Dietary survey in Japanese patients with type 2 diabetes and the influence of dietary carbohydrate on glycated hemoglobin: The Sleep and Food Registry in Kanagawa study

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ABSTRACT
Aims/Introduction: The present study investigated the relationship between the macronutrient energy ratio, dietary carbohydrate and glycated hemoglobin levels in Japanese patients with type 2 diabetes, to generate a potential optimal dietary intake of macronutrients for such patients.

Materials and Methods: In total, 3,032 patients participating in the Sleep and Food Registry in Kanagawa study were evaluated. Their diets were assessed for macronutrient content through a brief self-administered dietary history questionnaire. Relevant biochemical assays were carried out.

Results: The mean energy intake (± standard deviation) was 1,711 ± 645 kcal/day. The proportion of energy supplied by protein, fat and carbohydrate were 16.3, 26.8 and 52.3%, respectively. Total fiber intake was 12.6 ± 5.7 g/day. The high glycated hemoglobin (HbA1c) group (HbA1c > 8%) had significantly lower protein and higher carbohydrate intake than the low HbA1c group (HbA1c < 6.5%). Higher HbA1c levels were positively correlated with unfavorable metabolic factors, including elevated body mass index and excess carbohydrate intake, and negatively correlated with age, protein intake and fiber intake. Multiple regression analysis showed a significant association between HbA1c and carbohydrate intake after adjusting for sex, age and body mass index (0.104, P < 0.0001). Additionally, patients within the uppermost tertile for the percentage of total energy intake from carbohydrate (>60%) were more likely to have high HbA1c levels. HbA1c was significantly correlated with carbohydrate (%E) in all age groups and in patients taking one or two antidiabetic drugs.

Conclusions: The dietary carbohydrate-energy ratio has a positive correlation with HbA1c, suggesting that avoiding excessive carbohydrate intake (>60%) might help foster glycemic control.

INTRODUCTION
Dietary therapy plays a central role in diabetes management by preventing its onset, controlling blood glucose and preventing or delaying the onset of complications. One of the goals of nutrition therapy for patients with diabetes is to achieve and maintain blood glucose levels that are normal or as close to normal as possible. Good glycemic control can help to ameliorate or prevent common diabetic complications, such as
myocardial infarction and hypertension. While restriction of energy intake is widely recommended when treating type 2 diabetes mellitus, the optimal macronutrient composition remains debatable, as even intensive calorie intake reduction might not decrease the incidence of cardiovascular events in patients with type 2 diabetes who are overweight or obese. Although some studies have shown that low-carbohydrate diets might influence plasma glucose reduction, weight loss and the serum lipid profile in comparison with diets that are high in carbohydrates and low in fats, there have also been some mixed results. This could explain why some authors question the validity of calorie restriction intervention.

The recommendations of diabetologists, cardiologists and nutritionists regarding the optimal diet for patients with type 2 diabetes differ slightly. It is recommended that fat intake should be between <25 and 35%, and carbohydrate intake between 45% and 60% of the total energy intake. The American Diabetes Association recently noted a lack of ideal calorie intake from various macronutrients in patients with diabetes. This emphasizes the lack of clarity of optimal carbohydrate and protein intake to optimize glycemic control. Hence, it is suggested that assessment of individual dietary choices, patterns and metabolic objectives should determine macronutrient intake. Glycated hemoglobin (HbA1c) is increasingly being used as a biochemical indicator of the efficacy of this individualized assessment.

There are marked differences between dietary patterns in Asian and Western countries as a result of variations in foodstuffs, food composition and nutritional preferences. Many studies show a lower cardiovascular morbidity in Japan than in Western countries, and diet might be partly responsible for this. A survey of Spanish dietary choices reported a low-carbohydrate and high-fat diet. This diet is fairly prevalent in other Western countries, and affords the advantage of increased satiety and spontaneous reduction in energy intake; this might improve glycemic control and reduce hyperinsulinemia. In contrast, the Japan Diabetes Society (JDS) has recommended that patients with diabetes should obtain approximately 50–60% of their calorie intake from carbohydrates, 1.0–1.2 g/kg from protein and the remainder from fat. Few large-scale studies have reported on the food patterns in patients with type 2 diabetes in Asia, including Japan. Hence, the present study seeks to elucidate the diet of selected patients with type 2 diabetes in Japan, and their optimal energy distribution of macronutrients for improved glycemic control.

METHODS
The Sleep and Food Registry in Kanagawa (SOERKA), Japan, forms part of a multicenter prospective study (UMIN Clinical Trial Registry 000014318) aimed at evaluating the effects of modern treatments on the prognoses of patients with diabetes attending teaching hospitals certified by the JDS, or certified diabetes clinics within the Kanagawa Prefecture. To include a diverse array of participants, we randomly selected and registered 4,241 patients with diabetes aged ≥20 years, between July 2014 and March 2016, from 24 urban and rural hospitals and clinics around the city of Kanagawa (listed in the acknowledgements). Exclusion criteria were as follows: (i) drug-induced diabetes or current steroid therapy; (ii) a history of diabetic comaa or ketoacidosis six before the study; (iii) ongoing renal replacement therapy; (iv) ongoing or postsurgical care; (v) ongoing pregnancy or breast-feeding; (vi) comorbid diseases including malignancies and liver cirrhosis; and (vii) at the discretion of attending physicians. In all, 3,511 patients with type 2 diabetes were eligible.

In addition to the brief-type self-administered diet history questionnaire (BDHQ; Gender Medical Research Inc., Tokyo, Japan) completed by 3,116 (89%) patients, laboratory data were gathered for a month. Patients with energy intake <500 or >4,000 kcal/day (considered extremely low and high, respectively) and those without complete laboratory data were excluded. Thus, data of 3,032 patients (1,851 men and 1,181 women) were analyzed.

Ethical consideration
All patients provided informed consent. The study adhered to the 2013 Declaration of Helsinki (institutional ethics committee approval number: 000014318).

Dietary assessment
The BDHQ, evaluating the consumption frequency of 58 food items, was used to carry out the dietary survey. The BDHQ is a version of the diet history questionnaire used to assess dietary intake for a month. The diet history questionnaire comprises a 22-page semiquantitative questionnaire (estimated completion time: 30–40 min), and uses self-reported consumption frequency and portion proportions of 150 food-related items to evaluate dietary intake. The BDHQ is a four-page fixed-por-

Blood sampling and biochemical analysis
The plasma glucose level was measured by the glucose oxidase method; total serum cholesterol, triglycerides and high-density lipoprotein cholesterol, by enzymatic methods; and HbA1c, by high-performance liquid chromatography with low-density lipoprotein cholesterol measurement using a Cholestest®LDL kit (Sekisui Medical Co., Osaka, Japan), all at SRL Inc. The simplified Modification of Diet in Renal Disease equation was used for the estimated glomerular filtration rate. Urine albumin concentration was measured using an immunoturbidimetric
method (N-assay TIA MicroAlb; Nittobo Medical, Tokyo, Japan), while the urine albumin : creatinine ratio was measured on a spot urine specimen collected between the morning and afternoon.

Statistical analysis
Statistical analyses were carried out using SPSS for Windows (version 24.0; IBM Corporation, Armonk, New York, USA). The results are expressed as mean ± standard deviation and as numbers with percentages. Either ANOVA or the χ²-test was used to determine differences in mean values and proportions of the participants’ characteristics. One-way ANOVA and the Tukey multiple comparison method or Bonferroni correction were used for comparisons amongst three or more categories. The dietary intake of the relevant macronutrients was divided into arbitrary groups to show the cut-off points based on different nutritional recommendations; that is, total carbohydrate intake of <45, 45–50, 50–55, 55–60 or ≥60%. To identify factors that were independently correlated with HbA1c, univariate and multivariate linear regression analyses were carried out. HbA1c was the dependent variable, and age, sex, body mass index (BMI), energy kcal/day, energy intake, animal % energy, plant % energy, fat % energy, animal % energy, plant % energy, carbohydrate % energy, fiber % energy, the use of insulin and use of antidiabetic drugs were independent variables. Univariate analysis was carried out first, and all the variables that satisfied P < 0.05 were entered en bloc in the multivariate analyses, with age, sex, BMI and energy (kcal/day) as background variables. All independent variables in the multiple linear regression analysis were tested for multicollinearity. If the variance inflation factor exceeded 2.5, the variable was considered collinear. Statistical significance was based on a two-sided P-value <0.05.

RESULTS
General characteristics
Table 1 presents the baseline characteristics of the 3,032 patients, stratified by sex. The mean age was 63.2 ± 11.9 years for women and 62.9 ± 11.7 years for men. Mean BMI of the participants was 25.3 ± 4.7 and mean HbA1c was 7.5 ± 1.6, with

| Table 1 | Characteristics of patients and dietary composition |
|---------|-----------------------------------------------|
|         | Total | Male | Female | P-value |
|         |       |      |        |         |
| n       | 3,032 | 1,851 | 1,181  |         |
| Age (years) | 63.2 ± 11.8 | 62.9 ± 11.9 | 63.7 ± 11.9 | 0.06 |
| Bodyweight (kg) | 66.9 ± 25.4 | 71.0 ± 148 | 60.6 ± 14.1 | 0.00 |
| BMI (kg/m²) | 25.3 ± 4.7 | 25.1 ± 4.4 | 25.5 ± 5.2 | 0.06 |
| HbA1c (%) | 7.5 ± 1.6 | 7.5 ± 1.7 | 7.5 ± 1.5 | 0.92 |
| Total cholesterol (mmol/L) | 4.8 ± 1.0 | 4.7 ± 1.0 | 5.0 ± 1.0 | <0.001 |
| TG (mmol/L) | 1.8 ± 1.4 | 1.8 ± 1.4 | 1.7 ± 1.4 | 0.02 |
| HDL-C (mmol/L) | 1.4 ± 0.4 | 1.3 ± 0.4 | 1.5 ± 0.4 | 0.001 |
| OHA use (%) | 80.1 | 80.0 | 80.0 | 0.57 |
| Insulin use (%) | 25.9 | 26.9 | 24.6 | |
| Hypertension (%) | 62 | 62 | 61 | 0.05 |
| Dyslipidemia (%) | 74 | 71 | 78 | <0.001 |
| eGFR (ml/min/1.73 m²) | 713 ± 225 | 707 ± 221 | 722 ± 23.1 | 0.032 |
| Energy (kcal) | 1,711.8 ± 649.7 | 1,844.1 ± 6580 | 1,507.9 ± 5790 | <0.001 |
| Protein (g/day) | 69.2 ± 30.2 | 72.3 ± 31.0 | 64.6 ± 28.2 | <0.001 |
| Protein (%E) | 163.3 ± 3.6 | 157.3 ± 3.4 | 172.3 ± 3.7 | <0.001 |
| Fat (g/day) | 51.0 ± 23.1 | 54.0 ± 242 | 46.5 ± 20.7 | <0.001 |
| Fat (%E) | 268.6 ± 64 | 263.6 ± 64 | 273.6 ± 61 | <0.001 |
| Carbohydrate (g/day) | 222.0 ± 87.9 | 236.7 ± 90.5 | 199.4 ± 78.7 | <0.001 |
| Carbohydrate (%E) | 52.3 ± 9.2 | 51.8 ± 9.7 | 52.3 ± 8.3 | <0.001 |
| Animal protein (g/day) | 40.8 ± 23.2 | 42.6 ± 24.3 | 38.2 ± 21.4 | <0.001 |
| Plant protein (g/day) | 28.4 ± 10.6 | 29.7 ± 10.8 | 26.4 ± 10.0 | <0.001 |
| Animal fat (g/day) | 24.3 ± 13.5 | 25.7 ± 14.2 | 22.3 ± 12.0 | <0.001 |
| Plant fat (g/day) | 26.7 ± 12.1 | 28.3 ± 12.5 | 24.2 ± 11.0 | <0.001 |
| Total fiber (g/day) | 126.5 ± 5.7 | 125.5 ± 5.7 | 127.5 ± 5.6 | 0.55 |
| Total fiber (%E) | 0.76 ± 0.29 | 0.70 ± 0.26 | 0.86 ± 0.30 | <0.001 |
| SDF (g/day) | 3.1 ± 1.5 | 3.1 ± 1.5 | 3.2 ± 1.5 | 0.37 |
| IDF (g/day) | 9.0 ± 3.9 | 9.0 ± 4.0 | 9.0 ± 3.9 | 0.90 |

Data are presented as the mean ± standard deviation or number (%). The χ²-test and t-test were carried out to evaluate sex-stratified significant differences. BMI, body mass index; E, energy; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; IDF, insoluble dietary fiber; OHA, oral hypoglycemic agent; SDF, soluble dietary fiber; TG, triglycerides.
which was slightly higher than the target of <7.0% recommended by the JDS.

**Dietary characteristics**

The mean daily energy intake of all participants was 1,711.8 ± 649.7 kcal/day, comprising 1,844.1 ± 658.0 kcal/day in men, and 1,507.9 ± 579.0 kcal/day in women. This was lower than the daily intake of the general population. The mean proportions of total energy intake accounted for by protein, fat and carbohydrates were 16.3, 26.8 and 52.3%, respectively.

Intake of all macronutrients was higher in women than in men, suggesting that intake of other nutrients was higher in men. The percentage of energy obtained from animal and plant protein, as well as from animal and plant fat, was higher in men compared with women. Total fiber intake was 12.6 g/day, which was lower than the recommended value.

**Associations between diet and HbA1c**

Using the glycemic levels as indicated by HbA1c, the participants were divided into five groups (Table 2). Compared with the low HbA1c group (HbA1c <6.5%), total energy intake was significantly greater in the high HbA1c group (HbA1c >8%), but not significantly different from that in the moderate HbA1c group (HbA1c 6.5–8%). In the high HbA1c group, a significantly lower percentage of total energy intake (%E) was derived from protein compared with that of the low HbA1c group (HbA1c <7.5%), while intake of carbohydrate was higher. Intake of fiber was also significantly lower in the high HbA1c group. There was a significant positive correlation between HbA1c and unfavorable metabolic factors by the univariate linear regression analysis, whereas HbA1c was negatively correlated with age, protein (%E) and fiber intake. Fat intake (%E), including animal and plant fat, was not associated with HbA1c.

We carried out investigations regarding the presence of therapeutic agents. Although the presence of oral hypoglycemic drugs did not show a correlation, insulin use was observed to be correlated with HbA1c. As shown in Table 3, the correlation of HbA1c with carbohydrate (%E) was significant after adjusting for sex, age, energy intake and BMI (β = 0.104, P < 0.0001).

To investigate the effect of age and use of antidiabetic drugs on the association between carbohydrate (%E) and HbA1c, participants were stratified by age and use of antidiabetic drugs. Univariate and multivariate regression analyses were carried out. As shown in Table 2, HbA1c was significantly correlated with carbohydrate (%E) in all age groups (<55, 55–65, >65 years) and in participants taking one or two antidiabetic drugs. This correlation was absent in participants taking more than three antidiabetic drugs.

**Carbohydrate intake and HbA1c**

Based on the percentage of the participants’ total energy intake (%E) from carbohydrates, five groups were defined, namely (C1: <45%, C2: 45% to <50%, C3: 50% to <55%, C4: 55% to <60% and C5: ≥60%). The relationship between carbohydrate (%E) and HbA1c suggested that increasing carbohydrate intake from 45% to 60% significantly elevate HbA1c (Figure 1).

### Table 2 | Distribution of nutritional intake according to glycated hemoglobin

| HbA1c (<6.5%) | HbA1c 6.5–7.0% | HbA1c 7.0–7.5% | HbA1c 7.5–8.0% | HbA1c >8.0% | Total |
|---------------|----------------|----------------|----------------|------------|-------|
| n             | 616            | 729            | 597            | 339        | 751   | 3,032 |
| Age (years)   | 16.3 ± 11.1    | 164 ± 11.2     | 165 ± 10.6     | 164 ± 11.4 | 164 ± 11.4 | 169 ± 11.9 |
| BMI (kg/m²)   | 24.6 ± 4.7     | 24.5 ± 4.4     | 25.1 ± 4.3     | 25.7 ± 4.6 | 26.7 ± 4.6 | 25.3 ± 4.7 |
| Nutritional intake |            |                |                |            |        |       |
| Energy (kcal/day) | 1,636 ± 599 | 1,719 ± 611    | 1,732 ± 644    | 1,706 ± 630| 1,767 ± 630| 1,715 ± 647 |
| Protein (g/day)  | 67.2 ± 27.9    | 70.7 ± 31.0    | 71.2 ± 31.3    | 690 ± 27.3 | 686 ± 30.7 | 694 ± 30.0 |
| %Energy         | 166 ± 3.8      | 165 ± 3.5      | 164 ± 3.5      | 164 ± 3.5 | 158 ± 3.7 † | 163 ± 3.6 |
| Fat (g/day)     | 48.4 ± 20.8    | 52.1 ± 22.6    | 52.1 ± 23.8    | 503 ± 21.6 | 519 ± 24.7 | 511 ± 23.0 |
| %Energy         | 26.7 ± 6.3     | 27.3 ± 6.2     | 27.0 ± 6.5     | 265 ± 60  | 265 ± 66  | 268 ± 64  |
| Carbohydrate (g/day) | 2,093 ± 798 | 2,198 ± 804    | 2,227 ± 844    | 2,249 ± 872| 2,345 ± 101.7| 2,224 ± 879 |
| %Energy         | 51.7 ± 9.6     | 51.6 ± 9.1     | 52.1 ± 9.2     | 530 ± 83  | 534 ± 92 †‡ | 523 ± 92 |
| Animal Protein (g/day) | 39.8 ± 21.6 | 42.1 ± 24.8    | 42.4 ± 24.2    | 399 ± 20.5| 400 ± 23.2 | 409 ± 23.2 |
| Plant Protein (g/day) | 27.5 ± 10.1 | 28.6 ± 10.0    | 28.8 ± 10.5    | 29.1 ± 10.5| 28.5 ± 11.5 | 28.5 ± 10.6 |
| Animal fat (g/day) | 22.8 ± 11.9 | 24.9 ± 13.9    | 25.0 ± 13.9    | 238 ± 12.5| 249 ± 14.0 | 244 ± 13.4 |
| Plant fat (g/day) | 25.5 ± 11.4    | 27.2 ± 11.5    | 27.1 ± 12.1    | 264 ± 11.4| 270 ± 13.3 | 267 ± 12.0 |
| Fiber (g/day)   | 12.6 ± 5.9     | 13.0 ± 5.4     | 12.8 ± 5.7     | 12.7 ± 5.7 | 12.1 ± 5.5 | 12.6 ± 5.6 |
| Fiber (%E)      | 0.79 ± 0.32    | 0.78 ± 0.28    | 0.76 ± 0.27    | 0.72 ± 0.28| 0.76 ± 0.29| 0.76 ± 0.29 |
| SDF (g/day)     | 3.2 ± 1.6      | 3.3 ± 1.5      | 3.2 ± 1.5      | 3.2 ± 1.5 | 3.0 ± 1.5 †‡ | 3.1 ± 1.5 |
| IDF (g/day)     | 9.0 ± 4.1      | 9.3 ± 3.8      | 9.2 ± 4.0      | 9.1 ± 4.0 | 8.6 ± 3.8 †‡ | 9.0 ± 3.9 |

*P < 0.01 versus glycated hemoglobin (HbA1c) <6.5%; † versus 6.5–7.0%; ‡ versus 7.0–7.5%; ‡ versus 7.5–8%; § Tukey honest significant difference and Bonferroni correction. BMI, body mass index; E, energy; IDF, insoluble dietary fiber; SDF, Soluble dietary fiber.
The influence of meals, with varying portions of fat and carbohydrates, on glycemic control in Japanese patients with type 2 diabetes has not been elucidated. The present study examined the relationships amongst macronutrients and calorie intake and HbA1c in these patients. The present data showed that the mean proportions of total energy intake supplied by protein, fat and carbohydrates were 16.3, 26.8 and 52.3%, respectively. The carbohydrate : energy ratio positively correlated with HbA1c levels. Higher HbA1c in patients with >60% carbohydrate intake suggested that in average Japanese patients with type 2 diabetes, the %E supplied by carbohydrates should be <60%.

Some dietary surveys show that patients with type 2 diabetes obtain approximately 45% of their calories from carbohydrates, 36–40% from fat and the remaining 16–18% from protein. However, most (if not all) of these studies have been carried out in Western countries. It is known that various characteristics of diabetes, especially insulin secretion and resistance, differ between Western and Asian countries. Thus, dietary investigation of Japanese patients with type 2 diabetes is relevant, especially considering the paucity of data in the literature. Japanese-specific studies have previously shown the national dietary profile of patients with type 2 diabetes, identifying considerable differences between Japanese and Western patients. However, these studies are 15–20 years old. As dietary trends tend to change over time, the present study might help clarify the contemporary dietary patterns of Japanese patients with type 2 diabetes. It might also show differences between the current and earlier trends.

The National Health and Nutrition Survey reported that energy intake in men and women (aged 60–69 years) were 2,213 and 1,719 kcal/day, respectively. Patients in the SOREKA study had energy-restricted diets, with a reduction of 400 kcal/day for men and 200 kcal/day women, when compared with the general Japanese population. The present study showed that the mean proportions of total energy intake by protein, fat and carbohydrates were 16.3, 26.8 and 52.3%, respectively. This indicates that Japanese patients might be consuming diets that are low in fat and high in carbohydrate, compared with their Western counterparts.

However, carbohydrate consumption was lower and fat consumption was higher in these patients compared with other Asian patients. Additionally, the total energy intake accounted for by carbohydrates and proteins were 53.6 and 15.7%, respectively, in the Japan Diabetes Complications Study (JDCS), and 59 and 15.2%, respectively, in the Japanese Elderly Diabetes Intervention Trial (J-EDIT). This shows a decreased carbohydrate and increased protein intake compared with previous Japanese studies. The JDS recommends that patients with diabetes should derive approximately 50–60% of their calories...
from carbohydrates, 20% from protein and the remaining 20–30% from fat. However, the reason for the decline in carbohydrate intake despite most patients being on standard nutrition therapy based on the JDS recommendation is unclear. This might be partly due to the progressive Westernization of diet and lifestyle in Asia. It might also relate to recommendations for a low-carbohydrate diet in patients with diabetes by several diabetes associations. For example, the American Diabetes Association has reported on the effectiveness of such a diet for regulating blood glucose. Finally, low-carbohydrate diets have recently become popular in Japan, and patients might have spontaneously reduced their carbohydrate intake.

The current study investigated the parameters that could shape poor control of HbA1c, and to our knowledge, might be the first to evaluate the dietary pattern in a large cohort of patients with type 2 diabetes in Japan, and to explore the association of variations in dietary fat and carbohydrate intake with glycemic control in real-world clinical practice. As expected, the results of the present study showed a significant positive association between higher calorie intake and increased HbA1c, even after adjustment for total energy intake. A previous cross-sectional Korean study and two prospective studies obtained similar results, though the sample sizes were small. In contrast, both JDCS and J-EDIT found no correlation between the carbohydrate energy ratio and HbA1c. This discrepancy might be due to the use of different methods for dietary intake assessment. For instance, the food frequency questionnaire of Horigawa et al. was used in the JDCS and J-EDIT studies; however, BDHQ was used in the present study. The food frequency questionnaire assesses average weekly intake, whereas the BDHQ determines monthly intake and thus might reflect long-term dietary patterns. Furthermore, carbohydrates accounted for 55–65% of total energy intake in most patients in the J-EDIT study, and this narrow distribution of %E provides some insight into the lack of correlation between carbohydrate consumption and HbA1c. However, Mayer et al. reported that lowering dietary carbohydrate intake might foster glycemic control beyond its weight loss effects.

Carbohydrate intake is known to induce postprandial hyperglycemia. Most studies have confirmed that the total carbohydrate intake from snacks and meals is a consistent predictor of postprandial glucose, in both single-meal and mixed-meal studies. However, a consideration of both the quality and the quantity of dietary carbohydrate offers further insight. Carbohydrates comprise starch, sugar and fiber. Intake of fiber improves glycemic control by slowing the release and absorption of macronutrients due to increased intraluminal viscosity. Consistent with this pattern, Perfect et al. reported that increased consumption of dietary fiber enhanced fasting plasma glucose and HbA1c in a randomized cross-over study of patients with type 2 diabetes. The current study showed a slightly lower fiber consumption than that in the JDCS (14.7 g/day), Western patients (11.4–20.5 g/day) and general population of Japan (14.3 g/day). Fiber consumption was also lower in the group with high HbA1c (HbA1c >8%) compared with the group with good glycemic control (HbA1c <7.5%), suggesting that the high HbA1c group had an increased intake of non-fiber carbohydrates.

Fat and protein intake were not associated with glycemic control (Table 3), as previously reported. This might result from the fact that although high-fat and high-protein diets induce late sustained hyperglycemia, the intake of fat in the present study was lower than in Western countries. The influence of protein intake on glycemic control is complex. Some studies have reported deleterious metabolic sequela as a result of high protein intake, because acute intravenous infusion of amino acids and acute protein intake reportedly reduce insulin sensitivity, whereas a diet that is high in protein might cause insulin resistance and an increased risk of diabetes. However, the high HbA1c group had a relatively low protein intake, and there was no clear association between protein intake and HbA1c in the present study. Although the data generated in the present study show no significant relationship between fat intake and protein intake and glycemic control, additional studies should shed more biological insights on the relationship between these biological variables.

A review of the nutritional management of diabetes found that HbA1c decreased with a low-carbohydrate diet in six of the 10 studies in which it was measured. In contrast, three randomized control trials found no significant changes of HbA1c with a very low-carbohydrate diet. Another randomized control trial reported no difference with a moderately low-carbohydrate diet. Considered together, these pieces of information suggest that the role of diets that are low in carbohydrates on HbA1c remains inconclusive. In the present study, obtaining >60% of the total energy intake from carbohydrates tended to have a negative effect on glycemic control. However, the lower limit of carbohydrate intake could not be determined. To determine the optimal percentage of total energy intake as carbohydrates for patients with type 2 diabetes in Asia, a prospective observational study investigating the relationship between carbohydrate intake and glycemic control is required.

The present study had some merits. First, the participants were average Japanese patients with type 2 diabetes, which allows some measure of generalization for clinical management. Second, the study used a relatively large patient population size, further enhancing the generalizability. However, the study had some attendant limitations. First, quantitative and qualitative examination of carbohydrate intake based on measures such as the glycemic index or glycemic load or the types of grains ingested were not investigated. Second, some inaccuracy could have been introduced into the data based on the use of a self-reported questionnaire. Third, information about adherence to medications for diabetes, hypertension and dyslipidemia was not obtained. Fourth, by including patients who were taking medication during the study, the effects of diet could not be completely separated from those of medication. In order to eliminate these interferences by confounders, we carried out
multivariate linear regression analyses and subsequently showed a positive association thereto. We also stratified participants by age and use of antidiabetic drugs, and established a positive association between carbohydrate (%E) and HbA1c level. However, it is difficult to remove interference completely. Being a cross-sectional study, establishing a causal relationship between carbohydrate intake and glycemic control was not also possible.

In conclusion, the present study shows that the carbohydrate : energy ratio has a positive correlation with HbA1c levels, and that the percentage of total energy intake from carbohydrates should probably be <60% in patients with type 2 diabetes in Japan, though its lower limit could not be determined. Nevertheless, these data reiterate the need for patients with diabetes to avoid excessive carbohydrate consumption to maintain suitable glycemic control.

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