Intakes of Dietary Fiber, Vegetables, and Fruits and Incidence of Cardiovascular Disease in Japanese Patients With Type 2 Diabetes

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OBJECTIVE—Foods rich in fiber, such as vegetables and fruits, prevent cardiovascular disease (CVD) among healthy adults, but such data in patients with diabetes are sparse. We investigated this association in a cohort with type 2 diabetes aged 40–70 years whose HbA_{1c} values were ≥ 6.5% in Japan Diabetes Society values.

RESEARCH DESIGN AND METHODS—In this cohort study, 1,414 patients were analyzed after exclusion of patients with history of CVDs and nonresponders to a dietary survey. Primary outcomes were times to stroke and coronary heart disease (CHD). Hazard ratios (HRs) of dietary intake were estimated by Cox regression adjusted for systolic blood pressure, lipids, energy intake, and other confounders.

RESULTS—Mean daily dietary fiber in quartiles ranged from 8.7 to 21.8 g, and mean energy intake ranged from 1,442.3 to 2,058.9 kcal. Mean daily intake of vegetables and fruits in quartiles ranged from 228.7 to 721.4 g. During the follow-up of a median of 8.1 years, 68 strokes and 96 CHDs were observed. HRs for stroke in the fourth quartile vs. the first quartile were 0.39 (95% CI 0.12–1.29, P = 0.12) for dietary fiber and 0.35 (0.13–0.96, P = 0.04) for vegetables and fruits. There were no significant associations with CHD. The HR per 1-g increase was smaller for soluble dietary fiber (0.48 [95% CI 0.30–0.79], $P < 0.01$) than for total (0.82 [0.73–0.93], $P < 0.01$) and insoluble (0.79 [0.68–0.93], $P < 0.01$) dietary fiber.

CONCLUSIONS—Increased dietary fiber, particularly soluble fiber, and vegetables and fruits were associated with lower incident stroke but not CHD in patients with type 2 diabetes.

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Type 2 diabetes is a significant cause of premature mortality and morbidity related to cardiovascular disease (CVD), and medical nutritional therapy is an essential component of diabetes care aimed toward prevention of CVD. Current guidelines for diabetes care in many countries encourage consumption of dietary fiber, nondigestible carbohydrates, and lignin that are intrinsic and intact in plants, setting a variety of goals for daily intake of total dietary fiber (14 g/1,000 kcal in the U.S. [1], 40 g in Europe [2], 25–50 g in Canada [3], and 20–25 g in Japan [4]). An increase in dietary fiber can reduce CVD risk through a variety of mechanisms, such as decreasing total and LDL cholesterol (5), reducing postprandial glucose concentration and insulin secretion (6), lowering blood pressure (7), reducing clotting factors (8), and reducing inflammation (9). Lipid-lowering effects were attributable to soluble fiber (5), which reduces absorption of fat and binds bile acids (10). The effects of an unfortified high-fiber (50 g per day) diet on glycemic control and lipids were also demonstrated in a randomized trial in patients with type 2 diabetes (11).

Cohort studies of healthy adults suggest that foods rich in fiber protect against coronary heart disease (CHD) (12) and stroke (Supplementary Table 1) (13–19), but data on patients with type 2 diabetes are sparse (20–22) despite the integral role of medical nutritional therapy. All of the earlier studies in diabetes were conducted in the U.S. and Europe, and the effects of dietary fiber on CVD remain unknown for Asian patients, who account for >60% of the diabetic population worldwide (23). In comparison with type 2 diabetic patients in Western countries, those in East Asian countries, including Japan, are known to have different features regarding cardiovascular complications (24) including a much lower incidence rate of CHD than in Western countries (25) and obesity as a lesser cardiovascular risk factor (20). Therefore, it is still uncertain whether dietary recommendations established by the earlier studies are universally applicable to patients with type 2 diabetes, particularly to Japanese patients. This study therefore aimed to investigate the incidence rates of stroke and CHD in relation to intake of dietary fiber in total, soluble form, and insoluble form and vegetables and fruits in a cohort of Japanese patients with type 2 diabetes.

RESEARCH DESIGN AND METHODS—This study is part of the Japan Diabetes Complications Study

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(JDCS), an open-labeled randomized trial originally designed to evaluate the efficacy of a long-term therapeutic intervention mainly focused on lifestyle education. The original primary end points were CHD, stroke, diabetic retinopathy, and overt nephropathy. The primary results (26) of the JDCS have previously been described. Eligibility criteria were previously diagnosed patients with type 2 diabetes aged 40–70 years whose HbA_{1c} levels were ≥6.5% in Japan Diabetes Society values. From outpatient clinics in 59 university and general hospitals nationwide that specialize in diabetes care, 2,205 patients were initially registered from January 1995 to March 1996. Of the 2,033 patients who met the eligibility criteria and were randomized, 1,588 patients responded to the baseline dietary survey. There was no notable difference in baseline characteristics between responders and nonresponders (27). After exclusion of 174 patients with impaired glucose tolerance, a history of angina pectoris, myocardial infarction, stroke, peripheral artery disease, familial hypercholesterolemia, type III hyperlipidemia (diagnosed by broad β-band on electrophoresis), or nephrotic syndrome (urine protein >3.5 g/day and serum total protein <6.0 mg/dL) or serum creatinine levels >1.3 mg/dL (120 μmol/L) at baseline, 1,414 patients were included in the current analysis. We analyzed follow-up data collected until March 2003. The protocol was approved by the institutional review boards of all of the participating institutes. We obtained written informed consent from all patients.

Outcome measures

A fatal or first nonfatal manifestation of CHD comprised of angina pectoris or myocardial infarction was diagnosed according to criteria defined by the World Health Organization/Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (WHO/MONICA) project, and angina pectoris was defined as typical effort-dependent chest pain or oppression relieved at rest or by use of nitroglycerine as validated by an exercise-positive electrocardiogram or angiography. A patient with a first percutaneous coronary intervention or coronary artery bypass graft was also counted as having a CHD event. Diagnosis of stroke was according to guidelines defined by the Ministry of Health, Labour and Welfare of Japan and WHO criteria. Stroke events were defined as a constellation of focal or global neurological deficits or disturbance of cerebral function that was sudden or rapid in onset and for which there was no apparent cause other than a vascular accident such as epilepsy or brain tumors on the basis of a detailed history, neurological examination, and ancillary diagnostic procedures such as computed tomography, magnetic resonance imaging, cerebral angiography, and lumbar puncture. Stroke events were classified as cerebral infarction (including embolus), intracranial hemorrhage (including subarachnoid hemorrhage), transient ischemic attack, or stroke of undetermined type in accordance with WHO criteria. No cases of asymptomatic lesions detected by brain imaging (i.e., silent infarction) were included. Only first-ever CHD or stroke events during the study period were counted in the analysis and in a patient having both CHD and stroke events; each event was counted separately. Information regarding primary outcome and other clinical variables for each subject was collected through an annual report that included detailed findings at the time of the event from each participating diabetologist who was providing care to those patients. Adjudication of CHD and stroke events was by central committees comprised of experts who were masked to risk factor status and was based on additional data such as a detailed history, sequential changes in ECG and serum cardiac biomarkers, and results of coronary angiography or brain imaging.

Dietary assessment

The Food Frequency Questionnaire based on food groups (FFQg) (28) was administered at baseline. In brief, the FFQg elicited information on the average intake per week of 29 food groups and 10 kinds of cookery in commonly used units or portion sizes. The FFQg was externally validated by comparison with dietary records for seven continuous days of 66 subjects aged 19–60 years (28). The ratios of the estimates obtained by the FFQg against those by the dietary records ranged from 72 to 121%, and the average was 104% (1,666 kcal/1,568 kcal for total energy, 10.0 g/9.5 g for total dietary fiber, 51.0 g/48.0 g for green-yellow vegetables, and 64.8 g/54.7 g for fruits). After patients completed the questionnaire, the dietitian reviewed the answers and in the case of questionable responses interviewed the patient. We use standardized software for population-based surveys and nutrition counseling in Japan to calculate nutrient and food intakes (Excel EIYO-KUN, version 4.5, developed by Shikoku University Nutrition Database; KENPAKUSHA, Tokyo, Japan).

Statistical analysis

Hazard ratios (HRs) and 95% CIs for the incidence of stroke or CHD in relation to dietary intakes were estimated by Cox regression with adjustment for age, sex, BMI, HbA_{1c}, diabetes duration, diabetic retinopathy, treatment by insulin, treatment by oral hypoglycemic agents, systolic blood pressure (SBP), LDL cholesterol, HDL cholesterol, triglycerides (log transformed), current smoking, physical activity, alcohol intake, proportions of total fat, saturated fatty acids, n-6 fatty acids and n-3 fatty acids, cholesterol intake, and sodium intake as confounders. In addition to the multivariate adjustment, we applied the standard multivariate method for energy adjustment. We performed both quartile and linear Cox regression analyses, and the primary analysis was conducted using linear regression. Potential nonlinear relationships between dietary fiber and stroke were explored by a spline function, a smooth curve of incidence rate of stroke depending on dietary fiber. The spline function and 95% CI were estimated by energy-adjusted generalized additive models, and the degree of freedom was determined by generalized cross-validation. Potential effect modification by age ≥60 years, sex, HbA_{1c} ≥9%, duration of diabetes ≥10 years, overweight (BMI ≥25 kg/m^2), smoking status, hypertension (SBP ≥130 mmHg, diastolic blood pressure ≥85 mmHg, or treatment by antihypertensive agents), and dyslipidemia (LDL cholesterol ≥120 mg/dL, HDL cholesterol <40 mg/dL, triglycerides ≥150 mg/dL, or treatment by lipid-lowering agents) was explored by subgroup analysis and Wald tests for interaction terms using energy-adjusted Cox regression. All *P* values are two-sided, and the significance level is 0.05. All statistical analyses and data management were conducted at a central data center using SAS, version 9.2 (SAS Institute, Cary, NC).

RESULTS—The baseline characteristics and daily dietary intake of the 1,414 patients according to quartiles of total dietary fiber are shown in Table 1. Mean total dietary fiber in quartiles ranged from 8.7 to 21.8 g. Mean energy intake in quartiles ranged from 1,442.3 to 2,058.9 kcal.

Table 1—*Background characteristics and dietary intake for 1,414 patients with type 2 diabetes according to quartiles of total dietary fiber*

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P_{trend}
N	352	349	353	360	
Total dietary fiber (g/day)	8.7 ± 1.6	12.5 ± 0.9	15.8 ± 1.0	21.8 ± 4.0	<0.01
Soluble dietary fiber (g/day)	2.1 ± 0.4	2.9 ± 0.2	3.7 ± 0.3	5.1 ± 1.2	<0.01
Insoluble dietary fiber (g/day)	6.3 ± 1.2	9.0 ± 0.7	11.4 ± 0.9	15.8 ± 2.9	<0.01
Age (years)	57.5 ± 7.5	58.4 ± 7.2	59.5 ± 6.5	59.0 ± 6.4	<0.01
Women (%)	36.6	46.7	52.4	56.1	<0.01
HbA_{1c} (% in NGSP value)	8.2 ± 1.2	8.3 ± 1.2	8.4 ± 1.5	8.4 ± 1.4	0.03
HbA_{1c} (mmol/mol)	66.0 ± 12.7	66.9 ± 13.3	68.3 ± 16.5	68.1 ± 15.1	0.03
Fasting plasma glucose (mg/dL)	158.1 ± 42.5	158.8 ± 41.0	162.6 ± 46.9	161.9 ± 43.9	0.16
Years after diagnosis	11.1 ± 6.7	11.1 ± 7.1	11.1 ± 7.2	10.6 ± 7.1	0.37
BMI (kg/m^2)	22.8 ± 2.8	22.9 ± 3.1	22.8 ± 2.8	23.2 ± 3.1	0.10
SBP (mmHg)	131.3 ± 16.5	131.1 ± 17.2	132.5 ± 15.2	131.6 ± 15.9	0.57
Diastolic blood pressure (mmHg)	76.3 ± 10.3	76.7 ± 10.0	76.3 ± 9.8	76.7 ± 9.6	0.80
LDL cholesterol (mg/dL)	122.5 ± 31.6	122.7 ± 33.2	123.3 ± 31.5	121.3 ± 32.1	0.69
HDL cholesterol (mg/dL)	53.9 ± 16.8	54.5 ± 16.8	55.3 ± 16.8	55.2 ± 16.9	0.24
Triglycerides (mg/dL)*	101.0 ± 65.0	103.0 ± 71.0	97.0 ± 70.0	98.0 ± 68.0	0.26
Treated by insulin (%)	22.7	22.7	21.0	19.5	0.24
Treated by OHA without insulin (%)	65.6	66.2	66.0	64.2	0.68
Treated by antihypertensive agents (%)	25.6	27.7	26.9	23.1	0.41
Treated by lipid-lowering agents (%)	19.7	25.3	28.0	23.3	0.18
Current smoker (%)	39.6	27.8	23.7	19.9	<0.01
Physical activity (kJ/day)*	424.8 ± 956.3	546.4 ± 1,033.3	600.6 ± 1,041.3	702.9 ± 1,342.2	<0.01
Alcohol intake (%)					
Never	52.1	59.8	63.2	67.1	<0.01
≤1 drink†	40.3	33.9	32.4	27.4	
>1 drink†	7.7	6.3	4.4	5.4	
Grains (g/day)	184.5 ± 51.1	192.0 ± 56.3	194.4 ± 51.1	193.7 ± 49.0	0.02
Vegetables (g/day)	158.6 ± 64.7	258.3 ± 71.2	351.7 ± 86.1	518.3 ± 159.6	<0.01
Fruits (g/day)	70.1 ± 57.0	113.5 ± 74.0	147.3 ± 86.8	203.1 ± 139.3	<0.01
Seafood (g/day)	75.9 ± 44.4	86.2 ± 45.2	106.3 ± 54.5	128.1 ± 73.3	<0.01
Meat (g/day)	40.9 ± 31.2	45.1 ± 34.7	50.1 ± 35.8	59.9 ± 46.3	<0.01
Energy intake (kcal/day)	1,442.3 ± 315.7	1,617.5 ± 300.0	1,787.6 ± 310.0	2,058.9 ± 407.4	<0.01
Protein (% energy)	15.0 ± 2.5	15.3 ± 2.2	16.0 ± 2.3	16.6 ± 2.4	<0.01
Fat (% energy)	26.5 ± 5.3	27.3 ± 5.1	27.5 ± 4.4	28.6 ± 5.1	<0.01
Carbohydrate (% energy)	53.6 ± 6.9	54.2 ± 6.4	53.9 ± 5.9	53.2 ± 7.1	0.36
Saturated fatty acid (% energy)	7.8 ± 2.0	8.0 ± 1.7	7.9 ± 1.5	7.9 ± 1.6	0.35
Dietary cholesterol (mg/day)	260.1 ± 99.7	287.1 ± 90.1	321.4 ± 105.7	371.4 ± 135.8	<0.01
Sodium (g/day)	2.7 ± 0.7	3.7 ± 0.8	4.4 ± 0.9	5.9 ± 1.4	<0.01

Data are means ± SD unless otherwise indicated. OHA, oral hypoglycemic agents. *Median ± interquartile range. †One drink is equivalent to 12.6 g ethanol based on the U.S. Department of Agriculture definition.

Intake of total dietary fiber was positively associated with proportions of protein and fat intake but not with the proportion of carbohydrate intake. Patients in higher quartiles were significantly older and included more women and had preferable lifestyles such as a lower smoking proportion and increased physical activity. However, there were no significant trends in blood pressure, lipids, and medications, and the difference in HbA_{1c} values was only marginal. Total dietary fiber was positively associated with not only intakes of grain, vegetables, and fruits but also intakes of seafood, meat, and sodium.

During the follow-up of a median of 8.1 years, the numbers of incident CVD according to quartiles of total dietary fiber were 21, 24, 27, and 24 for CHD; 22, 15, 13, and 18 for stroke; and 19, 12, 11, and 15 for cerebral infarction, respectively. The 68 stroke events included 58 cerebral infarctions, 5 intracranial hemorrhages, 4 transient ischemic attacks, and 1 stroke of undetermined type in accordance with WHO criteria. The crude incidence rates per 1,000 patient-years for CHD, stroke, and cerebral infarction were 9.70, 6.81, and 5.69, respectively, and the follow-up rate at 8 years was 78%. There was no notable difference in baseline characteristics between patients who completed 8-year follow-up and the other patients (27).

Tables 2 and 3 show HRs for dietary fiber, vegetables, and fruits estimated by Cox regression models unadjusted (top model), adjusted for risk factors (middle model), and further adjusted for total energy intake (bottom model). The energy-adjusted HRs for stroke in the fourth quartile compared with the first quartile were 0.39 (95% CI 0.12–1.29, $P = 0.12$) for total dietary fiber and 0.35 (95% CI 0.13–0.96, $P = 0.04$) for vegetables and fruits (Table 2). There were no significant decreasing trends between grain intake, a major source of dietary fiber, and incident stroke (data not shown). The HR per 1-g increase was smaller for soluble dietary fiber (0.48 [95% CI 0.30–0.79], $P < 0.01$) than for total (0.82 [95% CI 0.73–0.93], $P < 0.01$) and insoluble (0.79 [95% CI 0.68–0.93], $P < 0.01$) dietary fiber. The HRs for cerebral infarction were similar to those for stroke (Supplementary Table 2). In contrast, both the quartile and linear analyses showed no significant trends toward a decreased incidence rate of CHD (Table 3). Supplementary Fig. 1 shows results of subgroup analysis according to risk factors for CVD. None of these associations indicated significant interactions, suggesting lack of clear evidence of effect modifications.

To explore potentially nonlinear relationships between total dietary fiber and the incidence of stroke, we fitted the energy-adjusted generalized additive models (Fig. 1). As shown graphically, decreasing trends according to higher values for dietary fiber were clearly shown, with the relationships appearing to be nonlinear. Notably, the estimated incidence rate was very low, i.e., <0.90/1,000 patient-years, among patients consuming total dietary fiber >25 g. Indeed, the maximum total dietary fiber in the 68 cases of stroke was 24 g.

CONCLUSIONS—This 8-year follow-up study of Japanese patients with type 2 diabetes revealed an ~60% risk reduction of stroke in the fourth quartile of total dietary fiber and vegetables/fruits compared with the first quartile. The estimated incidence rate of stroke was very low in patients consuming >25 g/day of total dietary fiber, suggesting a potential threshold of ~20–25 g. The association in relation to soluble fiber seemed to be stronger, but there were no significant associations between CHD and any types of dietary fiber. Our findings are in line with results of earlier cohort studies on the incidence of stroke among healthy adults, as summarized in Supplementary Table 1.

In comparison with people in Western countries, diabetic patients in East Asian countries, including Japan, are known to have quite different features such as the much lower incidence rate of CHD than in Western countries (25) and the low prevalence of obesity (20). As expected, the incidence rate of stroke among patients in this cohort, 6.81/1,000 patients-years, was 2–10 times higher than those in earlier studies (14–19)

Table 2—Cox regression analysis of incidence of stroke and intake of total, soluble, and insoluble dietary fiber and vegetables and fruits*

	Quartile analysis				
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	Linear analysis
Total dietary fiber	8.7 ± 1.6	12.5 ± 0.9	15.8 ± 1.0	21.8 ± 4.0	
Age and sex adjusted	Ref.	0.62 (0.32–1.21); 0.16	0.58 (0.29–1.16); 0.12	0.69 (0.36–1.31); 0.26	0.96 (0.91–1.01); 0.09
Adjusted for risk factors†	Ref.	0.46 (0.22–0.98); 0.04	0.41 (0.18–0.95); 0.04	0.45 (0.15–1.35); 0.16	0.86 (0.77–0.95); <0.01
Further adjusted for energy‡	Ref.	0.44 (0.20–0.95); 0.04	0.37 (0.15–0.91); 0.03	0.39 (0.12–1.29); 0.12	0.82 (0.73–0.93); <0.01
Soluble dietary fiber	2.1 ± 0.4	2.9 ± 0.2	3.7 ± 0.3	5.1 ± 1.2	
Age and sex adjusted	Ref.	0.66 (0.34–1.25); 0.20	0.56 (0.27–1.13); 0.10	0.58 (0.30–1.11); 0.10	0.82 (0.66–1.02); 0.08
Adjusted for risk factors†	Ref.	0.47 (0.22–1.00); 0.05	0.41 (0.17–0.95); 0.04	0.37 (0.13–1.09); 0.07	0.57 (0.37–0.87); 0.01
Further adjusted for energy‡	Ref.	0.45 (0.21–0.96); 0.04	0.37 (0.15–0.89); 0.03	0.32 (0.10–1.02); 0.05	0.48 (0.30–0.79); <0.01
Insoluble dietary fiber	6.3 ± 1.2	9.0 ± 0.7	11.4 ± 0.9	15.8 ± 2.9	
Age and sex adjusted	Ref.	0.72 (0.37–1.37); 0.31	0.55 (0.27–1.12); 0.10	0.72 (0.38–1.38); 0.33	0.95 (0.88–1.01); 0.10
Adjusted for risk factors†	Ref.	0.57 (0.27–1.19); 0.13	0.38 (0.16–0.92); 0.03	0.49 (0.17–1.45); 0.20	0.83 (0.72–0.95); 0.01
Further adjusted for energy‡	Ref.	0.55 (0.26–1.16); 0.11	0.36 (0.15–0.89); 0.03	0.44 (0.14–1.40); 0.16	0.79 (0.68–0.93); <0.01
Vegetables and fruits	228.7 ± 84.0	371.9 ± 83.0	499.0 ± 93.8	721.4 ± 197.3	
Age and sex adjusted	Ref.	0.87 (0.47–1.62); 0.65	0.63 (0.31–1.27); 0.19	0.58 (0.29–1.17); 0.13	0.999 (0.997–1.000); 0.04
Adjusted for risk factors†	Ref.	0.72 (0.36–1.45); 0.36	0.45 (0.20–1.05); 0.07	0.36 (0.13–0.97); 0.04	0.997 (0.996–0.999); <0.01
Further adjusted for energy‡	Ref.	0.72 (0.36–1.44); 0.35	0.45 (0.19–1.04); 0.06	0.35 (0.13–0.96); 0.04	0.997 (0.996–0.999); <0.01

Data are means ± SD or HR (95% CI); *P*. HR data for linear analyses are HR per 1-g increase. *The numbers of incident stroke were 22, 15, 13, and 18 in total dietary fiber quartiles; 22, 17, 12, and 17 in soluble dietary fiber quartiles; 21, 17, 12, and 18 in insoluble dietary fiber quartiles; and 21, 20, 13, and 14 in vegetable and fruit quartiles, respectively. †Adjusted for age, sex, BMI, HbA_{1c}, diabetes duration, diabetic retinopathy, treatment by insulin, treatment by oral hypoglycemic agents, SBP, LDL cholesterol, HDL cholesterol, triglycerides, current smoking, physical activity, alcohol intake, and proportions of total fat, saturated fatty acid, n-6 fatty acid and n-3 fatty acid, dietary cholesterol, and sodium intake. ‡Further adjusted for total energy intake.

Table 3—*Cox regression analysis of incidence of CHD* and intake of total, soluble, and insoluble dietary fiber and vegetables and fruits*

	Quartile analysis				Linear analysis
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	
Total dietary fiber	8.7 ± 1.6	12.5 ± 0.9	15.8 ± 1.0	21.8 ± 4.0	
Age and sex adjusted	Ref.	1.09 (0.61–1.97); 0.77	1.18 (0.66–2.12); 0.57	1.09 (0.60–1.96); 0.78	1.02 (0.98–1.06); 0.36
Adjusted for risk factors†	Ref.	1.06 (0.57–1.97); 0.86	0.91 (0.46–1.80); 0.79	0.62 (0.25–1.58); 0.32	0.97 (0.91–1.05); 0.49
Further adjusted for energy‡	Ref.	1.06 (0.56–2.01); 0.87	0.91 (0.44–1.89); 0.81	0.62 (0.23–1.72); 0.36	0.98 (0.90–1.06); 0.57
Soluble dietary fiber	2.1 ± 0.4	2.9 ± 0.2	3.7 ± 0.3	5.1 ± 1.2	
Age and sex adjusted	Ref.	0.93 (0.51–1.70); 0.82	1.22 (0.68–2.19); 0.50	1.06 (0.59–1.89); 0.85	1.07 (0.93–1.24); 0.36
Adjusted for risk factors†	Ref.	0.90 (0.48–1.71); 0.76	0.94 (0.48–1.85); 0.87	0.62 (0.25–1.51); 0.29	0.88 (0.64–1.21); 0.43
Further adjusted for energy‡	Ref.	0.91 (0.47–1.74); 0.77	0.95 (0.46–1.95); 0.89	0.62 (0.24–1.64); 0.34	0.88 (0.61–1.26); 0.48
Insoluble dietary fiber	6.3 ± 1.2	9.0 ± 0.7	11.4 ± 0.9	15.8 ± 2.9	
Age and sex adjusted	Ref.	0.97 (0.53–1.77); 0.92	1.34 (0.76–2.36); 0.32	0.99 (0.54–1.80); 0.96	1.03 (0.97–1.08); 0.35
Adjusted for risk factors†	Ref.	0.92 (0.49–1.75); 0.81	1.01 (0.52–1.95); 0.99	0.51 (0.20–1.30); 0.16	0.97 (0.87–1.07); 0.49
Further adjusted for energy‡	Ref.	0.92 (0.48–1.77); 0.80	1.00 (0.50–2.02); 1.00	0.50 (0.18–1.38); 0.18	0.97 (0.86–1.08); 0.56
Vegetables and fruits	228.7 ± 84.0	371.9 ± 83.0	499.0 ± 93.8	721.4 ± 197.3	
Age and sex adjusted	Ref.	1.44 (0.80–2.60); 0.23	1.44 (0.79–2.63); 0.24	1.25 (0.68–2.30); 0.47	1.000 (1.000–1.001); 0.28
Adjusted for risk factors†	Ref.	1.23 (0.66–2.29); 0.52	1.31 (0.67–2.55); 0.43	0.79 (0.35–1.76); 0.56	1.000 (0.998–1.001); 0.76
Further adjusted for energy‡	Ref.	1.25 (0.66–2.34); 0.50	1.34 (0.68–2.63); 0.40	0.81 (0.36–1.84); 0.61	1.000 (0.998–1.001); 0.82

Data are means ± SD or HR (95% CI); *P*. HR data for linear analyses are HR per 1-g increase. *The numbers of incident CHD were 21, 24, 27, and 24 in total dietary fiber quartiles; 21, 22, 27, and 26 in soluble dietary fiber quartiles; 21, 22, 31, and 22 in insoluble dietary fiber quartiles; and 19, 27, 25, and 25 in vegetables and fruits quartiles, respectively. †Adjusted for age, sex, BMI, HbA_{1c}, diabetes duration, diabetic retinopathy, treatment by insulin, treatment by oral hypoglycemic agents, SBP, LDL cholesterol, HDL cholesterol, triglycerides, current smoker, physical activity, alcohol intake, and proportions of total fat, saturated fatty acid, n-6 fatty acid and n-3 fatty acid, dietary cholesterol, and sodium intake. ‡Further adjusted for total energy intake.

(Supplementary Table 1). The "metabolically obese" phenotype (20) characterized by normal body weight with increased abdominal adiposity was also common (Table 1). Furthermore, most patients typically had a "low-fat energy-restricted diet," i.e., the proportions of protein, fat, and carbohydrate consumption met the Western guidelines (1–3), which recommended carbohydrate intake ranging from 45 to 65%, fat intake <30–35%, and protein intake from 10 to 20%. On the other hand, despite the possible difference in dietary habits, the distribution of dietary fiber intake substantially overlaps with those in populations of healthy adults except for cohorts in Finland and Sweden (Supplementary Table 1). The current goals for daily intake of total dietary fiber in guidelines are similar between Japan (20–25 g [4]) and the U.S. (14 g/1,000 kcal [1]). We observed a lower incidence of stroke around intake of 20–25 g (Fig. 1), supporting these dietary goals. Achieving such intake would be realistic given the national average in Japanese adults, i.e., 14.6 g (29).

The estimated risk reduction by dietary fiber in this cohort was seemingly stronger than those in the earlier cohort studies (Supplementary Table 1). The HRs of the fifth quintile of total dietary fiber compared with the first quintile ranged from 0.64 (95% CI 0.46–0.88) to 1.05 (0.73–1.51), showing moderate heterogeneity across studies. Data on the effects of dietary fiber in diabetic patients are limited (20–22). The Nurses' Health Study reported that whole-grain and bran intakes were associated with reduced all-cause and cardiovascular mortality among U.S. women with type 2 diabetes (20). Inverse associations with all-cause and cardiovascular mortality were also observed in a study of self-reported diabetes nested within the European Prospective Investigation into Cancer and Nutrition (EPIC) study (21). The EURODIAB Prospective Complications Study reported that higher dietary fiber consumption, especially that of soluble fiber, was associated with CVD in type 1 diabetic patients (22). Taken together, high intake of dietary fiber would reduce the incidence of stroke not only in healthy adults but also in patients with type 2 diabetes. However, it is unclear whether dietary fiber is more beneficial for diabetic patients.

The precise mechanisms for our findings cannot be clarified merely from epidemiological studies, but it is important

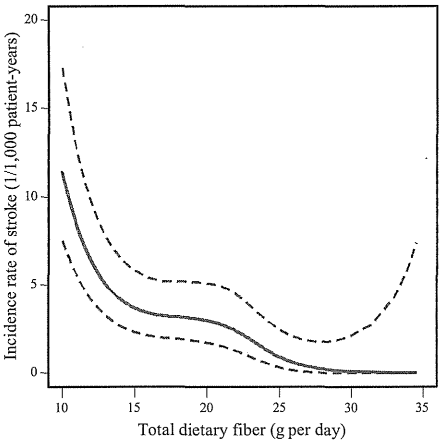

Figure 1—*Incidence rate (solid curve) and 95% CI (broken curve) of stroke in relation to total dietary fiber intake estimated by the generalized additive model.*

to note that the energy-adjusted HR was smaller for soluble dietary fiber (0.48/g) than for total (0.82/g) and insoluble (0.79/g) dietary fiber. Soluble fiber is mainly derived from fruits, vegetables, and legumes in typical Japanese diets. This type of fiber specifically decreases LDL cholesterol by −2.2 mg/dL per 1 g (5) and SBP by −1.32 mmHg (7) if given as supplements. Furthermore, lipids and blood pressure are the leading risk factors for CHD and stroke in Japanese patients, respectively (24). Our observations therefore support the hypothesis that the effects of dietary fiber on some types of stroke are mediated by lipids and blood pressure, but given that the degree of improvement in LDL cholesterol and SBP by dietary fiber is small, the entire risk reduction for stroke does not seem to be attributable to merely the effect on lipids and blood pressure. Other possibilities include reducing postprandial glucose concentration and insulin secretion (6), reducing clotting factors (8), and decreasing inflammation (9). These protective factors against CVD are biologically interrelated, so it may be possible that synergism among them results in the 60% risk reduction of stroke.

Another important finding of this study was that only stroke but not CHD was significantly reduced by dietary fiber. The Japan Public Health Center Study (18) also reported a significant association for only stroke, while dietary fiber was correlated with only CHD—not stroke—in the Japan Collaborative Cohort Study (17) (Supplementary Table 1). However, these three cohorts in Japan consistently reported HRs for CHD of <1 in higher quartiles of dietary fiber, showing weak decreasing trends in CHD (though statistically nonsignificant). Furthermore, our post hoc power calculation suggested that the power of our study may not be sufficient. For example, the observed HR for CHD between the first and fourth quartiles was 0.62, and $P = 0.36$ (Table 3), but the power to detect a true HR of 0.62 was only 11%, given the 45 CHD incidents in the first and fourth quartiles. Therefore, it is possible that the association between CHD and dietary fiber would become significant by conducting pooled analysis of cohorts.

To the best of our knowledge, this is the first study on dietary fiber and CVD in which patients with type 2 diabetes are prospectively registered based on their HbA_{1c} levels—not retrospectively selected based on self-reported diabetes status. Other strengths include treatment and follow-up plans that were conducted in institutes specializing in diabetes care and adjudication of cardiovascular events by an independent central committee. Our study has several limitations. First, the potential for bias, such as measurement errors in dietary assessments, confounding factors, and informative censoring, cannot be ruled out entirely. However, we found no notable difference in baseline characteristics between patients who completed 8-year follow-up and the other patients (27). Second, in an observational study rather than a randomized trial, it is impossible to conclude whether medical nutritional treatment encouraging dietary fiber or intake of vegetables and fruits would reduce incident stroke in clinical practice. The apparent preferable effects of dietary fiber might be due to a generally healthy lifestyle among high dietary fiber consumers. This possibility cannot be not entirely excluded; patients in higher quartiles of dietary fiber had a relatively low smoking rate and high level of physical activity, although they had adverse dietary behaviors such as increased intake of energy, saturated fatty acid, cholesterol, and sodium. Furthermore, it is difficult, although not impossible under strong assumptions for mediation analysis, to separate the effects specific to dietary fiber and the generic effect mediated by the quantity of energy consumed in this observational study. Finally, our results may not be generally applicable to populations with different lifestyle or genetic factors. For example, BMI and body weight are markedly different between patients in Japan and Western countries (30). Our systematic review found that earlier studies were conducted in U.S., Europe, and Japan and that the findings were moderately heterogeneous. Furthermore, a cohort study suggests that dietary fiber intake may modify the association between TCF7L2 rs7903146 and the incidence of type 2 diabetes, leading to preventive effects of dietary fiber from type 2 diabetes only among non–risk allele carriers (31). The contribution of such ethnic and genetic differences remains uncertain and is worthy of further research. These limitations notwithstanding, we conclude that high intakes of dietary fiber, particularly soluble fiber, and vegetables and fruits reduce incident stroke but not CHD in patients with type 2 diabetes.

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Sh.T. performed statistical analysis and drafted the manuscript. Y.Y. performed the dietary survey. C.K. contributed to the writing of the manuscript. Sa.T. was responsible for statistical analysis and data management. C.H. and R.O. contributed to the writing of the manuscript. H.I. contributed to the design and conduct of the JDCS. Y.O. was responsible for statistical analysis and data management. Y.A. contributed to the design and conduct of the JDCS. N.Y. and H.S. are the principal investigators of the JDCS. H.S. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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ORIGINAL ARTICLE

Dietary intake in Japanese patients with type 2 diabetes: Analysis from Japan Diabetes Complications Study

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ABSTRACT

Aims/Introduction: Though there are many differences in dietary habits and in the metabolic basis between Western and Asian people, the actual dietary intake in Asian patients with diabetes has not been investigated in a nationwide setting, unlike in Western countries. We aimed to clarify dietary intake among Japanese individuals with type 2 diabetes, and identify differences in dietary intake between Japanese and Western diabetic patients.

Materials and Methods: Nutritional and food intakes were surveyed and analyzed in 1,516 patients with type 2 diabetes aged 40–70 years from outpatient clinics in 59 university and general hospitals using the food frequency questionnaire based on food groups (FFQg).

Results: Mean energy intake for all participants was 1737 ± 412 kcal/day, and mean proportions of total protein, fat, and carbohydrate comprising total energy intake were 15.7, 27.6 and 53.6%, respectively. They consumed a 'low-fat energy-restricted diet' compared with Western diabetic patients, and the proportion of fat consumption was within the suggested range that has been traditionally recommended in Western countries. As a protein source, consumption of fish (100 g) and soybean products (71 g) was larger than that of meat (50 g) and eggs (29 g). These results imply that dietary content and food patterns among Japanese patients with type 2 diabetes are quite close to those reported as suitable for prevention of obesity, type 2 diabetes, cardiovascular disease, and total mortality in Europe and America.

Conclusions: A large difference was shown between dietary intake by Japanese and Western patients. These differences are important to establish ethnic-specific medical nutrition therapy for diabetes.

INTRODUCTION

Medical nutritional therapy is an essential constituent in managing existing diabetes and preventing, or at least slowing, the development of diabetes complications[1]. Thus, it is necessary to determine and assess dietary patterns in diabetes patients. However, there have been no large-scale studies of dietary patterns in nationwide settings from Asian regions except a recent study of elderly diabetic patients[2], although there have been many such studies among populations with diabetes in Western countries, such as the Diabetes Nutrition and Complications Trial, Strong Heart Study, National Health and Nutrition

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Examination Survey, and European Diabetes Centers Study of Complications in Patients with Insulin-Dependent Diabetes Mellitus Complications Study Group[3–6].

Dietary patterns in Asia are quite different from those of Western countries because of differences in food culture, food supply, dietary consumption and nutritional intake. For example, according to a report of the Food and Agriculture Organization (FAO) of the United Nations in 2007[7], the total energy supply and the energy supply from animal products in Asia were lower than those in Western regions (2668 and 402 kcal/day in Asia, 3748 and 1028 kcal/day in the USA, and 3406 and 942 kcal/day in European regions, respectively), although the percentage of energy from vegetable products was higher than in Western regions (85% in Asia, 73% in the USA and 72% in European regions).

In addition, in their joint position statement on the treatment of hyperglycemia, the American Diabetes Association and European Association for the Study of Diabetes encourage the development of individualized treatment plans built around racial and ethnic differences[8]. We reported previously that Japanese type 2 diabetic patients had a much lower body mass index (BMI) than Western patients, even though energy intake was the same, and both groups were similar with regard to age, diabetes duration, hemoglobin A1c (HbA1c) and other clinical variables[9,10]. This suggests a different metabolic basis between East Asians and Western patients with diabetes, such as the degree and influence of insulin deficiency and resistance[11]. Furthermore, it was reported that the profiles of the incidence of complications in diabetic patients differ between Asian and Western countries, such as much lower risks of myocardial infarction, stroke and congestive heart failure in Asian patients compared with Western patients, despite a higher risk of end-stage renal disease in Asian patients[12]. It could be possible that differences in eating patterns influence, at least partly, the differences in profiles of complications between the two groups.

Thus, given the differences in dietary habits and metabolic basis between Western and Asian people, it is necessary to clarify the actual dietary intake among Asian individuals with type 2 diabetes and compare it with that of Western diabetic patients in order to rationally develop effective medical nutritional therapy for diabetes. Our aim of the present study was to elucidate the actual dietary intake among Japanese middle-aged individuals with type 2 diabetes who participated in a nationwide cohort study, and to identify differences between Japanese and Western diabetic patients' dietary intake.

METHODS

Study Population

The Japanese Diabetes Complications Study (JDCS) is a nationwide cohort study of Japanese patients with type 2 diabetes from outpatient clinics in 59 university and general hospitals. Participants were previously diagnosed patients with type 2 diabetes aged 40–70 years whose HbA1c levels were ≥6.5%. Details of the study procedure were published elsewhere[13]. The protocol for the study, which is in accordance with the Declaration of Helsinki and the Ethical Guidelines for Clinical/Epidemiological Studies of the Japanese Ministry of Health Labor and Welfare, received ethical approval from the institutional review boards of all of the participating institutes. Written informed consent was obtained from all patients enrolled. A dietary survey was carried out in the baseline year of 1996. Nutrition and food intakes were assessed by the Food Frequency Questionnaire based on food groups (FFQg). A total of 1,516 of the eligible 2,033 patients completed the FFQg, and their data were analyzed in the present study.

Dietary Assessment

Nutrition and food intakes were assessed by the FFQg. The FFQg is composed of items on 29 food groups and 10 kinds of cookery, and elicits information on the average intake per week of each food or food group in commonly used units or portion sizes. After participants completed the questionnaire, a dietician reviewed the completed questionnaire with the participant. The FFQg was externally validated by comparison with weighed dietary records for seven continuous days of 66 subjects aged 19–60 years[14].

The correlation coefficients between the FFQg and dietary records for energy, protein, fat, carbohydrate, and calcium intakes were 0.47, 0.42, 0.39, 0.49, and 0.41, respectively. Intakes of 26 of the 31 nutrients were not significantly different between the two methods by paired *t*-tests. We used standardized software for population-based surveys and nutrition counseling in Japan (EIYO-KUN v.4.5, manufactured at the site of the Shikoku University Nutrition Database)[15] to calculate nutrient and food intakes, which were based on Japan Dietary Reference Intakes in 1996.

Other Assessments

Other measurements in addition to the dietary survey included a physical examination, blood pressure measurement, neurological/ophthalmological examination, and laboratory tests that included HbA1c, fasting plasma glucose/insulin/C-peptide, serum lipids/creatinine/urea nitrogen and urine analyses[13]. HbA1c assays were standardized by the Lab Test Committee of the Japan Diabetes Society (JDS)[13]. HbA1c values were converted from JDS values into National Glycohemoglobin Standardization Program (NGSP) equivalent values. NGSP equivalent values were calculated using the following formula: NGSP equivalent value (%) = JDS value (%) + 0.4[16]. Physical activity and smoking status were determined by a detailed questionnaire.

Statistical Analysis

All data are presented as means ± standard deviation unless otherwise stated. Differences in the major characteristics between participants who completed and did not complete the FFQg were examined by *t*-tests. All *P*-values are two-sided, and the significance level is 0.05. All statistical analyses were carried out using SAS packages version 9.1 (SAS Institute, Cary, NC, USA).

RESULTS

Table 1 shows the characteristics of the 1,516 type 2 diabetes patients. Their mean BMI was 22.7 kg/m^2, and 23% of the patients had a BMI ≥25 kg/m^2. Their mean age was 59 years, and mean $HbA1_C$ value was 7.9%.

Table 1 | Characteristics of 1,516 diabetic patients who participated in the nutritional and food intake survey of the Japanese Diabetes Complications Study

	Men (*n* = 807)		Women (*n* = 709)		Total (*n* = 1,516)	
	Mean	SD	Mean	SD	Mean	SD
Age (years)	58.4	±7.0	59.0	±6.8	58.7	±6.9
Diabetes duration (years)	11.5	±7.4	10.4	±6.7	11	±7.1
Weight (kg)	62	±8.6	54.2	±8.3	58.4	±9.3
BMI (kg/m^2)	22.7	±2.6	23.2	±3.3	22.9	±3.0
<18.5 kg/m^2	4.0%		6.8%		5.3%	
≥25 kg/m^2	19.3%		28.1%		23.4%	
Waist circumference (cm)	81.9	±7.8	76.6	±9.4	79.4	±9.0
Waist-to-hip ratio	0.89	±0.06	0.83	±0.07	0.86	±0.1
Fasting plasma glucose (mmol/L)	8.9	±2.4	9.0	±2.5	8.9	±2.4
HbA1c (%)	7.7	±1.2	8.1	±1.3	7.9	±1.3
Systolic blood pressure (mmHg)	131	±15.7	131	±16.3	131.4	±16.0
Diastolic blood pressure (mmHg)	77	±9.8	76	±9.9	76.6	±9.9
Total serum cholesterol (mmol/L)	5.0	±0.9	5.4	±0.9	5.2	±0.9
Serum LDL cholesterol (mmol/L)	3.0	±0.9	3.3	±0.8	3.2	±0.8
Serum HDL cholesterol (mmol/L)	1.4	±0.4	1.5	±0.5	1.4	±0.4
Serum triacylglycerol† (mmol/L)	1.2	±0.8	1.1	±0.8	1.1	±0.8
eGFR† (mL/min per 1.73 m^2)	79.4	±33.0	81.8	±36.6	80.3	±33.7
Treated by insulin (%)	18.1%		22.1%		20.0%	
Treated by OHA without insulin (%)	64.7%		67.1%		65.8%	
Current smoker (%)	46.4%		8.7%		28.7%	

eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; LDL, low-density lipoprotein; OHA, oral hypoglycemic agent; SD, standard deviation. †Median and interquartile range.

Table 2 shows the nutritional intake per day and the percentage of participants who met nutritional recommendations[17–19]. The mean daily energy intake for all participants was 1737 ± 412 kcal/day, and the mean proportions of total protein, fat and carbohydrate comprising total energy intake were 15.7, 27.6, and 53.6%, respectively. Saturated fatty acid intake comprised 28.6% of total fat intake. Additionally, we evaluated energy and nutritional intakes, respectively, by patients grouped according to sex, age, intensity of physical activity during work, HbA1C level and diabetes duration. Features of energy intake and nutritional intake, and the percentage of participants who met the nutritional recommendations by Japan and major Western guidelines were similar for each comparison with the exception that the men consumed 180 kcal/day more energy than the women (1820 and 1640 g/day, respectively; Table 2). As for intake of selected food groups per day, the mean total vegetable intake for all participants was 324 g/day (Table 3). As a protein source, consumption of fish (100 g) and soybean products (71 g) was larger than that of meat (50 g) and eggs (29 g). The male patients consumed approximately eightfold more alcoholic beverages than the female patients (115 and 14 g/day, respectively), but the characteristics of food intake did not differ greatly among the patient groups.

Table 4 summarizes the dietary composition of various study populations with diabetes, including the current JDCS participants. The JDCS patients had higher carbohydrate consumption and lower fat consumption than reported among diabetic patients in Western countries (37–50% energy and 35–45% energy, respectively)[3–6]. However, it is necessary to note differences in methods for measurement of dietary intake among the studies. In contrast, the JDCS patients had lower carbohydrate consumption and higher fat consumption than reported for type 2 diabetic patients in Korea[20] and South Africa[21]. The energy intake of JDCS patients was similar to that for Western diabetic patients[3–6], although the Western diabetic patients had a higher BMI than the Japanese diabetic patients.

DISCUSSION

In the present study, we determined the actual dietary intake among Japanese with type 2 diabetes in a nationwide large-scale setting. We clarified that the JDCS patients consumed a 'high-carbohydrate low-fat' diet compared with Western diabetic patients, and that their energy intake was similar to that of Western diabetic patients. In addition, the features of energy intake, and nutritional and food intake among the JDCS patients were similar regardless the differences in sex, age, intensity of physical activity during work, HbA1C level, and diabetes duration.

According to the National Health and Nutrition Survey[22] carried out the same year as the dietary survey of JDCS, energy intake by Japanese men and women aged 40–69 years in the general population ranged from 2214 kcal/day to 2319 kcal/day and

Table 2 | Nutritional intake per day, and percentage of participants who met the nutritional recommendations of the Japan Diabetes Society, Canadian Diabetes Association and American Diabetes Association

	Men (*n* = 807)		Women (*n* = 709)		Age <60 years (*n* = 755)		Age ≥60 years (*n* = 761)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Nutritional intake								
Energy								
kcal	1819	400	1643	405	1760	420	1714	403
Carbohydrate								
% Energy	53.0	6.8	54.2	6.3	52.9	6.7	54.2	6.5
g	239.6	55.4	220.1	48.5	230.9	54.4	230.0	52.0
Protein								
% Energy	15.2	2.3	16.2	2.4	15.6	2.4	15.8	2.4
g	69.7	20.8	67.2	22.7	69.0	22.1	68.0	21.4
Fat								
% Energy	26.7	4.9	28.7	4.8	28.1	5.1	27.2	4.8
g	54.3	17.1	53.2	18.9	55.3	18.5	52.3	17.3
SFAs								
% Energy	7.6	1.7	8.3	1.6	8.0	1.7	7.9	1.6
MUFAs								
% Energy	8.8	2.0	9.3	2.0	9.3	2.1	8.8	2.0
PUFAs								
% Energy	6.4	1.5	6.9	1.5	6.8	1.6	6.5	1.5
n6								
% Energy	5.2	1.3	5.5	1.4	5.5	1.4	5.2	1.3
n3								
% Energy	1.5	0.4	1.6	0.4	1.6	0.4	1.6	0.4
Cholesterol								
mg	316.9	116.9	306.9	118.1	313.1	116.5	311.3	118.6
Ca								
mg	619.6	228.3	661.0	229.5	628.9	228.3	648.9	230.8
Fe								
mg	8.0	2.5	8.2	2.7	8.1	2.6	8.1	2.5
Dietary fiber, total								
g	14.1	5.3	15.4	5.3	14.5	5.4	14.9	5.2
Sodium								
g	4.1	1.5	4.3	1.6	4.1	1.6	4.3	1.5
Recommendation met								
Carbohydrate†								
<55% Energy	61%		55%		61%		55%	
55–60% Energy	24%		29%		25%		27%	
≥60% Energy	15%		17%		13%		18%	
Fat†								
<25% Energy	38%		21%		27%		33%	
SFAs‡								
<7% Energy	35%		17%		26%		27%	
Fiber (total)†								
≥20 g	13%		17%		14%		16%	
Sodium†								
<3.9 g	50%		45%		50%		46%	

Table 2 | (Continued)

	Sedentary occupation (*n* = 1,032)		Non-sedentary occupation (*n* = 366)		HbA1c <7% (*n* = 1,266)		HbA1c ≥7% (*n* = 250)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Nutritional intake								
Energy								
kcal	1,714	400	1,774	436	1,736	407	1,739	437
Carbohydrate								
% Energy	53.6	6.5	53.9	6.9	53.4	6.7	54.6	6.2
g	227.7	51.1	237.2	59.1	229.5	52.1	235.4	57.9
Protein								
% Energy	15.7	2.4	15.3	2.4	15.7	2.4	15.5	2.2
g	67.9	21.0	68.6	23.1	68.6	21.7	67.9	21.7
Fat								
% Energy	27.7	4.8	27.1	5.3	27.6	5.0	27.8	4.8
g	53.2	17.3	53.9	19.0	53.7	17.9	54.2	18.2
SFAs								
% Energy	8.0	1.6	7.7	1.8	7.9	1.7	8.2	1.7
MUFAs								
% Energy	9.0	2.0	8.8	2.1	9.0	2.1	9.1	2.0
PUFAs								
% Energy	6.6	1.5	6.6	1.6	6.7	1.5	6.5	1.4
n6								
% Energy	5.3	1.3	5.3	1.4	5.4	1.4	5.2	1.2
n3								
% Energy	1.6	0.4	1.5	0.4	1.6	0.4	1.5	0.4
Cholesterol								
mg	311.8	116.2	305.0	118.6	312.2	117.8	312.2	116.2
Ca								
mg	637.4	222.5	631.2	242.4	637.2	232.4	648.0	215.6
Fe								
mg	8.1	2.4	8.1	2.7	8.1	2.6	8.1	2.5
Dietary fiber, total								
g	14.7	5.2	14.4	5.5	14.6	5.3	15.1	5.5
Sodium								
g	4.2	1.5	4.2	1.6	4.2	1.5	4.2	1.6
Recommendation met								
Carbohydrate†								
<55% Energy	58%		57%		59%		52%	
55–60% Energy	26%		26%		26%		28%	
≥60% Energy	16%		17%		15%		20%	
Fat†								
<25% energy	28%		36%		31%		28%	
SFAs‡								
<7% Energy	26%		30%		27%		23%	
Fiber, total†								
≥20 g	16%		12%		15%		17%	
Sodium†								
<3.9 g	49%		50%		48%		48%	

Table 2 | (Continued)

	Diabetes duration <10 years (*n* = 737)		Diabetes duration ≥10 years (*n* = 779)		Total (*n* = 1516)	
	Mean	SD	Mean	SD	Mean	SD
Nutritional intake						
Energy						
kcal	1,762	425	1,708	397	1,737	412
Carbohydrate						
% Energy	53.3	6.5	53.9	6.7	53.6	6.6
g	232.8	55.2	228.0	51.0	230.5	53.2
Protein						
% Energy	15.6	2.4	15.7	2.4	15.7	2.4
g	69.5	22.6	67.3	20.7	68.5	21.7
Fat						
% Energy	27.9	4.9	27.3	5.0	27.6	5.0
g	55.1	18.3	52.4	17.5	53.8	18.0
SFAs						
% Energy	7.9	1.7	7.9	1.7	7.9	1.7
MUFAs						
% Energy	9.1	2.0	8.9	2.0	9.0	2.0
PUFAs						
% Energy	6.7	1.5	6.5	1.5	6.6	1.5
n6						
% Energy	5.4	1.4	5.2	1.3	5.3	1.4
n3						
% Energy	1.6	0.4	1.5	0.4	1.6	0.4
Cholesterol						
mg	316.1	120.2	307.2	114.1	312.2	117.5
Ca						
mg	644.5	238.8	632.3	220.2	639.0	229.7
Fe						
mg	8.3	2.6	7.9	2.5	8.1	2.6
Dietary fiber Total						
g	15.0	5.4	14.4	5.2	14.7	5.3
Sodium						
g	4.3	1.6	4.1	1.5	4.2	1.5
Recommendation met						
Carbohydrate†						
<55% Energy	59%		57%		58%	
55–60% Energy	27%		25%		26%	
≥60% Energy	13%		19%		16%	
Fat†						
<25% Energy	28%		32%		30%	
SFAs‡						
<7% Energy	27%		27%		27%	
Fiber, total†						
≥20 g	17%		13%		15%	
Sodium†						
<3.9 g	48%		49%		48%	

MUFAs, mono-unsaturated fatty acids; n3, n-3 fatty acids; n6, n-6 fatty acids; PUFAs, poly-unsaturated fatty acids; SD, standard deviation; SFAs, saturated fatty acids. †Carbohydrate intake, 50–60% of total energy; fat intake, <25% total energy; fiber, >20 g/day; and sodium, <3.9 g (<10 g as salt) were recommended by the Japan Diabetes Society[17]. ‡Saturated fat intake should be <7% of total energy as recommended by the Canadian Diabetes Association[18] and the American Diabetes Association.[19]

Table 3 | Intake of selected food groups per day

	Men (*n* = 807)		Women (*n* = 709)		Age <60 years (*n* = 755)		Age ≥60 years (*n* = 761)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Grains (g)	207	58	173	40	194	54	189	52
Potato/aroid (g)	50	40	58	50	50	41	57	49
Soybeans/soy products (g)	68	49	75	54	71	51	72	52
Fruits (g)	121	101	148	108	126	107	140	103
Green-yellow vegetables (g)	130	69	147	66	136	67	140	68
Other vegetables (g)	174	103	200	99	184	100	188	104
Meat (g)	52	37	47	39	54	40	46	36
Fish (g)	103	61	97	59	101	61	100	60
Eggs (g)	30	18	28	16	29	16	29	17
Milk/dairy products (g)	165	109	177	94	168	108	173	97
Sweets/snacks (g)	16	20	20	21	18	21	17	20
Oil (g)	17	9	17	9	18	9	16	8
Alcoholic beverages (g)	155	195	14	48	99	180	80	142
Other beverages (g)	44	85	28	67	41	84	33	70

	Sedentary occupation (*n* = 1032)		Non-sedentary occupation (*n* = 366)		HbA1c <7% (*n* = 1266)		HbA1c ≥7% (*n* = 250)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Grains (g)	187	50	202	62	191	53	194	54
Potato/aroid (g)	53	42	55	45	53	42	57	58
Soybeans/soy products (g)	70	49	72	57	72	53	67	44
Fruits` (g)	139	105	118	109	132	104	141	112
Green-yellow vegetables (g)	139	68	132	67	137	67	143	70
Other vegetables (g)	188	102	176	100	184	102	195	103
Meat (g)	49	37	48	39	49	38	52	42
Fish (g)	99	60	100	62	102	61	93	58
Eggs (g)	29	17	28	16	29	17	30	16
Milk/dairy products (g)	170	101	169	107	168	102	184	105
Sweets/snacks (g)	18	20	19	22	17	20	20	23
Oil (g)	17	9	17	9	17	9	17	9
Alcoholic beverages (g)	83	160	103	166	96	169	54	116
Other beverages (g)	35	77	45	83	36	76	41	85

	Diabetes duration <10 years (*n* = 737)		Diabetes duration ≥10 years (*n* = 779)		Total (*n* = 1,516)	
	Mean	SD	Mean	SD	Mean	SD
Grains (g)	191	54	192	53	191	53
Potato/aroid (g)	56	45	51	45	54	45
Soybeans/soy products (g)	73	55	69	48	71	52
Fruits (g)	138	116	129	93	133	105
Green-yellow vegetables (g)	141	67	135	69	138	68
Other vegetables (g)	191	100	181	104	186	102
Meat (g)	51	39	48	37	50	38
Fish (g)	102	62	98	58	100	60
Eggs (g)	29	17	29	16	29	17
Milk/dairy products (g)	169	107	172	98	170	103
Sweets/snacks (g)	19	22	17	19	18	21
Oil (g)	18	9	16	9	17	9

Table 3 (Continued)

	Diabetes duration <10 years (n = 737)		Diabetes duration ≥10 years (n = 779)		Total (n = 1,516)	
	Mean	SD	Mean	SD	Mean	SD
Alcoholic beverages (g)	91	174	86	147	89	162
Other beverages (g)	38	81	35	73	37	77

HbA1c, glycated hemoglobin; SD, standard deviation.

1836 kcal/day to 1916 kcal/day, respectively. Thus, the JDCS patients consumed an energy-restricted diet reduced by 400–500 kcal/day in men and 200–300 kcal/day in women compared with Japanese men and women in the general population.

In addition, the energy intakes by the JDCS patients and Western patients with type 2 diabetes were similar. However, the mean BMI of the JDCS patients was within the normal range, and was much lower than in Western diabetic patients[3–6]. The differences in energy intake between the two groups were too small to explain the large difference in BMI. In terms of the biological aspects of ethnic differences, it is known that Asian people are more susceptible to pancreatic β-cell secretory defects and pronounced dysfunction in early insulin secretion than Western people[23]. In contrast, among Asian populations, the proportion of body fat and prevalence of prominent abdominal obesity are higher than in individuals of European origin with similar BMI values[23]. Also, ethnic differences in biological factors based on genetics, such as the basal metabolic rate, are assumed between Asian and Western people. Further studies are required to clarify the mechanism of the development of type 2 diabetes in consideration of an ethnic-specific constitution, and it should be investigated whether results of dietary assessments and actual food intake differ consistently between Asian and Western patients with diabetes.

The proportions of protein, fat and carbohydrate consumed by JDCS patients met the major current Western guidelines (American Association of Clinical Endocrinologists[24], European Association for the Study of Diabetes[25], Canadian Diabetes Association[18]), which recommend carbohydrate intake ranging from 45 to 65%, fat intake <30–35% and protein intake from 10 to 20%. Furthermore, mean carbohydrate intake as a percentage of energy intake (53.6%) met the current recommendations of the JDS (50–60%)[17], and mean fat intake (27.6%) was 2.6% higher than the recommendation (25% or less)[17]. Therefore, it was clarified that Japanese type 2 diabetic patients consumed a 'low-fat energy-restricted diet', which has been traditionally recommended in Western countries (generally 25–35% of energy from fat)[18,26,27], although the guidelines of the American Diabetes Association for 2011[19] stated the possibility of the effectiveness of both a low-carbohydrate and a low-fat calorie-restricted diet. These proportions of intake by the JDCS patients did not differ much according to sex, age, intensity of physical activity during work, HbA1C level and diabetes duration. In addition, the proportion of fat consumption by the JDCS patients met the definition of low fat intake reported in the recent systematic review by the American Diabetes Association, which might improve glycemic control, total cholesterol and low-density lipoprotein (LDL) cholesterol, but might also lower high-density lipoprotein (HDL) cholesterol[26]. However, the JDCS patients and Western type 2 diabetic patients had similar HDL cholesterol levels (1.4 mmol/L and 1.1–1.2 mmol/L, respectively)[3,4], which is probably a result of the fact that the serum level of HDL cholesterol is naturally higher in East Asians than in Western populations.

The proportions of protein, fat and carbohydrate as percentages of energy supply in the JDCS patients were similar to those reported in elderly Japanese type 2 diabetic patients (fat/carbohydrate: 25.6/59.0%)[2], the general Japanese population (25.8/59.3%)[27], and a comprehensive picture of the pattern of the country's food supply reported in the FAO Balance Sheet (27.3/59.5%)[7]. Furthermore, according to the report of the FAO in 1996[7], fat and carbohydrate as percentages of energy supply in the USA, European region, Spain, Korea, and South Africa were 34.5/53.1%, 33.5/54.4%, 39.5/47.5%, 20.0/68.9%, and 22.0/67.7%, respectively. Thus, the proportions of protein, fat and carbohydrate consumed by diabetic patients in each country were similar to those reported in the FAO Balance Sheet, which reflects dietary patterns for each country[7]. As well as in these countries, it can be estimated that Japanese type 2 diabetes patients' 'low-fat energy-restricted diet' is deeply ingrained in the ethnic-specific dietary pattern of Japan.

As a protein source, consumption of fish and soybean products was larger than that of meat and eggs, and this pattern was similar without regard to sex, age, intensity of physical activity during work, HbA1C level and diabetes duration. These results imply that dietary content and food patterns among Japanese patients with type 2 diabetes were quite close to those in Western countries that have been reported as decreasing the risk of obesity[28], type 2 diabetes[29] and mortality as a result of cardiovascular disease[29], which is known to be higher in Western countries than in Japan. Conversely, the American Diabetes Association noted that soy-derived supplements were not associated with a significant reduction in glycemic measures or risk factors for cardiovascular disease, and that there is limited evidence in relation to protein sources[26].

Table 4 | Summary of literature on dietary composition of diabetic patients including the current Japanese Diabetes Complications Study results

Study name or author	Method for measurement of dietary intake	Years carried out	Study population	Type of diabetes	No. participants (No. men)	Mean age (years)†	Energy intake (kcal)†	Carbohydrate intake (% energy)†	Fat intake (% energy)†	BMI†
Present study (JDCS)	FFQg	1996	Japanese	Type 2 diabetes	1,516 (805)	M: 58.4 W: 59.0	M: 1,819 W: 1,643	M: 53.0 W: 54.2	M: 26.7 W: 28.7	M: 22.7 W: 23.2
EURODIAB IDDM Complications Study Group[6]	3-day record	NA	European	IDDM	2,868 (1458)	33	M: 2,202 W: 1,604	M: 43.1 W: 41.9	M: 37.9 W: 37.9	M: 26 W: 28
	7-day food diaries	1993–1994	Spanish	Type 1 diabetes,	144 (70)	M: 25.0 W: 27.1	M: 2,217 W: 1,623	M: 39.5 W: 40.0	M: 41.5 W: 40.5	M: 22.4 W: 23.2
DNCT[3]				Type 2 diabetes	193 (81)	M: 62.2 W: 62.5	M: 1,788 W: 1453	M: 39.0 W: 38.0	M: 38.5 W: 36.0	M: 25.8 W: 28.5
Strong Heart Study (SHS)[5]	24-h dietary recall	1997–1999	American Indians	Diabetes	1,008 (316)	M: 63.5 W: 63.5	M: 1,595 W: 1,422	M: 48.7 W: 48.7	M: 35.3 W: 35.9	M: 30.6 W: 32.8
NHANES[5]	24-h dietary recall	1999–2000	General US population	Diabetes	373 (190)	M: 64.9 W: 65.3	M: 1,852 W: 1,384	M: 48.4 W: 49.8	M: 34.7 W: 33.8	M: 30.5 W: 32.8
Diabetic Educational Eating Plan study[4]	7-day dietary recall	2005–2006	Clinical trial participants in USA White 85%, Black 5%, Asian 5%, other 5%	Type 2 diabetes	40 (19)	53.5	1,778	36.7	44.6	35.8 <25 5.0% 25–30 17.5% ≥30 77.5%
Lee *et al.*[20]	24-h dietary recall	2003–2004	Korean	Type 2 diabetes	154 (78)	61	M: 1,788 W: 1,546	M: 66.7‡ W: 68.4‡	M: 16.3‡ W: 16.2‡	M: NA W: NA
Kamada *et al.*[2]	FFQg	2001	Japan	Type 2 diabetes	912 (417)	M: 71.4 W: 72.3	M: 1,802 W: 1,661	M: 59.5 W: 58.6	M: 25.4 W: 25.8	M: 23.5 W: 24.0
Nthangeni *et al.*[21]	24-h dietary recall	1998	South African	Type 2 diabetes	290 (133)	<40§	M: 1,971¶ W: 1,712¶	M: 66.7 W: 65.8	M: 13.4 W: 14.4	M: ≥30 15.8% W: ≥30 40.8%

BMI, body mass index; DNCT, Diabetes Nutrition and Complications Trial; EURODIAB IDDM, European Diabetes Centers Study of Complications in Patients with Insulin-Dependent Diabetes Mellitus; IDDM, insulin-dependent diabetes mellitus; JDCS, Japan Diabetes Complications Study; M, men; NA, not available; NHANES, National Health and Nutrition Examination Survey; SHS, Strong Heart Study; W, women. †Maximum value and minimum value are shown if mean value was not available. ‡Estimated from mean value. §Age range was described because mean age was not reported. ¶1 kcal = 4.184 kJ.

Further studies are required to clarify whether glycemic control and risk of cardiovascular disease are affected by soy consumption and other protein sources over a long time period.

Furthermore, 73% of the JDCS patients met the recommendations for saturated fatty acid (SFA) intake (<7% of energy intake[18,19]), and their mean SFA intake was lower than those of Western type 2 diabetes participants (7.9% and 11.2–14.5%, respectively)[3–5].

Just 15% of the JDCS patients ingested 20 g or more of fiber per day, and their mean fiber intake (14.7 g/day) was similar to that of Western type 2 diabetes participants (11.4–20.5 g/day)[3–5] and the general Japanese population (15.7 g/day)[27]. More fiber consumption is recommended for JDCS patients, because it was reported that a high intake of dietary fiber improved fasting plasma glucose and HbA1c values in patients with type 2 diabetes in randomized crossover studies[26]. Increasing fiber intake is recommended to keep diabetes under good control.

The JDCS patients consumed excess sodium, and their mean sodium intake was 4.2 g/day. Thus, their mean sodium intake was lower than in the general Japanese population (4.6 g/day)[27], and higher than in the USA and UK general populations (3.6 and 3.4 g/day, respectively)[30], and a diabetic population in the USA (2.5–3.4 g/day)[5]. High sodium intake directly increases the risk of stroke, and the risk of stroke is decreased by 6% for each 1.15-g/day reduction in sodium intake[31]. Given a 1.15 g/day sodium reduction in JDCS patients, which would result in a sodium intake equal to that in Western diabetes patients, it could be expected that the morality risk of stroke in JDCS patients would be reduced from 7.5 per 1,000 patient-years[32] to 7.0 per 1,000 patient-years.

The present study had several limitations. First, the survey data were collected in 1996, 17 years ago. However, according to results of the National Health and Nutrition Survey[22] in 1996 and 2006, energy intake was slightly decreased (50–100 kcal/day) from 1996 to 2006, and the proportions of fat and carbohydrate did not differ greatly as reported in the FAO Balance Sheet (in 1996: 27.3/59.5%, 2006: 28.7/58.1%, respectively)[7]. Additionally, the characteristics of energy intake and nutritional and food intake by the JDCS patients differed very little between patients <60 years and those aged 60 years or over.

Second, inaccuracies in participants' reported dietary composition on the self-recording questionnaire are possible. Previous data show that being a woman, being obese or desiring to reduce bodyweight are factors related to the likelihood of underreporting energy intake[33]. However, the Japanese type 2 diabetic patients had a much lower BMI compared with Western patients[8]. An additional limitation is that just 74.5% of participants completed the FFQg, and their characteristics were slightly different from those who did not complete the FFQg; therefore, the differences between those who did and did not complete the questionnaire could have potentially influenced the cross-study comparisons of dietary intake. Finally, the method of dietary assessment for type 2 diabetes patients was different in each study that we examined. Establishment of a method that would allow a more direct country-by-country comparison is required.

In conclusion, we clarified that Japanese with type 2 diabetic patients had a 'high-carbohydrate low-fat' diet in comparison with Western diabetic patients, but had an energy intake similar to Western patients with diabetes. Furthermore, the proportions of protein, fat, and carbohydrate consumption and food intake were also quite close to the food pattern that has been traditionally recommended in Western countries.

The present study was a descriptive epidemiological examination to elucidate the actual dietary intake among Japanese middle-aged patients with type 2 diabetes who participated in a nationwide cohort study, and to compare findings with those of Western diabetic patients. Thus, we could not establish a cause–effect model between the risk of diabetes complications and the characteristics of food or nutritional intake, although medical nutritional therapy is an essential constituent for diabetes management.

However, the mean BMI of the JDCS patients was within normal range, whereas the BMI in the Western diabetic patients was higher, even though energy intake in both groups was similar. Additionally, the features of energy intake, and nutritional and food intake also did not differ greatly among the JDCS patients regardless of the differences in sex, age, intensity of physical activity during work, HbA1C level and diabetes duration.

It is possible that the difference in the dietary pattern and ethnic-specific characteristics, such as those related to body fat, prominent abdominal obesity and insulin deficiency and resistance, between Asian and Western people would result in different effects from medical nutritional therapy. Considering ethnic-specific dietary patterns and characteristics is important to explore effective medical nutritional therapy.

Based on preliminary findings, more research is required to survey how food and nutritional intakes among Asian type 2 diabetes patients are associated with the risk of development of diabetic complications, and results should be compared with those in Western patients.

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Predicting Macro- and Microvascular Complications in Type 2 Diabetes

The Japan Diabetes Complications Study/the Japanese Elderly Diabetes Intervention Trial risk engine

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OBJECTIVE—To develop and validate a risk engine that calculates the risks of macro- and microvascular complications in type 2 diabetes.

RESEARCH DESIGN AND METHODS—We analyzed pooled data from two clinical trials on 1,748 Japanese type 2 diabetic patients without diabetes complications other than mild diabetic retinopathy with a median follow-up of 7.2 years. End points were coronary heart disease (CHD), stroke, noncardiovascular mortality, overt nephropathy defined by persistent proteinuria, and progression of retinopathy. We fit a multistate Cox regression model to derive an algorithm for prediction. The predictive accuracy of the calculated 5-year risks was cross-validated.

RESULTS—Sex, age, HbA_{1c}, years after diagnosis, BMI, systolic blood pressure, non-HDL cholesterol, albumin-to-creatinine ratio, atrial fibrillation, current smoker, and leisure-time physical activity were risk factors for macro- and microvascular complications and were incorporated into the risk engine. The observed-to-predicted (O/P) ratios for each event were between 0.93 and 1.08, and Hosmer-Lemeshow tests showed no significant deviations between observed and predicted events. In contrast, the UK Prospective Diabetes Study (UKPDS) risk engine overestimated CHD risk (O/P ratios: 0.30 for CHD and 0.72 for stroke). C statistics in our Japanese patients were high for CHD, noncardiovascular mortality, and overt nephropathy (0.725, 0.696, and 0.767) but moderate for stroke and progression of retinopathy (0.636 and 0.614). By combining macro- and microvascular risks, the classification of low- and high-risk patients was improved by a net reclassification improvement of 5.7% ($P = 0.02$).

CONCLUSIONS—The risk engine accurately predicts macro- and microvascular complications and would provide helpful information in risk classification and health economic simulations.

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Risk classification for vascular complications is of particular importance in diabetes care, and there is a need for validated diabetes-specific risk engines (1,2). Asian populations account for >60% of the world's diabetes patients (3,4), but data used for most of the engines specific to diabetes include only a limited number of Asians (5–9). Asian patients with diabetes have several important features. We previously reported that Japanese patients have a markedly low prevalence of obesity and low incidence rates of overt nephropathy and diabetic retinopathy (10–13). Furthermore, the risk factor profiles of diabetes complications are quite different between Japanese and Western subjects with diabetes (14). In cohort studies of multiple ethnic groups, lower incidence rates of cardiovascular disease (CVD) were observed in Asian patients than in whites (15,16). Given the overestimation of risks of coronary heart disease (CHD) and stroke in Chinese patients by the UK Prospective Diabetes Study (UKPDS) risk engine (17,18), risk engines for non-Asian populations may not be transportable to Asian patients. To our knowledge, only the Hong Kong Diabetes Registry (HKDR) has developed risk engines for Asian patients with diabetes (17–20).

Most risk engines have focused on classical cardiovascular risk factors such as control of HbA_{1c}, blood pressure, and lipids (5–9,17–20), but, increasingly, studies have suggested the importance of lifestyle factors. In fact, exercise has been shown to reduce all-cause mortality (21,22) and is encouraged by guidelines for type 2 diabetes (23,24). A recent survey of general practitioners in Germany indicated that those physicians thought that to be useful, risk engines should link estimated risks with appropriate recommendations for lifestyle changes (25). Another concern is the lack of capacity to assess multiple diseases simultaneously (25). However, just combining the results of risk engines specific to each vascular complication may yield biased estimates