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Relationship Between Dietary Inflammatory Index and Carotid Artery Calcification in Patients with Ischemic Stroke

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Background and Purpose: Diet may influence systemic inflammatory status, vascular calcification, and, therefore, the development of atherosclerosis. The Dietary Inflammatory Index (DII) is a measure of the inflammatory potential of diet. Although previous studies have examined the relationship between DII and cardiovascular diseases, its specific association with carotid artery calcification in ischemic stroke patients remains insufficiently explored. This study aimed to evaluate the relationship between Dietary Inflammatory Index (DII) and carotid artery calcification in patients with ischemic stroke.

Methods: This is a retrospective cross-sectional analysis based on a prospective registry database. Patients with ischemic stroke were enrolled via Nanjing Stroke Registry Program. DII was calculated based on 39 food components with the help of a food frequency questionnaire. Carotid artery calcification was quantified as calcification score using the Agatston method based on computed tomography angiography. The data were compared among patients stratified by tertiles of DII. Multiple logistic regression models were used to evaluate the influence of DII on carotid artery calcification. Spearman analysis was used to evaluate the relationship between DII and ln-transformed carotid artery calcification score.

Results: Of the 601 enrolled, carotid artery calcification was detected in 368 (61.23%) patients. Compared with patients with the lowest DII, those with higher DII had a higher ratio of stroke subtypes of large artery atherosclerosis (p =0.050), a higher calcification score (p <0.001), and a higher ratio of calcification (p <0.001). Other baseline characteristics, including sex and age, showed no significant differences across the DII tertiles. Patients with carotid artery calcification had significantly higher DII scores compared to those without calcification (p = 0.018). Logistic regression analysis showed that patients with the highest DII tertile had a higher risk of carotid artery calcification after adjusting for significant cofounders (OR =1.880, 95% CI, 1.205−2.932; p =0.005). Spearman correlation analysis indicated that DII was associated with ln-transformed carotid artery calcification score in patients with carotid artery calcification (R =0.110, p =0.035).

Conclusion: DII was associated with carotid artery calcification in patients with ischemic stroke. Considering a possible causal relationship, the mechanism of this relationship warrants further investigation.

Keywords: dietary inflammatory index, artery calcification, carotid, ischemic stroke

Introduction

Atherosclerotic diseases pose a heavy healthcare burden worldwide.[1,2] Plaque calcification, a common phenomenon during progress of atherosclerosis, is a result of ectopic calcium phosphate deposition in artery wall.[3] Artery calcification,

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as a key marker of atherosclerotic progression, has been widely associated with increased cardiovascular events and mortality risks.[4,5] Artery calcification could be detected with Computed Tomography Angiography (CTA) and quantified with Agatston Calcification Score (ACaS).[6,7]

Both artery calcification and atherosclerosis could be influenced by systemic inflammation.[8] Chronic systemic low-grade inflammation was affected by diet, making dietary patterns a potential factor influencing vascular calcification.[9] A recent population-based study inversely associated cruciferous vegetable intake with extensive abdominal aortic calcification in elderly women.[10] Similarly, a meta-analysis related vitamin K supplementation to reduced artery calcification.[11] However, the impacts of overall dietary inflammatory potential on artery calcification have not been thoroughly evaluated to date.

The overall inflammation effect of diet could be well reflected by the Dietary Inflammatory Index (DII).[12] DII was a tool developed to assess the inflammatory potential of various foods and nutrients based on their effects on serum inflammatory markers such as interleukin-1β (IL-1β), interleukin-4 (IL-4), interleukin-6 (IL-6), interleukin-10 (IL-10), tumor necrosis factor-α (TNF-α) and C-reactive protein (CRP).[12] A higher DII indicates a more pro-inflammatory diet. DII has been associated with obesity, diabetes mellitus, cardiovascular disease,[9,13] vascular plaque instability,[14] and abdominal artery calcification.[15] As carotid artery calcification has been recognized as a significant factor in vascular health, understanding the association between pro-inflammatory diets and calcification in patients with ischemic stroke holds clinical relevance. Identifying potential dietary interventions to mitigate calcification may contribute to improved vascular health and reduced stroke recurrence.

Several studies have also highlighted the association between DII and stroke. For instance, a study on ischemic stroke patients demonstrated that a higher DII was associated with increased carotid artery plaque vulnerability,[14] while large-scale cohort studies based on NHANES data confirmed the relationship between DII and stroke risk.[16] However, the specific association between DII and carotid artery calcification in ischemic stroke patients has not been fully explored.

Given that artery calcification is a significant marker of vascular pathology, understanding the role of dietary inflammation in this process is of clinical importance. This study aimed to determine whether DII is associated with carotid calcification in patients with ischemic stroke, providing insights into the potential mechanisms by which pro-inflammatory diets might influence vascular health and calcification.

Subjects and Methods

Patients

Consecutive patients with ischemic stroke were screened for eligibility via Nanjing Stroke Registry Program from February 2016 to April 2021. This study is a retrospective cross-sectional analysis of a prospective cohort. A total of 601 patients were included in the final analysis. Ischemic stroke was diagnosed based on the Chinese Guidelines for Diagnosis and Treatment of Acute Ischemic Stroke, combining clinical symptoms and neuroimaging findings.

Patients were included if they were: (1) aged 18 years or older; (2) diagnosed with ischemic stroke in seven days; (3) completed the 298-item semi-quantitative food-frequency questionnaire (FFQ); and (4) underwent carotid CTA scans at our center. Patients were excluded if they: (1) had malignant tumors; (2) had gastrointestinal diseases that may significantly affect diet pattern; (3) had severe cardiac, hepatic, and renal insufficiency; (4) had calcium and phosphorus metabolism disorders; (5) had a history of carotid stenting or endarterectomy; or (6) had carotid occlusion.

Clinical and Laboratory Data Collection

Basic clinical data were collected for all patients, including sex, age, body mass index (BMI), smoking history, hypertension, diabetes mellitus, atrial fibrillation, dyslipidemia, coronary heart disease history, and regular physical exercise. The Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification system was used to subtype stroke etiology.

Fasting venous blood samples were collected within 24 hours of hospital admission in the early morning. The key laboratory parameters measured included lymphocyte count, neutrophil count, and serum creatinine. The neutrophil-to-lymphocyte ratio (NLR) was calculated, and the estimated glomerular filtration rate (eGFR) was determined using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation based on serum creatinine levels.

Information on hypertension, diabetes mellitus, dyslipidemia, and atrial fibrillation was based on the patients' prior medical history, obtained through interviews, medical records, or diagnosed during the current hospitalization according to relevant guidelines. Coronary heart disease history was defined as a previous diagnosis from other hospitals. Regular physical exercise was defined as engaging in moderate exercise at least twice a week. TOAST subtypes refer to the classification of ischemic stroke into five subtypes: large artery atherosclerosis, small artery occlusion, cardioembolism, stroke of other determined etiology, and stroke of undetermined etiology, based on the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria.

Dietary Intake Assessment

The 298-item semi-quantitative food-frequency questionnaire (FFQ) was conducted during the patients' hospital stay and was administered by professionally trained clinicians. Dietary data were collected using the FFQ, which were designed to measure individual nutrient based on long-term dietary habits. The questionnaire is the Chinese version of FFQ used in National Health and Nutrition Examination Surveys, with common Chinese food items added. The individual foods were divided into 8 groups: staple foods, vegetables, fruits, nuts, meats and fish, beverages, dietary supplements, and condiments. The frequency and quantity of each food item in the past 12 months were recalled. These semi-quantitative assessments were sequentially transformed into nutrient contents according to the Nutrient Database established by the US Department of Agriculture (USDA). The food components were then standardized by the national average energy. Patients who missed significant food items in the FFQ and those with extremely high (for males >4200 kcal/d, for females >3500 kcal/d) or extremely low energy intakes (for males <800 kcal/d, for females <500 kcal/d) were excluded from data analysis.

Dietary Inflammatory Index

DII was calculated by 45 pro- and anti-inflammatory food components with the Shivappa algorithm according to their potentials for changing serum inflammatory biomarkers.[12] This study calculated DII with 39 food components that are commonly consumed in the Chinese population: alcohol, vitamin B_{12}, vitamin B_6, β-carotene, caffeine, carbohydrate, cholesterol, energy, total fat, fiber, folic acid, ginger, garlic, iron, magnesium, monounsaturated fatty acids, niacin, omega-3 fatty acids, omega-6 fatty acids, onion, protein, polyunsaturated fatty acids, riboflavin, saturated fat, selenium, thiamin, vitamin A, vitamin E, vitamin C, vitamin D, zinc, green/black tea, flavan-3-ol, flavones, flavonols, flavonones, isoflavones, anthocyanins, and pepper. Certain Western food items such as Eugenol, Turmeric, Rosemary, Thyme/Oregano, and Saffron were excluded due to their infrequent use in China. Additionally, trans fat was not included due to difficulties in obtaining accurate estimates for its consumption. Although the original DII uses 45 components, studies have shown that it can be reliably estimated with a minimum of 25 components, ensuring the validity of our calculation with 39 components.[9] All food components were adjusted by energy density approach.

Z-scores for each dietary component were calculated based on the global daily mean intake and standard deviation (SD) derived from a reference database. The Z-score was calculated using the following formula: Z score = (individual food component intake - global daily mean intake) / global daily intake SD. The Z score was converted to a percentile score which was normalized, and the resulting value was then multiplied by the reported DII of 39 corresponding food components. The DII scores of individual food components were then summed to obtain the overall DII. Theoretically, the overall DII of a patient ranged from −8.87 (minimally anti-inflammatory diet) to +7.89 (maximally pro-inflammatory diet). Patients were then stratified into three groups based on DII terciles.

Carotid Artery Calcification

Carotid computed tomography (CTA) was performed with a dual-source 64-slice CT system (Siemens, Germany). Imaging was acquired by scanning from 4 cm below the aortic arch to the superior border of the orbit in the craniocaudal direction. Calcification scores in the carotid artery were measured with the Syngo Calcium Scoring system (Siemens, Germany). Artery Calcification was defined as a focus of ≥4 contiguous pixels accompanied by a CT density of ≥130 hounsfield units (HU). According to the Agatston method,[6] calcification was divided into 4 grades: 130–199 hU (grades 1), 200–299 hU (grades 2),

300–399 hU (grades 3), and >399 hU (grades 4). The total Agatston score was defined as the sum of each lesion's Agatston score, which could be calculated by calcification area times maximal cofactor.

Sample Size

The sample size was determined based on the availability of eligible patients during the study period. No formal sample size calculation was performed.

Statistical Analysis

Missing data for baseline characteristics were imputed using multiple imputations by chained equations (MICE). DII and carotid artery calcification variables had no missing data, ensuring complete primary outcomes. Continuous data were demonstrated as mean ±standard deviation (SD) or quartiles [M (P25, P75)] and analyzed by one-way ANOVA or Kruskal–Wallis *H*-test. Categorical data were expressed as frequency (rate) and analyzed by chi-square test. DII was adjusted for energy by the energy density approach.

Binary logistic regression models (forward LR method) were applied to explore the relationship between DII and carotid artery calcification. The independence of variables was considered to ensure the validity of the regression analysis. Additionally, the linearity assumption between continuous independent variables and the log odds of the dependent variable was tested using the Box-Tidwell test. Since the age variable did not meet this assumption, we transformed it using the natural logarithm (ln-transformed age) to satisfy the linearity requirement. Collinearity among variables was examined using the variance inflation factor (VIF), and no significant multicollinearity was found. Variables with $p< 0.1$ from univariate analyses, along with those previously reported as being associated with carotid artery calcification, were selected for multivariable analysis. During the forward selection process, variables that did not contribute significantly to the model were removed.

In the multivariable logistic regression analysis, the following covariates were adjusted for: ln-transformed age, sex, body mass index (BMI), history of diabetes mellitus, history of coronary heart disease, history of hypertension, smoking history, regular physical exercise, TOAST subtypes, and estimated glomerular filtration rate (eGFR).

Considering the extremely left-skewed distribution of the carotid artery calcification score, we added 1 to the score to account for zero values and then applied a natural logarithm (ln) transformation. This transformation was performed to normalize the distribution for more robust statistical analysis. Spearman analysis was used to evaluate the relationship between DII and ln-transformed carotid artery calcification score. Statistical analysis was performed using SPSS Statistics version 28.0 (IBM, New York). P <0.05 was deemed a statistical significance.

Ethical Approval

This study is a retrospective analysis of data from the Nanjing Stroke Registry Program. All participants provided written informed consent as part of the registry. The study was approved by the Ethics Review Committee of Jinling Hospital (2010NLY - 018) and conducted in accordance with the principles of the Declaration of Helsinki.

Results

Between February 2016 and April 2021, a total of 660 patients with ischemic stroke were screened for eligibility from the Nanjing Stroke Registry Program (NSRP). Based on the study design, 59 patients were excluded due to the following reasons: malignant tumor (n = 9), chronic gastrointestinal diseases (n = 18), calcium or phosphorus metabolism disorder (n = 1), carotid artery stenting (n = 1), incomplete food frequency questionnaire (FFQ) (n = 1), extreme energy intake (n = 29). After applying these exclusion criteria, a total of 601 patients were included in the final analysis. Of the 601 analyzed patients, 368 (61.2%) were detected with and 233 (38.8%) without carotid artery calcification. The DII ranged from −6.59 to 6.81, where negative values represent anti-inflammatory diets and positive values represent pro-inflammatory diets. Compared with patients with the lowest tertile of DII (T1), patients with higher tertile of DII (T2 and T3) had a higher ratio of stroke subtypes of large artery atherosclerosis (T1: 38.0%, T2: 42.7%, T3: 45.5%, P = 0.050) and a higher intake of staple foods (T1: 543.4 g/d [428.1, 735.1], T2: 626.7 g/d [489.6, 822.9], T3: 664.2 g/d [529.4, 893.6], P < 0.001) and lower intakes of vegetables (T1: 554.7 g/d [397.8, 736.5], T2: 376.9 g/d [291.0, 504.0], T3: 220.3 g/d [148.7, 329.0], P < 0.001), fruits (T1: 204.1 g/d [102.6, 374.6], T2:

134.4 g/d [64.89, 241.8], T3: 58.27 g/d [21.77, 120.5], $P < 0.001$), nuts (T1: 17.68 g/d [6.557, 37.29], T2: 9.430 g/d [3.831, 23.58], T3: 5.894 g/d [0.221, 16.08], $P < 0.001$), meat (T1: 73.08 g/d [40.45, 113.4], T2: 57.01 g/d [30.65, 94.30], T3: 44.79 g/d [21.75, 79.56], $P < 0.001$), and dairy products (T1: 0.00 g/d [0.00, 16.80], T2: 0.00 g/d [0.00, 7.073], T3: 0.00 g/d [0.00, 0.221], $P = 0.036$).

Patients with the highest tertile of DII (T3) had higher calcification scores (T1: 0.45 [0, 49.4], T2: 18.4 [0, 126], T3: 18.6 [0, 97.0], $P < 0.001$) and a higher ratio of calcification (T1: 50.5%, T2: 69.8%, T3: 63.4%, $P < 0.001$) than patients with the lowest tertile of DII (T1) (Table 1). The baseline characteristics of patients stratified by carotid artery calcification status have been previously published.[17] To avoid redundancy, we provide a detailed comparison of DII categories stratified by carotid artery calcification status in the Supplementary Materials. Patients with carotid artery calcification had higher DII than patients without carotid artery calcification (0.17 [−1.39, 1.97] vs −0.55 [−2.37, 1.89], $P = 0.018$, (suppl. Table 1).

In the univariate binary logistic regression analysis (Crude model), factors such as ln-transformed age (OR = 279.7, P < 0.001), history of diabetes mellitus (OR = 1.940, $P < 0.001$), estimated glomerular filtration rate (eGFR) (OR = 0.974, $P < 0.001$), TOAST subtypes (LAA subtype: OR = 1.725, p = 0.032), and DII (T2: OR = 2.271, $P < 0.001$; T3: OR = 1.695, $P = 0.009$) were significantly associated with carotid artery calcification (Table 2). However, after adjusting for potential confounders in the multivariate logistic regression model (Model 1), only ln-transformed age (OR = 317.7, $P < 0.001$), history of diabetes mellitus (OR = 1.928, $P = 0.001$), and DII (T2: OR = 2.584, $P < 0.001$; T3: OR = 1.880, $P = 0.005$) remained significant. These results suggest that the association between DII and carotid artery calcification is robust even after accounting for key clinical and demographic factors (Table 2).

Table 1 Patient Characteristics According to DII

Characteristics	Dietary Inflammatory Index			p[a]
	T1 (n =200)	T2 (n =199)	T3 (n =202)	
Age, year, mean ±SD	64.6 ±10.1	65.6 ±10.3	64.8 ±11.4	0.621
Female gender, n (%)	67 (33.5)	55 (27.6)	72 (35.6)	0.208
BMI, kg/m^2 median (P25, P75)	24.5 (23.1, 26.9)	25.1 (22.9, 26.9)	24.2 (22.5, 26.7)	0.371
Regular physical exercise, n (%)	179 (89.5)	171 (85.9)	180 (89.1)	0.480
Smoking history, n (%)	89 (44.5)	106 (53.3)	102 (50.5)	0.201
Hypertension history, n (%)	144 (72.0)	151 (75.9)	140 (69.3)	0.335
Diabetes mellitus history, n (%)	68 (34.0)	63 (31.7)	74 (36.6)	0.575
Dyslipidemia history, n (%)	11 (5.5)	10 (5.0)	15 (7.4)	0.562
Atrial fibrillation history, n (%)	15 (7.5)	19 (9.5)	15 (7.4)	0.679
Coronary heart disease history, n (%)	33 (16.5)	27 (13.6)	23 (11.4)	0.329
NLR, median (P25, P75)	2.18 (1.67, 3.03)	2.15 (1.58, 3.23)	2.03 (1.56, 3.11)	0.806
eGFR, mL/min, median (P25, P75)	109 (99.5, 120)	107 (95.9, 119)	109 (100, 119)	0.262
TOAST subtypes, n (%)				0.050
LAA	76 (38.0)	85 (42.7)	92 (45.5)	
SVD	103 (51.5)	82 (41.2)	76 (37.6)	
Others	21 (10.5)	32 (16.1)	34 (16.8)	
Staple foods, g/d, median (P25, P75)	543.4 (428.1, 735.1)	626.7 (489.6, 822.9)	664.2 (529.4, 893.6)	<0.001
Vegetables, g/d, median (P25, P75)	554.7 (397.8, 736.5)	376.9 (291.0, 504.0)	220.3 (148.7, 329.0)	<0.001
Fruits, g/d, median (P25, P75)	204.1 (102.6, 374.4)	134.4 (64.89, 241.8)	58.27 (21.77, 120.5)	<0.001
Nuts, g/d, median (P25, P75)	17.68 (6.557, 37.29)	9.430 (3.831, 23.58)	5.894 (0.221, 16.08)	<0.001
Meat, g/d, median (P25, P75)	73.08 (40.45, 113.4)	57.01 (30.65, 94.30)	44.79 (21.75, 79.56)	<0.001
Dairy products, g/d, median (P25, P75)	0 (0, 16.80)	0 (0, 7.073)	0 (0, 0.221)	0.036
Supplement Use, n (%)	27 (13.5)	17 (8.5)	19 (9.4)	0.224
Calcification Score, median (P25, P75)	0.45 (0, 49.4)	18.4 (0, 126)	18.6 (0, 97.0)	<0.001
Calcification, n (%)	101 (50.5)	139 (69.8)	128 (63.4)	<0.001

Notes: [a]Calculated using one-way ANOVA, Kruskal–Wallis *H*-test or chi-square test.

Abbreviations: BMI, body mass index; NLR, neutrophil to lymphocyte ratio; eGFR, estimated glomerular filtration rate; TOAST, Trial of ORG 10172 Acute Stroke Treatment classification system; LAA, large-artery atherosclerosis; SVD, small vascular disease.

Table 2 Logistic Regression Analysis for Exploring the Association Between DII and Carotid Artery Calcification

	Crude model		Model 1	
	OR (95% CI)	***p***	**OR (95% CI)**	***p***
Ln-transformed age	279.7 (81.52–959.7)	<0.001	317.7 (88.74–1137)	<0.001
Male	0.993 (0.699–1.411)	0.970	–	–
BMI	0.976 (0.927–1.029)	0.368	–	–
Smoking history	0.897 (0.646–1.246)	0.518	–	–
Regular physical exercise	2.111 (1.281–3.479)	0.003	–	–
Hypertension history	1.304 (0.906–1.875)	0.153	–	–
Diabetes mellitus history	1.940 (1.351–2.785)	<0.001	1.928 (1.293–2.876)	0.001
Coronary heart disease history	1.663 (1.003–2.758)	0.049	–	–
eGFR	0.974 (0.965–0.984)	<0.001	–	–
TOAST subtypes		0.015	–	–
Others	Ref	–		
LAA	1.725 (1.048–2.840)	0.032	–	–
SVD	1.064 (0.653–1.734)	0.803	–	–
DII		<0.001		<0.001
DII (T1, n= 200)	Ref	–	–	–
DII (T2, n= 199)	2.271 (1.506–3.423)	<0.001	2.584 (1.638–4.078)	<0.001
DII (T3, n= 202)	1.695 (1.138–2.525)	0.009	1.880 (1.205–2.932)	0.005

Notes: Variables that were significant in the univariate analysis but not included in the multivariate model did not meet the criteria to remain in the model during the forward LR selection process due to lack of statistical significance after adjustment. Ln-transformed age: Age was log-transformed due to the non-linearity detected in the Box-Tidwell test. The natural logarithm of age was used to meet the linearity assumption in the logistic regression model. DII was adjusted by energy. eGFR, estimated glomerular filtration rate; TOAST, Trial of ORG 10172 Acute Stroke Treatment classification system. Model 1, adjusted for age, male, BMI, and history of smoking, regular physical exercise, TOAST, history of hypertension, diabetes mellitus, coronary heart disease, and eGFR.
Abbreviations: LAA, large-artery atherosclerosis; SVD, small vascular disease; DII, Dietary Inflammatory Index; OR, odds ratio; CI, confidence interval; BMI, body mass index.

To evaluate the predictive ability of the Dietary Inflammatory Index (DII) for carotid artery calcification, we performed ROC curve analysis. The area under the curve (AUC) for DII alone was 0.557 (95% CI: 0.509–0.605), indicating a weak predictive ability. The optimal cutoff value for DII was −1.302, which was determined based on maximizing the Youden Index, with a sensitivity of 73.9% and a specificity of 42.5% (Table 3). After adjusting for confounding factors in the multivariate logistic regression model (Model 1), including ln-transformed age, sex, body mass index (BMI), history of smoking, regular physical exercise, TOAST subtypes, history of hypertension, diabetes mellitus, coronary heart disease, and eGFR, the predictive ability of the model significantly improved. The AUC for the multivariate model was 0.751 (95% CI: 0.710–0.791), with a sensitivity of 80.4% and a specificity of 59.7% at an optimal cutoff value of 0.566. This suggests that while DII alone is not a strong predictor of carotid calcification, its predictive value improves when combined with other clinical and demographic variables in the multivariate model.

Spearman test detected that DII was associated with ln-transformed carotid artery calcification score (R =0.110, *P* =0.035, Figure 1) in patients with carotid artery calcification.

Table 3 Results of ROC Analysis

Predictor Variable	AUC (95% CI)	Cutoff Value	Sensitivity (%)	Specificity (%)	Youden Index
DII	0.557 (0.509–0.605)	−1.302	73.9	42.5	0.164
Model 1	0.751 (0.710–0.791)	0.566	80.4	59.7	0.401

Notes: DII was adjusted by energy; Model 1, Multivariate logistic regression model adjusted for ln-transformed age, male, BMI, and history of smoking, regular physical exercise, TOAST, history of hypertension, diabetes mellitus, coronary heart disease, and eGFR.
Abbreviation: DII, Dietary Inflammatory Index.

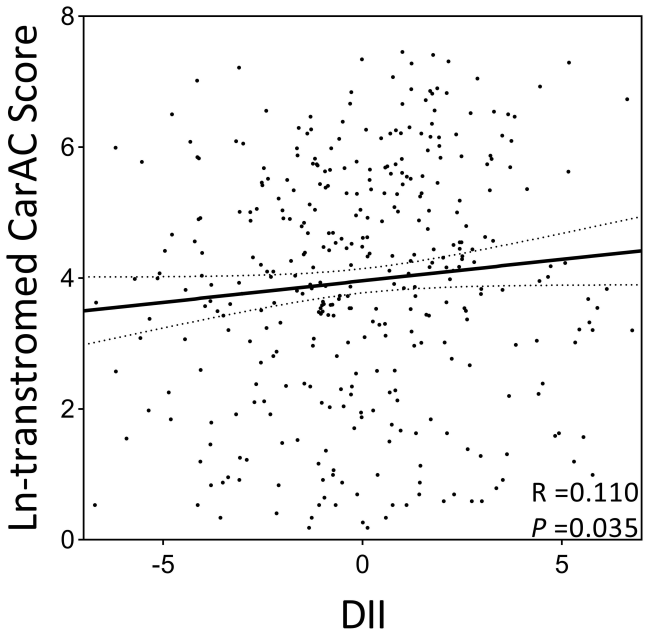

Figure 1 Association between Dietary Inflammatory Index and Ln-transformed Carotid Artery Calcification Score.
Abbreviations: CarAC, carotid artery calcification score.

Discussion

This cross-sectional study observed a positive relationship between DII level and carotid artery calcification in patients with ischemic stroke. Even after adjusting for potential confounders such as age, BMI, smoking history, and physical activity in the multivariate logistic regression model, DII remained independently associated with carotid artery calcification. These findings suggest that dietary inflammation may contribute to the development of vascular calcification in ischemic stroke patients, potentially worsening their cardiovascular risk profile. While the ability of DII alone to predict calcification is limited, its association with vascular calcification highlights the need for further investigation into how dietary factors may influence vascular health in this vulnerable population. This could inform dietary interventions aimed at reducing inflammation and preventing vascular complications in ischemic stroke patients.

Several studies have linked individual nutrients to vascular calcification. For example, higher vitamin C intake is associated with lower abdominal aortic calcification (AAC) scores and reduced AAC risk.[18] Additionally, flavonoid intake has been linked to reduced carotid artery calcification, with studies suggesting that flavonoids may influence the initiation and progression of atherosclerosis through their antioxidant and anti-inflammatory properties.[17] Furthermore, vitamin K has been shown to inhibit the progression of vascular calcification by suppressing the NF-κB signaling pathway, which plays a critical role in inflammation.[19] While these studies highlight the connection between individual nutrients and calcification, they fail to provide a comprehensive evaluation of overall diet. In contrast, the DII incorporates these individual nutrients alongside many others, offering a more holistic perspective on the long-term relationship between dietary inflammatory potential and calcification. Although the original DII uses 45 components, our study included 39, which previous research has shown is sufficient to accurately reflect dietary inflammatory potential.[9]

Similar to our findings, an analysis based on the 2013–2014 National Health and Nutrition Examination Survey (NHANES) reported a positive association between DII and AAC.[15] Both studies suggest that pro-inflammatory diets contribute to vascular calcification across different vascular beds. However, NHANES focused on a community population, whereas our study examined stroke patients, who are likely to have a greater atherosclerotic burden. This makes our findings particularly significant for secondary prevention in stroke patients. Additionally, our study was conducted in a Chinese population, which may reveal important racial and lifestyle differences from the US-based NHANES findings.

DII may affect the systemic inflammatory status and accelerate the process of artery calcification and atherosclerosis. DII was a reliable indicator of dietary inflammation and has been associated with different inflammatory biomarkers,[9,20]

such as interleukin-1β (IL-1β),[21] interleukin-4 (IL-4),[22] interleukin-6 (IL-6),[23] tumor necrosis factor-α (TNF-α),[24] and C-reactive protein (CRP).[25] These biomarkers are directly linked to systemic inflammation. Both cross-sectional and follow-up studies found that higher DII scores (pro-inflammatory diet) predicted increased inflammatory biomarker concentrations, and these studies support the use of DII in elderly populations.[26]

Dietary inflammation can promote vascular calcification through several mechanisms.[27] For example, IL-1β plays a critical role in regulating atherosclerotic calcification by inducing endothelial-to-mesenchymal transition, mobilizing mesodermal progenitor cells, and activating tissue-nonspecific alkaline phosphatase[21]. Similarly, IL-6 has been shown to enhance the expression of bone morphogenetic protein 2 (BMP2) in vascular smooth muscle cells (VSMCs), a key factor driving vascular calcification.[28] TNF-α, primarily released by M1 macrophages, upregulates enzymes like carbonic anhydrase 1 and 2 (CA1 and CA2) in VSMCs, promoting calcification pathways.[29] Additionally, oxidative stress amplifies the inflammatory response, further accelerating calcification. Oxidized lipids interact with immune cells, such as macrophages and endothelial cells, triggering an inflammatory cascade that leads to increased calcification of the vascular walls.[27] This intricate relationship between dietary inflammation, oxidative stress, and inflammatory biomarkers highlights how pro-inflammatory diets, as measured by DII, can contribute to vascular calcification and overall cardiovascular risk.

Our findings underscore the role of dietary inflammation in the progression of carotid artery calcification among ischemic stroke patients. This could suggest that targeted dietary interventions focused on reducing inflammation may offer a novel avenue for secondary stroke prevention, particularly by improving vascular health and mitigating cardiovascular risks in this vulnerable population. Unlike studies in general or community-based populations, our research focuses specifically on stroke patients, adding a new dimension to how diet might influence the management of cardiovascular risk in this group.

Our study demonstrated that DII was associated with vascular calcification, but the association was weak. Possible reasons are as follows. Some confounding factors cannot be collected and adjusted, such as gastrointestinal microbiome, which may affect the absorption of diets. In addition, FFQ can only obtain information about the patient's diet in the past year, but vascular calcification is a long-term and complex process. Besides, it is hard to find microcalcifications with Carotid CTA that were strongly associated with inflammation.

Several limitations should be addressed when interpreting the results. In particular, the study did not collect comprehensive data on the history of medication use, which could influence vascular health and calcification. This study also did not specifically deal with the population of dietary supplements. Although 10.5% of patients reported taking dietary supplements, their use was intermittent and irregular, and the types of supplements varied widely, making it difficult to include them in a standardized analysis. Furthermore, no significant associations were found between supplement use and either DII categories or carotid calcification status. Given the heterogeneous nature of supplement intake and the lack of standardized data on dosage or frequency, further studies are needed to explore the potential role of dietary supplements in this population. The 6 components involved in DII were not collected in FFQ including eugenol, trans fat, turmeric, thyme/oregano, and rosemary, which could affect DII value. Besides, this is a single-center and cross-sectional study that may limit the generalization of the results to other populations. Then, the memory bias of FFQ could affect the evaluation of food component intake.

Conclusions

This study identified a significant association between the Dietary Inflammatory Index (DII) and carotid artery calcification in ischemic stroke patients. Even after controlling for confounding factors, DII remained significantly correlated with the presence of calcification. These findings suggest that a pro-inflammatory diet may exacerbate vascular calcification, potentially increasing cardiovascular risk. While dietary interventions targeting inflammation may offer a strategy for improving vascular health, further longitudinal studies are essential to validate these results and investigate the underlying mechanisms in greater detail.

Data Sharing Statement

Anonymized data and material supporting the research is available by request from qualified investigators.

Ethical Approval

The studies involving human participants were reviewed and approved by Ethic committee of Jinling Hospital, Medical School of Nanjing University (2010NLY −018). The participants provided their written informed consent to participate in this study.

Informed Consent

Written informed consent was obtained from all subjects before the study.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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