Original Article

Premorbid dietary intake of protein is associated with early outcomes but not with severity of ischemic stroke

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Background and Objectives: Dietary protein intake has been associated with reduced risk of stroke. This study aimed to examine the relationship between premorbid dietary intake of protein and both stroke severity and neurological outcomes in patients with acute ischemic stroke. **Methods and Study Design:** Consecutive patients with first-ever ischemic stroke in Jinling Hospital were screened for eligibility of participation. A validated food-frequency questionnaire (FFQ) was performed to collect necessary data for calculating pre-stroke dietary intakes. Stroke severity was assessed by the National Institutes of Health Stroke Scale (NIHSS) at baseline. Neurological outcomes were assessed by the modified Rankin scale (mRS) 90 days after stroke onset. Multivariable logistical regression was applied to analyze the impacts of dietary protein intake on stroke severity or neurological outcomes. **Results:** Of the 201 enrolled patients, 110 (54.7%) were classified as minor (NIHSS ≤5) and 91 (45.3%) as major stroke (NIHSS ≥6). After adjusting for potential confounders, multivariable logistic regression did not detect significant association between total (odds ratio (OR)=0.98, p=0.15), animal (OR=1.01, p=0.87) or plant protein intake (OR=0.96, p=0.07) and stroke severity. According to the 90-day mRS, 127 patients (63.2%) were determined with good (mRS ≤2), and 74 (36.8%) with poor outcomes (mR 3-6). Multivariable logistic regression detected that premorbid dietary intake of total protein was positively associated with good neurological outcomes (OR=1.05, p=0.04). **Conclusions:** Higher level of premorbid protein intake may be associated with favorable neurological outcomes independent of stroke severity.

Key Words: diet, protein intake, stroke severity, outcome, ischemic stroke

INTRODUCTION

Stroke is the second leading cause of death and third leading cause of Disability-Adjusted Life Years (DALYs) worldwide.[1] Previous studies indicated that lifestyle factors, such as dietary habit, may influence the risk of stroke.[2,3] Higher dietary protein has been associated with lower risk of stroke in our previous meta-analysis involving 254,489 participants.[4] The proposed mechanisms underlying this association include: the beneficial effects of dietary protein on blood pressure,[5] delay of stroke onset,[6] and substitution effects of carbohydrates.[7,8]

The association between dietary protein intake and stroke risk has been explored extensively, but the impacts of premorbid dietary protein intake on stroke outcomes remained largely undetermined, although limited data indicated that protein supplement after stroke may improve neurological rehabilitation.[9] This study aimed to assess the impacts of premorbid protein intake on severity and neurological outcomes of ischemic stroke in a cohort of Chinese patients.

METHODS

Study population

Consecutive patients with first-ever ischemic stroke were screened in Jinling Hospital (Nanjing, China) from January 2015 to July 2015. All subjects in this study were limited to in-hospital patients. In this center, stroke patients were treated following a pre-established protocol adapted according to the latest guidelines. Patients received same rehabilitation regimes given that their stroke severity were similar. Patients and their relatives received uniform health education during their hospital stay. Patients were included if they: had a first-ever ischemic stroke within 7 days; aged 18 years or older; willing to participate the study. Patients were excluded if they: had major neurological deficit before the index stroke; had severe heart, lung, liver or renal diseases; had malignant tumor; or had disease of digestive tract which may influence their dietary pattern. The study protocol was approved by the Institutional Review Board of Jinling Hospital (Nanjing, China) and the informed consent was obta-

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ined from all patients or their proxies (2010NLY-018).

Baseline assessment

Demographic profiles (age, sex), educational levels, family history of ischemic stroke, body mass index (BMI), major risk factors for cardiovascular diseases (hypertension, diabetes, atrial fibrillation (AF), hyperlipidemia) were collected at baseline. Current status of cigarette smoking and alcohol drinking was also recorded. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured at baseline assessment. Fasting blood samples were collected for testing total cholesterol (TC), triacylglycerol (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and C-reactive protein (CRP). Stroke etiologies were determined according to criteria of the Trial of Org 10172 in Acute Stroke Treatment Classification (TOAST).[10]

Assessment of dietary intake

The parameters concerning premorbid dietary intakes were assessed with a semi-quantitative food frequency questionnaire (FFQ) which contained 95 items. This FFQ was adapted from the 81-item FFQ used in Shanghai Men's Health Study (SMHS).[11] To increase the representativeness of the initial FFQ, 14 items were added. The reproducibility and validity of the 81-item FFQ in measuring dietary intakes have been validated in Chinese population.[12] The FFQ was administrated by trained interviewers during a face-to-face interview. For patients unable to answer the FFQ, such as those with obvious cognitive impairment, a surrogate who was familiar with the patient's dietary pattern was asked to answer the FFQ.

Consumption of food or food groups were calculated as the frequency of intake multiplied by the portion sizes. Individual intake of food item was converted to g/day. Nutrients and energy intakes were calculated according to China Food Composition Table 2002 and USDA National Nutrient Database for Standard Reference.[13,14] All nutrient intakes and food intakes were adjusted for total energy intake according to previously reported methods.[15] To exclude extremely skewed data, male patients with energy intakes of >4.20 or <0.80 $\times 10^3$ Kcal/day, and female patients with energy intakes >3.50 or <0.50 $\times 10^3$ Kcal/day were excluded from data analysis.[16]

Major contributors of dietary protein intake included red meat, poultry, eggs, dairy products, fish, legumes and nuts. The total protein intake was defined as a summation of these animal and plant protein intake.

Assessment of stroke severity

National Institutes of Health Stroke Scale (NIHSS) was used to evaluate the severity of ischemic stroke at baseline.[17] Stroke severity was dichotomized. Minor stroke was defined as NIHSS ≤5 and major stroke as NIHSS ≥6.[18] The NIHSS was rated by two trained physicians who were blind to the results of FFQ.

Assessment of early neurological outcomes

The modified Rankin scale (mRS) was used to assess early neurological outcomes of stroke.[19] The mRS was performed in 90 days after the index stroke via a telephone interview. The mRS is a widely used scale for evaluating the stroke outcomes with scores ranging from 0 (no symptoms) to 6 (death). In this study, a good neurological outcome was defined as a mRS ≤2 and a poor neurological outcome as a mRS 3-6 following that in the previous studies.[20] The mRS was rated by a physician who was blind to the results of FFQ.

Statistical analysis

Statistical analysis was performed with SPSS software package (version 22.0, Armonk, NY: IBM Corp). Continuous variables were reported as mean±standard deviation (SD) or median (interquartile range (IQR)). Categorical variables were reported as number (percentage). Continuous variables were compared by Student's, Mann-Whitney U or Kruskal-Wallis test. Categorical variables were compared by Chi-square or Fisher exact test. To determine which dietary factors might be associated with the severity of stroke and neurological outcomes, univariate analysis was first performed, and then multivariate logistical regression analysis was performed with potential confounders being adjusted. Results were presented as odds ratio (OR), 95% confidence interval (CI) and p value. All statistical significance was defined as a 2-tailed $p<0.05$.

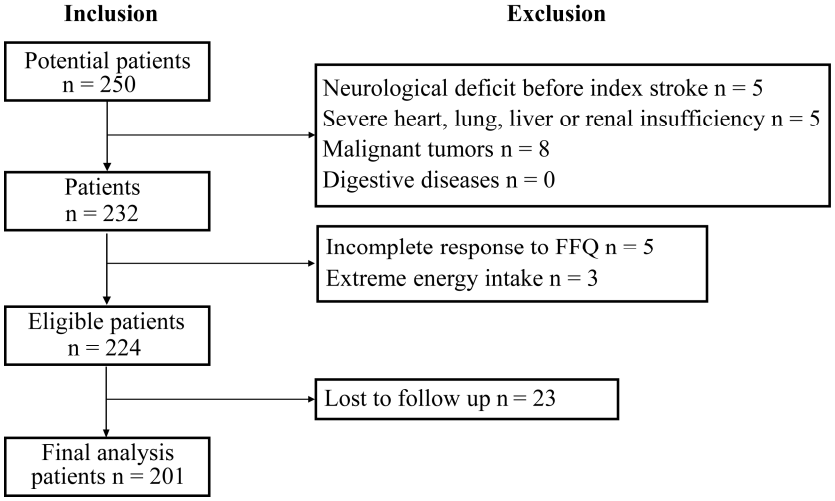

Figure 1. Flowchart of patient selection

RESULTS

Figure 1 is a flowchart for patient selection. A total of 224 patients were screened for eligibility, of which 23 (10.3%) patients lost to follow up. Finally, 201 patients, 139 (69.2%) male and 62 (30.8%) female, entered the data analysis. Of the 201 patients, the mean duration from stroke onset to NIHSS assessment was 38 (18-73) hours. The mean age of these analyzed 201 patients was 60.7±12.7 years. The total energy intake was 1.36 (1.11-1.70) $\times 10^3$ Kcal/day. The energy-adjusted intake of total protein was 55.6±54.3 g/day. Dietary intake of animal protein was 17.8±10.7 g/day, and dietary intake of plant protein was 37.8±11.8 g/day. Of the 201 patients, 110 (54.7%) were classified as with minor (NIHSS ≤5) and 91 (45.3%) as with major stroke (NIHSS ≥6). According to the 90-day mRS, 127 (63.2%) patients were classified as with good outcomes (mRS ≤2), and 74 (36.8%) as with poor outcomes (mRS 3-6).

Table 1 shows baseline characteristics of the included patients according to stroke severity. Patients with minor

Table 1. Baseline characteristics according to stroke severity[†]

	Minor stroke (NIHSS ≤5)	Major stroke (NIHSS ≥6)	*p* value
Patients, n (%)	110 (54.7)	91 (45.3)	
Age, years, mean±SD	59.2±12.4	62.5±12.9	0.07
Male, n (%)	74 (67.3)	65 (71.4)	0.54
BMI, kg/m^2, mean±SD	25.3±3.3	24.4±2.9	0.05
Hypertension, n (%)	79 (71.8)	58 (63.7)	0.23
Diabetes, n (%)	37 (33.6)	24 (26.4)	0.28
AF, n (%)	9 (8.2)	22 (24.2)	0.003**
Smoking, n (%)	47 (42.7)	39 (42.9)	1.00
TC, mmol/L, mean±SD	4.6±1.2	4.7±1.1	0.66
TG, mmol/L, median (IQR)	1.7 (1.2-2.4)	1.4 (1.0-1.8)	0.02*
HDL-C, mmol/L, median (IQR)	1.0 (0.9-1.2)	1.0 (0.9-1.2)	0.51
LDL-C, mmol/L, mean±SD	2.6±0.9	3.0±1.0	0.01*
CRP, mg/L, median (IQR)	1.5 (0.0-3.4)	2.2 (0.4-9.0)	0.02*
Stroke onset to NIHSS assessment, hours, median (IQR)	39 (22-83)	38 (10-72)	0.26
TOAST, n (%)			<0.001***
LAA	40 (36.4)	49 (53.8)	
CE	8 (7.3)	19 (20.9)	
SAO	35 (31.8)	5 (5.5)	
SOE & SUE	27 (24.5)	18 (19.8)	
Total energy intake, $\times 10^3$ Kcal/day, median (IQR)	1.36 (1.17-1.68)	1.37 (1.08-1.80)	0.31
Total protein intake, g/day, mean±SD	57.1±14.4	53.7±12.3	0.08
Animal protein intake, g/day, mean±SD	19.5±10.8	15.8±10.3	0.02*
Plant protein intake, g/day, mean±SD	37.7±13.0	37.9±10.3	0.89
Fiber intake, g/day, median (IQR)	8.0 (6.2-10.8)	7.3 (5.7-11.7)	0.47
Carbohydrate intake, g/day, mean±SD	249±52	273±50	0.001**
SFA intake, g/day, mean±SD	14.1±3.9	12.6±4.0	0.01*
K^+ intake, g/day, median (IQR)	1.3 (1.2-1.7)	1.3 (1.1-1.7)	0.75
Na^+ intake, g/day, mean±SD	4.8±1.5	4.9±1.7	0.74
Red meat intake, g/day, median (IQR)	41.0 (18.9-73.8)	27.4 (9.9-57.0)	0.03*
Poultry intake, g/day, median (IQR)	8.6 (0-16.3)	5.9 (0-11.3)	0.07
Eggs intake, g/day, median (IQR)	16.4 (0-60.6)	4.1 (0-59.5)	0.33
Dairy intake, g/day, median (IQR)	0 (0-11.5)	0 (0-0)	0.42
Fish intake, g/day, median (IQR)	15.9 (4.0-34.4)	11.4 (1.0-24.6)	0.15
Legumes intake (dry), g/day, median (IQR)	3.9 (0-7.9)	4.1 (0.7-7.4)	0.89
Nuts intake, g/day, median (IQR)	2.1 (0-8.2)	0 (0-5.6)	0.04*

AF: atrial fibrillation; BMI: body mass index; CE: cardioembolism; CRP: C-reactive protein; HDL-C: high-density lipoprotein cholesterol; LAA: large-artery atherosclerosis; LDL-C: low-density lipoprotein cholesterol; NIHSS: National Institutes of Health Stroke Scale; SAO: small-vessel occlusion; SOE: stroke of other determined etiology; SUE: stroke of undermined etiology; SFA: saturated fatty acid; TC: total cholesterol; TG: triacylglycerol; TOAST: the Trial of Org 10172 in Acute Stroke Treatment Classification.

[†]*p* values are based on univariate analysis (Student's, Mann-Whitney U, Kruskal-Wallis, Chi-square or Fisher exact test) as appropriate. Significance is shown by $^*p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

Table 2. Dietary protein intake and major stroke (NIHSS ≥6)[†]

	OR	95% CI	*p* value
Total protein intake, g/day	0.98	0.95-1.01	0.15
Animal protein intake, g/day	1.01	0.95-1.06	0.87
Plant protein intake, g/day	0.96	0.92-1.00	0.07

AF: atrial fibrillation; CI: confidence interval; CRP: C-reactive protein; LDL-C: low-density lipoprotein cholesterol; OR: odds ratio; SFA: saturated fatty acid; TG: triacylglycerol; TOAST: the Trial of Org 10172 in Acute Stroke Treatment Classification.

[†]Multivariate logistical regression analysis adjusted for age, AF, TG, LDL-C, CRP, TOAST, dietary carbohydrate intake and dietary SFA intake.

stroke had lower AF rate (8.2 vs 24.2 %, p=0.003), higher TG (1.7 vs 1.4 mmol/L, p=0.02), lower LDL-C (2.6 vs 3.0 mmol/L, p=0.01) and lower CRP (1.5 vs 2.2 mg/L, p=0.02) than patients with major stroke. Concerning the duration from stroke onset to NIHSS assessment, no significant difference was detected between patients with minor and with major stroke (39 vs 38 hours, p=0.26). Compared with patients with major stroke, patients with minor stroke had higher intake of animal protein (19.5 vs 15.8 g/day, p=0.02) and saturated fatty acid (SFA, 14.1 vs 12.6 g/day, p=0.01), and had lower intake of carbohydrate intake (249 vs 273 g/day, p=0.001) before stroke onset. Patients with minor stroke had higher red meat intake (41.0 vs 27.4 g/day, p=0.03) and higher nuts intake (2.1 vs 0 g/day, p=0.04) than patients with major stroke.

As in Table 2, no associations between total (OR=0.98, 95% CI: 0.95-1.01, p=0.15), animal (OR=1.01, 95% CI: 0.95-1.06, p=0.87), plant protein intake (OR=0.96, 95% CI: 0.92-1.00, p=0.07) and stroke severity were detected after adjusting for age and other major confounders (AF, TG, LDL-C, CRP, TOAST, dietary carbohydrate intake, dietary SFA intake).

Table 3 exhibits the baseline characteristics of the included patients according to stroke outcomes. As expected, ages (63.8 vs 58.9 years, p=0.01) were more advanced, AF rate (24.3 vs 10.2 %, p=0.01) and serum CRP (2.6 vs 1.5 mg/L, p=0.003) were higher, and serum TG levels (1.3 vs 1.6 mmol/L, p=0.01) were lower in patients with poor outcomes. No significant difference was detected concerning the duration from stroke onset to NIHSS assessment between patients with good and with poor neurological outcomes (37 vs 44 h, p=0.76). Patients with poor outcomes had higher baseline NIHSS scores (10 vs 4, p<0.001) than those with good outcomes. Total protein intake (52.5 vs 57.4 g/day, p=0.01), fiber intake (7.2 vs 8.0 g/day, p=0.045) and fish intake (10.6 vs 15.8 g/day, p=0.04) were lower in patients with poor outcomes than those with good outcomes.

Table 3. Baseline characteristics according to the stroke outcomes[†]

	Good outcomes (mRS ≤2)	Poor outcomes (mR 3-6)	p value
Patients, n (%)	127 (63.2)	74 (36.8)	
Age, years, mean±SD	58.9±12.5	63.8±12.5	0.01*
Male, n (%)	90 (70.9)	49 (66.2)	0.53
BMI, kg/m^2, mean±SD	25.1±3.3	24.5±2.9	0.19
Hypertension, n (%)	84 (66.1)	53 (71.6)	0.44
Diabetes, n (%)	36 (28.3)	25 (33.8)	0.43
AF, n (%)	13 (10.2)	18 (24.3)	0.01*
Smoking, n (%)	54 (42.5)	32 (43.2)	1.00
TC, mmol/L, mean±SD	4.7±1.2	4.6±1.1	0.68
TG, mmol/L, median (IQR)	1.6 (1.1-2.3)	1.3 (1.1-1.7)	0.01*
HDL-C, mmol/L, median (IQR)	1.0 (0.8-1.2)	1.0 (0.9-1.2)	0.30
LDL-C, mmol/L, mean±SD	2.7±0.9	3.0±1.0	0.08
CRP, mg/L, median (IQR)	1.5 (0.0-3.4)	2.6 (0.8-9.7)	0.003**
Baseline NIHSS scores, median (IQR)	4 (1-7)	10 (5-13)	<0.001***
Stroke onset to NIHSS assessment, hours, median (IQR)	37 (19-72)	44 (11-88)	0.76
TOAST, n (%)			0.004**
LAA	49 (38.6)	40 (54.1)	
CE	13 (10.2)	14 (18.9)	
SAO	33 (26.0)	7 (9.5)	
SOE&SUE	32 (25.2)	13 (17.6)	
Total energy intake, ×10^3 Kcal/day, median (IQR)	1.37 (1.16-1.71)	1.32 (1.07-1.70)	0.33
Total protein intake, g/day, mean±SD	57.4±14.4	52.5±11.5	0.01*
Animal protein intake, g/day, mean±SD	18.4±10.7	16.8±10.8	0.32
Plant protein intake, g/day, mean±SD	39.0±13.0	35.6±9.0	0.05
Fiber intake, g/day, median (IQR)	8.0 (6.3-11.0)	7.2 (5.4-9.6)	0.045*
Carbohydrate intake, g/day, mean±SD	259±53	261±51	0.79
SFA intake, g/day, mean±SD	13.6±4.3	13.3±3.8	0.52
K^+ intake, g/day, median (IQR)	1.4 (1.2-1.7)	1.3 (1.0-1.7)	0.23
Na^+ intake, g/day, mean±SD	4.8±1.5	5.0±1.8	0.50
Red meat intake, g/day, median (IQR)	33.4 (15.8-72.6)	34.4 (13.4-65.3)	0.60
Poultry intake, g/day, median (IQR)	6.5 (0-12.3)	7.7 (0-16.2)	0.49
Eggs intake, g/day, median (IQR)	12.8 (0-59.9)	9.0 (0-61.1)	0.71
Dairy intake, g/day, median (IQR)	0 (0-0)	0 (0-0)	0.99
Fish intake, g/day, median (IQR)	15.8 (4.0-34.5)	10.6 (0-24.7)	0.04*
Legumes intake (dry), g/day, median (IQR)	3.9 (0-8.0)	4.1 (0.5-7.2)	0.80
Nuts intake, g/day, median (IQR)	0.7 (0-6.5)	0.2 (0-7.1)	0.93

AF: atrial fibrillation; BMI: body mass index; CE: cardioembolism; CRP: C-reactive protein; HDL-C: high-density lipoprotein cholesterol; LAA: large-artery atherosclerosis; LDL-C: low-density lipoprotein cholesterol; mRS: the Modified Rankin scale; NIHSS: National Institutes of Health Stroke Scale; SAO: small-vessel occlusion; SFA: saturated fatty acid; SOE: stroke of other determined etiology; SUE: stroke of undermined etiology; TC: total cholesterol; TG: triacylglycerol; TOAST: the Trial of Org 10172 in Acute Stroke Treatment Classification.

[†]p values are based on univariate analysis (Student's, Mann-Whitney U, Kruskal-Wallis, Chi-square or Fisher exact test) as appropriate. Significance is shown by *p<0.05, **p<0.01, ***p<0.001.

Table 4. Dietary protein and source food intake and good outcomes (mRS ≥2) of stroke[†]

Dietary protein and source food (g/day)	OR	95% CI	*p* value
Total protein intake	1.05	1.00-1.10	0.04*
Animal protein intake	1.01	0.98-1.05	0.50
Plant protein intake	1.07	1.00-1.15	0.06
Protein-source food intake			
Red meat intake	1.00	0.99-1.01	0.98
Poultry intake	0.98	0.95-1.01	0.18
Eggs intake	1.01	1.00-1.02	0.35
Dairy products intake	1.00	1.00-1.00	0.70
Fish intake	1.01	0.99-1.02	0.47
Legumes intake (dry)	1.04	1.00-1.08	0.08
Nuts intake	0.99	0.95-1.02	0.46

AF: atrial fibrillation; CI: confidence interval; CRP: C-reactive protein; NIHSS: National Institutes of Health Stroke Scale; OR: odds ratio; TG: triacylglycerol; TOAST: the Trial of Org 10172 in Acute Stroke Treatment Classification.
[†]Multivariate logistical regression analysis adjusted for age, sex, AF, TG, CRP, TOAST, baseline NIHSS scores and dietary fiber intake.
Significance is shown by *$p<0.05$.

After adjusting for age, sex, AF, TG, CRP, TOAST, baseline NIHSS scores and dietary fiber intake, multivariate logistic regression indicated that total protein intake was positively associated with good outcomes of ischemic stroke (OR=1.05, 95% CI: 1.00-1.10, p=0.04). However, animal protein intake (OR=1.01, 95% CI: 0.98-1.05, p=0.50) and plant protein intake (OR=1.07, 95% CI: 1.00-1.15, p=0.06) were not associated with good outcomes (Table 4).

After adjusting for age, sex, AF, TG, CRP, TOAST, baseline NIHSS scores and dietary fiber intake, no association was detected between dietary intake of red meat (OR=1.00, 95% CI: 0.99-1.01, p=0.98), poultry (OR=0.98, 95% CI: 0.95-1.01, p=0.18), eggs (OR=1.01, 95% CI: 1.00-1.02, p=0.35), dairy products (OR=1.00, 95% CI: 1.00-1.00, p=0.70), fish (OR=1.01, 95% CI: 0.99-1.02, p=0.47), legumes (OR=1.04, 95% CI: 1.00-1.08, p=0.08), or nuts (OR=0.99, 95% CI: 0.95-1.02, p=0.46) and neurological outcomes in this cohort of stroke patients.

DISCUSSION

This study detected an independent and positive association between premorbid dietary intake of total protein and good outcomes in patients with ischemic stroke. No association was detected between premorbid dietary intake and stroke severity.

Previous studies indicated that higher dietary protein intake may be helpful for the functional recovery after stroke.[9,21-24] Inadequate protein and energy intakes have been related to the disability and neurological deficit 6 months after stroke.[22] Increasing dietary protein intake in 30 days after stroke could improve neurological and cognitive recoveries.[23] Besides, protein supplementation may enhance the spontaneous recovery of neurological alterations in patients with ischemic stroke. In a controlled study, Aquilani and colleagues observed that patients with protein supplementation achieved more improved motor performances compared with patients with placebo 21 days after the intervention.[9] Supplementation of essential amino acids (EAAs) may decrease the risk of complications, such as nosocomial infections, in rehabilitation stage of stroke patients.[25] Data from this study demonstrated that premorbid protein intake was positively and independently associated with favorable outcomes of ischemic stroke, which is consistent with findings from previous studies.

Baseline NIHSS score, an indicator of stroke severity, has been demonstrated as a powerful predictor for outcome of ischemic stroke.[17,26] However, an expected significant association between premorbid dietary intake and stroke severity was not observed in this patient cohort. These results may indicate that higher premorbid protein intake improve neurological outcomes via mechanisms other than reducing stroke severity. To confirm this finding, larger studies with longer follow-up are warranted.

The underlying mechanisms concerning the effects of dietary protein on neurological outcomes of ischemic stroke remains largely unclear. The observed positive effects of dietary protein on neurological functions after stroke may be explained by its influences on cortical plasticity and neurotransmission, and its favorable actions on concomitant infection and blood pressure. Experimental and clinical researches demonstrated that protein may play an important role in the cortical plasticity and neurotransmission which were favorable for functional recovery.[27,28] Several experimental studies reported that the protein synthesis can be suppressed in the endangered neural cells (e.g. ischemic penumbra) in the circumstance of focal cerebral ischemia.[29] However, protein synthesis is very important to axonal sprouting and new cortical networks. If the amino acid from protein intake was increased, the process of protein synthesis may be reactivated and the formation of axonal sprouting and new cortical networks can be activated.[30] Furthermore, amino acids from protein may exhibit the function of improving chemical neurotransmission in spared tissue, which may also enhance the retrieval after stroke.[31]

Previous study indicated that EAAs, the important components of protein, may reduce the infection risk by acting on immune cells.[21] EAAs can enhance the defense capacities by inducing protein synthesis which is crucial for the immune responses.[32] Some amino acids, such as cysteine, can also affect metabolic pathways which are related to the immune function.[25] Cysteine plays a vital role in the glutathione metabolism and redox activity.[33]

Additionally, dietary protein may have a favorable effect on blood pressure. The International Study on Macronutrients and Blood Pressure (INTERMAP) and a clini-

cal trial of comprehensive lifestyle modification for blood pressure control (PREMIER) showed an inverse relationship between dietary protein intake and blood pressure.[34-36] In a Japanese population study, increased protein intake (19.2 g/day) was associated with decreased systolic blood pressure (1.5 mmHg) in men.[37] Studies reported that amino acids hydrolyzed from protein, such as glutathione, can reduce blood pressure by means of inhibiting oxidative injury and enhancing the effects of nitric oxide.[38,39] Since high blood pressure can influence the outcomes of stroke, it may be possible that dietary protein can be in favor of the function recovery by decreasing blood pressure.

There were several limitations of our study. First, dietary intake was assessed during a face-to-face interview and no biomarkers of dietary protein were used. Thus, memory biases may exist in the assessment of dietary protein intake. Besides, this was a hospital-based study, which may limit the feasibility for generalizing the results. The incomplete data prevented us to analyze the impacts of protein intake on follow-up blood pressure. Our study has strengths as well. To the best of our knowledge, few studies evaluated the associations between premorbid dietary intake of protein and neurological outcomes in patients with ischemic stroke. This was a prospective study and we investigated effects of major protein sources on the good outcomes.

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AUTHOR DISCLOSURES

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