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The Association Between Inflammatory Dietary Pattern and Risk of Cognitive Impairment Among Older Adults with Chronic Diseases and Its Multimorbidity: A Cross-Sectional Study

Lili Wang[1], Le Cheng[1], Chenhui Lv[1], Jie Kou[1], Wenjuan Feng[1], Haoran Xie[1], Ruolin Yan[1], Xi Wang[1], Shuangzhi Chen[1], Xin Song[1], Lushan Xue[1], Cheng Zhang[1], Xuemin Li[2], Haifeng Zhao[1,3]

[1]Department of Nutrition and Food Hygiene, School of Public Health, Shanxi Medical University, Taiyuan, People's Republic of China; [2]Center for Disease Control and Prevention in Shanxi Province, Taiyuan, People's Republic of China; [3]MOE Key Laboratory of Coal Environmental Pathogenicity and Prevention (Shanxi Medical University), Ministry of Education, Taiyuan, People's Republic of China

Correspondence: Haifeng Zhao, Department of Nutrition & Food Hygiene, School of Public Health, Shanxi Medical University, Taiyuan, Shanxi, 030001, People's Republic of China, Tel/Fax +86-351-4135046, Email haifengzao75@163.com

Background: The present study aimed to explore the association between the inflammatory potential of diet, assessed by energy-adjusted dietary inflammatory index (E-DII) and reduced rank regression (RRR)-derived inflammatory dietary pattern, and the risk for cognitive impairment (CI) in community-dwelling older adults, especially in older adults with chronic diseases and multimorbidity.

Methods: A total of 549 older adults from Taiyuan city were included in the present cross-sectional study. The Chinese Version of the Mini-Mental State Examination (CMMSE) was used for the evaluation of cognitive function. E-DII score was calculated based on semi-quantitative food frequency questionnaire (FFQ). Blood samples, including interleukin (IL)-1β, interleukin (IL)-18, tumor necrosis factor-α (TNF-α) and C-reactive protein (CRP), were tested for calculating RRR-derived inflammatory dietary pattern. Logistic regression was used to assess the association between inflammatory dietary pattern and risk of CI. In addition, patients with diabetes, hypertension, hyperlipidemia and multimorbidity were screened for further analysis among 549 older adults.

Results: In those 549 older adults, adjusting for demographic characteristics and chronic disease status, there was no association between E-DII score tertile (OR_{T3VST1}: 1.357, 95%*CI*:0.813~2.265, P_{trend} = 0.267), RRR-derived inflammatory dietary pattern score tertile (OR_{T3VST1}: 1.092, 95%*CI*:0.679~ 1.758, P_{trend} = 0.737) and risk of CI. However, in older adults with diabetes and multimorbidity, the score tertile of E-DII and RRR-derived inflammatory dietary pattern were positively correlated with risk of CI in a dose-responsive manner (All $P_{trend} < 0.05$). There is insufficient evidence to reach similar conclusion in patients with hypertension and hyperlipidemia (All $P_{trend} > 0.05$).

Conclusion: In the present study, pro-inflammatory diet contributed to the increased risk of CI in older adults with diabetes and multimorbidity. These results supplemented vital evidence for the prevention and treatment of CI in older adults with chronic diseases.

Keywords: chronic diseases, multimorbidity, cognitive impairment, inflammatory dietary pattern, dietary inflammatory index, reduced rank regression

Introduction

Populations around the world are aging at an unprecedented pace, particularly in China. According to the seventh national census in China, 190.63 million people are aged 65 years or older, representing 13.5% of the total population of 1.40 billion people in 2020.[1] Result from this drastic demographic shift, the direct medical expenses per capita of aging-related cognitive impairment (CI) is also expected to increase further.[2] A systematic review reported that the global prevalence of CI ranged from 5.1% to 41% with a median of 19.0%.[3] In China, the latest report showed that the overall prevalence of dementia was 6.0% and of mild cognitive impairment (MCI) was 15.5% in adults aged 60 years or older.[4]

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Loss of memory, learning difficulties and a decrease in the ability to concentrate on a task characterizes CI in the older adults, which would lead to the decline of patients' life quality. Due to the lack of medical technologies that could significantly and sustainably restore cognitive function, preventing CI represents a matter of great public health interest.

The mechanisms of cognitive aging are complex and are closely associated with aging-related chronic disease, such as diabetes, hypertension, hyperlipidemia et al. Many studies have revealed that the long-lasting decompensation of these chronic diseases, often diagnosed in middle age, may accelerate cognitive decline in older patients.[5–7] Besides, it is a common observation that older patients with accumulation of multimorbidity tend to experience accelerated worsening of their cognitive function.[8] Since a prolonged exposure time to risk factors increases the risks of having such conditions, understanding the risk factors of CI in older adults with chronic diseases is an important step to identify targets for preventive strategies.

One of the signs of senility is the establishment of a chronic systemic low-grade inflammation state, manifested as high circulating levels of pro-inflammatory cytokines, including interleukin (IL)-1β, interleukin (IL)-18, tumor necrosis factor-α (TNF-α), and C-reactive protein (CRP).[9] There is strong evidence that IL-1β and IL-18 are the proinflammatory cytokine produced during inflammation following inflammasome activation, have been shown to mediate key aspects of neuronal and cognitive dysfunction.[10] TNF-α can influence the synthesis of Amyloid β-protein (Aβ) plaques, and the formation of neurofibrillary tangles and therefore can curb the progression of CI pathology.[11] Elevated levels of CRP predict poorer cognitive function and increased dementia risk in cognitively healthy middle-aged and older adults as well.[12] Simultaneously, chronic diseases associated with aging will further aggravate inflammation at peripheral and central inflammatory levels, inducing Aβ deposition, which leads to cognitive dysfunction.[13–15] This cognitive decline may not evolve to frank dementia and even improve if the underlying inflammatory condition is successfully controlled.

Increasing evidence suggests that diet might play a critical role in alleviating inflammation and reducing the risk of CI.[16] Dietary pattern has been recommended for a wide range of applications, because it takes into account the diversity and complexity of diets. Some recognized healthy diets such as Mediterranean Diet (MD) and Dietary Approaches to Stop Hypertension (DASH) have been proved to have effects of anti-inflammatory and neuroprotective. However, most of these studies have just focused on the bidirectional relationship between diet and inflammation, diet and cognition, or inflammation and cognition.[17,18] It is necessary to further clarify the relationship between diet-related inflammation and cognitive health. Inflammatory dietary pattern which could predict the concentrations of inflammatory markers have been proposed in recent years, such as dietary inflammatory index (DII), reduced rank regression (RRR)-derived inflammatory dietary pattern, thus providing a shortcut to better explore the effect of inflammatory diet on treating disease. The DII was developed based on evidence from a large number of human population study, qualifying cell culture and animal experiments.[19] Considering the impact of overall consumption of dietary energy on the overall inflammatory potential of the diet, the energy-adjusted dietary inflammatory index (E-DII) was further developed.[20] It focus more on most nutrients and bioactive ingredients related to inflammation, and has few regional uniqueness and ethnic specificity, and has a wide range of applications.[21] In cross-sectional and prospective studies, E-DII scores were positively associated with the impaired cognitive function in older adults.[22–24] RRR-derived dietary pattern allows the integration of disease-related inflammatory markers in the analysis, is also considered an appropriate method.[25,26] Furthermore, compared with E-DII, RRR-derived dietary pattern can focus on food categories and may be more valuable in assessing complex diet-disease interactions value.[27] These two mutually reinforce each other. It has been shown that RRR-derived dietary pattern associated with high CRP level contributed to the increased risk of CI.[28] Although few scholars have explored the relationship between inflammatory dietary pattern and CI in patients with chronic diseases and multimorbidity, previous research provided support to explore associations between the inflammatory potential of diet and CI in older adults with chronic diseases and multimorbidity.

Unlike previous studies on dietary inflammation and cognition, considering the respective advantages of E-DII and RRR-derived inflammatory dietary pattern, we simultaneously use the two methods to explore and verify the relationship between inflammatory diet and cognitive ability in older adults in Taiyuan city. Furthermore, given the prevalent comorbid condition of CI in severe chronic illness, we further focus the relationship between inflammatory diet and cognitive ability in older adults with chronic diseases and multimorbidity in the current study. It will be critical to provide offer guidance for the prevention of memory decline in older adults with or without chronic diseases in public practice.

Materials and Methods

Study Participants and Design

In this cross-sectional study, individuals aged 65 or older (respectively from six major communities of six urban areas in Taiyuan, Shanxi, China) were recruited using a cluster-sampling. We excluded subjects if they 1) had CI caused by other non-vascular factors such as degenerative disease, ischemic cerebrovascular disease, systemic disease, taking medicine that affect cognition, 2) had disorders of consciousness, delirium or mental, 3) had severe aphasia, hearing, visual impairment and movement, sensory impairment, 4) used dietary supplements. The data of sociodemographic characteristics, dietary intake and cognitive function were gathered through trained interviewers. In our study, the chronic disease status in all older participants was confirmed by asking the following question, "Has a doctor or other health professional ever told you that you had diabetes, or hypertension, or hyperlipidemia?". Furthermore, the multimorbidity was defined when a person had more than two of the above diseases. After collating and excluding patients with missing data, 549 older individuals were included in our analysis. All subjects voluntarily joined our study and signed the informed consent form as documentary proof. The study protocol has been approved by the Medical Ethics Committee of Shanxi Medical University, China.

Calculation of Sample Size

The required sample size was calculated by following formula:

$$n = (Z_{\alpha})^{2} \times P(1 - P) / d^{2}$$

α=the type I error of 5%.

P=the prevalence rate of CI in older adults based on Jianping Jia's study: 15.5%.[4]

d=the accuracy of estimation which was considered 20% of P: 0.031.

In summary, 524 participants were needed in the current cross-sectional study. Therefore, data from 549 participants were sufficient in our analysis.

Assessment of Cognitive Function

In our study, the Chinese Version of the Mini-Mental State Examination (CMMSE) was used to assess the cognitive performance in older adults, which was appropriate for the seniors with Chinese cultural backgrounds.[29] It has been validated and used in prior studies.[30–33] The CMMSE consists of thirty points grouped into seven categories: orientation to place, orientation to time, registration, attention, concentration, language and visual construction. The total score ranges from 0 to 30 points. With 27 points as the critical value, ≥27 points are considered cognition normal (CN), and <27 points are considered CI.[34]

Assessment of Dietary Intake

Dietary intake was evaluated through a semiquantitative food frequency questionnaire (FFQ), administered by trained interviewers. In our study, the design of FFQ was appropriately adjusted according to the dietary characteristics of Shanxi people, especially the people in Taiyuan, based on the FFQ used the China National Nutrition and Health Survey. The participants' intake of various foods were surveyed by the FFQ over the past 1 year. The dietary questionnaire was divided into 18 food groups, such as cereals, tubers, fresh vegetables, fresh fruits, livestock and poultry meat, milk and its products, eggs, beans and their products, nuts, pickles, sugar-sweetened beverages (SSBs), wine, etc. In addition, using the China Food Composition Table, the average daily intake of different foods and nutrients were calculated based on the frequency of intake and portion size information of individuals.

Measurement of Inflammatory Biomarker

The fasting blood samples were collected by venipuncture into 5 mL blood collection tubes. Then, blood was centrifuged at 2000 × g for 10 min from each participant, and stored in −80°C until use. The plasma levels of IL-1β, IL-18, TNF-α and CRP were measured using ELISA (Human IL-1β, IL-18, TNF-α and CRP, Enzyme-linked Biotechnology, Wuhan, China).

Inflammatory Dietary Pattern

Energy-Adjusted Dietary Inflammatory Index (E-DII)

The development and validation of the DII has been elaborated elsewhere.[19–21] Briefly, the calculation of DII consists of two main parts which were the overall inflammatory effect score for specific food parameters and the individual's standardized dietary intake data. The overall inflammatory effect score for specific food parameter was obtained based on literature that illustrated the relationship of 6 important inflammatory biomarkers (IL-1β, IL-6, TNF-α, CRP, IL-4 and IL-10) and 45 food parameters (macronutrients, micronutrients, bioactive compounds and foods/spices). Meanwhile, based on a database containing data from 11 countries around the world, the average daily dietary intake data of individuals were normalized. The normalized average daily dietary intake was converted to a percentile score, and each percentile score was doubled and then "1" was subtracted to achieve a symmetrical distribution with values centred on 0 and bounded between −1 and +1.[19] Ultimately, the centred percentile value for each food parameter were multiplied by the corresponding inflammatory effect score and summed to obtain an overall DII score for each individual.[19]

In the present study, 25 of 45 food parameters were incorporated, including energy, carbohydrate, protein, total fat, saturated fatty acids (SFA), monounsaturated fatty acids (MUFA), polyunsaturated fatty acids (PUFA), fiber, cholesterol, vitamin A, β carotene, vitamin E, thiamine, riboflavin, niacin, folic acid, vitamin C, magnesium, iron, zinc, selenium, anthocyanin, isoflavones, alcohol and green tea.[19] Furthermore, the DII were calculated as per 1000 kcal/d consumed, the so-called E-DII, to control for the effect of different total energy intake among participants.[20] A positive value indicates that the diet has a pro-inflammatory tendency, a negative value indicates that the diet has an anti-inflammatory tendency, and a zero value indicates that the diet has no inflammatory effect.

RRR-Derived Inflammatory Dietary Pattern

The RRR method was realised by the procedure PLS of the SAS software (method = RRR).[25] In this analysis, we used the standardized dietary intake of 18 food groups as predictor variables and serum concentrations of log-transformed IL-1β, IL-18, TNF-α and CRP as response variables. The food parameters and inflammatory biomarkers were selected based on published research investigating their association with cognition, as well as the inflammatory potential of various types of foods.[35–37] The inflammatory dietary pattern score was calculated by multiplying the standardized dietary intake by the corresponding factor load. Foods with absolute factor loadings of >0.20 were used to describe the dietary pattern, but all foods contributed to calculation of the dietary pattern score. The number of RRR-derived inflammatory dietary pattern was determined by the number of inflammatory factors entered into the regression model. The first factor obtained by RRR was retained for subsequent analyses, as it accounts for most of the variation in the 18 foods and 4 inflammatory factors. The rest of the dietary patterns explained rather low cumulative variance, therefore, were not considered in the present analysis. When the higher the score, the more the preference of the dietary pattern of the person corresponding to the proinflammatory dietary pattern, and the lower the score, the more deviation from the dietary pattern.[38]

Statistical Analysis

Continuous variables were expressed as the means ± standard deviation (SD) or medians (interquartile ranges [IQR]) based on the test of normality. Categorical variables were presented as frequencies and percentages. The Student's *t*-test and chi-square tests were performed to compare the differences in the distributions of sample characteristics between groups. Spearman's correlation was conducted to analyze the relationship between inflammatory biomarkers and dietary pattern scores. The E-DII and RRR-derived inflammatory dietary pattern scores were divided into tertiles by scoring. Thus, tertile 1, the lowest scoring group, is the most anti-inflammatory group, whereas tertile 3, the highest scoring

group, is the most pro-inflammatory group. Logistic regression was used to assess the association between inflammatory dietary pattern and risk of CI. Odds ratio (OR) and corresponding 95% confidence intervals (CIs) were calculated. Model 1 was used to calculate the crude OR. Model 2 adjusted for age, gender, educational level, income level, BMI, physical activity, smoking habit, alcohol intake, tea intake. Model 3 adjusted for diabetes, hypertension and hyperlipidemia. All the statistical analysis were performed using SPSS 22.0 and SAS 9.4 softwares. A two-sided *P*-value of < 0.05 was considered statistically significant.

Results

Characteristics of the Study Population

The characteristics of 549 older adults are shown in Table 1. The median age was approximately 72 years. Males and females accounted for 39.7% and 60.3% of the older adults, respectively. Patients with diabetes, hypertension and

Table 1 Characteristics of Whole Older Adults

Characteristics		Whole older adults (n=549)	CN (n=326)	CI (n=223)	z /χ^2	*P* value
Sex	Males	218 (39.7)	134 (41.1)	84 (37.6)	0.701	0.403
	Females	331 (60.3)	192 (58.9)	139 (62.4)		
Age (year)		72.00 (68.00, 77.00)	71.00 (67.00, 75.00)	75.00 (68.00, 79.00)	−5.328	< 0.001
Age	65~69	191 (34.8)	128 (39.3)	63 (28.3)	28.816	< 0.001
	70~74	149 (27.1)	103 (31.6)	46 (20.6)		
	75~79	136 (24.8)	66 (20.2)	70 (31.4)		
	≥ 80	73 (13.3)	29 (8.9)	44 (19.7)		
Educational level	illiteracy	125 (22.8)	36 (11.0)	89 (39.9)	83.450	< 0.001
	≤ 6 years	140 (25.5)	74 (22.7)	66 (29.6)		
	> 6 years	284 (51.7)	216 (66.3)	68 (30.5)		
Income level	< 3000	187 (34.1)	96 (29.4)	91 (40.8)	13.217	0.004
	3000~	277 (50.4)	173 (53.1)	104 (46.6)		
	7000~	57 (10.4)	43 (13.2)	14 (6.3)		
	≥ 10,000	28 (5.1)	14 (4.3)	14 (6.3)		
BMI (kg/m^2)		24.03 (21.80, 26.50)	24.22 (22.20, 26.67)	23.61 (21.26, 26.04)	1.948	0.052
BMI	< 18.5	27 (4.9)	12 (3.7)	15 (6.7)	3.643	0.303
	18.5~23.9	242 (44.1)	141 (43.3)	101 (45.3)		
	24.0~27.9	193 (35.2)	117 (35.9)	76 (34.1)		
	≥ 28.0	87 (15.8)	56 (17.1)	31 (13.9)		
Physical activity	Yes	383 (69.8)	231 (70.9)	152 (68.2)	0.457	0.499
	No	166 (30.2)	95 (29.1)	71 (31.8)		
Smoking habit	Yes	132 (24.0)	65 (19.9)	67 (30.0)	7.406	0.007
	No	417 (76.0)	261 (80.1)	156 (70.0)		
Alcohol intake	Yes	72 (13.1)	48 (14.7)	24 (10.8)	1.824	0.177
	No	477 (86.9)	278 (85.3)	199 (89.2)		
Tea intake	Yes	132 (24.0)	89 (27.3)	43 (19.3)	4.662	0.031
	No	417 (76.0)	237 (72.7)	180 (80.7)		
Diabetes	Yes	92 (16.8)	63 (19.3)	29 (13.0)	3.792	0.051
	No	457 (83.2)	263 (80.7)	194 (87.0)		
Hypertension	Yes	251 (45.7)	145 (44.5)	106 (47.5)	0.498	0.480
	No	298 (54.3)	181 (55.5)	117 (52.5)		
Hyperlipidemia	Yes	152 (27.7)	98 (30.1)	54 (24.2)	2.260	0.133
	No	397 (72.3)	228 (69.9)	169 (75.8)		
IL-1β, ng/ml [M, (P25, P75)]		6.45 (5.84, 7.31)	6.27 (5.81, 7.14)	6.81 (5.98, 7.62)	−3.831	< 0.001
IL-18, ng/ml [M, (P25, P75)]		225.00 (200.37, 254.72)	217.32 (189.63, 250.15)	236.15 (211.22, 258.21)	−2.938	0.003
TNF-α, pg/ml [M, (P25, P75)]		280.50 (197.42, 432.16)	255.75 (199.29, 382.94)	327.42 (190.09, 644.27)	−7.692	< 0.001
CRP, ng/ml [M, (P25, P75)]		13.93 (10.75, 27.14)	13.54 (10.42, 23.57)	14.99 (11.01, 31.83)	−2.819	0.005

hyperlipidemia accounted for 16.8% (92 cases), 45.7% (251 cases) and 27.7% (152 cases), respectively. Compared the characteristics of older adults in different cognitive groups, we found that older adults with CI were more likely to be ripe old age, less educated, low-income earners, smokers and non-tea drinkers. In addition, they were likely to have higher levels of IL-1β, IL-18, TNF-α and CRP (all *P*-value <0.05).

Moreover, the characteristics of the screened patients with diabetes, hypertension, hyperlipidemia and multimorbidity were further analyzed. It was found that the levels of the above 4 inflammatory factors in the CN group were lower than those in the CI group (all *P*-value <0.05) (Supplement Tables 1–4)

E-DII of the Study Population

Figure 1A-E presented the range of E-DII score in older adults and older adults with various chronic diseases. The median E-DII scores showed that the diets of these people were pro-inflammatory as a whole. Moreover, analysing E-DII scores in different cognitive groups, we found that compared with the CN participants, the CI patients had higher E-DII scores (all *P*-values < 0.05) (Table 2). In order to identify the specific dietary components that cause the increase of E-DII in CI patients, the intake of food components constituting E-DII were compared among different cognitive groups, as shown in Table 3. In whole older adults, patients with CI had lower intake of protein, fiber, cholesterol, folic acid, magnesium, iron, zinc, and anthocyanin (*P*-values < 0.05). In older adults with diabetes, we found that the intake of fiber, folic acid, magnesium and zinc were lower in CI group (*P*-values < 0.05). In older adults with hypertension, participant of CI group had lower intake of protein, fiber, cholesterol, folic acid, magnesium, iron, zinc, and anthocyanin (*P*-values < 0.05). In older adults with hyperlipidemia, the intake of protein, iron, and folic acid were lower in the CI group (*P*-values < 0.05). In addition, it was found that the daily intake of protein, fiber, cholesterol, riboflavin, folic acid, magnesium, iron, zinc, and selenium in the CI group were lower than those in the CN group among older adults with multimorbidity (*P*-values < 0.05).

RRR-Derived Inflammatory Dietary Pattern

The results of the factor loadings of all 18 food items derived by RRR in older adults and older adults with chronic diseases were showed in Table 4 and Figure 2. In whole older adults, the RRR-derived inflammatory dietary pattern

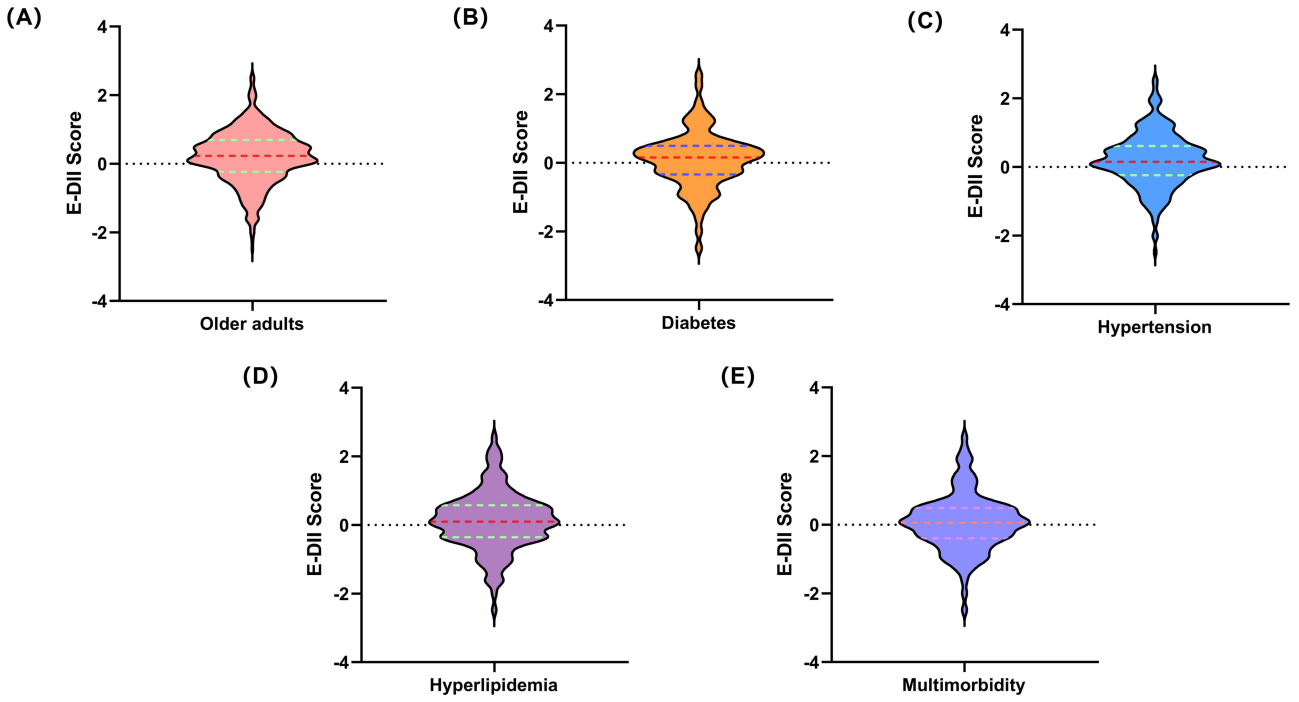

Figure 1 The E-DII score in different study population.
Notes: (**A**) Whole older adults. (**B**) Older adults with diabetes. (**C**) Older adults with hypertension. (**D**) Older adults with hyperlipidemia. (**E**) Older adults with multimorbidity.

Table 2 Comparison of E-DII Score Between CN and CI Group in Different Study Population

Subject	Score of E-DII	CN	CI	z /χ^2	*P* value
Whole older adults	0.23 (−0.23, 0.69)	0.17 (−0.31, 0.60)	0.27 (−0.04, 0.74)	−2.404	0.016
Diabetes	0.16 (−0.34, 0.49)	−0.01 (−0.59, 0.40)	0.37 (0.13, 0.74)	−3.257	0.001
Hypertension	0.15 (−0.24, 0.61)	0.03 (−0.39, 0.51)	0.28 (0.01, 0.73)	−3.253	0.001
Hyperlipidemia	0.10 (−0.36, 0.57)	0.04 (−0.40, 0.47)	0.25 (−0.11, 0.70)	−2.137	0.033
Multimorbidity	0.06 (−0.39, 0.49)	−0.09 (−0.61, 0.40)	0.24 (−0.03, 0.67)	−3.241	0.001

explained 4.45% of the response variation. For individual response variable, the explained variation ranged from 1.78% (for CRP) to 7.86% (for IL-1β). The dietary pattern was characterized by high intake of cereals and low intake of nuts and wine, and positively correlated with levels of IL-1β, IL-18, TNF-α and CRP (Table 4, Figure 2A).

In addition, in order to in depth the inflammatory diet of chronic disease patients, we further extracted the RRR-derived inflammatory dietary pattern in older adults with chronic diseases and multimorbidity. In patients with diabetes, the RRR-derived inflammatory dietary pattern was positively correlated with levels of IL-1β, IL-18, TNF-α and CRP, and characterized by high intake of SSBs, pickles, and low intake of tubers, aquatic products, beans and nuts. It explained 13.04% of the variation in inflammatory factors, ranging from 7.58% (for CRP) to 23.37% (for IL-1β) (Table 4, Figure 2B). In hypertension patients, the RRR-derived inflammatory dietary pattern was characterized by low intakes of nuts, accounting for 4.42% of the response variation (Table 4, Figure 2C). In patients with hyperlipidemia, the RRR-derived inflammatory dietary pattern was characterized by low intakes of nuts and wine, accounting for 13.12% of the response variation (Table 4, Figure 2D). In patients with multimorbidity, the results showed that the RRR-derived inflammatory dietary pattern was characterized by low intakes of tubers, beans and nuts, which was positively correlated with levels of IL-1β, IL-18, TNF-α and CRP, and accounted for 12.79% of the total variation, ranging from 4.11% (for CRP) to 25.87% (for IL-1β) (Table 4, Figure 2E).

Correlation Analysis of the Inflammatory Dietary Pattern Score and Inflammatory Markers

Spearman's correlation analysis was used to explore the correlation of E-DII, RRR-derived inflammatory dietary pattern score with levels of IL-1β, IL-18, TNF-α and CRP (Table 5, Table 6). Except for patients with hypertension, the scores of E-DII and RRR-derived inflammatory dietary pattern were found to be positively correlated with the above four inflammatory factors in rest of the population (All *P*-values < 0.05). However, the scores of E-DII and RRR-derived inflammatory dietary pattern were positively correlated only with levels of IL-1β and IL-18 in patients with hypertension (*P*-values < 0.05).

The Association Between Inflammatory Dietary Pattern and CI

Logistic regression was performed to investigate the association between inflammatory dietary pattern and CI. According to the tertiles score of inflammatory dietary pattern, the unadjusted and adjusted ORs for the CI were shown in Tables 7 and 8.

In the 549 older adults, adjusting for demographic characteristics and chronic disease status, there was no association between E-DII score tertile (OR_{T3VST1}: 1.357, 95%*CI*: 0.813~2.265, P_{trend} = 0.267), RRR-derived inflammatory dietary pattern score tertile (OR_{T3VST1}: 1.092, 95%*CI*: 0.679~1.758, P_{trend} = 0.737) and increased risk of CI. Besides, the relationship between inflammatory dietary patterns and cognition in older adults with various chronic diseases and multimorbidity were further analyzed. In the RRR-derived inflammatory dietary pattern, after adjusting for age, gender, education, economic status, BMI, smoking status, drinking status, exercising status and chronic disease status, the results showed that the inflammatory dietary pattern was associated with risk of CI in a dose-response manner in older adults with diabetes and multimorbidity (All P_{trend} < 0.05). However, in the older adults with hypertension and hyperlipidemia, the relationship between the RRR-derived inflammatory dietary pattern and CI wasn't observed (All P_{trend} > 0.05). The same conclusion was found for E-DII.

Table 3 Intake Status of Dietary Components in Different Study Population/1000 Kcal

Dietary components	Whole older adults		*P* value	Diabetes		*P* value	Hypertension		*P* value	Hyperlipidemia		*P* value	Multimorbidity		*P* value
	CN (n=326)	CI (n=223)		CN (n=63)	CI (n=29)		CN (n=145)	CI (n=106)		CN (n=98)	CI (n=54)		CN (n=81)	CI (n=45)	
Carbohydrate (g)	136.76 (123.76, 152.05)	139.44 (123.65, 154.49)	0.293	136.01 (112.86, 143.86)	134.92 (123.14, 154.13)	0.467	139.30 (126.80, 151.79)	140.44 (125.89, 155.29)	0.550	141.25 (127.75, 152.35)	140.83 (125.37, 151.66)	0.814	136.89 (121.96, 150.70)	132.90 (123.54, 152.07)	0.638
Protein (g)	37.61 (34.71, 41.08)	36.71 (33.26, 40.00)	0.022	38.52 (35.49, 42.10)	38.24 (34.15, 41.76)	0.378	37.78 (35.35, 41.34)	36.62 (33.46, 39.77)	0.024	38.01 (35.43, 41.63)	36.75 (32.38, 39.35)	0.012	38.67 (36.31, 42.09)	36.68 (33.13, 39.45)	0.005
Fat (g)	35.63 (29.50, 42.18)	34.05 (28.25, 41.45)	0.254	36.58 (32.24, 44.06)	34.34 (26.27, 41.21)	0.244	34.82 (29.64, 40.68)	33.53 (28.13, 40.84)	0.420	34.55 (28.83, 40.51)	35.90 (29.58, 43.05)	0.603	35.26 (29.79, 41.92)	36.75 (30.06, 42.50)	0.620
SFA (g)	8.02 (6.85, 9.57)	8.06 (6.49, 9.54)	0.541	8.36 (7.10, 9.90)	8.24 (7.62, 10.14)	0.953	7.88 (6.87, 9.38)	7.95 (6.46, 9.45)	0.451	7.78 (7.00, 9.39)	7.65 (6.52, 8.69)	0.167	7.88 (7.00, 9.53)	8.01 (6.74, 9.31)	0.671
MUFA (g)	11.81 (8.81, 15.25)	11.35 (8.45, 14.61)	0.270	11.97 (9.27, 15.00)	11.53 (8.37, 15.44)	0.668	11.66 (9.34, 15.23)	10.81 (8.17, 14.28)	0.110	11.93 (9.15, 14.93)	11.22 (8.09, 13.97)	0.297	11.47 (9.28, 14.81)	11.97 (8.67, 14.83)	0.754
PUFA (g)	8.58 (6.22, 11.15)	8.40 (5.99, 12.08)	0.553	9.31 (6.50, 12.13)	9.09 (5.01, 12.22)	0.542	8.28 (6.20, 11.00)	8.58 (6.30, 11.85)	0.302	8.66 (6.63, 12.04)	8.43 (5.43, 12.43)	0.500	8.80 (6.53, 11.71)	9.55 (5.55, 13.18)	0.774
Fiber (g)	6.47 (4.83, 8.15)	5.91 (4.41, 7.76)	0.018	6.81 (5.16, 8.60)	5.49 (4.51, 6.14)	0.004	6.68 (5.16, 8.46)	5.85 (4.35, 7.84)	0.012	7.10 (5.48, 8.70)	6.44 (5.45, 8.47)	0.393	7.38 (5.59, 9.13)	5.88 (4.85, 8.28)	0.011
Cholesterol (mg)	160.73 (93.19, 201.70)	134.36 (79.04, 178.73)	0.001	179.67 (105.77, 218.51)	139.71 (75.46, 197.22)	0.092	158.66 (99.21, 208.25)	115.68 (69.85, 168.96)	< 0.001	150.84 (90.58, 205.86)	134.54 (78.40, 172.18)	0.137	173.82 (99.11, 212.11)	111.98 (73.81, 170.56)	0.007
VA (RAE)	141.89 (98.63, 185.67)	133.85 (91.99, 184.98)	0.624	162.85 (135.49, 188.88)	135.81 (102.96, 169.01)	0.058	135.88 (98.54, 180.04)	134.21 (90.31, 170.67)	0.297	140.36 (97.74, 170.14)	133.96 (103.02, 168.67)	0.923	143.12 (110.17, 180.04)	135.80 (100.67, 168.55)	0.353
β-carotene (μg)	203.45 (136.15, 322.52)	216.28 (130.45 300.31)	0.637	202.39 (143.68, 289.22)	183.24 (126.05, 232.93)	0.362	205.74 (129.13, 317.02)	201.08 (126.55, 292.97)	0.339	202.93 (142.50, 304.70)	219.96 (137.90, 296.13)	0.630	202.39 (143.36, 310.23)	195.48 (137.03, 291.33)	0.750
Thiamine (mg)	3.30 (2.17, 5.04)	3.07 (1.91, 5.12)	0.127	3.79 (2.18, 5.23)	3.07 (2.27, 6.04)	0.963	2.98 (2.02, 4.68)	3.20 (2.00, 5.62)	0.446	3.32 (2.35, 4.88)	3.09 (1.94, 4.69)	0.236	3.29 (2.14, 4.67)	3.03 (1.98, 4.69)	0.660

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Riboflavin (mg)	0.38 (0.31, 0.44)	0.36 (0.30, 0.44)	0.286	0.42 (0.35, 0.48)	0.39 (0.32, 0.45)	0.153	0.38 (0.31, 0.44)	0.35 (0.29, 0.42)	0.088	0.40 (0.31, 0.44)	0.37 (0.31, 0.43)	0.410	0.41 (0.34, 0.45)	0.36 (0.31, 0.42)	0.047
Niacin (mg)	6.01 (5.32, 6.83)	5.97 (5.26, 6.93)	0.638	6.12 (5.40, 6.93)	5.83 (5.14, 6.57)	0.238	6.04 (5.40, 6.83)	5.92 (5.14, 6.58)	0.216	6.11 (5.41, 6.93)	5.98 (5.23, 6.94)	0.364	6.10 (5.41, 6.92)	5.89 (5.13, 6.58)	0.200
Folic acid (μg)	141.96 (120.12, 166.83)	129.06 (106.52, 156.82)	< 0.001	148.51 (131.69, 172.53)	113.34 (106.23, 140.39)	0.001	146.70 (126.40, 173.35)	124.35 (102.22, 149.80)	< 0.001	149.40 (124.23, 170.50)	134.05 (107.67, 167.83)	0.048	152.32 (132.44, 177.26)	122.59 (106.58, 137.85)	< 0.001
VC (mg)	41.96 (31.04, 54.57)	40.89 (28.04, 55.69)	0.317	46.31 (34.89, 54.63)	44.10 (28.36, 60.20)	0.696	42.02 (31.89, 55.36)	41.96 (27.20, 57.47)	0.563	42.44 (32.62, 52.56)	44.76 (29.44, 56.23)	0.636	45.36 (34.93, 53.97)	44.09 (29.34, 60.20)	0.986
VE (mg)	17.89 (14.11, 21.58)	17.34 (13.47, 21.68)	0.345	19.17 (15.38, 23.31)	17.78 (11.37, 2.25)	0.262	17.98 (14.12, 21.89)	17.46 (14.32, 21.72)	0.680	18.21 (13.88, 21.75)	17.20 (14.00, 20.80)	0.498	18.62 (14.11, 22.82)	18.54 (15.51, 22.25)	0.957
Mg (mg)	212.79 (186.24, 241.70)	206.50 (181.83, 230.41)	0.049	222.69 (194.33, 249.54)	205.79 (180.58, 222.95)	0.044	218.41 (193.49, 242.25)	206.73 (180.61, 229.70)	0.016	223.15 (192.14, 247.80)	211.03 (189.44, 236.54)	0.189	226.42 (194.79, 250.39)	208.35 (183.30, 227.56)	0.031
Fe (mg)	9.00 (8.10, 10.15)	8.54 (7.38, 9.49)	< 0.001	9.01 (8.23, 10.13)	8.45 (7.98, 9.49)	0.080	9.18 (8.09, 10.43)	8.40 (7.38, 9.49)	0.001	8.91 (8.20, 10.30)	8.36 (7.43, 9.42)	0.032	9.04 (8.17, 10.49)	8.34 (7.50, 9.63)	0.037
Zn (mg)	4.34 (3.70, 5.02)	3.93 (3.44, 4.74)	< 0.001	4.65 (4.05, 5.39)	4.06 (3.52, 4.88)	0.014	4.38 (3.78, 5.02)	3.93 (3.35, 4.72)	0.004	4.42 (3.79, 5.18)	4.21 (3.53, 4.80)	0.051	4.56 (3.97, 5.20)	4.06 (3.57, 4.84)	0.030
Se (μg)	16.64 (14.91, 18.79)	16.67 (14.56, 18.90)	0.713	16.86 (15.33, 19.20)	16.67 (14.40, 18.88)	0.608	16.64 (15.54, 18.66)	16.10 (14.25, 18.73)	0.129	16.84 (14.63, 18.74)	15.91 (14.01, 18.22)	0.167	16.83 (15.60, 18.87)	15.81 (13.39, 17.80)	0.020
Anthocyanidin (mg)	6.85 (3.10, 17.15)	4.72 (2.30, 12.96)	0.008	6.19 (3.76, 17.91)	6.19 (2.56, 12.82)	0.199	6.86 (3.89, 17.92)	4.63 (1.96, 13.06)	0.003	6.91 (3.59, 21.19)	7.93 (2.66, 25.75)	0.936	6.86 (4.01, 17.25)	6.75 (2.55, 21.54)	0.388
Isoflavone (mg)	9.37 (5.26, 14.77)	9.41 (4.48, 14.76)	0.597	10.03 (7.06, 18.88)	10.36 (4.23, 14.56)	0.295	9.60 (5.42, 16.52)	9.49 (3.72, 14.47)	0.323	9.67 (6.12, 15.79)	10.45 (4.33, 14.86)	0.636	10.79 (7.16, 20.18)	9.58 (3.83, 13.90)	0.150

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Table 4 Factor Loadings of RRR-Derived Inflammatory Dietary Pattern in Different Study Population

Food groups	Whole older adults	Diabetes	Hypertension	Hyperlipidemia	Multimorbidity
Cereal	0.22*	0.19	0.11	0.14	0.15
Tuber	−0.12	−0.41*	−0.18	−0.19	−0.41*
Vegetable	−0.06	0.18	0.09	−0.18	0.02
Fruit	0.03	−0.01	−0.08	−0.16	−0.04
Livestock meat	0.07	0.10	0.05	0.07	0.05
Poultry meat	−0.14	0.07	−0.14	−0.05	0.10
Aquatic product	0.01	−0.29*	−0.02	−0.09	−0.16
Milk and dairy product	0.13	0.20	0.16	0.19	0.19
Egg	−0.14	0.01	−0.13	−0.09	−0.12
Bean	−0.09	−0.29*	−0.05	−0.05	−0.21*
Nut	−0.26*	−0.41*	−0.21*	−0.34*	−0.39*
oil	0.07	−0.08	−0.01	0.09	0.05
Salt	0.02	0.08	0.09	0.18	0.10
SSBs	−0.05	0.30*	0.08	0.14	0.15
Wine	−0.26*	0.07	0.00	−0.33*	−0.08
Fried pasta	0.02	0.13	−0.01	0.08	0.13
Pickle	−0.06	0.22*	0.06	−0.03	0.12
Pastry	0.04	−0.03	0.00	0.08	0.03
Total variation of food (%)	8.71	5.72	7.16	7.87	6.65
Total variation of inflammatory factor (%)	4.45	13.04	4.42	13.12	12.79
IL-1β	7.86	23.37	9.33	22.56	25.87
IL-18	6.04	18.08	6.94	16.81	16.74
TNF-α	2.14	3.12	1.22	7.22	4.42
CRP	1.78	7.58	0.20	5.90	4.11

Note: * Factor loadings > 0.20 or <−0.20 are shown.

Discussion

This cross-sectional study derived dietary pattern that reflected plasma inflammation factors using the RRR and E-DII. We found that pro-inflammatory diet was associated with a higher risk of CI in older adults with diabetes and multimorbidity, providing new insights into the prevention of CI by adjusting dietary pattern to optimize the level of inflammation in older adults in Taiyuan, Shanxi Province, China.

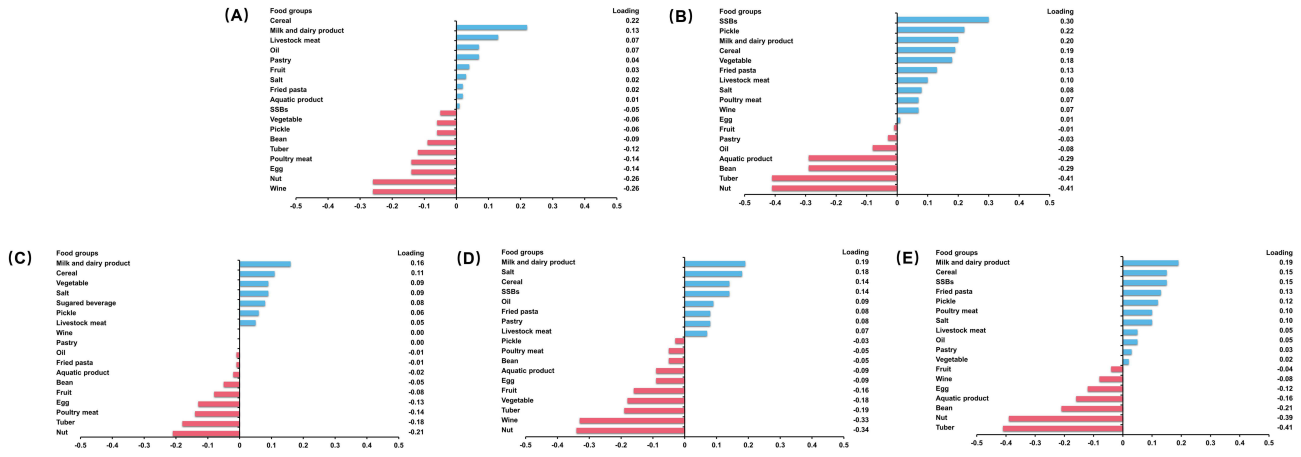

Figure 2 The RRR-derived inflammatory dietary pattern in different study population.
Note: (**A**) Whole older adults. (**B**) Older adults with diabetes. (**C**) Older adults with hypertension. (**D**) Older adults with hyperlipidemia. (**E**) Older adults with multimorbidity.

Table 5 Correlation Analysis of E-DII Score and Inflammatory Markers

Inflammatory marker	Whole older adults		Diabetes		Hypertension		Hyperlipidemia		Multimorbidity	
	r value	*P* value	r value	*P* value	r value	*P* value	r value	*P* value	r value	*P* value
IL-1β	0.186	< 0.001	0.281	0.007	0.186	0.003	0.271	0.001	0.253	0.004
IL-18	0.129	0.002	0.211	0.043	0.128	0.042	0.271	0.001	0.222	0.012
TNF-α	0.107	0.012	0.258	0.013	0.121	0.055	0.210	0.009	0.245	0.006
CRP	0.297	< 0.001	0.344	0.001	0.283	< 0.001	0.313	< 0.001	0.241	0.007

Table 6 Correlation Analysis of RRR-Inflammatory Dietary Pattern Score and Inflammatory Markers

Inflammatory marker	Whole older adults		Diabetes		Hypertension		Hyperlipidemia		Multimorbidity	
	r value	*P* value	r value	*P* value	r value	*P* value	r value	*P* value	r value	*P* value
IL-1β	0.236	< 0.001	0.510	< 0.001	0.304	< 0.001	0.366	< 0.001	0.459	< 0.001
IL-18	0.259	< 0.001	0.522	< 0.001	0.309	< 0.001	0.371	< 0.001	0.455	< 0.001
TNF-α	0.115	0.007	0.272	0.009	0.098	0.123	0.220	0.006	0.246	0.005
CRP	0.115	0.007	0.255	0.014	0.055	0.382	0.259	0.001	0.178	0.047

Table 7 The Relationship Between the RRR-Derived Inflammatory Dietary Pattern and CI

Subject	RRR-derived inflammatory dietary pattern	Model 1	Model 2	Model 3
Whole older adults	T_1	1 (Ref)	1 (Ref)	1 (Ref)
	T_2	1.384 (0.906, 2.113)	1.279 (0.796, 2.056)	1.281 (0.795, 2.064)
	T_3	1.581 (1.037, 2.410)	1.082 (0.673, 1.739)	1.092 (0.679, 1.758)
	P_{trend}	0.034	0.764	0.737
Diabetes	T_1	1 (Ref)	1 (Ref)	1 (Ref)
	T_2	10.472 (2.113, 51.903)	14.286 (2.430, 84.008)	15.595 (2.407, 101.022)
	T_3	12.687 (2.555, 62.992)	16.331 (2.782, 95.866)	16.475 (2.604, 104.241)
	P_{trend}	0.001	0.002	0.005
Hypertension	T_1	1 (Ref)	1 (Ref)	1 (Ref)
	T_2	2.782 (1.463, 5.289)	2.411 (1.167, 4.978)	2.487 (1.193, 5.181)
	T_3	2.467 (1.295, 4.700)	1.901 (0.919, 3.931)	1.946 (0.934, 4.053)
	P_{trend}	0.007	0.103	0.099
Hyperlipidemia	T_1	1 (Ref)	1 (Ref)	1 (Ref)
	T_2	1.000 (0.433, 2.308)	0.968 (0.357, 2.622)	0.998 (0.355, 2.807)
	T_3	1.719 (0.762, 3.877)	1.074 (0.397, 2.907)	1.182 (0.425, 3.289)
	P_{trend}	0.188	0.880	0.736
Multimorbidity	T_1	1 (Ref)	1 (Ref)	-
	T_2	1.833 (0.690, 4.871)	1.808 (0.602, 5.435)	-
	T_3	4.033 (1.554, 10.470)	3.901 (1.276, 11.930)	-
	P_{trend}	0.004	0.016	-

Note: Model 1: Crude model. Model 2: Adjusted for age, gender, education, economic status, BMI, smoking status (yes/no), drinking status (yes/no), exercising status (yes/no). Model 3: Adjusted for diabetes (yes/no), hypertension (yes/no) or hyperlipidemia (yes/no).

Low-grade inflammation appears to play a pathogenic role in aging-related neurodegenerative diseases, especially among older adults with chronic diseases.[39] Most studies had confirmed that chronic diseases including diabetes, particularly in the context of aging, can release many pro-inflammatory mediators into the vessels, promoting substantial blood brain barrier (BBB) disruption and further strengthening marked neuroinflammation in brain, which probably

Table 8 The Relationship Between the E-DII and CI

Subject	E-DII	Model 1	Model 2	Model 3
Whole older adults	T_1	1 (Ref)	1 (Ref)	1 (Ref)
	T_2	1.664 (1.089, 2.544)	1.512 (0.925, 2.472)	1.531 (0.936, 2.506)
	T_3	1.628 (1.065, 2.489)	1.328 (0.798, 2.211)	1.357 (0.813, 2.265)
	P_{trend}	0.026	0.301	0.267
Diabetes	T_1	1 (Ref)	1 (Ref)	1 (Ref)
	T_2	5.895 (1.464, 23.734)	9.099 (1.702, 48.650)	7.131 (1.286, 39.555)
	T_3	8.167 (2.034, 32.789)	23.561 (3.671, 151.217)	20.082 (3.103, 129.982)
	P_{trend}	0.003	0.001	0.002
Hypertension	T_1	1 (Ref)	1 (Ref)	1 (Ref)
	T_2	2.818 (1.475, 5.386)	2.228 (1.077, 4.611)	2.214 (1.069, 4.583)
	T_3	2.887 (1.508, 5.527)	2.051 (0.969, 4.341)	2.011 (0.945, 4.282)
	P_{trend}	0.002	0.070	0.079
Hyperlipidemia	T_1	1 (Ref)	1 (Ref)	1 (Ref)
	T_2	1.930 (0.816, 4.563)	0.444 (0.155, 1.274)	1.794 (0.614, 5.236)
	T_3	2.769 (1.180, 6.498)	0.904 (0.361, 2.264)	1.958 (0.668, 5.737)
	P_{trend}	0.020	0.150	0.239
Multimorbidity	T_1	1 (Ref)	1 (Ref)	-
	T_2	3.750 (1.135, 10.357)	5.014 (1.439, 17.473)	-
	T_3	4.545 (1.651, 12.512)	8.250 (2.165, 31.440)	-
	P_{trend}	0.004	0.002	-

Note: Model 1: Crude model. Model 2: Adjusted for age, gender, education, economic status, BMI, smoking status (yes/no), drinking status (yes/no), exercising status (yes/no). Model 3: Adjusted for diabetes (yes/no), hypertension (yes/no) or hyperlipidemia (yes/no).

contributes to the exacerbation of CI in those older adults.[40–43] In our study, the plasma levels of IL-1β, IL-18, TNF-α and CRP in older adults with diabetes, hypertension, hyperlipidemia and multimorbidity in CI group were significantly higher than those in CN group, suggesting that inflammation may affect the occurrence of CI in older adults with chronic diseases. The result of a systematic review and meta-analysis showed that CI among T2DM patients was associated with systemic inflammation.[44] This is consistent with our research results. The study by Jessica Youwakim also revealed that inflammation caused by long-term high blood pressure is an important predisposing factor of vascular damage for neurodegenerative diseases.[45] In addition, multiple studies have also shown that older adults with multimorbidity have higher levels of inflammation compared to those without multimorbidity, which may further increases the risk of CI.[46,47] These support an increased inflammatory–vascular interaction associated with CI in patients with chronic diseases. Consequently, considering how to reduce vascular inflammation or restore vascular functions, they could all be potential therapeutic strategies to prevent chronic disease and its associated cerebrovascular risks.

The E-DII and RRR-derived inflammatory dietary patterns can be used to objectively assess the inflammatory potential of a diet, which has been validated in several studies.[23,48] Our results showed that RRR-derived inflammatory dietary pattern and E-DII were associated with signs of inflammation in plasma of the whole older adults and the older adults with chronic diseases and multimorbidity, further providing evidence to explain the association between inflammatory dietary patterns and blood inflammation. In addition, similar to RRR-derived inflammatory dietary pattern, the Empirical Dietary Inflammatory Index (EDII) was developed based on the intake of food groups and inflammatory markers, and showed a strong ability to predict concentrations of plasma inflammatory markers as well.[49,50] However, considering that the selection of food groups tends to align with western dietary patterns, the use of EDII may be more applicable to populations with dietary structure similar to the developmental cohort. Choosing the appropriate method in different population studies contribute to developing more precise cognitive health maintenance strategies and customizing effective dietary intervention programs as well.

Previous studies demonstrated that greater pro-inflammatory diet potential were associated with an increased risk for CI.[51,52] In our study, the inflammatory dietary pattern among older adults was characterized by high intake of grain and

low intake of nut and wine. The staple foods of older adults in Taiyuan are mainly higher consumption of refined grains. A study has found that chronic consumption of refined carbohydrates has been linked to relative neurocognitive deficits across the lifespan.[53] A moderate consumption of nut and wine provides the protection against neurodegenerative diseases. This protective effect is most likely due to the presence of PUFA and phenolic compounds in nut and wine.[54,55] However, no significant association between the RRR-inflammatory dietary, E-DII and CI were found in the older adults in Taiyuan city. Further in-depth analysis revealed the significant association between pro-inflammatory diet and CI risk differed by the type and number of chronic diseases among the older adults in Taiyuan City. Statistically significant results were observed among the patients with diabetes and multimorbidity. In older adults with diabetes, the RRR-derived inflammatory dietary pattern was characterized by high consumption of SSBs, pickles, and low consumption of tubers, aquatic products, legumes, and nuts. Currently, for the prevention and control of T2DM and related vascular complications, it had been highly recommended to consume plenty of whole grains, vegetables, fruits, aquatic products, legumes and nuts, and limit the intake of processed meat products.[56] Interestingly, the actual intake of SSBs was very small in our participants, but we still found the relationship between SSBs and CI, which demands further research. It has been reported that the consumption of a great quantity of SSBs may cause high glycemic load (GL) and induce insulin resistance, which in turn exacerbates the inflammatory response.[57–59] Therefore, restricting the intake of SSBs may have a certain effect in preventing CI in older adults with diabetes.

Older adults rarely suffer from a single chronic condition. In contrast, multimorbidity is common after the age of 65. There is strong evidence demonstrating that CI is more common in older adults with higher multimorbidity.[60] Specially, a study that investigates the impact of specific multimorbidity pattern on the transitions across cognitive stages indicated that participants in the cardiovascular pattern exhibited an increased hazard of progression from MCI to dementia and for all transitions to death, which provides strong support for our current study on multimorbidity.[61] A study using NHANES data found that DII tended to be linearly associated with depression in patients with multimorbidity, and the ORs for risk of depression increased with the increase of DII, suggesting that pro-inflammatory diet may affect the brain nervous system of patients with multimorbidity.[62] Our results found that the pro-inflammatory diet, especially characterized by a low intake of tubers, legumes and nuts, could significantly increase the risk of CI in older adults with multimorbidity. This provides valuable data for the dietary prevention and treatment of CI in older adults with chronic diseases in Taiyuan city. Increasing scientific evidence has shown that nuts and legumes, can have anti-inflammatory properties and would benefit overall cognition level.[63,64] A very key reminder is that the beneficial effects are possible to come from wholesome nutritious diets rather than from individual nutrients.[65] So far, only a few studies have explored the connection between the inflammatory diet and CI of patients with multimorbidity. More research is still needed to elucidate the impact of inflammatory dietary pattern on cognitive deterioration in the patients with multimorbidity in the future.

This study also had a few limitations. First, due to the limited variety of nutritional components included in the China Food Composition Table, the parameters for calculating DII were incomplete. Second, we had only measurement of four pro-inflammatory markers, which may underestimate associations of the dietary indexes with the inflammatory markers. Third, only three chronic diseases including diabetes, hypertension and hyperlipidemia were included in the baseline survey. If more chronic diseases are taken into account, the results of the study will be more accurate. Fourth, due to the limited sample size of the survey population, patients with chronic diseases (diabetes or hypertension or hyperlipidemia) analyzed in this study may suffered from multiple diseases. Although other diseases besides the target disease were adjusted for the analysis, the results will still be affected to some extent. Last but not least, it is difficult to draw causal inferences regarding the etiological links between dietary inflammation and risk of CI using a cross-sectional design. More studies are warranted to replicate our work and verify the conclusions.

Conclusions

Our study provided new proof for the connection between inflammatory diet and risk of CI in patients with chronic diseases. Furthermore, this relationship varies depending on the type and quantity of chronic diseases. Specially, in older adults with diabetes and comorbidities, pro-inflammatory diet significantly increases the risk of CI. These results supplemented vital evidence for the prevention and treatment of CI in older adults with chronic diseases.

Abbreviations

CI, Cognitive Impairment; MCI, Mild Cognitive Impairment; IL-1β, Interleukin-1β; IL-18, Interleukin-18; TNF-α, Tumor Necrosis Factor-α; CRP, C-reactive Protein; Aβ, Amyloid β-protein; MD, Mediterranean Diet; DASH, Dietary Approaches to Stop Hypertension; DII, Dietary Inflammatory Index; RRR, Reduced Rank Regression; E-DII, Energy adjusted Dietary Inflammatory Index; CMMSE, Chinese Version of the Mini-Mental State Examination; CN, Cognitive Normal; FFQ, Food Frequency Questionnaire; SSBs, Sugar-sweetened Beverages; SFA, Saturated Fatty Acids; MUFA, Monounsaturated Fatty Acids; PUFA, Polyunsaturated Fatty Acids; SD, Standard Deviation; IQR, Interquartile Ranges; OR, Odds ratio; CIs, Confidence Intervals; BBB, Blood Brain Barrier; EDII, Empirical Dietary Inflammatory Index; GL, Glycemic load.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Informed Consent

This study adhered to the principles outlined in the Declaration of Helsinki. The study was reviewed and approved by the Medical Ethics Committee of Shanxi Medical University, China (protocol code 2014030 and date of approval 7th March, 2014). The patients/participants provided their written informed consent to participate in this study.

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An unauthorized version of the Chinese MMSE was used by the study team without permission, however this has now been rectified with PAR. The MMSE is a copyrighted instrument and may not be used or reproduced in whole or in part, in any form or language, or by any means without written permission of PAR (www.parinc.com). Therefore, we are very grateful to PAR Inc. for authorizing the use of the MMSE scale in this study.

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 report no conflicts of interest in this work.

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