Original Article

Dietary Glycemic Index and Glycemic Load in Relation to Atherosclerotic Stenosis of Carotid and Cardiovascular Risk Factors in Ischemic Stroke Patients

Min Peng[1], Xiang Li[2], Yujing Liu[2], Min Zou[3], Yaqian Xia[2] and Gelin Xu[1, 2]

Min Peng, Xiang Li and Yujing Liu contributed equally to this work.

[1]Department of Neurology, Jinling Hospital, Medical School of Nanjing University, Jiangsu, China
[2]Department of Neurology, Jinling Hospital, Jinling Clinical College of Nanjing Medical University, Jiangsu, China
[3]Department of Hematology, Xiangtan City Central Hospital, Hunan, China

Aim: Glycemic index (GI) and glycemic load (GL) influence postprandial glucose concentrations and insulin responses. This study aims to ascertain the connection between GI, GL, and carotid atherosclerotic stenosis and cardiovascular disease (CVD) risk factors.

Methods: A total of 669 patients with ischemic stroke within 7 days were enrolled. GI and GL were assessed with a validated food frequency questionnaire from patients. Computed tomography angiography (CTA) was used for the evaluation of carotid atherosclerotic stenosis. Traditional risk factors such as total cholesterol, tri-glycerides, LDL-C, HDL-C, C-reactive protein, homocysteine, neutrophil to lymphocyte ratio (NLR), fasting plasma glucose, and hemoglobin A1c were measured. GI/GL and its association with CVD risk factors and carotid stenosis were explored with Spearman analysis and multivariable logistic regression, respectively.

Results: The prevalence of carotid stenosis was 63.2% of all 669 participants. The mean value of GI/GL was 49.3/137. Spearman test did not detect significant relationships between GI/GL and CVD risk factors. In multivariable regression models, GI (4th vs. 1st quartile, OR=2.11; 95% CI, 1.30–3.42) and GL (4th vs. 1st quartile, OR=1.82; 95% CI, 1.12–2.96) were observed a significant association with carotid stenosis after adjustment for major confounding factors. The association between GL and carotid stenosis became more pronounced among youngers (4th vs. 1st quartile, OR=2.42; 95% CI, 1.13–4.76) and women (4th vs. 1st quartile, OR=3.81; 95% CI, 1.45–5.05).

Conclusion: Higher GI and GL were positively associated with a higher degree of carotid stenosis in these Chinese cerebral infarction patients, especially in younger patients and women.

See correspondence vol. 27: 1243-1244

Key words: Glycemic index, Glycemic load, Carotid stenosis, Ischemic stroke

Introduction

The concept of glycemic index (GI) was originally designed for recommendations of diabetics' diets and was proposed in 1981 by Jenkins *et al.* GI is a quantitation assessment on the ability of accumulated carbohydrate from the diet to increase blood glucose levels[1]. Glycemic load (GL) combines the quality and quantity of overall digested carbohydrates, calculating from multiplying GI of food items by the amount of consumed carbohydrates. Higher carbohydrates consumption leads to insulin secretion from pancreas; in response, the tissues took in more blood glucose. So we can predict the concentration of postprandial plasma insulin/glucose concentrations and the degree of insulin sensitive in the body through calculating

GI/GL[2].

Atherosclerosis is a predominant factor of stroke (ischemic or hemorrhagic) events. Approximately one third of ischemic stroke is caused by extracranial carotid stenosis. Research showed that carotid stenosis due to atherosclerosis accounted for 90% of the total carotid stenosis[3]. Therefore, the prevention of carotid atherosclerotic stenosis is of great importance to the occurrence of stroke.

High concentrations of postprandial glucose and plasma insulin will increase the chronic oxidative stress levels, influence endothelial function, and may play a key role in the generation of cardiovascular diseases (CVD). GI/GL was reported to be associated with blood pressure[4], type 2 diabetes[5], and cardiovascular disease risks[6].

In diabetes, poor glycemic control was associated with the severity of intracranial atherosclerosis[7]. But to date, the relationship between dietary GI/GL, one dominant factor of poor glycemic control, and carotid atherosclerotic stenosis has not been explored. This study aimed to investigate these relationships plus whether GI/GL influencing CVD risk factor in a large scale of symptomatic adults with ischemic stroke.

Materials and Methods

Study Population

The patients of this study were screened from 2016 to 2019 via the Nanjing Stroke Registry Program (NSRP) conducted by the Center of Clinical Research for Stroke Screening and Prevention of Jinling Hospital. This study protocol was approved by Jinling Hospital Ethic Review Committee. Informed consent was received from all participants or their proxies.

The including criteria were patients with ischemic stroke in 7 days and aged over 18 years old; the excluding criteria were patients who had cancer, severe liver/kidney insufficiency, chronic gastrointestinal diseases, and carotid endarterectomy history.

Dietary Intake Assessment

A validated food frequency questionnaire (FFQ) derived from the National Health and Nutrition Examination Surveys (NHNES)[8] was utilized to assess patients' eating habits during the previous 12 months. The NHNES questionnaire was first translated into Chinese. Then according to China National Nutrition and Health Surveys (which reported the food consumption frequency, but not consumption quantity), the 20–30 most frequently consumed foods in each classification were added if they were not included in NHNES questionnaire. A total of 298 food items classified into 8 groups constituted this Chinese FFQ including staple foods (grains, potatoes, and beans), vegetables, fruits, nuts, meats and fishes, beverages, dietary supplements, and condiments. Nutrients intake was estimated through a Food Composition Table[9] from the Chinese Center for Disease Control and Prevention and Institute of Nutrition and Food Safety. Participants with incomplete FFQ and reported extremely energy intake were excluded.

GI/GL Calculation

GI values were expressed as a percent of the glycemic response elicited by pure glucose as a standard food (GI for pure glucose=100). GI and GL calculation in this study was using Chinese Table of Glycemic Index Values[9] and International Tables of Glycemic Index Values 2008 [10]. GL was calculated by multiplying the content of carbohydrate of food parameters by its GI values and then by its daily average consumption derived from FFQ. The overall GL was the summation of all food items. GL of each unit represents the equivalent of 1 g carbohydrate from pure glucose. The overall GI was then estimated by dividing the overall GL by the participants' daily average intake of carbohydrate.

Anthropometrics, Sociodemographic, and Physical Activity Measurement

Body mass index (BMI) was calculated by dividing the weight by the height squared. Body weight was measured using a digital electronic scale. Body height was measured with a wall-mounted rangefinder. According to annual family incomes, socioeconomic status was classified as high (200000 yuan or more), moderate (100000–199999 yuan), and low (less than 100000 yuan). Patients with at least 20 minutes physical activities a day for at least 3 days a week were deemed as "physically active"[11].

Biochemical Analysis of CVD Risk Factors

Subjects were fasting 8 hours for blood samples. Blood samples were usually collected at the first morning after hospitalization. Most patients (about 90%) were hospitalized within 24 hours of stroke onset; therefore blood samples were usually obtained within 48 hours of stroke onset. Fasting plasma glucose (FPG), hemoglobin A1c (HbA1c), serum total cholesterol (TC), triglycerides (TG), HDL cholesterol (HDL-C), LDL cholesterol (LDL-C), C-reactive protein (CRP), homocysteine, and white blood cells were measured using fresh blood samples by Jinling Hospital Biochemistry Laboratory.

Carotid Stenosis Measurement

The degree of carotid stenosis measurement was conducted with a dual-source multidetector CT scanner (Somaton Definition Flash, Siemens, Germany) using the standard scanning protocol: 120-kV tube voltage, 300-mA tube current, 0.75-mm slice thickness, 64 × 0.6-mm collimator width, and 160 mm-FOV. Two neurologists were in charge of the evaluation of carotid enhanced imagines with a carotid reconstruction software (Neurovascular, Siemens, Germany). The presence and extents of stenosis on carotid bifurcations were assessed by NASCET criteria that described as the maximal loss rate percentage of lumen diameter in the lesion region ([normal lumen diameter at distal point − minimal lumen diameter of obstruction lesion)/normal lumen diameter at distal point] × 100%) [12]. The degrees of carotid stenosis were classified according to NASCET criteria: no or mild (0–29%), moderate (30%–69%), and severe (70%–100%). Patients with poor imaging quality or who had carotid lesions other than atherosclerosis (e.g., artery dissection) in bifurcations were excluded.

Statistical Analysis

Continuous data were showed as means ± SD, while categorical data were showed as frequency number (rate). Least significant difference test was used for comparing the homogeneity of variance between groups. Carotid stenosis degree was divided into three groups. Baseline data were analyzed with one-way ANOVA, Kruskal–Wallis H test, or Chi-square test. Spearman test was used for investigating the association of CVD risk factors and GI/GL. In multivariable logistic analysis, GI and GL were categorized into quartiles. Ordinal logistic regression models were utilized for calculating odds ratios (OR) and 95% confidence intervals (CI) between GI/GL quartiles and carotid stenosis with (model 1) or without (model 0) controlling for confounding factors which $P < 0.1$. Stratified analyses among patients were additionally conducted by age (<65 years or ≥ 65 years) and sex (women or men). Statistical significance in logistic regression models was determined by the Wald test. Statistical analysis was conducted with SPSS Statistics version 22.0 (IBM, New York, USA). P value <0.05 was deemed as statistical significance.

Results

After excluding 7 patients from all 676 enrolled, 669 patients entered data analysis eventually. The screening process was presented in **Fig. 1**.

The mean age was 65.0 years (SD 10.8 years) and the percentage of men was 66.2%. The average

676 patients were enrolled from NSRP during 2016−2019

Exclusions (n = 7):
-Incomplete FFQ (n = 3)
-Extremely energy intake (n = 1)
-Carotid dissection (n = 3)
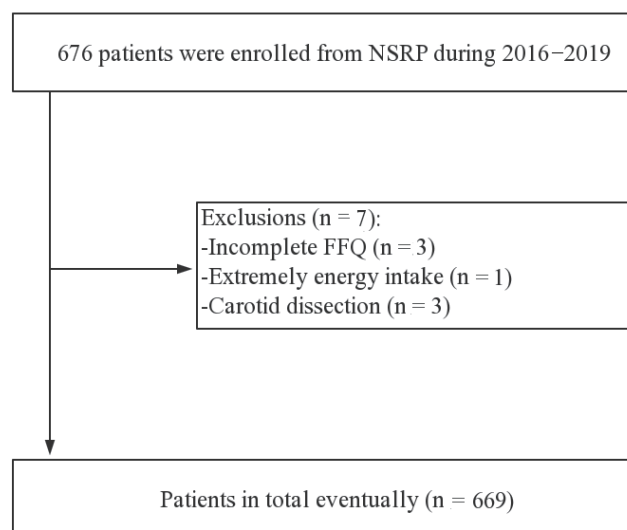
Patients in total eventually (n = 669)

Fig. 1. Flowchart of the included patients in this study

7 patients were excluded and 669 were eventually enrolled.

value of GI/GL was 49.3 (SD 24.5)/137 (SD 81.6). The prevalence of carotid stenosis was 63.2% (*n*= 423) in 669 participants, and 4.6% patients (*n*=31) had at least 1 carotid occlusion. The stenosis rate of 27.1% patients (*n*=181) were at 30%–69%, while 16.4% patients (*n*=128) were at 70%–100%.

Of all the 423 patients who had carotid stenosis, the infarction lesions of 277 patients resulted from internal carotid system, while 146 were caused by vertebral artery disease. In those 277 patients with anterior circulation infarction, 198 (71.5%) patients had cerebral infarction (cause of the index stroke) in the same side of dominant carotid stenosis, and 79 (28.5%) patients had cerebral infarction in the other side of dominant carotid stenosis.

Patients' baseline characteristics were shown in **Table 1**. Comparing to patients with no or mild stenosis, the severe stenosis patients were older (66.0 ± 9.87 vs. 62.9 ± 11.4, *p*=0.01) and more likely to be men (71.8% vs. 63.8%, *p*=0.04). Those in the severe stenosis participants had a higher prevalence of hypertension (78.2% vs. 64.3%, *p*=0.001), diabetes mellitus (40.0% vs. 27.5%, *p*<0.001), and heart disease (22.7% vs. 10.1%, *p*=0.002). TOAST subtypes were statistically significant between groups, and the proportion of large artery atherosclerosis (LAA) was higher in the most severe carotid stenosis group than the group with no or mild stenosis (56.4% vs. 16.1%, *p*<0.001). The severe stenosis patients had an obviously higher serum level of hemoglobin A1c (6.81 ± 2.09 vs. 6.19 ± 1.34, *p*=0.001) and higher glycemic index (60.2 ± 36.6 vs. 45.2 ± 15.9, *p*=0.001) and higher glycemic load (171 ± 104 vs. 120 ± 59.9, *p*<

1154

Table 1. Baseline data stratified by carotid stenosis in ischemic stroke patients[a]

Characteristics[b]	Carotid stenosis			p-value
	No or mild (0-29%) n=378, 56.5%	Moderate (30~69%) n=181, 27.1%	Severe (70%~100%) n=110, 16.4%	
Age (years)	62.9±11.4	68.7±8.87	66.0±9.87	0.01*
Sex (males, %)				0.04*
Men	241 (63.8)	133 (73.5)	79 (71.8)	
Women	137 (36.2)	48 (26.5)	31 (28.2)	
BMI (Kg/m²)	24.8±3.16	25.0±3.40	24.8±3.09	0.93
Socioeconomic states (%)				0.83
Low	109 (28.8)	49 (27.1)	37 (33.6)	
Medium	130 (34.4)	64 (35.4)	36 (32.7)	
High	139 (36.8)	68 (37.6)	37 (33.6)	
Physical activities (%)				0.22
Inactive	193 (51.1)	92 (50.8)	66 (60.0)	
Active	185 (48.9)	89 (49.2)	44 (40.0)	
Smoking history (%)	171 (45.2)	95 (52.5)	62 (56.4)	0.07
Hypertension (%)	243 (64.3)	140 (77.3)	86 (78.2)	0.001**
Diabetes mellitus (%)	104 (27.5)	83 (45.9)	44 (40.0)	<0.001***
Dyslipidemia (%)	77 (20.4)	36 (19.9)	15 (13.6)	0.27
Atrial fibrillation (%)	25 (6.6)	14 (7.7)	6 (5.5)	0.75
Heart disease (%)	38 (10.1)	28 (15.5)	25 (22.7)	0.002**
Stroke history (%)	72 (19.0)	46 (25.4)	30 (27.3)	0.09
TOAST subtypes (%)				<0.001***
LAA	61 (16.1)	68 (37.6)	62 (56.4)	
SVD	132 (34.9)	57 (31.5)	27 (24.5)	
CE	31 (8.2)	10 (5.5)	3 (2.7)	
Others	154 (40.7)	46 (25.4)	18 (16.4)	
NLR	2.36±1.28	2.62±1.91	2.65±1.43	0.05
CRP (mg/L)	3.27±7.67	4.98±15.9	4.66±11.6	0.24
Hcy (μmol/L)	14.1±7.60	13.9±6.63	14.3±8.03	0.81
HbA1c (mmol/L)	6.19±1.34	6.63±1.61	6.81±2.09	0.001**
FPG (mmol/L)	5.61±1.73	6.02±1.94	5.80±2.03	0.39
Glycemic index	45.2±15.9	51.2±31.0	60.2±36.6	0.001**
Glycemic load	120±59.9	152±95.5	171±104	<0.001***

[a] Data were presented as m ± SD or frequency (rate)
[b] LAA, large artery atherosclerosis; SVD, small vascular disease; CE, cardioembolism; NLR, neutrophil to lymphocyte ratio; CRP, C-reactive protein; Hcy, homocysteine; HbA1c, hemoglobin A 1c; FPG, fasting plasma glucose

0.001) than participants with no or mild stenosis.

In multiple regression models (**Table 2**), the odds were at 2.21 (4th vs. 1st quartile (Q), 95% CI, 1.46–3.35; p=0.001) of GI and 1.92 (4th vs. 1st Q, 95% CI, 1.27–2.92; p=0.002) of GL in the crude model. The OR of GI and GL tended to 2.11 (4th vs. 1st Q, 95% CI, 1.30–3.42; p=0.02) and 1.82 (4th vs. 1st Q, 95% CI, 1.12–2.96; p=0.02), respectively, after adjustment for age, sex, smoking history, TOAST subtypes, hypertension, diabetes mellitus, heart disease, stroke history,

NLR, and HbA1c levels.

Stratified logistic regression by age and sex was performed (**Table 3**). The results showed that GI was a risk factor for carotid stenosis among the youngers (4th vs. 1st Q; OR=2.17; 95% CI, 1.02–4.61; p=0.04) and women (4th vs. 1st Q; OR=3.36; 95% CI, 1.22–4.69; p=0.02). Higher GL had a pronounced relationship with carotid stenosis for younger patients compared to the old aged (4th vs. 1st Q; younger patients, OR=2.42; 95% CI, 1.13–4.76; p=0.02; elders,

Table 2. Multiple logistics regression between carotid stenosis and quartile of glycemic index and glycemic load

	Patients	Crude Model		Model 1	
		OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Glycemic index	Number				
Q1	168	1 (REF)		1 (REF)	
Q2	167	1.05 (0.68-1.95)	0.83	1.11 (0.68-1.83)	0.81
Q3	167	0.97 (0.63-2.60)	0.89	0.92 (0.56-1.53)	0.53
Q4	167	2.21 (1.46-3.35)	0.001**	2.11 (1.30-3.42)	0.02*
Glycemic load	Number				
Q1	167	1 (REF)		1 (REF)	
Q2	168	1.00 (0.65-1.54)	0.99	1.02 (0.62-1.70)	0.81
Q3	167	1.33 (0.87-2.03)	0.18	1.31 (0.80-2.14)	0.13
Q4	167	1.92 (1.27-2.92)	0.002**	1.82 (1.12-2.96)	0.02*

Model 1, adjusted for age, sex, smoking history, hypertension, diabetes mellitus, heart disease, stroke history, TOAST subtypes, neutrophil to lymphocyte ratio level and hemoglobin A 1c levels

Table 3. Stratified regression analysis between carotid stenosis and quartile of glycemic index and glycemic load according to age and sex [a]

Models [b]	Age		Sex	
	<65 years OR (95% CI)	≥ 65 years OR (95% CI)	Women OR (95% CI)	Men OR (95% CI)
GI				
Q1	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Q2	0.85 (0.37-1.94)	1.31 (0.64-2.45)	1.60 (0.58-3.32)	0.76 (0.13-3.49)
Q3	0.64 (0.28-1.45)	1.18 (0.53-2.37)	1.62 (0.56-4.39)	0.23 (0.02-2.31)
Q4	2.17 (1.02-4.61)	1.88 (0.76-3.58)	3.36 (1.22-4.69)	2.36 (0.58-4.61)
p-value	0.04*	0.06	0.02*	0.23
GL				
Q1	1 (REF)	1 (REF)	1 (REF)	1 (REF)
Q2	1.03 (0.44-2.39)	1.12 (0.58-2.17)	1.98 (0.74-3.70)	1.15 (0.26-5.06)
Q3	1.26 (0.56-2.84)	1.34 (0.70-2.54)	2.89 (1.06-4.17)	0.36 (0.03-3.59)
Q4	2.42 (1.13-4.76)	1.45 (0.76-2.77)	3.81 (1.45-5.05)	1.39 (0.04-6.26)
p-value	0.02*	0.26	0.007**	0.67

[a] GI, glycemic index; GL, glycemic load
[b] Adjusted for age, sex, smoking history, TOAST subtypes, hypertension, diabetes mellitus, heart disease, stroke history, neutrophil to lymphocyte ratio and hemoglobin A 1c levels

OR=1.45; 95% CI, 0.76–2.77; *p*=0.26). Higher GL had also shown a more significant connection with higher carotid stenosis among women compared to men (4th vs. 1st Q; women, OR=3.81; 95% CI, 1.45–5.05; *p*=0.007; men, OR=1.39; 95% CI, 0.04–6.26; *p*=0.67). However, no significant relationship between GI and carotid stenosis was observed in the elderly and men.

Spearman test has not shown statistical significance between GI/GL and total cholesterol, triglycerides, LDL-C, HDL-C, CRP, Hcy, NLR, FPG, and HbA1c (**Table 4**).

This study detected 930 plaques in total. Of all 669 patients, 285 (42.6%) had calcified plaques and 124 (18.5%) had ulcerated plaques (**Supplementary Table 1**).

Discussion

This is the first study that revealed that GI and GL had an independent effect on the development of atherosclerotic stenosis. This cross-sectional study observed increased 2.1-fold odds for higher carotid stenosis of GI and an increased 1.8-fold risk of GL.

Table 4. Spearman analysis between cardiovascular risk factors and glycemic index and glycemic load

CVD risk factors	Glycemic index		Glycemic load	
	r	p-value	r	p-value
Total cholesterol (mmol/L)	-0.01	0.86	-0.02	0.62
Triglycerides (mmol/L)	0.05	0.23	0.06	0.13
LDL-C (mmol/L)	0.01	0.80	-0.001	0.97
HDL-C (mmol/L)	0.02	0.59	-0.05	0.20
NLR	0.04	0.27	0.03	0.40
CRP (mg/L)	0.03	0.40	0.04	0.32
Hcy (μmol/L)	0.05	0.31	0.07	0.15
HbA1c (mmol/L)	0.01	0.87	0.03	0.42
FPG (mmol/L)	0.01	0.74	0.05	0.25

CVD, cardiovascular disease; NLR, neutrophil to lymphocyte ratio; CRP, C-reactive protein; Hcy, homocysteine; HbA1c, hemoglobin A 1c; FPG, fasting plasma glucose

The stratified results showed that the effect of GL was more pronounced in younger patients and women. The risk of GL increased by about 2.4-fold for younger patients and 3.8-fold for women.

Some previous literatures reported the association between GI/GL and cardiovascular diseases. Among a large sample of asymptomatic adults, one study showed that higher GI and GL were linked to a severe coronary artery calcium, and the association for GL was stronger[13]. The results showed that combining the quality and the quantity of carbohydrates intake was a more important determinant of atherosclerosis. One Chinese study in 2016 and three meta-analyses all concluded that higher glycemic load and higher glycemic index diets were associated with an increased risk of CVD in women[6, 14]. Those results were consistent with this study which also showed that women had a greater risk for carotid stenosis. With regard to cardiovascular risk factors, the results were mixed. A previous study showed that dietary GL have been related with increased diabetes risk and lower LDL-C levels[6]. This study did not find that GI/GL had a positive relationship with CVD risk factors which supported the conclusion of one randomized trial that included 163 overweight adults[15].

The mechanisms of GI/GL effect on pathological process of chronic diseases are not completely understood. Long-term high GI/GL diet leads to postprandial hyperglycemia and serum insulinemia[16]. Hyperglycemia decreases the microcirculation perfusion in macrovascular and microvascular by changing the physiological properties of red blood cells and increasing the plasma viscosity and fibrinogen levels. Insulinemia causes the decrease of insulin sensitivity for organs or tissues and produces a chain of endocrine disorders. Habitual high GI/GL diet also causes an imbalance of antioxidation-oxidation resulting in endothelial dysfunction and vascular inflammation which is the initial pathophysiological reaction in atherosclerosis[17]. The above consists of the most important determinants for the development and progression of atherosclerotic stenosis.

This study had some limitations. A cross-sectional design limited the ability to deduce causality. Considering the wide differences in dietary structures and eating habits, this scale may be less applicable in populations other than Chinese. In addition, a recall bias inevitably produced during the collection of the past 1-year FFQ data, this may be a cause for the high standard deviation of GI and GL. Atherosclerosis belongs to a systemic disease, but this study assessed carotid bifurcations only for analysis. However, no methods have access to evaluate atherosclerosis in the whole body yet.

Conclusion

The quantity and quality of carbohydrate may take part in the progression of atherosclerotic stenosis of carotid in conjunction with other factors. High-risk stroke population especially youngers and women should reduce their GI and GL for decreasing the unfavorable influence of carbohydrates and preventing cardiovascular diseases. Further research is still needed to carry out for exploring their temporal causality and exact underlying mechanism for the relationship of dietary GI/GL and carotid atherosclerotic stenosis risk.

Acknowledgements

Disclosure

Min Peng, Xiang Li, Yujing Liu, Min Zou, Yaqian Xia and Gelin Xu declare that they have no conflicts of interests.

References

1) Venn BJ, Green TJ. Glycemic index and glycemic load: Measurement issues and their effect on diet-disease relationships. Eur J Clin Nutr, 2007; 61 Suppl 1: S122-131

2) Glade MJ, Smith K. A glance at… Glycemic index. Nutrition, 2015; 31: 539-541

3) Bazan HA, Smith TA, Donovan MJ, Sternbergh WC 3rd. Future management of carotid stenosis: Role of urgent carotid interventions in the acutely symptomatic carotid patient and best medical therapy for asymptomatic carotid disease. Ochsner J, 2014; 14: 608-615

4) Evans CE, Greenwood DC, Threapleton DE, Gale CP, Cleghorn CL, Burley VJ. Glycemic index, glycemic load, and blood pressure: A systematic review and meta-analysis of randomized controlled trials. Am J Clin Nutr, 2017; 105: 1176-1190

5) Shao SY, Xu WJ, Tao J, Zhang JH, Zhou XR, Yuan G, Yang Y, Zhang J, Zhang HY, Xu Q, Deng XX, Hu SH, Zhang MX, Liu ZL, Yu XF. Glycemic index, glycemic load, and glycemic response to pomelo in patients with type 2 diabetes. J Huazhong Univ Sci Technolog Med Sci, 2017; 37: 711-718

6) Mirrahimi A, Chiavaroli L, Srichaikul K, Augustin LS, Sievenpiper JL, Kendall CW, Jenkins DJ. The role of glycemic index and glycemic load in cardiovascular disease and its risk factors: A review of the recent literature. Curr Atheroscler Rep, 2014; 16: 381

7) Choi N, Lee JY, Sunwoo JS, Roh H, Ahn MY, Park ST, Lee KB. Recently uncontrolled glycemia in diabetic patients is associated with the severity of intracranial atherosclerosis. J Stroke And Cerebrovascu Dis, 2017; 26: 2615-2621

8) Ahluwalia N, Dwyer J, Terry A, Moshfegh A, Johnson C. Update on nhanes dietary data: Focus on collection, release, analytical considerations, and uses to inform public policy. Adv nutr, 2016; 7: 121-134

9) Chinese Center for Disease Control and Prevention, Institution of Nutrition and Food Safety. China food composition, 2st ed 2009. Beijing, China

10) Atkinson FS, Foster-Powell K, Brand-Miller JC. International tables of glycemic index and glycemic load values: 2008. Diabetes care, 2008; 31: 2281-2283

11) Ren YJ, Su M, Liu QM, Tan YY, DU YK, Li LM, Lyu J. Validation of the Simplified Chinese-character Version of the International Physical Activity Questionnaire-Long Form in Urban Community-dwelling Adults: a Cross-sectional Study in Hangzhou, China. Bio Enviro Sci, 2017; 30: 255-263

12) North American Symptomatic Carotid Endarterectomy Trial Collaborators, Barnett HJM, Taylor DW, Haynes RB, Sackett DL, Peerless SJ, Ferguson GG, Fox AJ, Rankin RN, Hachinski VC, Wiebers DO, Eliasziw M. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. N Engl J Med, 1991; 325: 445-453

13) Choi Y, Chang Y, Ryu S, Cho J, Kim MK, Ahn Y, Lee JE, Sung E, Kim B, Ahn J, Kim CW, Rampal S, Zhao D, Zhang Y, Pastor-Barriuso R, Lima JA, Chung EC, Shin H, Guallar E. Relation of dietary glycemic index and glycemic load to coronary artery calcium in asymptomatic korean adults. Am J Cardiol, 2015; 116: 520-526

14) Yu D, Zhang X, Shu XO, Cai H, Li H, Ding D, Hong Z, Xiang YB, Gao YT, Zheng W, Yang G. Dietary glycemic index, glycemic load, and refined carbohydrates are associated with risk of stroke: A prospective cohort study in urban chinese women. Am J Clin Nutr, 2016; 104: 1345-1351

15) Sacks FM, Carey VJ, Anderson CA, Miller ER 3rd, Copeland T, Charleston J, Harshfield BJ, Laranjo N, McCarron P, Swain J, White K, Yee K, Appel LJ. Effects of high vs low glycemic index of dietary carbohydrate on cardiovascular disease risk factors and insulin sensitivity: The omnicarb randomized clinical trial. JAMA, 2014; 312: 2531-2541

16) Jenkins DJ, Wolever TM, Taylor RH, Barker H, Fielden H, Baldwin JM, Bowling AC, Newman HC, Jenkins AL, Goff DV. Glycemic index of foods: A physiological basis for carbohydrate exchange. Am J Clin Nutr, 1981; 34: 362-366

17) Ceriello A, Assaloni R, Da Ros R, Maier A, Piconi L, Quagliaro L, Esposito K, Giugliano D. Effect of atorvastatin and irbesartan, alone and in combination, on postprandial endothelial dysfunction, oxidative stress, and inflammation in type 2 diabetic patients. Circulation, 2005; 111: 2518-2524

Supplementary Table 1. Plaque characteristics at the maximal stenosis of patients

Plaque characteristics	Carotid Stenosis			
	No or mild (0~29%) $n = 378$, 56.5%	Moderate (30~69%) $n = 181$, 27.1%	Severe (70%~99%) $n = 79$, 11.8%	Occlusion (>99%) $n = 31$, 4.6%
Total plaque numbers	212	445	273	
Calcification (%)	86 (22.8)	143 (79.0)	56 (67.0)	
Ulceration (%)	25 (6.6)	66 (36.5)	33 (41.8)	