JDI Journal of Diabetes Investigation Open access
Official Journal of the Asian Association for the Study of Diabetes
ORIGINAL ARTICLE

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

Tadashi Yamakawa[1]*, Rika Sakamoto[1], Kenichiro Takahashi[1], Jun Suzuki[1], Minori Matuura-Shinoda[1], Mayumi Takahashi[1], Erina Shigematsu[2], Shunichi Tanaka[3], Mizuki Kaneshiro[4], Taro Asakura[4], Takehiro Kawata[5], Yoshihiko Yamada[6], Uru Nezu Osada[7], Tetsuo Isozaki[8], Atsushi Takahashi[9], Kazuaki Kadonosono[10], Yasuo Terauchi[11]

[1]Department of Endocrinology and Diabetes, Yokohama City University Medical Center, [2]Department of Endocrinology and Metabolism, Yokohama Medical Center, [3]Department of Medicine, Kanazawa Medical Clinic, Yokohama, [4]Kaneshiro Medical Clinic, Sagamihara, [5]Idogaya Kens Clinic, Yokohama, [6]International University of Health and Welfare, Atami Hospital, Atami, [7]Saiseikai Yokohama Nanbu Hospital, Yokohama, [8]Koiso Clinic, Yokosuka, [9]Takahashi Medical Clinic, Fujisawa, [10]Department of Ophthalmology, Yokohama City University Medical Center, and [11]Department of Endocrinology and Metabolism, Yokohama City University School of Medicine, Yokohama, Japan

Keywords
Dietary carbohydrate, Glycated hemoglobin, Type 2 diabetes

***Correspondence**
Tadashi Yamakawa
Tel.: +81-45-261-5656
Fax: +81-45-253-5715
E-mail address:
yamakat@yokohama-cu.ac.jp

J Diabetes Investig 2019; 10: 309–317

doi: 10.1111/jdi.12903

Clinical Trial Registry
University Hospital Medical Information Network Clinical Trial Registry
UMIN000014318

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 most 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[1]. Good glycemic control can help to ameliorate or prevent common diabetic complications, such as

Received 19 March 2018; revised 27 July 2018; accepted 29 July 2018

myocardial infarction and hypertension[2]. While restriction of energy intake is widely recommended when treating type 2 diabetes mellitus[3], 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[4]. 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,[5–7] there have also been some mixed results[8]. This could explain why some authors question the validity of calorie restriction intervention[9].

The recommendations of diabetologists, cardiologists and nutritionists regarding the optimal diet for patients with type 2 diabetes differ slightly[10–12]. It is recommended that fat intake should be between <25 and 35%, and carbohydrate intake between 45% and 60% of the total energy intake[13]. 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[14]. Hence, it is suggested that assessment of individual dietary choices, patterns and metabolic objectives should determine macronutrient intake[15]. Glycated hemoglobin (HbA1c) is increasingly being used as a biochemical indicator of the efficacy of this individualized assessment[16–18].

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[19]. 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[20]. 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[21]. Few large-scale studies have reported on the food patterns in patients with type 2 diabetes in Asia, including Japan[22,23]. 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 (SOREKA), 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 coma 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[6]. 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[24,25] to evaluate dietary intake. The BDHQ is a four-page fixed-portion questionnaire (estimated completion time 10–15 min) that evaluates dietary intake using self-reported consumption frequency of 58 food-related items. Dietary intake can be estimated using a purpose-built computer algorithm based on the Standard Tables of Food Composition in Japan[26]. The value of each item was energy-adjusted by density methods (g/1,000 kcal) in each patient. Previous studies have reported on the validity of ranking the energy-adjusted intake of different nutrients in an adult Japanese population[27].

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 χ^2-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 multivariable 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%,

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 ± 14.8	60.6 ± 14.1	0.00
BMI (kg/m^2)	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	
Insulin use (%)	25.9	26.9	24.6	
Hypertension (%)	62	62	61	0.57
Dyslipidemia (%)	74	71	78	<0.001
eGFR (mL/min/1.73 m^2) Composition of diet	71.3 ± 22.5	70.7 ± 22.1	72.2 ± 23.1	0.032
Energy (kcal)	1,711.8 ± 649.7	1,844.1 ± 658.0	1,507.9 ± 579.0	<0.001
Protein (g/day)	69.2 ± 30.2	72.3 ± 31.0	64.6 ± 28.2	<0.001
Protein (%E)	16.3 ± 3.6	15.7 ± 3.4	17.2 ± 3.7	<0.001
Fat (g/day)	51.0 ± 23.1	54.0 ± 24.2	46.5 ± 20.7	<0.001
Fat (%E)	26.8 ± 6.4	26.3 ± 6.4	27.7 ± 6.1	<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)	12.6 ± 5.7	12.5 ± 5.7	12.7 ± 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 χ^2-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[28]. 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[13].

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 ($\beta = 0.104$, $P < 0.0001$).

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 4, 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% might 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)	63.5 ± 11.1	64.4 ± 11.2	65.5 ± 10.6	64.6 ± 11.4	58.9 ± 13.2†,‡,§,¶	63.1 ± 11.9
BMI (kg/m^2)	24.6 ± 4.7	24.5 ± 4.4	25.1 ± 4.3	25.7 ± 4.6†,‡	26.7 ± 5.2†,‡,§,¶	25.3 ± 4.7
Nutritional intake						
Energy (kcal/day)	1,636 ± 599	1,719 ± 611	1,732 ± 644	1,706 ± 630	1,767 ± 717	1,715 ± 647
Protein (g/day)	67.2 ± 27.9	70.7 ± 31.0	71.2 ± 31.3	69.0 ± 27.3	68.6 ± 30.7	69.4 ± 30.0
%Energy	16.6 ± 3.8	16.5 ± 3.5	16.4 ± 3.5	16.4 ± 3.5	15.8 ± 3.7†	16.3 ± 3.6
Fat (g/day)	48.4 ± 20.8	52.1 ± 22.6	52.1 ± 23.8	50.3 ± 21.6	51.9 ± 24.7	51.1 ± 23.0
%Energy	26.7 ± 6.3	27.3 ± 6.2	27.0 ± 6.5	26.5 ± 6.0	26.5 ± 6.6	26.8 ± 6.4
Carbohydrate (g/day)	209.3 ± 79.8	219.8 ± 80.4	222.7 ± 84.4	224.9 ± 87.2	234.5 ± 101.7	222.4 ± 87.9
%Energy	51.7 ± 9.6	51.6 ± 9.1	52.1 ± 9.2	53.0 ± 8.3	53.4 ± 9.2†,‡	52.3 ± 9.2
Animal Protein (g/day)	39.8 ± 21.6	42.1 ± 24.8	42.4 ± 24.2	39.9 ± 20.5	40.0 ± 23.2	40.9 ± 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	23.8 ± 12.5	24.9 ± 14.0	24.4 ± 13.4
Plant fat (g/day)	25.5 ± 11.4	27.2 ± 11.5	27.1 ± 12.1	26.4 ± 11.4	27.0 ± 13.3	26.7 ± 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	0.77 ± 0.28	0.72 ± 0.28	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.

Table 3 | Univariate and multivariate linear regression analyses

	Univariate		Multivariate		VIF
	β	*P*	β	*P*	
Age (years)	−0.188	<0.001	−0.164	<0.001	1.164
Sex	0.020	0.24			1.078
BMI (kg/m^2)	0.121	<0.001	0.048	0.009	1.255
Energy (kcal/day)	0.089	<0.001	0.122	<0.0001	1.141
Protein %Energy	−0.102	<0.001	0.023	.491	1.516
Animal %Energy	−0.038	0.035	0.018	0.58	1.89
Plant % Energy	0.038	0.035	−0.042	.085	1.89
Fat %Energy	−0.035	0.056			
Animal %Energy	0035	0.051			
Plant % Energy	−0.035	0.051			
Carbohydrate %Energy	0.093	<0.001	0.092	<0.0001	1.023
Fiber %Energy	−0.113	<0.001	−0.037	0.051	1.234
Use of antidiabetic drug	−0.032	0.065			
Use of insulin	0.26	<0.001	0.254	<0.0001	1.010

Adjusted for age, sex and body mass index (BMI). VIF, variance inflation factor.

Table 4 | Effect of age and antidiabetic drug use on carbohydrate (%E) and Glycated hemoglobin association

	Univariate		Multivariate		VIF
	β	*P*	β	*P*	
Age (years)					
<55	0.117	0.001	0.114	0.002	0.992
55–65	0.138	<0.001	0.134	<0.001	1.01
>65	0.54	0.039	0.053	0.045	1.006
Use of antidiabetic drug					
0 or 1	0.077	0.03	0.074	0.004	1.007
2	0.137	<0.001	0.137	<0.001	1.002
>3	0.066	0.072			

Adjusted for sex and body mass index. VIF, variance inflation factor.

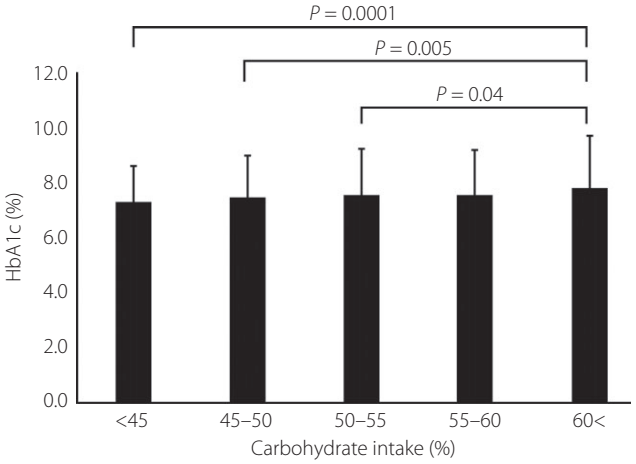

Figure 1 | The relationship between carbohydrate (%E) and glycated hemoglobin (HbA1c).

DISCUSSION

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[29–31]. 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[32,33]. 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[22,23]. However, these studies[32,33] 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[28] reported that energy intake in men and women (aged 60–69 years) were 2,213 and 1,719 kcal/day, respectively.[10]

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[19,34]. However, carbohydrate consumption was lower and fat consumption was higher in these patients compared with other Asian patients[35]. 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)[22,23]. 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[15]. 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[36] and two prospective studies[37,38] 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[22,23]. This discrepancy might be due to the use of different methods for dietary intake assessment. For instance, the food frequency questionnaire of Horikawa *et al.*[22] 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.*[16] 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[39]. 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[40,41]. Consistent with this pattern, Perfect *et al.*[42] 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)[19,34,43] and general population of Japan (14.3 g/day)[23]. 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[42]. This might result from the fact that although high-fat and high-protein diets induce late sustained hyperglycemia,[44] 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[45,46], whereas a diet that is high in protein might cause insulin resistance and an increased risk of diabetes[47,48]. 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[42] 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[49–51]. Another randomized control trial reported no difference with a moderately low-carbohydrate diet[52]. 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.

ACKNOWLEDGMENTS

This study was supported by Grants-in-Aid [17K09841] from the Ministry of Health, Labor and Welfare, Health and Labor Sciences Research Grants, Japan. Mrs Yamagiwa, Mrs Morimoto and Mrs Seki provided administrative assistance. Members of the Japan Epidemiology Collaboration on Occupational Health Study Group are: R Sakamoto, K Takahashi, M Matsura-Shinoda, J Nagakura, J Suzuki, T Masutani, M Takahashi, E Nara and H Ohki, Yokohama City University Medical Center, Yokohama, Japan; M Waseda, Waseda Medical Clinic, Fujisawa, Japan; K Danno and S-I Tanaka, Kanazawa Medical Clinic, Yokohama, Japan; H Tuchiya, Yokosuka City Hospital, Yokosuka, Japan; T Takano, Fujisawa City Hospital, Fujisawa, Japan; E Shigematsu, Yokohama Medical Center, Yokohama, Japan; J Nagakura, Yata Ikeda Clinic, Mishima, Japan; Y Okamoto, Seikyo Totsuka Clinic, Yokohama, Japan; M Takai, Takai Medical Clinic, Kamakura, Japan; F Minagawa, Minagawa Medical Clinic, Yokohama, Japan; M Ishikawa, Ishikawa Medical Clinic, Yokohama, Japan; M Kaneshiro and T Asakura, Kaneshiro Medical Clinic, Sagamihara, Japan; T Isozaki, Koiso Clinic, Yokosuka, Japan; A Takahashi, Takahashi Medical Clinic, Fujisawa, Japan; S Nakajima and Y Hamamoto, Nakajima Medical Clinic, Yokosuka, Japan; K Hoshino, Hoshino Medical Clinic, Fujisawa, Japan; K Shinoda, Konandai Medical Clinic, Yokohama, Japan; Y Ishihara and M Ishihara, Fureai Medical Clinic, Yokohama, Japan; T Kawata, Idogaya Kens Clinic, Yokohama, Japan; Y Noguchi, Fureai Yokohama Hospital, Yokohama, Japan; Y Yamada, International University of Health and Welfare Atami Hospital, Atami, Japan; U Osada, Saiseikai Yokohama Nanbu Hospital, Yokohama, Japan; Y Terauchi, Department of Endocrinology and Metabolism, Yokohama City University School of Medicine, Yokohama, Japan. Editorial support in the form of medical writing was provided by Editage (www.editage.com).

DISCLOSURE

Yasuo Terauchi received honoraria for lectures from MSD K.K.; Ono Pharmaceutical Co., Ltd.; Nippon Boehringer Ingelheim Co., Ltd.; Novartis Pharma K.K.; Takeda Pharmaceutical Co., Ltd.; Mitsubishi Tanabe Pharma Corp.; Daiichi Sankyo Co., Ltd.; Sanwa Kagaku Kenkyusho Co., Ltd.; Kowa Pharmaceutical Co., Ltd.; Novo Nordisk Pharma Ltd.; Eli Lilly Japan K.K.; Sanofi K.K.; Shionogi & Co., Ltd.; Bayer Yakuhin, Ltd.; and AstraZeneca K.K.; and obtained research support from MSD K.K.; Ono Pharmaceutical Co., Ltd.; Nippon Boehringer Ingelheim Co., Ltd.; Novartis Pharma K.K.; Takeda Pharmaceutical Co., Ltd.; Mitsubishi Tanabe Pharma Corp.; Daiichi Sankyo Co., Ltd.; Sanwa Kagaku Kenkyusho Co., Ltd.; Novo Nordisk Pharma Ltd.; Eli Lilly Japan K.K.; Sanofi K.K.; Dainippon Sumitomo Pharma Co., Ltd.; Shionogi & Co., Ltd.; Bayer Yakuhin, Ltd.; Astellas Pharma, Inc.; Pfizer Japan, Inc.; and AstraZeneca K.K. Tadashi Yamakawa received honoraria for lectures from MSD K.K.; Kowa Pharmaceutical Co., Ltd.; Novo Nordisk Pharma Ltd.; and obtained research support from AstraZeneca K.K. The authors declare that although they are affiliated with a department that is supported financially by a pharmaceutical company, the authors received no current funding for this study and this does not alter their adherence to all the journal policies on sharing data and materials. The other authors declare no conflict of interest.

REFERENCES

1. Franz MJ, Boucher JL, Green-Pastors J, *et al*. Evidence-based nutrition practice guidelines for diabetes and scope and standards of practice. *J Am Diet Assoc* 2008; 108: S52–S58.
2. Benjamin EM. Glycemic control in the elderly: risks and benefits. *Clin Diabetes* 2002; 20: 118–121.
3. Heilbronn LK, Noakes M, Clifton PM. Effect of energy restriction, weight loss, and diet composition on plasma lipids and glucose in patients with type 2 diabetes. *Diabetes Care* 1999; 22: 889–895.
4. Look ARG, Wing RR, Bolin P, *et al*. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. *N Engl J Med* 2013; 369: 145–154.
5. Feinman RD. Fad diets in the treatment of diabetes. *Curr Diab Rep* 2011; 11: 128–135.
6. Accurso A, Bernstein RK, Dahlqvist A, *et al*. Dietary carbohydrate restriction in type 2 diabetes mellitus and metabolic syndrome: time for a critical appraisal. *Nutr Metab* 2008; 5: 9.
7. Volek JS, Fernandez ML, Feinman RD, *et al*. Dietary carbohydrate restriction induces a unique metabolic state positively affecting atherogenic dyslipidemia, fatty acid partitioning, and metabolic syndrome. *Prog Lipid Res* 2008; 47: 307–318.
8. American Diabetes Association. 4. Lifestyle Management: standards of Medical Care in Diabetes—2018. *Diabetes Care* 2018; 41: S38–S50.
9. Lustig RH, Malhotra A. The cholesterol and calorie hypotheses are both dead—it is time to focus on the real culprit: insulin resistance. *Stroke* 2018; 13: 57.

10. Nutrition Subcommittee of the British Diabetic Association's Professional. Advisory Committee. Dietary recommendations for people with diabetes: an update for the 1990s. *Diabet Med* 1992; 9: 189–202.
11. American Diabetes Association. Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications. *Diabetes Care* 2002; 25: 202–212.
12. Krauss RM, Eckel RH, Howard B, *et al.* AHA Dietary Guidelines: revision 2000: a statement for healthcare professionals from the Nutrition Committee of the American Heart Association. *Circulation* 2000; 102: 2284–2299.
13. Ajala O, English P, Pinkney J. Systematic review and meta-analysis of different dietary approaches to the management of type 2 diabetes. *Am J Clin Nutr* 2013; 97: 505–516.
14. American Diabetes Association. 3. Foundations of care and comprehensive medical evaluation. *Diabetes Care* 2016; 39: S23–S35.
15. Wheeler ML, Dunbar SA, Jaacks LM, *et al.* Macronutrients, food groups, and eating patterns in the management of diabetes: a systematic review of the literature, 2010. *Diabetes Care* 2012; 35: 434–445.
16. Mayer SB, Jeffreys AS, Olsen MK, *et al.* Two diets with different haemoglobin A1c and antiglycaemic medication effects despite similar weight loss in type 2 diabetes. *Diabetes Obes Metabol* 2014; 16: 90–93.
17. McKenzie AL, Hallberg SJ, Creighton BC, *et al.* A novel intervention including individualized nutritional recommendations reduces hemoglobin A1c level, medication use, and weight in type 2 diabetes. *JMIR Diabetes* 2017; 2: e5.
18. Parker L. The effect of reduced carbohydrate diet education on hemoglobin A1c in patients with type 2 diabetes. Evidence-Based Practice Project Reports, 2016; 81. Available from: https://scholar.valpo.edu/ebpr/81. Accessed February 6, 2018.
19. Manzano P, Camarero E, Pico A, *et al.* Diabetes nutrition and complications trial (DNCT): food intake and targets of diabetes treatment in a sample of Spanish people with diabetes. *Diabetes Care* 1997; 20: 1078–1080.
20. Noakes TD, Windt J. Evidence that supports the prescription of low-carbohydrate high-fat diets: a narrative review. *Br J Sports Med* 2017; 51: 133–139.
21. Tajima N, Noda M, Origasa H, *et al.* Evidence-based practice guideline for the treatment for diabetes in Japan 2013. *Diabetol Int* 2015; 6: 151–187.
22. Horikawa C, Yoshimura Y, Kamada C, *et al.* Dietary intake in Japanese patients with type 2 diabetes: analysis from Japan diabetes complications study. *J Diabetes Investig* 2014; 5: 176–187.
23. Kamada C, Yoshimura H, Okumura R, *et al.* Optimal energy distribution of carbohydrate intake for Japanese elderly patients with type 2 diabetes: the Japanese Elderly Intervention Trial. *Geriatr Gerontol Int* 2012; 12: 41–49.
24. Sasaki S, Yanagibori R, Amano K. Self-administered diet history questionnaire developed for health education: a relative validation of the test-version by comparison with 3-day diet record in women. *J Epidemiol* 1998; 8: 203–215.
25. Sasaki S, Ishihara J, Tsugane S, *et al.* Validity of a self-administered food frequency questionnaire in the 5-year follow-up survey of the JPHC Study Cohort I to assess sodium and potassium intake: comparison with dietary records and 24-hour urinary excretion level. *J Epidemiol* 2003; 13: S102–S105.
26. The Council for Science and Technology, Ministry of Education, Culture, Sports, Science, and Technology, Japan. Standard Tables of Food Composition in Japan: Fatty Acid Section, 5th revised and enlarged. Tokyo: Printing Bureau of the Ministry of Finance, 2005: 321. (Japanese and English)
27. Kobayashi S, Honda S, Murakami K, *et al.* Both comprehensive and brief self-administered diet history questionnaires satisfactorily rank nutrient intakes in Japanese adults. *J Epidemiol* 2012; 22: 151–159.
28. National Health and Nutrition Survey. Ministry of Health Law, Japan 2014. Available from: http://www.e-stat.go.jp/SG1/estat/GL08020103.do?_toGL_&listID=000001151595&requestSender=dsearch. Accessed January 31, 2017 (Japanese)
29. Delahanty LM, Nathan DM, Lachin JM, *et al.* Association of diet with glycated hemoglobin during intensive treatment of type 1 diabetes in the Diabetes Control and Complications Trial. *Am J Clin Nutr* 2009; 89: 518–524.
30. Vitolins MZ, Anderson AM, Delahanty L, *et al.* Action for Health in Diabetes (Look AHEAD) trial: baseline evaluation of selected nutrients and food group intake. *J Am Diet Assoc* 2009; 109: 1367–1375.
31. Oza-Frank R, Cheng YJ, Narayan KM, *et al.* Trends in nutrient intake among adults with diabetes in the United States: 1988–2004. *J Am Diet Assoc* 2009; 109: 1173–1178.
32. Tripathy D, Carlsson M, Almgren P, *et al.* Insulin secretion and insulin sensitivity in relation to glucose tolerance: lessons from the Botnia Study. *Diabetes* 2000; 49: 975–980.
33. Fukushima M, Usami M, Ikeda M, *et al.* Insulin secretion and insulin sensitivity at different stages of glucose tolerance: a cross-sectional study of Japanese type 2 diabetes. *Metabolism* 2004; 53: 831–835.
34. Ma Y, Olendzki BC, Hafner AR, *et al.* Low-carbohydrate and high-fat intake among adult patients with poorly controlled type 2 diabetes mellitus. *Nutrition* 2006; 22: 1129–1136.
35. Lee H, Kim M, Daly BJ. Nutritional patterns of Korean diabetic patients: an exploratory study. *Int Nurs Rev* 2008; 55: 442–446.
36. Woo MH, Park S, Woo JT, *et al.* A comparative study of diet in good and poor glycemic control groups in elderly patients with type 2 diabetes mellitus. *Korean Diabetes J* 2010; 34: 303–311.

37. Peterson MD, Haapala HJ, Chaddha A, *et al.* Abdominal obesity is an independent predictor of serum 25-hydroxyvitamin D deficiency in adults with cerebral palsy. *Nutr Metab* 2014; 11: 22.
38. Yamada Y, Uchida J, Izumi H, *et al.* A non-calorie-restricted low-carbohydrate diet is effective as an alternative therapy for patients with type 2 diabetes. *Intern Med* 2014; 53: 13–19.
39. Gannon MC, Nuttall FQ, Westphal SA, *et al.* Acute metabolic response to high-carbohydrate, high-starch meals compared with moderate-carbohydrate, low-starch meals in subjects with type 2 diabetes. *Diabetes Care* 1998; 21: 1619–1626.
40. Dikeman CL, Fahey GC. Viscosity as related to dietary fiber: a review. *Crit Rev Food Sci Nutr* 2006; 46: 649–663.
41. Karhunen LJ, Juvonen KR, Flander SM, *et al.* A psyllium fiber-enriched meal strongly attenuates postprandial gastrointestinal peptide release in healthy young adults. *J Nutr* 2010; 140: 737–744.
42. Perfect MM, Patel PG, Scott RE, *et al.* Sleep, glucose, and daytime functioning in youth with type 1 diabetes. *Sleep* 2012; 35: 81–88.
43. Eilat-Adar S, Xu J, Zephier E, *et al.* Adherence to dietary recommendations for saturated fat, fiber, and sodium is low in American Indians and other U.S. adults with diabetes. *J Nutr* 2008; 138: 1699–1704.
44. Smart CE, Evans M, O'Connell SM, *et al.* Both dietary protein and fat increase postprandial glucose excursions in children with type 1 diabetes, and the effect is additive. *Diabetes Care* 2013; 36: 3897–3902.
45. Smith GI, Yoshino J, Stromsdorfer KL, *et al.* Protein ingestion induces muscle insulin resistance independent of leucine-mediated mTOR activation. *Diabetes* 2015; 64: 1555–1563.
46. Robinson MM, Soop M, Sohn TS, *et al.* High insulin combined with essential amino acids stimulates skeletal muscle mitochondrial protein synthesis while decreasing insulin sensitivity in healthy humans. *J Clin Endocrinol Metab* 2014; 99: E2574–E2583.
47. Tinker LF, Sarto GE, Howard BV, *et al.* Biomarker-calibrated dietary energy and protein intake associations with diabetes risk among postmenopausal women from the Women's Health Initiative. *Am J Clin Nutr* 2011; 94: 1600–1606.
48. American Diabetes Association. 4. Lifestyle Management. *Diabetes Care* 2017; 40: S33–S43.
49. Daly ME, Paisey R, Paisey R, *et al.* Short-term effects of severe dietary carbohydrate-restriction advice in Type 2 diabetes–a randomized controlled trial. *Diabet Med* 2006; 23: 15–20.
50. Davis NJ, Tomuta N, Schechter C, *et al.* Comparative study of the effects of a 1-year dietary intervention of a low-carbohydrate diet versus a low-fat diet on weight and glycemic control in type 2 diabetes. *Diabetes Care* 2009; 32: 1147–1152.
51. Dyson PA, Beatty S, Matthews DR. A low-carbohydrate diet is more effective in reducing body weight than healthy eating in both diabetic and non-diabetic subjects. *Diabet Med* 2007; 24: 1430–1435.
52. Wolever TM, Gibbs AL, Mehling C, *et al.* The Canadian Trial of Carbohydrates in Diabetes (CCD), a 1-y controlled trial of low-glycemic-index dietary carbohydrate in type 2 diabetes: no effect on glycated hemoglobin but reduction in C-reactive protein. *Am J Clin Nutr* 2008; 87: 114–125.