Dietary inflammatory index is associated with severe depression in older adults with stroke: a cross-sectional study

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Running title: Diet and depression in adults with stroke

This peer-reviewed article has been accepted for publication but not yet copyedited or typeset, and so may be subject to change during the production process. The article is considered published and may be cited using its DOI
10.1017/S0007114524000850
The British Journal of Nutrition is published by Cambridge University Press on behalf of The Nutrition Society

Abstract

Inflammation is involved in the pathogenesis of stroke and depression. We aimed to investigate the association between the dietary inflammatory index (DII) and depression in American adults with stroke. Adults with stroke were enrolled from the National Health and Nutrition Examination Survey between 2005 and 2018 in the United States. The DII was obtained from a 24-h dietary recall interview for each individual. Multivariate regression and restricted cubic spline analyses were conducted to evaluate the association between DII and depression in adults with stroke. The mean age of the 1,239 participants was 63.85 years (50.20% women), and the prevalence of depression was 18.26%. DII showed a linear and positive association with severe depression in adults with stroke (OR, 1.359; 95% CI, 1.021, 1.810; p for non-linearity=0.493). Compared with those in the lowest tertile of the DII, adults with stroke in the third tertile of the DII had a 3.222-fold higher risk of severe depression (OR, 3.222; 95% CI, 1.150, 9.026). In the stratified analyses, the association between DII score and severe depression was more significant in older adults (p for interaction=0.010) but not significant with respect to sex (p for interaction=0.184) or smoking status (p for interaction=0.396). No significant association was found between DII and moderate-to-moderately severe depression in adults with stroke. In conclusion, an increase in DII score was associated with a higher likelihood of severe depression in older adults with stroke.

Keywords: dietary inflammatory index, depression, stroke, older adults

Introduction

Stroke is a major cause of mortality and disability worldwide (1). Stroke survivors face great life challenges because of severe sequelae (such as paralysis, aphasia, cognitive impairment, and psychological disorders)(2), and depression is one of the most common mental diseases after stroke (3). Post-stroke depression further leads to poor quality of life and higher mortality (4, 5).

The mechanisms of post-stroke depression are multifactorial and not fully understood (6, 7). The possible mechanisms of post-stroke depression included hypothalamic-pituitary-adrenal (HPA) axis dysregulation, reduced monoamine levels, abnormal neurotrophic responses (6, 7), neuronal ischaemic change and neuroinflammation (7, 8). In addition, the concentrations of the pro-inflammatory cytokines TNF-α and IL-6 in peripheral blood were significantly elevated in patients with depression(9). Cytokines alter the production, metabolism, and transport of neurotransmitters that synergistically affect mood and also affect neuronal growth and survival to promote depressive episodes(10). Increasing evidence indicates that foods and nutrients may play a role in depressive episodes because of their anti-inflammatory and pro-inflammatory properties. A meta-analysis showed that an increased intake of total dietary fibre is associated with lower odds of depression (11). Adhere to healthy dietary patterns (12) , such as Mediterranean diet (13) and traditional Brazilian diet (14) rich in vegetables, fruits, fish, and olive oil are thought to be associated with reduced risk of depression, whereas Western-type dietary patterns are characterised by high consumption of red or processed meat, refined grains, sweets, high-fat dairy products, and low intake of fruits and vegetables aggravate depressive episodes (15), and a recent meta-analysis also suggested that ultra-processed food was associated with an increased risk of anxiety and depression (16). The association between diet and depression may be partially mediated by inflammatory markers (17).

Studies have investigated the relationship between the inflammatory potential of diet and post-stroke depression (18, 19). A U.S. population study showed that increasing dietary

antioxidant intake may prevent depressive symptoms in adults with stroke (19). However, the relationship between certain food antioxidants and depression remains controversial, which may be related to different food questionnaires and methods used to assess dietary intake in previous studies (17, 20). The dietary inflammatory index (DII) is a dietary index that provides a quantitative means to study the relationship between pro-and anti-inflammatory diets and disease (21). A study of postmenopausal women suggested that DII can be used to predict the incidence of menopausal complications (22). Ghazizadeh et al. found that DII is significantly associated with major depression in women (23). However, the relationship between the DII and depression in adults with stroke remains unclear.

Thus, the objective of this study was to investigate the association between DII and depression in American adults with stroke using data from the National Health and Nutrition Examination Survey (NHANES).

Materials and methods

1.1. Data source and study population

The present study was a cross-sectional analysis using data from NHANES 2005–2018. The NHANES is a nationally representative cross-sectional survey of the non-institutionalised US population with data collected in 2-year cycles. During each cycle, the NHANES was conducted based on a stratified multistage probability sampling design and included two components: a household interview and a health examination. This study included individuals older than 18 years who participated in the 2005–2018 NHANES survey cycles. From a total of 1,658 participants with stroke, we excluded those with missing data, including the 9-item Patient Health Questionnaire (PHQ-9) score (n=304), DII score (n=59), and participants with missing data on covariates of interest (n=56). The final sample size for the analysis was 1,239. All participants provided written informed consent before participating in the survey. The NHANES survey was approved by the Research Ethics Review Board of the National Centre for Health Statistics, and the procedures followed the principles of the

Declaration of Helsinki. The NHANES data used in this study are publicly available (https://wwwn.cdc.gov/nchs/nhanes/) and do not require ethical or administrative approval.

1.2. Covariates selection

Sociodemographic and lifestyle information, including age, sex, race, marital status, smoking status, education level, and sleep status, were obtained through standardised questionnaires. Race was classified as non-Hispanic White, non-Hispanic Black, Mexican American, or other. Smoking status was defined as a non-smoker, former smoker, or current smoker. Education was classified as less than high school and high school or above. Sleep status was obtained by participants answering the following questionnaire: over the last 2 weeks, how often have you been bothered by trouble falling or staying asleep or sleeping too much? And it was defined as not at all, several days, more than half the days, and nearly every day. Body mass index (BMI) was provided by the Mobile Examination Centre. A history of hypertension and diabetes was assessed using a combination of questionnaires and examination results. Hypertension was defined as follows: (1) average systolic blood pressure/average diastolic blood pressure ≥ 140/90 mmHg, (2) previous diagnosis by a doctor or health professional, or (3) currently taking antihypertensive medications. Diabetes was defined as (1) self-reported diagnosis of diabetes, (2) fasting HbA1c level > 6.4%, or (3) current use of hypoglycaemic drugs. Stroke data were self-reported personal interview data obtained from the medical status section of the NHANES. In this questionnaire, stroke was identified as a stroke diagnosis by a physician or health professional.

1.3. Depressive symptom assessment

A validated PHQ-9 was used to assess depressive symptoms. PHQ-9 consists of a 9-item depression module to assess the frequency of depressive symptoms over the past 2 weeks. With each of the 9 items ranging from “0” (not at all) to “3” (nearly every day), PHQ-9 has total scores ranging from 0 to 27. A higher PHQ-9 score was associated with more severe depressive symptoms. PHQ-9 scores of 5, 10, 15, and 20 represented mild, moderate, moderately severe,

and severe depression, respectively (24). Depression was defined as PHQ-9 scores ≥ 10 in clinical practice (24). In this study, we categorised depression into three grades based on the PHQ-9 scores: no clinical depression (PHQ-9: ≤ 9), moderate-to-moderately severe depression (PHQ-9: 10–19), and severe depression (PHQ-9: 20–27).

1.4. Dietary data and computation of DII scores

Dietary data were derived from self-reports, and DII was calculated by adding the scores of each dietary component consumed by each participant within a 24-h period. Higher DII scores were associated with a more pro-inflammatory diet, whereas lower DII scores indicated a more anti-inflammatory diet. The method for calculating DII was reported in detail by Shivappa et al (21). DII scores were based on 11 food consumption datasets worldwide (21), which provides reliable estimates of the mean and standard deviation of 45 food parameters. A participant's exposure relative to the standard global mean was calculated as a z-score, which was calculated by subtracting the mean of the energy-adjusted regionally representative database from each food parameter and dividing this value by the standard deviation of the parameter. These z-scores were converted to central proportion scores by multiplying by 2 and subtracting 1 to reduce the effect of "right-skewing". The final values were multiplied by the overall food parameter-specific inflammatory effect score to obtain a food parameter-specific DII score. DII scores for specific food parameters were added to obtain an overall DII score for each individual. In this study, the NHANES 2008–2015 database provided 28 of the 45 food parameters to calculate DII. Previous studies revealed that the DII scores were still available even if the nutrients used to calculate DII were <30 (21). These food parameters and other basic information for calculating DII are shown in **Table S1**.

1.5. Statistical Analysis

Descriptive data on participants' characteristics were expressed as means and standard errors (SEs) or medians; interquartile ranges (IQRs) for continuous variables; and numbers and weighted percentages for categorical variables. One-way analysis of variance and chi-squared tests were used to compare continuous and categorical variables, respectively. The weight prevalence of different degrees of depression was evaluated in all participants. Multivariate logistic regression analyses were used to estimate the association between DII scores and different degrees of depression in adults with stroke. Model 1 shows the age-adjusted results. Variables were entered in the multivariate logistic regression models if the p-value was ≤ 0.10 in the univariable analysis. In the multivariate-adjusted model, we adjusted for baseline age, sex, race, educational status, marital status, and smoking status. Restricted cubic spline (RCS) was used to evaluate the potential non-linear relationship between DII and depression in adults with stroke. Stratification analysis was performed to estimate the relationship between DII and severe depression according to age, sex, and smoking status. Data were weighted to ensure that they were representative of U.S. adults using complex survey sampling analysis methods. All data analyses were performed using the R software (version R-4.1.0; Cary, NC, USA). Two-sided p values <0.05 were considered statistical significance.

Results

Characteristics of the Study Population

This study included 1,239 adults with stroke. The mean age of the participants was 63.85 years, and 622 (50.20%) were women. Among the 1,239 participants, the weight prevalence of moderate-to-moderately severe and severe depression was 14.62% and 3.64%, respectively (**Figure 1**).

Table 1 presents the characteristics of the participants and DII score tertiles. Compared with participants in the lowest DII score tertile (tertile 1), those in the highest DII score tertile (tertile

3) were more likely to be female, highly educated, and current smokers. There were no differences in the distribution of age, race, marital status, BMI, sleep status, or history of diabetes or hypertension.

Associations between DII and depression in adults with stroke

Table 2 shows that the DII score was positively associated with severe depression in adults with stroke. The age-adjusted ORs (95% CIs) for severe depression across the DII score tertiles were 1.00 (reference), 0.995 (0.332, 2.976), and 3.853 (1.417, 10.476), respectively (Table 2). The ORs for severe depression were similar following additional adjustments for sex, race, education, smoking, and marital status (1.00 (reference), 0.942(0.327, 2.718), and 3.222(1.150, 9.026) across the DII tertiles). When modelling the DII score continuously, a similar positive association was observed in the fully adjusted models (Model 2 in Table 2). A one-unit increase in the DII score was associated with 35.9% higher odds (p=0.026) of severe depression in adults with stroke. No significant association between the DII and depression was found for total depression (p=0.283) or moderate-to-moderately severe depression (p=0.871). In **Figure 2**, the non-linear relationship between DII and severe depression was not significant in the RCS model (p for non-linearity > 0.05).

Stratification Analysis

In the stratified analyses (**Figure 3)**, no interactions were observed between the DII and sex (p-interaction=0.184) or smoking status (p-interaction=0.396). However, the DII-severe depression association was stronger in older individuals (p-interaction=0.010).

Discussion

In this cross-sectional study of a representative US sample, we found that older adults with stroke with higher DII scores were significantly associated with a higher risk of severe depression. No significant association was found in adults with stroke and moderate-to-moderately severe depression. These findings may provide clinical and public health implications for preventing depression in adults with stroke.

The DII level is related to the pro-and anti-inflammatory ability of the diet(21), with a higher DII indicating a stronger pro-inflammatory ability. Inflammation is a defence mechanism that prevents harmful substances from entering the body; however, sustained and prolonged inflammation is detrimental to health (25). Increasing evidence indicates that the inflammatory properties of diet are associated with a variety of diseases (such as coronary heart disease, various types of cancer) (26). A pro-inflammatory diet can promote depression by affecting the HPA axis, oxidative stress, gut-brain axis, and other pathways to increase neuroinflammation and change the secretion of neurotransmitters (27, 28, 29). In a previous meta-analysis, participants with the highest DII scores had a 23% higher risk of depression than those with the lowest DII scores (30). A significant association between DII and depression has been confirmed in the general population (31) and in individuals with comorbid chronic diseases (such as diabetes and coronary heart disease) (32). A cohort study from Iran showed that DII is significantly associated with major depression in women (23). However, few studies have reported the association between DII scores and depression severity in adults with stroke. We found a significant association between the DII and severe depressive episodes in adults with stroke, whereas this relationship was not observed for moderate-to-moderately severe depression. It should be noted that the DII score was not significantly associated with depression in adults with stroke before the degree of depression was graded, contradicting to the positive results of previous studies in other populations (30, 31, 32). Depression is a multifactorial disease (33). Post-stroke depression is directly related to cerebrovascular injury (7). Compared with the general population, the composition of risk factors for depression in the

stroke population may be different (7, 34), which may lead to different conclusions on the correlation between DII and depression in different populations. In addition, the crude diagnosis of depression may mask the actual relationship between the DII and different degrees of depression. The complex composition of risk factors for depression and the relationship between diet and different levels of depression in different populations needs to be further explored.

We further performed a subgroup analysis of the association between the DII score and severe depression in adults with stroke. A higher DII score conferred a higher risk of major depressive episodes in older adults. In line with previous studies, older age was a risk factor for depression (33). Ageing, increased levels of accompanying diseases, lower activity, and lower living standards predispose older adults to psychological problems (35), which may be attributed to immune dysregulation, most notably, high blood levels of pro-inflammatory immunogenic stimuli(36, 37). Additionally, DII promotes the onset of depression by increasing pro-inflammatory factors in the body(28, 29); therefore, there may be a synergistic effect between DII and ageing.

Depression plays an important role in the progression and prognosis of stroke (3). Diet appears to be a modifiable risk factor for depression (14, 38). Our results extend the association between dietary inflammation potential and depression in the stroke population, with a more detailed classification of the degree of depression and a relative subgroup analysis to identify special populations.

Despite the significance of our findings, this study has a few limitations. First, the NHANES is a cross-sectional observational study; therefore, causality cannot be established, and residual confounding factors cannot be completely ruled out. Second, dietary data were obtained from only one 24-h dietary recall, this may not represent habitual diet, although 24-h dietary recalls have been widely used in previous studies (39, 40). Third, history of antidepressant use, and some other characteristic data were not available due to the limitations of the NHANES

database. Finally, stroke, depression and dietary recalls were self-reported and may be limited by underlying cognitive difficulties in a stroke population, which may have introduced a bias. However, these questionnaires have been widely used to assess stroke, depression and DII (41, 42, 43). Future longitudinal studies are needed to explore the relationship between DII and depression in different populations.

Conclusions

A high DII was associated with a higher likelihood of having severe depression in older adults with stroke. Future studies with prospective designs or clinical trials are needed to confirm the results of this study.

Acknowledgements

We would like to thank Editage (www.editage.cn) for English language editing.

Conflict of Interest

None.

Financial support

This study was funded by the Clinical Research Award of the First Affiliated Hospital of Xi'an Jiaotong University (Grant No. XJTU1AF2018CRF-024) and by the horizontal subject of the First Affiliated Hospital of Xi'an Jiaotong University (Grant No. HX201872). The study funders were not involved in the design of the study.

Authorship contributions

Y.G. and Y.R.Z. designed the research; P.P.Z. conducted research and wrote the manuscript; P.P.Z. and Y.R.Z. analyzed data; X.X. and Y.B.W. revised the tables and images; Y.G. and Y.R.Z. provided important revisions for the final content. All authors reviewed and approved the final version of the manuscript.

Abbreviations: dietary inflammatory index (DII); hypothalamic-pituitary-adrenal (HPA); National Health and Nutrition Examination Survey (NHANES); 9-item Patient Health Questionnaire (PHQ-9); standard errors (SEs); interquartile ranges (IQRs); Restricted cubic spline (RCS); Body mass index (BMI).

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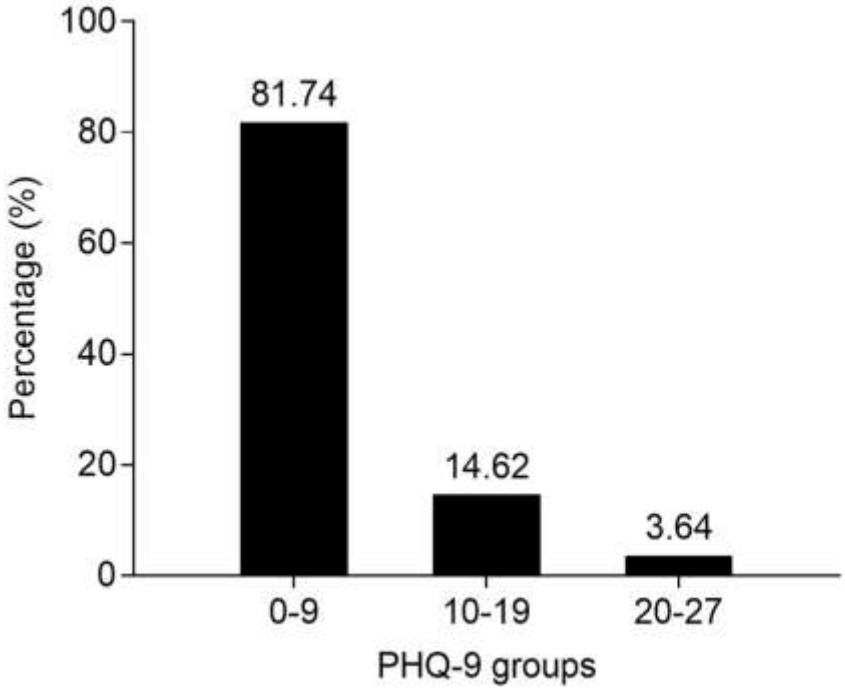

Figure 1. Percentage (%) of depression status in adults with stroke, NHANES 2005–2018.

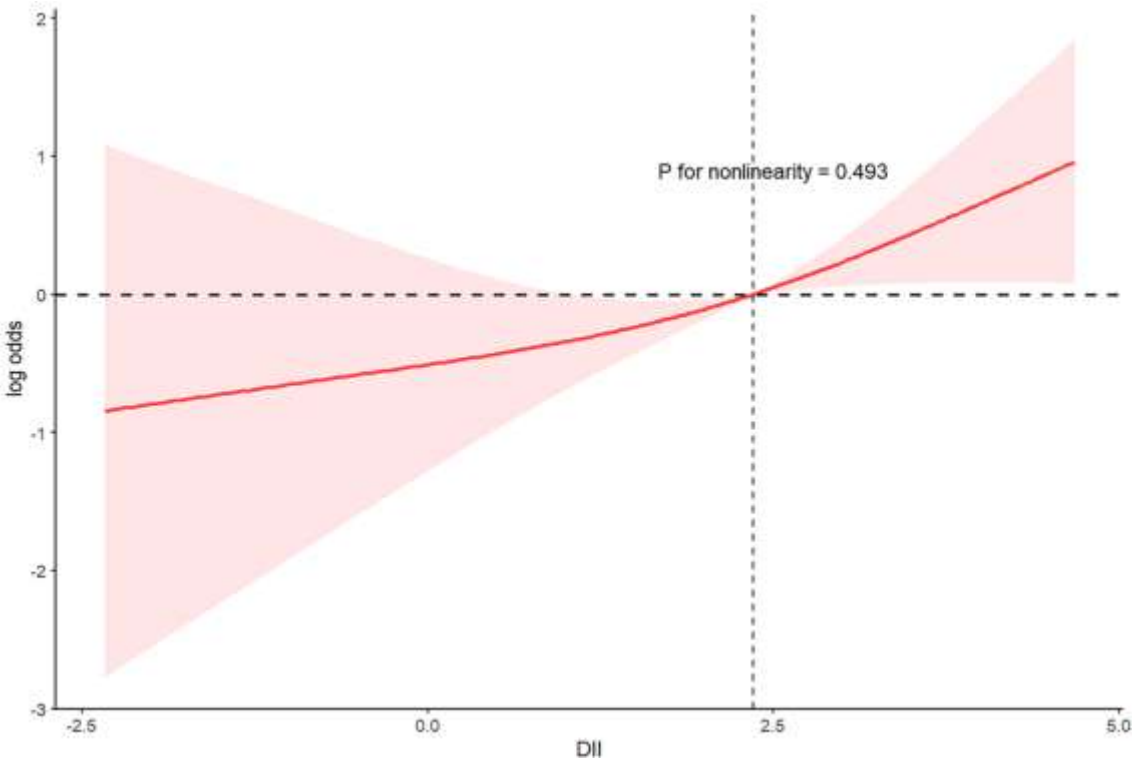

Figure 2. Restricted cubic spline (RCS) of dietary inflammatory index (DII) with severe depression.

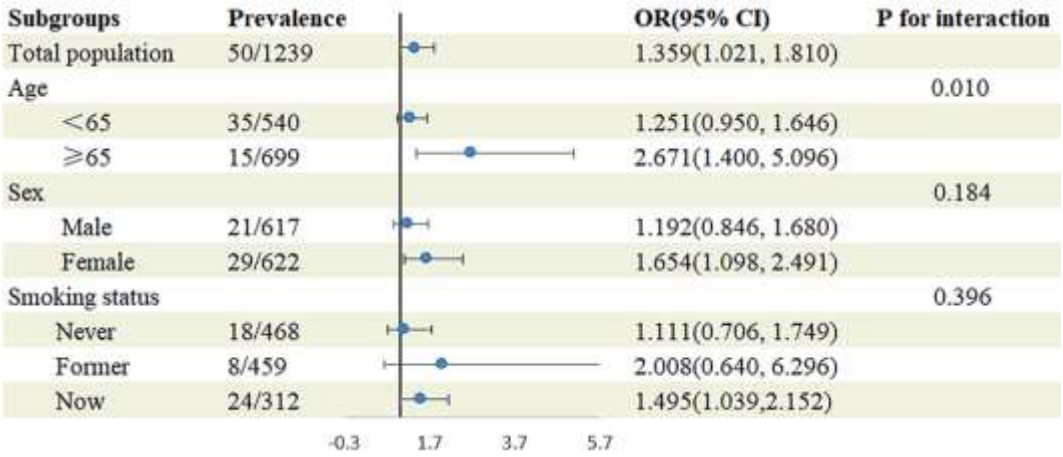

Figure 3. Subgroup analysis of the association of the dietary inflammatory index with severe depression in adults with stroke.

Results were adjusted for all covariates except the corresponding stratification variable.

Table 1. Baseline characteristics of adults with stroke by the dietary inflammatory index (DII) tertiles (Q) from NHANES 2005 –2018

Characteristic	DII score				
	Total(N=1,239)	Q1(N=413)	Q2(N=413)	Q3(N=413)	P-value
Age, years[a]	63.85(0.58)	65.38(0.82)	62.56(0.93)	63.67(0.95)	0.06
Female, n (%)	622(50.20)	158(38.92)	204(58.04)	260(68.69)	< 0.001
Race, n (%)					0.08
Non-Hispanic White	627(50.61)	219(71.62)	202(69.82)	206(70.56)	
Non-Hispanic Black	341(27.52)	96(11.75)	115(14.66)	130(18.10)	
Mexican American	115(9.28)	43(5.72)	40(4.19)	32(3.94)	
Other race	156(12.59)	55(10.91)	55(11.33)	46(7.40)	
Education Status, n (%)					0.01
Less than high school	404(32.61)	121(20.12)	123(22.65)	160(30.94)	
High school or above	835(67.39)	292(79.88)	289(77.35)	254(69.06)	
Smoking status, n (%)					0.05
Never	468(37.77)	148(38.99)	159(40.20)	161(39.60)	
Former	459(37.05)	177(41.34)	155(34.81)	127(30.06)	

Current	312(25.18)	88(19.66)	98(24.99)	126(30.35)	
Marital status, n (%)					0.08
Married/living with partner	653(52.7)	224(61.47)	230(62.02)	199(52.04)	
Never married	102(8.23)	31(6.63)	29(5.13)	42(8.64)	
Widowed/divorced/separated	484(39.06)	158(31.91)	153(32.85)	173(39.32)	
Body mass index (kg/m^2)[a]	30.33(0.27)	29.62(0.41)	30.84(0.53)	30.54(0.41)	0.13
Sleep disorders, n (%)					0.21
Not at all	643(51.9)	211(53.00)	224(51.38)	208(45.16)	
Several days	243(19.61)	92(22.03)	81(20.77)	70(19.38)	
More than half the days	131(10.57)	47(9.31)	40(10.73)	44(11.57)	
Nearly every day	222(17.92)	63(15.66)	67(17.12)	92(23.89)	
Medical history, n (%)					
Diabetes	442(35.67)	131(28.32)	155(33.23)	156(34.21)	0.29
Hypertension	1,012(81.68)	327(79.03)	336(77.54)	349(79.55)	0.88

[a]Mean (SE)

Table 2. Associations of the dietary inflammatory index (DII) with depression in adults with stroke

Depressive symptom severity	Variables	Prevalence rate	Model 1 OR (95% CI)	P-value	Model 2 OR (95% CI)	P-value
Clinical depression	DII (Continu	232/1239	1.104(0.992,1.228)	0.07	1.065(0.949,1.195)	0.283
	Tertile1	64/413	reference		reference	
	Tertile2	68/413	1.044(0.702,1.553)	0.829	0.994(0.658,1.503)	0.978
	Tertile3	100/413	1.620(1.109,2.367)	0.013	1.411(0.926,2.149)	0.108
Moderate-to-moderately severe depression	DII (Continu	182/1,239	1.049(0.932,1.181)	0.424	0.989(0.862,1.134)	0.871
	Tertile1	57/413	reference		reference	
	Tertile2	56/413	1.054(0.699,1.589)	0.800	1.011(0.655,1.559)	0.962
	Tertile3	69/413	1.292(0.824,2.025)	0.261	1.135(0.699,1.841)	0.606
Severe depression	DII (Continu	50/1,239	1.437(1.066,1.938)	0.018	1.359(1.021, 1.810)	0.036
	Tertile1	7/413	reference		reference	
	Tertile2	12/413	0.995(0.332, 2.976)	0.992	0.942(0.327, 2.718)	0.911

Model 1: Adjusted for age. Model 2: Adjusted for age, sex, race, education status, marital status, smoking status.

Clinical depression: PHQ-9≥10; Moderate-to-moderately severe depression: PHQ-9 scores:10-19; Severe depression: PHQ-9 ≥20.