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High Dietary Glycemic Load is Associated with Poor Functional Outcome in Patients with Acute Cerebral Infarction

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Background and Purpose Elevated postprandial blood glucose is a critical risk factor for stroke. The dietary glycemic load (GL) and glycemic index (GI) are frequently used as markers of the postprandial blood glucose response to estimate the overall glycemic effect of diets. We hypothesized that high dietary GL, GI, or total carbohydrate intake is associated with a poor functional outcome in patients with acute ischemic stroke.

Methods We prospectively included 263 first-ever ischemic stroke patients who completed a semiquantitative food-frequency questionnaire. The dietary GL, GI, and total carbohydrate intake were investigated by examining the average frequency of intake during the previous year based on reference amounts for various food items. Poor functional outcome was defined as a score on the modified Rankin Scale (mRS) of ≥3 at 3 months after stroke.

Results The patients were aged 65.4±11.7 years (mean±standard deviation), and 58.2% of them were male. A multivariate analysis adjusted for age, sex, marital status, prestroke mRS score, diabetes mellitus, hyperlipidemia, body mass index, triglycerides, low-density lipoprotein, hemoglobin A1c, stroke classification, and National Institutes of Health Stroke Scale score, early neurological deterioration, and high-grade white-matter hyperintensities revealed that the dietary GL and total carbohydrate intake were associated with a poor functional outcome, with odds ratios for the top quartile relative to the bottom quartile of 28.93 (95% confidence interval=2.82−296.04) and 36.84 (95% confidence interval=2.99−453.42), respectively (p for trend=0.002 and 0.002, respectively). In contrast, high dietary GI was not associated with a poor functional outcome (p for trend=0.481).

Conclusions Increased dietary GL and carbohydrate intake were associated with a poor short-term functional outcome after an acute ischemic stroke.

Key Words glycemic load, glycemic index, carbohydrate intake, stroke, outcome.

INTRODUCTION

Elevated postprandial blood glucose is a critical risk factor for stroke regardless of the presence of diabetes mellitus,[1,2] and increased postprandial blood glucose is mostly impacted by the dietary carbohydrate intake.[3] Because carbohydrates vary in size, fiber content, and chemical structure, the increase in postprandial blood glucose may vary depending on type of carbohydrate ingested.[4] The dietary glycemic load (GL) and glycemic index (GI) are frequently used as markers of the postprandial blood glucose response to estimate the overall impact of dietary carbohydrate intake.[5]

Previous epidemiological cohort studies have revealed that high GL and GI are associated with the risk of stroke.[6-8] An increased GI predicted a greater risk of mortality after stroke in

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population-based studies in Japan[8] and Australia.[9] Because stroke can cause serious handicaps and the short-term function after a first ischemic stroke is associated with the long-term outcome,[10] risk factors for poor functional outcome should be evaluated after a stroke. The association of the dietary GL or GI with functional outcome at 3 months after ischemic stroke has not been reported.

A high carbohydrate intake related to a high dietary GL or GI has an unfavorable impact on glucose and lipid metabolism,[11] and the impact could potentially increase the risk of vascular events and poor stroke prognosis.[12,13] We therefore hypothesized that high dietary GL, GI, or total carbohydrate intake is associated with a poor functional outcome in patients with acute ischemic stroke. In this study, we investigated the relationship between the dietary GL or GI and the functional outcome after an acute ischemic stroke.

METHODS

Subjects

We prospectively included 263 patients who were admitted to Ewha Womans University Mokdong Hospital within 7 days after they experienced their first symptomatic ischemic stroke. Patients were evaluated for past medical history, family history, and using brain imaging studies (CT or MRI), vascular imaging studies (digital subtraction angiography, CT angiography, or MR angiography), chest X-ray, 12-lead electrocardiography, transthoracic echocardiography, routine blood tests, and with electrocardiography monitoring for a median period of 3 days at a stroke intensive care unit. Blood samples were collected within 24 hours of admission and after fasting for more than 12 hours, and the following parameters were analyzed: white blood cell count, hemoglobin, fasting glucose, triglycerides, low-density lipoprotein, hemoglobin A1c (HbA1c), insulin, and C-reactive protein.

Strokes were classified according to the Trial of Org 10172 in Acute Stroke Treatment system.[14] The severity of neurological deficits was determined by using the National Institutes of Health Stroke Scale (NIHSS) at admission.[15,16] Early neurological deterioration was defined as any increase in the NIHSS score within 7 days after admission.[17] The extent of white-matter hyperintensities (WMHs) was determined on fluid-attenuated inversion recovery images of periventricular white matter or deep white matter according to the Fazekas scoring system. A Fazekas score of ≥2 for the periventricular white matter and/or of ≥2 for the deep white matter was considered indicative of high-grade WMHs.[18] The presence of symptomatic cerebral atherosclerosis was defined as >50% stenosis and/or occlusion of extracranial and/or intracranial arteries that could explain stroke-related symptoms based on the North American Symptomatic Carotid Endarterectomy Trial[19] or Warfarin-Aspirin Symptomatic Intracranial Disease study,[20] respectively. To assess functional outcome, the modified Rankin Scale (mRS) was used. Prestroke mRS score and mRS score at 3 months after the index stroke was assessed by a stroke neurologist and/or a well-trained stroke specialist nurse. This study was conducted with the approval of the Institutional Review Board of Ewha Womans University Mokdong Hospital (approval no. ECT 11-59-21). Informed consent was received from patients and their caregivers.

Semiquantitative food-frequency questionnaire, dietary glycemic load, and glycemic index

The survey was conducted through one-on-one interviews with patients and their caregivers, each of which typically took 20−30 minutes. Dietary intake was assessed with a validated Korean version of a semiquantitative food-frequency questionnaire (SQFFQ).[21] The SQFFQ comprised a list of 111 foods, with the average frequency of intake of each food during the previous year reported based on a reference amount. The frequency of food intake was categorized into 'almost never,' 'once a month,' 'two or three times a month,' 'one or two times a week,' 'three or four times a week,' 'once a day,' 'two times a day,' and 'three times a day.' The amount of each food consumed was categorized into 'less than the reference amount,' 'the reference amount,' and 'more than the reference amount.' Food and nutrient intakes were calculated with the aid of the Computer-Aided Nutritional Analysis Program (version 4.0, Korea Nutrition Society, Seoul, Korea).[21]

The GI is a measure of the postprandial blood glucose response to carbohydrate intake when compared with a reference foodstuff (either glucose or white bread). The GI can be considered an indicator of the quality of dietary carbohydrates that are consumed. The GI values of foods can be obtained from an international table[22] or the www.glycemicindex.com website. The dietary GI can be calculated as the sum of GI values of each consumed food item, multiplied by the percentage of carbohydrate content and consumption frequency and divided by the total carbohydrate consumption. The GL is calculated by multiplying the GI of a food item with available carbohydrate content but without dividing by the total carbohydrate consumption, which indicates both the quality and quantity of carbohydrate intake.[6] The total carbohydrate intake is measured by summing the scores on validated food-frequency questionnaires.

Risk factors

Hypertension was defined as a resting systolic blood pressure of ≥140 mm Hg or diastolic blood pressure of ≥90 mm Hg on

repeated measurements, or treatment with antihypertensive medications. Diabetes mellitus was diagnosed if a patient had a fasting blood glucose level of ≥7.0 mmol/L or was being treated with oral hypoglycemic agents or insulin. Hyperlipidemia was diagnosed for low-density lipoprotein ≥4.1 mmol/L or total cholesterol ≥6.2 mmol/L. Subjects with a recent weekly alcohol intake that regularly exceeded 300 g of ethanol were classified as heavy drinkers. Patients were defined as smokers if they were current smokers or had stopped smoking within the previous year. Body mass index was calculated by dividing body weight by height squared (in units of kg/m^2). Patients who had exercised more than once weekly for the past 6 months were classified as performing regular exercise.[23,24] The marital status was categorized into single (including never married, divorced, separated, or bereaved) and married.

Statistical analysis

Statistical analyses were conducted with the Windows SPSS software package (version 18.0, SPSS Inc., Chicago, IL, USA). The independent *t*-test, Mann-Whitney U test, one-way analysis of variance with Bonferroni post-hoc analysis, and Kruskal-Wallis test for continuous variables and the chi-square test or Fisher's exact test for categorical variables were applied to quartiles of the dietary GL, GI, and total carbohydrate intake. Trends across quartiles were tested by using the median of each quartile as the predictor in linear models for continuous variables and in logistic models for categorical variables. Functional outcome was dichotomized into good (mRS score <3) or poor (mRS score ≥3) in a binary logistic regression analysis, and subdivided into mRS scores of 0, 1, 2, and 3–6 in an ordinal logistic regression analysis. Univariate and multivariate binary and ordinal logistic regression analyses–with a dependent variable of the mRS score at 3 months after the index stroke–were conducted to determine predictive factors for functional outcome. Multivariate analyses were adjusted for age, sex, variables with $p<0.1$ in the univariate analysis (marital status, prestroke mRS score, hyperlipidemia, body mass index, stroke classification, NIHSS score, early neurological deterioration, and high-grade WMHs), and variables related to GL, GI, or total carbohydrate intake (diabetes mellitus, triglycerides, low-density lipoprotein, and HbA1c).

There was no interaction of dietary GL with diabetes mellitus or HbA1c (p=0.964 and 0.484, respectively). Multicollinearity was present between dietary GL and the total carbohydrate intake (variance inflation factor was higher than 6 when the dependent variable was defined as the functional outcome at 3 months after the index stroke in multivariate linear regression), and so dietary GL, GI, and total carbohydrate intake were analyzed separately in multivariate analyses. A two-tailed p value of <0.05 was considered indicative of statistical significance.

RESULTS

We first included 306 patients who completed an SQFFQ and were confirmed as having experienced an acute ischemic stroke by brain CT, MRI, or both imaging modalities. Because our study used a survey, patients suspected of having cognitive impairment (Mini-Mental State Examination score <24) or aphasia were not enrolled (n=15).[25] After excluding patients for whom clinical information or blood laboratory findings were lacking (n=11), whose daily calorie intake was outside of the range of 500–5,000 kcal (n=4), who had rare causes of stroke such as arterial dissection (n=2) or venous thrombosis (n=1), and for whom outcome data at 3 months after the index stroke were not available (n=10), finally 263 patients were included in this study (Fig. 1).

The included patients were aged 65.4±11.7 years (mean±standard deviation), and 153 (58.2%) of them were male. Their dietary GL and GI were 158.7±72.7 and 59.6±4.8, respectively. Stroke classifications of large-artery atherosclerosis, lacune, and cardioembolism were most common. The median NIHSS score at admission was 3, with an interquartile range of 1–6. Demographic data for the study subjects and comparative analyses according to quartiles of the dietary GL are summarized in Table 1. The prevalence of male sex

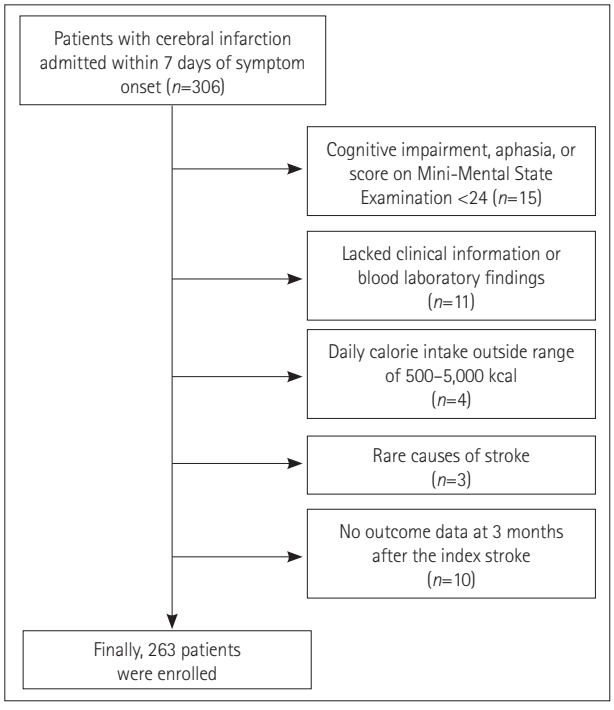

Fig. 1. Flow chart depicting the participation of subjects in this study.

Table 1. Comparison of demographic and clinical data according to quartiles of dietary GL

Variables	Q1 (*n*=66)	Q2 (*n*=65)	Q3 (*n*=66)	Q4 (*n*=66)	Total (*n*=263)	*p**	*p* for trend†
GL	90.2 [77.0–98.0]	125.3 [113.8–135.8]	170.6 [163.2–182.1]	222.2 [201.9–268.8]	144.9 [106.0–188.5]		
Demographic data							
Sex, male	32 (48.5)	36 (55.4)	43 (65.2)	42 (63.6)	153 (58.2)	0.042	0.042
Age, years	65.8±13.3	65.9±12.2	66.1±10.9	63.8±10.4	65.4±11.7	0.654	0.116
Marital status, married	39 (59.1)	44 (67.7)	45 (68.2)	44 (66.7)	172 (65.4)	0.375	0.375
Education, >7 years	14 (21.2)	14 (21.5)	10 (15.2)	11 (16.7)	49 (18.6)	0.718	0.352
Prestroke mRS score	0 [0–1]	0 [0–1]	0 [0–1]	0 [0–1]	0 [0–1]	0.165	0.520
Risk factors							
Hypertension	25 (37.9)	32 (49.2)	32 (48.5)	32 (48.5)	121 (46.0)	0.502	0.257
Diabetes mellitus	12 (18.2)	22 (33.8)	26 (39.4)	34 (51.5)	94 (35.7)	0.001	0.001
Hyperlipidemia	11 (16.7)	20 (30.8)	13 (19.7)	10 (15.2)	54 (20.5)	0.113	0.487
Alcohol intake	24 (36.4)	27 (41.5)	31 (47.0)	36 (54.5)	118 (44.9)	0.734	0.029
Smoking	23 (34.8)	22 (33.8)	29 (43.9)	29 (43.9)	103 (39.2)	0.466	0.166
Body mass index, kg/m^2	24.2±3.5	27.3±2.4	23.7±2.8	24.0±3.5	24.8±2.2	0.307	0.442
Regular exercise	22 (33.3)	22 (33.8)	26 (39.4)	25 (37.9)	95 (36.1)	0.858	0.470
Laboratory findings							
White blood cell count, ×10^3/μL	7.0±3.1	6.9±1.9	7.8±2.6	7.9±3.3	7.4±2.8	0.099	0.208
Hemoglobin, mg/dL	13.4±1.6	13.2±1.4	13.3±2.0	13.3±1.6	13.3±1.6	0.946	0.953
Fasting glucose, mg/dL	112.7±36.0	114.6±36.0	124.1±38.8	127.2±45.7	119.7±39.6	0.100	0.001
Triglycerides, mg/dL	104.9±48.9	131.8±72.0	123.0±37.0	138.6±92.6	124.5±67.0	0.024	0.012
Low-density lipoprotein, mg/dL	114.6±31.6	118.7±33.6	112.2±27.7	120.3±36.0	116.4±32.3	0.468	0.549
HbA1c, %	5.8±0.8	6.3±1.6	6.5±1.4	6.9±1.7	6.6±1.4	0.001	0.001
Insulin, μIU/mL	6.4±4.5	6.4±5.1	8.0±7.6	7.3±8.6	7.0±6.7	0.439	0.071
C-reactive protein, mg/dL	0.7±1.8	0.8±2.3	0.8±1.7	0.6±1.4	0.7±1.8	0.916	0.725
Stroke classification						0.770	N/A
Large-artery atherosclerosis	18 (27.3)	20 (30.8)	27 (40.9)	26 (39.4)	91 (34.6)		
Lacune	26 (39.4)	25 (38.5)	19 (28.8)	19 (28.8)	89 (33.8)		
Cardioembolism	14 (21.2)	11 (16.9)	11 (16.7)	9 (13.6)	45 (17.1)		
Multiple causes	2 (3.0)	5 (7.7)	4 (6.1)	6 (9.1)	17 (6.5)		
Negative evaluation	6 (9.1)	4 (6.2)	5 (7.6)	6 (9.1)	21 (8.0)		
NIHSS score	3 [1–6]	2 [1–6]	3 [1–5]	3 [2–5]	3 [1–6]	0.404	0.695
Early neurological deterioration	5 (7.6)	6 (9.2)	6 (9.1)	3 (4.5)	20 (7.6)	0.722	0.529
High-grade WMHs	15 (22.7)	14 (21.5)	13 (19.7)	26 (39.4)	68 (25.9)	0.035	0.047
Symptomatic cerebral atherosclerosis	18 (27.3)	20 (30.8)	19 (28.8)	25 (37.9)	82 (31.2)	0.566	0.244
SQFFQ data							
GI	59.6 [56.1–62.4]	58.5 [54.9–62.3]	59.4 [56.4–62.4]	60.6 [57.3–63.4]	59.6 [56.2–62.7]	0.038	0.004
Total carbohydrates, g/day	148.5 [125.0–169.4]	215.2 [197.2–232.1]	286.2 [268.8–306.3]	372.0 [328.4–450.5]	245.6 [180.7–321.1]	0.001	0.001
Total energy, kcal	1,231.6±444.1	1,665.4±424.3	2,081.7±559.3	2,863.5±803.8	1,961.7±833.9	0.001	0.001
Fat, g/day	38.1±24.6	47.3±22.3	56.9±30.0	76.7±35.3	54.8±31.8	0.001	0.001
Protein, g/day	54.2±24.7	69.6±25.9	85.0±32.8	109.6±36.7	79.6±36.6	0.001	0.001
Dietary fiber, g/day	16.2±7.2	22.9±10.5	29.4±10.2	35.7±13.9	26.0±12.9	0.001	0.001
Grains, g/day	260.7±229.6	355.6±605.9	307.4±162.2	456.7±261.2	345.1±362.7	0.013	0.004
Starch, g/day	42.5±59.1	72.6±159.7	45.3±54.6	63.1±81.8	55.8±98.3	0.001	0.165
Sugar, g/day	32.7±54.1	31.0±35.6	32.7±35.6	40.3±46.8	34.2±43.7	0.625	0.070

Data are median [interquartile range], *n* (%), or mean±standard deviation values.
Q1 and Q4, top and bottom quartiles of the GI, respectively.
**p*<0.05, †*p*<0.1.
GI: glycemic index, GL: glycemic load, HbA1c: hemoglobin A1c, mRS: modified Rankin Scale, NIHSS: National Institutes of Health Stroke Scale, SQFFQ: semiquantitative food-frequency questionnaire, WMHs: white-matter hyperintensities.

Table 2. Comparison of demographic and clinical data according to quartiles of total carbohydrate intake

Variables	Q1 (*n*=65)	Q2 (*n*=66)	Q3 (*n*=66)	Q4 (*n*=66)	Total (*n*=263)	*p**	*p* for trend†
Total carbohydrates, g/day	147.4 [124.6–169.0]	214.6 [200.0–227.9]	285.4 [269.6–304.7]	374.9 [341.2–450.5]	245.6 [180.7–321.1]		
Demographic data							
Sex, male	34 (52.3)	33 (50.0)	44 (66.7)	42 (63.6)	153 (58.2)	0.139	0.064
Age, years	66.8±12.0	65.0±13.4	65.0±11.3	64.8±10.2	65.4±11.7	0.751	0.368
Marital status, married	41 (63.1)	43 (65.2)	45 (68.2)	43 (65.2)	172 (65.4)	0.943	0.726
Education, >7 years	11 (16.9)	15 (22.7)	15 (22.7)	8 (12.1)	49 (18.6)	0.330	0.498
Prestroke mRS score	0 [0–1]	0 [0–1]	0 [0–1]	0 [0–1]	0 [0–1]	0.157	0.513
Risk factors							
Hypertension	23 (35.4)	35 (53.0)	32 (48.5)	31 (47.0)	121 (46.0)	0.217	0.278
Diabetes mellitus	15 (23.1)	23 (34.8)	26 (39.4)	30 (45.5)	94 (35.7)	0.054	0.007
Hyperlipidemia	9 (13.8)	21 (31.8)	15 (22.7)	9 (13.6)	54 (20.5)	0.029	0.651
Alcohol intake	24 (36.9)	28 (42.4)	30 (45.5)	36 (54.5)	118 (44.9)	0.228	0.387
Smoking	23 (35.4)	21 (31.8)	31 (47.0)	28 (42.4)	103 (39.2)	0.276	0.179
Body mass index, kg/m^2	27.2±3.5	24.3±3.4	24.1±3.0	23.6±3.3	24.8±2.2	0.336	0.109
Regular exercise	21 (32.3)	24 (36.4)	22 (33.3)	28 (42.4)	95 (36.1)	0.621	0.304
Laboratory findings							
White blood cell count, ×10^3/μL	7.1±3.2	6.8±1.9	8.2±3.1	7.6±2.8	7.4±2.8	0.040	0.073
Hemoglobin, mg/dL	13.4±1.5	13.2±1.5	13.3±2.1	13.3±1.3	13.3±1.6	0.932	0.942
Fasting glucose, mg/dL	114.5±35.6	117.0±38.8	114.6±35.1	132.7±45.9	119.7±39.6	0.023	0.018
Triglycerides, mg/dL	107.8±51.3	128.2±67.2	129.5±62.9	132.4±81.5	124.5±67.0	0.136	0.043
Low-density lipoprotein, mg/dL	111.2±26.5	122.4±36.0	113.3±29.4	118.7±35.8	116.4±32.3	0.179	0.451
HbA1c, %	6.0±0.8	6.4±1.6	6.4±1.4	6.9±1.7	6.6±1.4	0.007	0.001
Insulin, μIU/mL	6.4±4.5	6.3±6.9	8.0±7.7	7.3±8.2	7.0±6.7	0.342	0.174
C-reactive protein, mg/dL	0.7±1.8	0.7±2.3	0.5±1.2	0.9±1.9	0.7±1.8	0.839	0.849
Stroke classification						0.635	N/A
Large-artery atherosclerosis	16 (24.6)	22 (33.3)	28 (42.4)	25 (37.9)	91 (34.6)		
Lacune	28 (43.1)	22 (33.3)	19 (28.8)	20 (30.3)	89 (33.8)		
Cardioembolism	14 (21.5)	10 (15.2)	10 (15.2)	11 (16.7)	45 (17.1)		
Multiple causes	2 (3.1)	7 (10.6)	4 (6.1)	4 (6.1)	17 (6.5)		
Negative evaluation	5 (7.7)	5 (7.6)	5 (7.6)	6 (9.1)	21 (8.0)		
NIHSS score	3 [1–5]	2 [1–6]	3 [1–5]	3 [2–5]	3 [1–6]	0.301	0.151
Early neurological deterioration	5 (7.7)	6 (9.1)	5 (7.6)	4 (6.1)	20 (7.6)	0.934	0.661
High-grade WMHs	16 (24.6)	15 (22.7)	15 (22.7)	22 (33.3)	68 (25.9)	0.449	0.279
Symptomatic cerebral atherosclerosis	16 (24.6)	23 (34.8)	19 (28.8)	24 (36.4)	82 (31.2)	0.437	0.256
SQFFQ data							
GL	90.0 [77.0–98.3]	126.4 [112.8–136.1]	170.7 [163.2–183.2]	222.2 [195.7–268.8]	144.9 [106.0–188.5]	0.001	0.001
GI	60.9 [58.1–62.9]	58.4 [54.6–62.7]	60.4 [57.4–62.8]	59.6 [55.3–62.1]	59.6 [56.2–62.7]	0.174	0.286
Total energy, kcal	1,170.6±395.6	1,660.8±375.4	2,056.8±453.8	2,946.5±768.4	1,961.7±833.9	0.001	0.001
Fat, g/day	34.2±21.7	47.2±20.1	55.7±26.5	81.6±35.8	54.8±31.8	0.001	0.001
Protein, g/day	49.1±19.8	69.0±20.7	83.8±27.4	116.3±37.4	79.6±36.6	0.001	0.001
Dietary fiber, g/day			28.4±9.3	39.2±13.2	26.0±12.9	0.001	0.001
Grains, g/day	253.2±224.9	364.2±601.8	301.2±128.1	460.2±278.5	345.1±362.7	0.007	0.005
Starch, g/day	35.9±37.3	75.0±164.3	40.4±42.1	71.7±86.7	55.8±98.3	0.035	0.183
Sugar, g/day	32.9±54.4	29.0±34.4	33.4±33.6	41.4±48.7	34.2±43.7	0.422	0.213

Data are median [interquartile range], *n* (%), or mean±standard-deviation values.
*$p<0.05$, †$p<0.1$.
GI: glycemic index, GL: glycemic load, HbA1c: hemoglobin A1c, mRS: modified Rankin Scale, NIHSS: National Institutes of Health Stroke Scale, SQFFQ: semiquantitative food-frequency questionnaire, WMHs: white-matter hyperintensities.

and a history of diabetes mellitus increased with the dietary GL. In addition, the fasting glucose, triglycerides, HbA1c, high-grade WMHs, dietary GI, total energy intake, total carbohydrate intake, and intakes of fat, protein, dietary fiber, and grains increased with the quartiles of the dietary GL.

The results of comparative analyses according to quartiles of the total carbohydrate intake are summarized in Table 2. The prevalence of a history of diabetes mellitus increased with the intake of total carbohydrate. In addition, fasting glucose, triglycerides, HbA1c, dietary GL, total energy intake, and intakes of fat, protein, dietary fiber, and grains increased with the quartiles of total carbohydrate intake.

The results of a comparative analysis between good and poor outcome groups are presented in Supplementary Table 1 (in the online-only Data Supplement). A multivariate binary logistic analysis revealed that a high dietary GL was associated with an increased risk of a poor functional outcome [odds ratio (OR) for top quartile relative to bottom quartile=28.93, 95% confidence interval (CI)=2.82–296.04, *p* for linear trend=0.002]. The total carbohydrate intake was associated with an increased risk of a poor functional outcome (OR for top quartile relative to bottom quartile=36.84, 95% CI=2.99–453.42, *p* for linear trend=0.002). In contrast, a high dietary GI was not associated with a poor functional outcome (OR for top quartile relative to bottom quartile=3.60, 95% CI=0.54–23.76, *p* for linear trend=0.481) (Table 3 and Supplementary Tables 2–5 in the online-only Data Supplement). A multivariate ordinal logistic analysis found that a high dietary GL was associated with an increased risk of a poor functional outcome (OR for top quartile relative to bottom quar-

Table 3. Associations of dietary GL, GI, and total carbohydrate intake with a poor functional outcome

Variables	GL	GI	Total carbohydrates
Binary logistic regression (mRS score=0–2 versus 3–6)			
Continuous variables, OR (95% CI), *p*	1.01 (1.00–1.02), 0.003	1.00 (0.89–1.12), 0.982	1.01 (1.00–1.02), 0.005
Ordinal variables, quartile; OR (95% CI), *p* for trend	3.38 (1.66–6.90), 0.002	1.20 (0.71–2.03), 0.481	3.08 (1.50–6.32), 0.002
Q1, Reference	1	1	1
Q2, OR (95% CI), *p*	6.31 (0.59–67.39), 0.127	4.25 (0.69–25.94), 0.117	12.64 (1.12–142.14), 0.040
Q3, OR (95% CI), *p*	32.78 (2.81–381.86), 0.005	1.83 (0.26–12.63), 0.538	20.64 (1.68–253.56), 0.018
Q4, OR (95% CI), *p*	28.93 (2.82–296.04), 0.005	3.60 (0.54–23.76), 0.182	36.84 (2.99–453.42), 0.005
Ordinal logistic regression (mRS score=0, 1, 2, 3–6)			
Continuous variables, OR (95% CI), *p*	1.00 (1.00–1.03), 0.005	1.03 (0.95–1.11), 0.519	1.00 (1.00–1.03), 0.006
Ordinal variables, quartile; OR (95% CI), *p* for trend	1.58 (1.10–2.27), 0.014	1.20 (0.86–1.69), 0.284	1.69 (1.16–2.45), 0.006
Q1, Reference	1	1	1
Q2, OR (95% CI), *p*	1.06 (0.51–6.63), 0.356	1.99 (0.67–5.91), 0.215	2.67 (0.73–9.72), 0.137
Q3, OR (95% CI), *p*	6.82 (1.99–23.57), 0.002	1.77 (0.57–5.46), 0.321	7.66 (2.08–28.22), 0.002
Q4, OR (95% CI), *p*	4.71 (1.32–16.78), 0.017	2.02 (0.66–6.20), 0.217	5.00 (1.35–18.62), 0.016

Adjusted for age, sex, variables with $p<0.1$ in univariate analysis (marital status, prestroke mRS score, hyperlipidemia, body mass index, stroke classification, National Institutes of Health Stroke Scale score, early neurological deterioration, and high-grade white-matter hyperintensities), and variables related to GL, GI, or total carbohydrate intake (diabetes mellitus, triglycerides, low-density lipoprotein, and hemoglobin A1c).
CI: confidence interval, GI: glycemic index, GL: glycemic load, mRS: modified Rankin Scale, OR: odds ratio.

Table 4. Associations of dietary GL, GI, and total carbohydrate intake with a poor functional outcome according to presence of diabetes mellitus

Variables	Continuous variables		Ordinal variables (quartiles)	
	OR (95% CI)	*p**	OR (95% CI)	*p* for trend*
Without diabetes mellitus				
GL	1.02 (1.01–1.07)	0.010	2.57 (1.10–6.01)	0.029
GI	0.92 (0.78–1.08)	0.336	0.75 (0.39–1.45)	0.403
Total carbohydrates	1.01 (1.01–1.02)	0.041	2.25 (1.03–4.91)	0.041
With diabetes mellitus				
GL	1.04 (1.01–1.09)	0.048	10.96 (1.06–112.52)	0.044
GI	1.27 (0.93–1.73)	0.121	4.71 (0.95–23.34)	0.058
Total carbohydrates	1.02 (1.01–1.04)	0.028	4.93 (1.02–23.82)	0.047

*Adjusted for age, sex, variables with $p<0.1$ in univariate analysis (marital status, prestroke modified Rankin Scale score, hyperlipidemia, body mass index, stroke classification, National Institutes of Health Stroke Scale score, early neurological deterioration, and high-grade white-matter hyperintensities), and variables related to GL, GI, or total carbohydrate intake (diabetes mellitus, triglycerides, low-density lipoprotein, and hemoglobin A1c).
CI: confidence interval, GI: glycemic index, GL: glycemic load, OR: odds ratio.

tile=4.71, 95% CI=1.32−16.78, *p* for linear trend=0.014). The total carbohydrate intake was associated with an increased risk of a poor functional outcome (OR for top quartile relative to bottom quartile=5.00, 95% CI=1.35−18.62, *p* for linear trend=0.006), while a high dietary GI was not related to a poor functional outcome (Table 4). In subgroup analysis, high dietary GL and total carbohydrate intake were significantly associated with a poor functional outcome regardless of the presence of diabetes mellitus (Table 4).

DISCUSSION

This study found that increased dietary GL and total carbohydrate intake were independently associated with a poor functional outcome at 3 months after an acute ischemic stroke even after adjusting for stroke classification, NIHSS score at admission, and early neurological deterioration, which are factors that strongly influence stroke outcome. These associations were not affected by diabetes mellitus. The correlations of GL, GI, and the carbohydrate intake with stroke risk and prognosis have not been demonstrated. A previous Italian cohort study found that an increased GL and carbohydrate intake (but not GI) were associated with an increased stroke risk.[26] In a Dutch population, high GL, GI, and carbohydrate intake were related to an increased risk of cardiovascular disease (including stroke) during a mean follow-up of 11.9 years.[27] The Takayama study revealed that a high dietary GI increased the risk of mortality from stroke in Japanese women.[8] A meta-analysis revealed that a high dietary GL was associated with an increased risk of coronary heart disease and stroke, and there was a linear dose-response relationship between the GL and the risk of coronary heart disease.[28] In contrast, the dietary GI was only weakly associated with the risk of coronary heart disease, and it was not associated with the risk of stroke or stroke-related death.[28] A Swedish study found that the GI and GL were not associated with long-term mortality in middle-aged men.[7] These discrepancies between our study and previous studies may be due to differences in study populations (general populations in other studies versus acute ischemic stroke patients in the present study), race, sex distribution, or dietary contributions to the GL and GI.[7] The present study has provided new insight into the association of the dietary GL and total carbohydrate intake with the functional outcome after acute ischemic stroke.[8,26,27]

Several mechanisms could explain the relationships of high GL and total carbohydrate intake with a poor functional outcome found in our study. Chronic hyperglycemia induced by a high dietary GL may impact the stroke outcome.[29] A previous study found that chronic hyperglycemia was related to a poor functional outcome in patients with acute ischemic stroke.[30] This tendency was also found in a large multicenter stroke registry from Japan.[31] Hyperglycemia was associated with more-severe cytotoxic injury, cerebral hypoperfusion, cerebral edema, and hemorrhagic transformation, which are strong prognostic factors after an acute ischemic stroke.[32-34] Chronic hyperglycemia leads to increased lactate production and promotes mitochondrial dysfunction by creating an acidotic intracellular environment,[35] which may aggravate the damage to ischemic tissue. Alternatively, a high dietary GL and GI can suddenly increase the blood sugar level, and such variability is associated with endothelial dysfunction in type 1 and type 2 diabetes mellitus.[36] Endothelial dysfunction is a risk factor for cardiovascular disease,[37] and impaired flow-mediated dilation (≤4.5%) is associated with a poor outcome in acute ischemic stroke patients with endothelial dysfunction.[38] Hyperglycemia and insulin resistance induced by a high dietary GL may impact hypercoagulability by increasing the serum levels of fibrinogen and von Willebrand factor.[39,40] Our results are also supported by increased thrombotic activity possibly predicting the 1-year functional outcome in patients with ischemic stroke.[39]

We found that an increased dietary GI was not independently related to a poor functional outcome, although a relationship was found in the univariate analysis. The dietary GL more accurately reflects the amount and quality of blood glucose and insulin increase when consuming carbohydrates than does the dietary GI.[41] We speculate that our findings were due to the study design or differences in the predictability of the dietary GL and GI. Further investigations are needed to confirm these differences.

This study was subject to some limitations. First, although patients with acute ischemic stroke were enrolled prospectively, patients with cognitive dysfunction or severe neurological deficit were excluded. This means that our study results are not representative of overall ischemic stroke. Second, this study was limited to Korean stroke patients. Because the dietary habits of Korean patients differ from those in other countries, the study results are difficult to generalize beyond Korea. Third, the smallness of the sample and the questionnaire survey design of our study may have caused selection and/or recall bias. Further large-scale and long-term cohort studies are therefore needed.

In conclusion, an increased dietary GL and total carbohydrate intake were associated with a poor functional outcome after an acute ischemic stroke. Low-GL food and a low-carbohydrate diet may improve the prognosis after an acute ischemic stroke.

Supplementary Materials

The online-only Data Supplement is available with this article at https://doi.org/10.3988/jcn.2018.14.2.165.

Conflicts of Interest

The authors have no financial conflicts of interest.

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