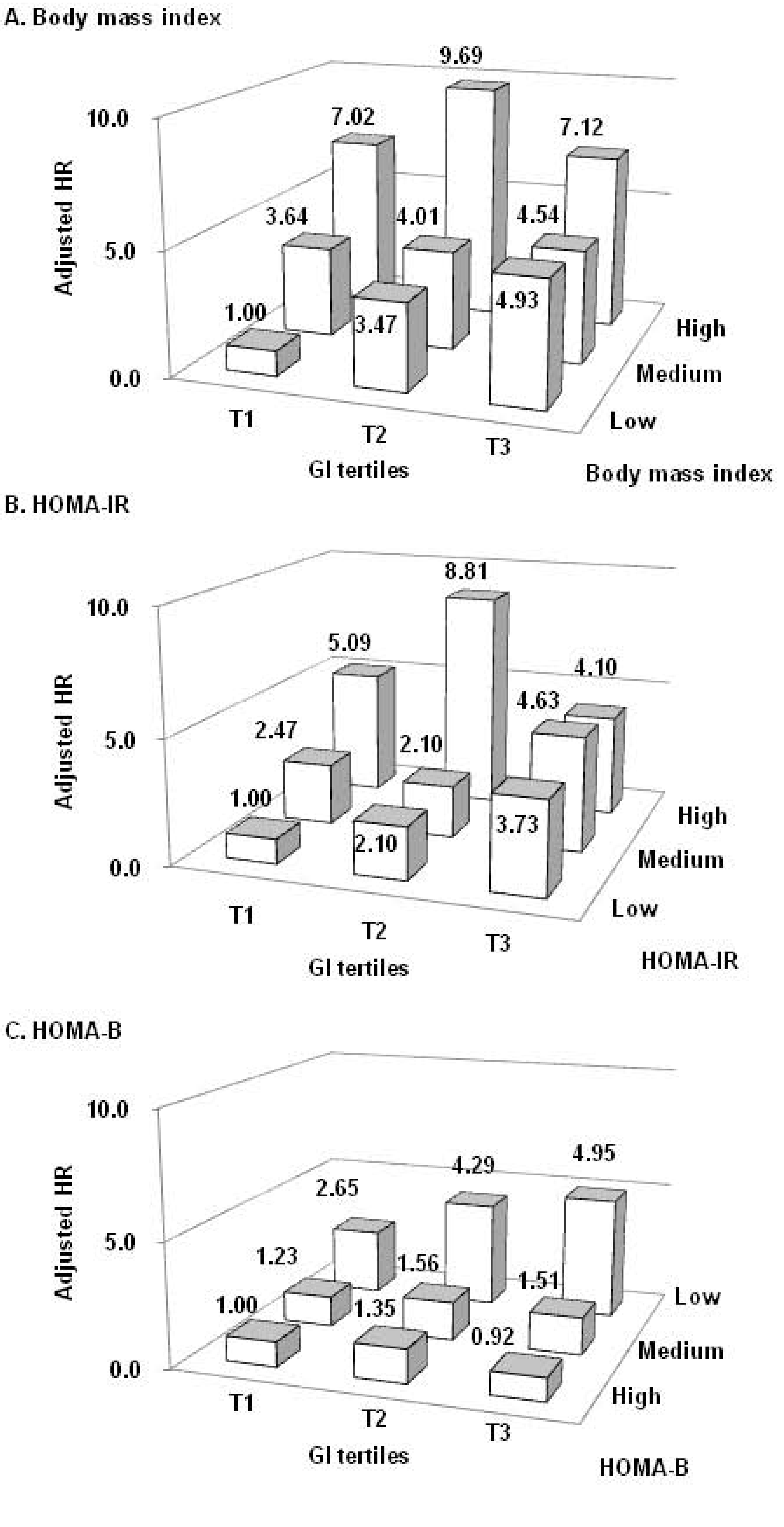
Figure 1.


A. Body mass index
Adjusted HR
10.0
5.0
0.0
9.69
7.02
7.12
3.64
4.01
4.54
1.00
3.47
4.93
High
Medium
Low
T1
T2
T3
GI tertiles
Body mass index
B. HOMA-IR
Adjusted HR
10.0
5.0
0.0
8.81
5.09
4.10
4.63
2.47
2.10
1.00
2.10
3.73
High
Medium
Low
T1
T2
T3
GI tertiles
HOMA-IR
C. HOMA-B
Adjusted HR
10.0
5.0
0.0
4.29
4.95
2.65
1.23
1.56
1.51
1.00
1.35
0.92
Low
Medium
High
T1
T2
T3
GI tertiles
HOMA-B