Postprint: Association Between Dietary Inflammatory Potential and Severity of Coronary Artery Lesions in Patients with Acute Coronary Syndrome

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Abstract

Background The occurrence and development of Acute Coronary Syndrome (ACS) are closely associated with inflammatory response, but the relationship between dietary inflammatory potential and the severity of coronary artery lesions in ACS patients remains unclear. Objective To evaluate the dietary inflammatory potential of ACS patients using the Dietary Inflammatory Index (DII) and explore its relationship with the severity of coronary artery lesions in ACS patients. Methods Using convenience sampling, 309 patients with first-time diagnosis of ACS confirmed by coronary angiography were selected from the Department of Cardiology, Second Affiliated Hospital of Harbin Medical University between April 2022 and March 2023. They were divided into 4 groups based on DII quartiles: DII-1 group (-8.35~-4.56), DII-2 group (-4.55~-0.77), DII-3 group (-0.76~3.02), DII-4 group (3.03~6.81), and into 4 groups based on Gensini score quartiles: Q1 group (4~32 points), Q2 group (34~52 points), Q3 group (54~84 points), Q4 group (86~192 points). Demographic characteristics, clinical features, overall DII, and nutrient DII were compared among ACS patients with different coronary artery lesion severities, and multivariate Logistic regression analysis was used to explore the relationship between DII and coronary artery lesion severity in ACS patients. Results There were statistically significant differences in education level, low-density lipoprotein cholesterol (LDL-C) level, lipoprotein(a) (LP-a) level, overall DII, and DII for total fat, saturated fatty acids, vitamin E, and carotene among ACS patients with different coronary artery lesion severities (P$ $0.05). Multivariate Logistic regression analysis showed that after adjusting for confounding factors including education level and LDL-C and LP-a levels, DII-4 group was an influencing factor for Q2 group [OR=15.389, 95%CI (1.595, 148.432)], Q3 group [OR=15.102, 95%CI (1.620, 140.788)], and Q4 group [OR=17.319, 95%CI (1.901, 157.807)] (P<0.05); DII for total fat [OR=3.831, 95%CI (1.195, 9.094)], saturated fatty acids [OR=8.562, 95%CI (1.519, 48.258)], and vitamin E [OR=0.640, 95%CI (0.460, 0.890)] were influencing factors for Q4 group (P<0.05). Conclusion Dietary inflammatory potential and inflammatory potential of nutrients including total fat, saturated fatty acids, and vitamin E are influencing factors for coronary artery lesion severity in ACS patients, and clinicians should further strengthen reasonable anti-inflammatory dietary guidance for ACS patients.

Full Text

Relationship between Dietary Inflammatory Potential and Severity of Coronary Artery Disease in Patients with Acute Coronary Syndrome

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Abstract

Background The pathogenesis and progression of acute coronary syndrome (ACS) are closely associated with inflammatory responses, yet the relationship between dietary inflammatory potential and the severity of coronary artery disease in ACS patients remains unclear.

Objective To evaluate the dietary inflammatory potential of ACS patients using the Dietary Inflammatory Index (DII) and investigate its association with coronary artery disease severity.

Methods Using a convenient sampling method, we enrolled 309 patients who were newly diagnosed with ACS via coronary angiography in the Department of Cardiology at The Second Affiliated Hospital of Harbin Medical University between April 2022 and March 2023. Patients were divided into four groups based on DII quartiles: DII-1 group (-8.35 to -4.56), DII-2 group (-4.55 to -0.77), DII-3 group (-0.76 to 3.02), and DII-4 group (3.03 to 6.81). Additionally, based on Gensini score quartiles, patients were categorized as Q1 group (4–32 points), Q2 group (34–52 points), Q3 group (54–84 points), and Q4 group (86–192 points). Demographic characteristics, clinical features, overall DII, and nutrient-specific DII values were compared across groups with varying coronary artery disease severity. Multivariate logistic regression analysis was employed to explore the relationship between DII and coronary artery disease severity in ACS patients.

Results Significant differences were observed among ACS patients with different coronary artery disease severities in terms of educational level, low-density lipoprotein cholesterol (LDL-C) levels, lipoprotein(a) [LP(a)] levels, overall DII, and DII values for total fat, saturated fatty acids, vitamin E, and carotene ($P \leq 0.05$). After adjusting for confounding factors including educational level and LDL-C and LP(a) levels, multivariate logistic regression revealed that DII-4 group membership was an influencing factor for Q2 group [OR=15.389, 95%CI (1.595, 148.432)], Q3 group [OR=15.102, 95%CI (1.620, 140.788)], and Q4 group [OR=17.319, 95%CI (1.901, 157.807)] ($P<0.05$). Furthermore, DII values for total fat [OR=3.831, 95%CI (1.195, 9.094)], saturated fatty acids [OR=8.562, 95%CI (1.519, 48.258)], and vitamin E [OR=0.640, 95%CI (0.460, 0.890)] were influencing factors for Q4 group ($P<0.05$).

Conclusion Dietary inflammatory potential, as well as the inflammatory potential of specific nutrients—total fat, saturated fatty acids, and vitamin E—are significant influencing factors for coronary artery disease severity in ACS patients. Clinicians should strengthen evidence-based anti-inflammatory dietary guidance for ACS patients.

Keywords Acute coronary syndrome; Diet, food, and nutrition; Root cause analysis; Dietary Inflammatory Index; Dietary nutrients; Gensini score

1. Introduction

Acute coronary syndrome (ACS) represents a group of clinical syndromes characterized by rupture of atherosclerotic plaques with thrombus formation in coronary arteries, featuring acute onset and high mortality rates that pose a serious threat to public health. Numerous studies have confirmed that inflammatory responses play a crucial role in the progression of coronary artery disease and the development of ACS. Epidemiological research indicates that unhealthy dietary patterns affect ACS progression and increase the risk of ACS incidence and mortality. Recent studies have demonstrated that the Dietary Inflammatory Index (DII) is closely associated with systemic inflammatory markers including interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α). However, the relationship between DII and the severity and progression of coronary artery disease in ACS patients remains unclear. This study employed DII to assess the dietary inflammatory potential of ACS patients and explore its relationship with coronary artery disease severity, aiming to provide a reference for developing targeted dietary intervention strategies for ACS patients in clinical practice.

1.1 Study Participants

Using a convenient sampling method, we selected 309 patients who were newly diagnosed with ACS via coronary angiography in the Department of Cardiology at The Second Affiliated Hospital of Harbin Medical University between April 2022 and March 2023. Inclusion criteria were: (1) meeting the diagnostic criteria for ACS in the *Guidelines for the Rapid Diagnosis and Treatment of Acute Coronary Syndrome (2019)*; (2) having resided in Heilongjiang Province for more than 12 months prior to enrollment; (3) providing informed consent and voluntary participation; and (4) having no intellectual deficits and being able to complete questionnaire assessments. Exclusion criteria included: (1) concomitant other organic heart diseases or peripheral vascular diseases; (2) severe hepatic, renal, pulmonary, or cerebral diseases; (3) digestive system diseases or absorption disorders; and (4) pregnancy or lactation. This study was approved by The Second Affiliated Hospital of Harbin Medical University (Approval No.: YJSKY2022-130).

1.2 Methods

A self-designed questionnaire was used to collect demographic and clinical characteristics of all participants. Demographic variables included sex, age, educational level, and duration of residence in Heilongjiang Province. Clinical features encompassed history of hypertension, diabetes, hyperlipidemia, and coronary heart disease family history, smoking and alcohol consumption habits, blood pressure, body mass index (BMI), waist circumference, fasting blood glucose, and levels of total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and lipoprotein(a) [LP(a)].

The semi-quantitative food frequency questionnaire (SQFFQ) is an internationally recognized dietary assessment tool commonly used in research on diet-disease relationships. The SQFFQ comprises three components: a food list, food intake frequency, and portion size per consumption, primarily collecting information on food consumption frequency and portion sizes over the past year. Based on the *2002 China National Nutrition and Health Survey* and local dietary patterns and consumption habits, we expanded and modified the food list in our SQFFQ to include 102 items. Food intake frequency and portion sizes were assessed using locally common containers and weight units, with intake frequency typically categorized into 5–10 intervals. Research has demonstrated that this SQFFQ has a content validity index (CVI) of 0.96 and a Cronbach’ s α coefficient of 0.853, indicating good reliability and validity.

DII was calculated based on SQFFQ data as follows: (1) Dietary nutrient intake calculation: Using the *China Food Composition Table Standard Edition* (6th edition), we listed the nutrient content per 100 grams for each food item. Referencing the global DII database, we assessed 21 nutrients (energy, protein, carbohydrate, total fat, saturated fatty acids, monounsaturated fatty acids, polyunsaturated fatty acids, dietary fiber, cholesterol, vitamin A, vitamin C, vitamin E, thiamin, riboflavin, magnesium, iron, zinc, selenium, folic acid, carotene, and niacin) and 5 food items (onion, garlic, alcohol, tea, and ginger). Nutrient intakes were calculated using R language matrix operations. Since the inflammatory potential of these five food items primarily relates to the global DII database, they were not further analyzed in this study. (2) DII quantification and grouping: Individual DII values were quantified by comparing dietary nutrient intakes with global mean and standard deviation values from 11 populations for 45 dietary nutrients to calculate Z-scores. These Z-scores were converted to proportions, doubled, and subtracted by 1 for centering (range: -1 to 1, centered at 0). The centered values were then multiplied by the corresponding nutrient inflammatory effect scores to obtain nutrient-specific DII values. The sum of all nutrient DII values yielded the overall DII for each individual. Based on quartiles, patients were divided into four DII groups: DII-1 group (-8.35 to -4.56), DII-2 group (-4.55 to -0.77), DII-3 group (-0.76 to 3.02), and DII-4 group (3.03 to 6.81), where DII-1 represented the lowest inflammatory potential and highest anti-inflammatory effect, while DII-4 represented the highest inflammatory potential and pro-inflammatory effect.

Coronary artery disease severity was quantitatively assessed using the Gensini scoring system based on coronary angiography results: (1) Stenosis severity was scored at the most severe lesion in each coronary artery, with <25% stenosis = 1 point, 25-49% = 2 points, 50-74% = 4 points, 75-89% = 8 points, 90-99% = 16 points, and $ $99% = 32 points. (2) Different coronary branches were weighted by specific coefficients: left main lesion $×$5.0, proximal left anterior descending artery $×$2.5, mid left anterior descending artery $×$1.5, distal left anterior descending artery $×$1.0, first diagonal branch $×$1.0, second diagonal branch $×$0.5, proximal left circumflex artery $×$2.5, distal left circumflex artery and posterior descending artery $×$1.0, posterolateral branch $×$0.5, and proximal, middle, and distal right coronary artery and posterior descending artery $×$1.0. (3) The Gensini score was calculated as the sum of each lesion' s stenosis score multiplied by its corresponding coefficient. Based on quartiles, patients were categorized into four Gensini score groups: Q1 group (4–32 points), Q2 group (34–52 points), Q3 group (54–84 points), and Q4 group (86–192 points), representing mild, moderate, moderately severe, and severe coronary artery disease, respectively.

1.3 Statistical Methods

Statistical analysis was performed using R language and SPSS 25.0 software. Normally distributed continuous variables were expressed as mean ± standard deviation (x̄±s) and compared among groups using one-way ANOVA. Non-normally distributed continuous variables were presented as median (interquartile range) [M(P25, P75)] and compared using the Kruskal-Wallis H test. Categorical data were expressed as frequencies and percentages and compared using the ^{2} test. Multivariate logistic regression analysis was used to explore the relationship between DII and coronary artery disease severity in ACS patients. Statistical significance was set at $P \leq 0.05$.

2. Results

2.1 Demographic and Clinical Characteristics

Among the 309 ACS patients, there were 82 in Q1 group, 74 in Q2 group, 80 in Q3 group, and 73 in Q4 group. No significant differences were observed among the four groups in sex, age, duration of residence in Heilongjiang Province, history of hypertension, diabetes, hyperlipidemia, coronary heart disease family history, smoking or alcohol consumption, systolic blood pressure, diastolic blood pressure, BMI, waist circumference, fasting blood glucose, or levels of TC, TG, and HDL-C ($P>0.05$). However, significant differences were found in educational level and levels of LDL-C and LP(a) among the groups ($P \leq 0.05$) .

2.2 Dietary Inflammatory Potential

Significant differences in overall DII were observed among patients with varying coronary artery disease severity ($P<0.05$) .

2.3 Inflammatory Potential of 21 Nutrients

No significant differences were found among the four groups in DII values for energy, protein, carbohydrate, monounsaturated fatty acids, polyunsaturated fatty acids, dietary fiber, cholesterol, vitamin A, vitamin C, thiamin, riboflavin, magnesium, iron, zinc, selenium, folic acid, or niacin ($P>0.05$). However, significant differences were observed in DII values for total fat, saturated fatty acids, vitamin E, and carotene ($P<0.05$) .

2.4 Relationship between DII and Coronary Artery Disease Severity

Using educational level (assigned values: junior high school or below=1, high school or college=2, bachelor’ s degree or above=3), LDL-C level (actual measured value), LP(a) level (actual measured value), and overall DII (DII-1 group=1, DII-2 group=2, DII-3 group=3, DII-4 group=4) as independent variables, with coronary artery disease severity as the dependent variable (Q1 group=1, Q2 group=2, Q3 group=3, Q4 group=4), multivariate logistic regression analysis showed that DII-4 group membership was an influencing factor for Q2, Q3, and Q4 groups ($P<0.05$). After adjusting for confounding factors including educational level and LDL-C and LP(a) levels, DII-4 group remained an influencing factor for Q2, Q3, and Q4 groups ($P<0.05$) .

2.5 Relationship between Nutrient DII and Coronary Artery Disease Severity

Using educational level, LDL-C level, LP(a) level, and DII values for total fat, saturated fatty acids, vitamin E, and carotene (all using actual measured values) as independent variables, with coronary artery disease severity as the dependent variable (Q1 group=1, Q2 group=2, Q3 group=3, Q4 group=4), multivariate logistic regression analysis revealed that DII values for total fat and saturated fatty acids were influencing factors for Q4 group ($P<0.05$). After adjusting for educational level and LDL-C and LP(a) levels, DII values for total fat, saturated fatty acids, and vitamin E were influencing factors for Q4 group ($P<0.05$) .

3. Discussion

3.1 Dietary Inflammatory Potential as an Influencing Factor for Coronary Artery Disease Severity in ACS Patients

Quantitative assessment of coronary artery disease severity using the Gensini scoring system demonstrated that after adjusting for confounding factors including educational level and LDL-C and LP(a) levels, DII-4 group membership was an influencing factor for Q2, Q3, and Q4 groups. The risk of increased coronary artery disease severity in the DII-4 group was 15–17 times higher than in the DII-1 group, indicating that elevated dietary inflammatory potential is an independent risk factor for increased coronary artery disease severity in ACS patients. These findings are consistent with previous research by FORMAN et al. Therefore, clinicians should strengthen evidence-based anti-inflammatory dietary guidance for ACS patients to delay coronary artery progression and shift the prevention and treatment of ACS to an earlier stage.

Recent studies on the relationship between DII and cardiovascular disease have revealed the predictive value of dietary inflammatory potential for coronary heart disease. AGRAIB et al. conducted a case-control study of 198 coronary heart disease patients and 190 healthy controls, finding that each 1.13-unit increase in DII was associated with an approximately 11% higher risk of coronary heart disease, suggesting that pro-inflammatory diets correlate with increased coronary heart disease risk. A large-scale study of 45,000 US adults found that increased DII was associated with elevated coronary heart disease risk after adjusting for age, sex, smoking, alcohol consumption, and other confounding factors. Our study focused on ACS, the most severe form of coronary heart disease, calculating DII based on SQFFQ data and coronary angiography results. The findings suggest that clinicians should enhance anti-inflammatory dietary counseling for ACS patients.

3.2 Nutrient Inflammatory Potential as an Influencing Factor for Coronary Artery Disease Severity in ACS Patients

Dietary pattern research indicates that the development of coronary artery disease is closely related to long-term dietary patterns, and adherence to healthy dietary patterns can effectively reduce coronary heart disease risk. The beneficial effects of healthy dietary patterns on coronary heart disease primarily stem from the potential anti-inflammatory effects of specific nutrients. Therefore, this study further analyzed the impact of nutrient inflammatory potential on coronary artery disease severity in ACS patients.

Elevated vitamin E DII was a protective factor against increased coronary artery disease severity in ACS patients. Previous research has confirmed that vitamin E provides both primary and secondary cardiovascular protection. A meta-analysis of randomized controlled trials demonstrated that vitamin E supplementation reduces the risk of acute myocardial infarction. Other studies have shown that decreased plasma vitamin E levels can accurately predict acute cardiovascular events, and that daily intake of 400–800 IU of vitamin E exerts coronary protective effects. VARDI and SAREMI et al. have shown that vitamin E regulates monocyte-macrophage release of inflammatory mediators by inhibiting activation of inflammatory initiators, thereby reducing inflammatory responses and delaying atherosclerosis development. Our results indicate that after adjusting for educational level and LDL-C and LP(a) levels, vitamin E DII was an influencing factor for Q4 group, with Q4 group patients having 0.640 times the risk of increased coronary artery disease severity compared to Q1 group. The average vitamin E intake among ACS patients in China is currently 18.91 mg/day, which meets the recommended intake for healthy populations (14 mg/day) but falls short of the intake recommended for cardiovascular protection. Therefore, clinicians should actively guide ACS patients to adjust their dietary patterns and incorporate vitamin E-rich fruits and vegetables to effectively delay coronary artery progression.

Elevated total fat DII was a risk factor for increased coronary artery disease severity in ACS patients. Prospective studies from the Japanese Public Health Center and community cohorts have shown that total fat intake is positively correlated with cardiovascular mortality in men, with higher total fat intake associated with increased coronary heart disease risk. Animal experiments have confirmed that high-fat diets not only increase blood viscosity and lipid levels but also activate inflammatory cells and promote lipid deposition and aggregation in vascular walls, thereby worsening coronary artery disease severity. The *Chinese Dietary Guidelines* recommend that total fat intake should not exceed 30% of total energy intake; however, current total fat intake among ACS patients in China accounts for approximately 31.9% of total energy intake. Our study found that after adjusting for confounding factors, total fat DII was an influencing factor for Q4 group, with Q4 group patients having 3.831 times higher risk of increased coronary artery disease severity compared to Q1 group. Therefore, clinicians should focus on reducing the proportion of total fat intake in ACS patients' total energy consumption to further delay coronary artery progression.

Elevated saturated fatty acid DII was also a risk factor for increased coronary artery disease severity in ACS patients. The *Dietary Guidelines for Americans* states that saturated fatty acid intake is closely related to cardiovascular disease development. The Japanese Public Health Center study identified saturated fatty acid intake >0.20 g/day as an important risk factor for acute myocardial infarction. The American Heart Association' s nutrition guidelines recommend strictly limiting saturated fatty acid intake to no more than 7% of total energy intake. Recent clinical studies have found that saturated fatty acids enhance inflammatory factor expression in cardiomyocytes, representing an important factor contributing to increased acute cardiovascular event rates. Currently, saturated fatty acid intake among ACS patients in China accounts for approximately 3.6% of total energy intake, which is within the recommended range of relevant dietary guidelines. Our results showed that after adjusting for educational level and LDL-C and LP(a) levels, saturated fatty acid DII was an influencing factor for Q4 group, with Q4 group patients having 8.562 times higher risk of increased coronary artery disease severity compared to Q1 group. Therefore, clinicians should advise ACS patients to reduce saturated fatty acid intake and its proportion in total energy intake to decrease saturated fatty acid-induced coronary inflammation and delay disease progression.

In summary, dietary inflammatory potential and the inflammatory potential of specific nutrients—total fat, saturated fatty acids, and vitamin E—are significant influencing factors for coronary artery disease severity in ACS patients. Clinicians should strengthen anti-inflammatory dietary guidance for ACS patients, helping them adjust dietary structure by increasing vitamin E intake while reducing total fat and saturated fatty acid intake to effectively alleviate diet-induced coronary inflammation, delay disease progression, and reduce ACS exacerbation risk. However, this study had a relatively small sample size from a single center, and the dietary patterns may have regional characteristics. Therefore, the results and conclusions require validation through larger-scale, multicenter studies. Additionally, the specific mechanisms by which dietary inflammatory potential influences coronary artery disease progression in ACS patients warrant further investigation.

Author Contributions and Conflicts of Interest

Author Contributions: Guiping Hu, Ping Lin, Zhenjuan Zhao, and Yini Wang conceived and designed the study and conducted feasibility analysis. Guiping Hu, Mingqiang Yan, and Xiao Sun were responsible for data collection and collation. Guiping Hu performed statistical analysis and drafted the manuscript. Ping Lin, Zhenjuan Zhao, and Yini Wang revised the manuscript. Ping Lin was responsible for quality control and final review, providing overall supervision and management.

Conflicts of Interest: The authors declare no conflicts of interest.

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Note: Figure translations are in progress. See original paper for figures.