Arthritis Research & Therapy

RESEARCH

Open Access

The comprehensive relationship between combined anti-inflammatory and healthy diets and all-cause mortality in rheumatoid arthritis: results from NHANES 2003–2018

Penghe Wang[1,2], Dongni Wang[1,2], Jiayu Sui[1,2], Shuang Liu[1,2], Yingjing Kong[1,2], Hongwei Lei[3*] and Maomao Zhang[1,2,4,5*]

Abstract

Background Rheumatoid arthritis (RA) is a chronic, systemic autoimmune inflammatory disorder. Diet is recognized as a modifiable factor that may influence inflammation and potentially accelerate RA progression. Nevertheless, the effects of diverse dietary patterns and their combined impact on RA progression and long-term mortality remain inadequately understood. This study examined the association between dietary patterns and mortality in patients with RA, focusing on the Healthy Eating Index (HEI-2015) and Dietary Inflammatory Index (DII) and evaluating their combined effects.

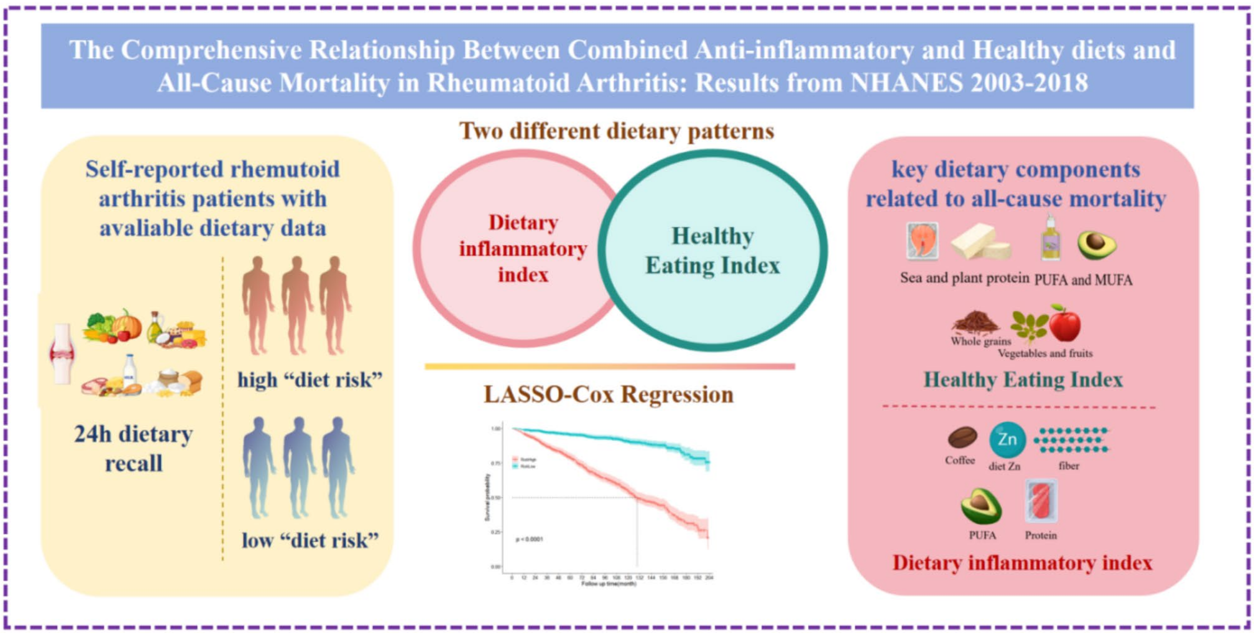
Methods The analysis included 2,069 patients with RA from the National Health and Nutrition Examination Survey (NHANES) spanning 2003–2018. Weighted multi-variable Cox regression models estimated the relationship between the DII, HEI-2015, combined dietary patterns, and all-cause mortality in patients with RA. Linear associations between the DII, HEI-2015, and all-cause mortality were analyzed using restricted cubic splines (RCS). Dietary factors associated with mortality were identified through the Least Absolute Shrinkage and Selection Operator (LASSO) method, and subgroup and sensitivity analyses were conducted to strengthen the findings.

Results Participants had a median age of 59 years (IQR: 48–69), with 42.1% male. Adjusting for potential confounders, the hazard ratio (HR) for individuals adhering to healthy and anti-inflammatory dietary patterns, as opposed to unhealthy and pro-inflammatory patterns, was 0.70 (95% CI: 0.53–0.92; adjusted $P = 0.01$; trend $P = 0.02$). In weighted Cox analyses of the DII and HEI-2015, higher quartiles showed no significant mortality risk difference from the lowest quartiles. The LASSO-Cox model identified 12 dietary components predictive of all-cause mortality in patients with RA, with an AUC of 0.749 (0.682–0.815) at 1 year, 0.763 (0.724–0.802) at 3 years, 0.783 (0.749–0.802) at 5 years, and 0.868 (0.712–0.938) for all death events. Kaplan-Meier analysis revealed that the low-risk dietary group exhibited significantly lower mortality compared to the high-risk group ($P < 0.001$).

*Correspondence:
Hongwei Lei
banboo428@163.com
Maomao Zhang
maomaolp1983@163.com
Full list of author information is available at the end of the article

Conclusions These findings suggest that combining a higher HEI-2015 with a lower DII score correlates with reduced all-cause mortality risk among patients with RA, supporting dietary modification as a potential strategy to prevent premature death in this population.

Graphic abstract



Keywords Rheumatoid arthritis, Dietary inflammatory index, HEI-2015, NHANES, All-cause mortality, United States

Background

Rheumatoid arthritis (RA) is an autoimmune disorder marked by progressive joint degradation, often leading to permanent disability and increased mortality. Long-term mortality risk factors in RA frequently involve comorbid conditions and elevated peripheral blood inflammatory markers [1, 2]. Notable among these are hypertension, coronary heart disease, diabetes, chronic inflammation, specific inflammatory markers like neutrophil-to-lymphocyte ratio (NLR), interleukin-6 (IL-6), C-reactive protein (CRP), and certain genetic loci [3–8].

Dietary factors have increasingly been acknowledged as significant modulators of systemic inflammation [9]. High-quality, well-balanced diets enriched with anti-inflammatory nutrients can effectively lower systemic inflammation levels [9–12]. Previous studies have examined dietary patterns and RA risk, including the association between the Mediterranean diet and reduced RA incidence [13, 14]; however, comprehensive research assessing RA mortality risk through dietary lenses remains limited.

Dietary factors influencing health outcomes often overlap, with different dietary indices capturing various dietary dimensions, addressing the limitations inherent in evaluating nutrients through isolated patterns. The Healthy Eating Index-2015 (HEI-2015) evaluates dietary quality by encompassing nutritional balance and micronutrient intake and is strongly linked with decreased mortality risk from cancer, cardiovascular diseases (CVD), frailty, and metabolic conditions [13, 15, 16]. Meanwhile, the Dietary Inflammatory Index (DII) gauges a diet's inflammatory potential and has been correlated with higher long-term mortality risk in cardiovascular, chronic kidney, and autoimmune diseases [17–19]. Although various dietary patterns, including the HEI-2015 and DII, have demonstrated effects on cardiovascular health and long-term mortality in the general population [13, 15, 16, 20–22], few studies have specifically examined these well-established dietary indices concerning long-term mortality in patients with RA, particularly within large-scale cohorts. Consequently, identifying dietary patterns that may reduce mortality risk in patients with RA is vital to addressing the research gap related to RA mortality and diet.

This study analyzed data from a large cohort within the National Health and Nutrition Examination Survey (NHANES) from 2003 to 2018 to evaluate associations between dietary health (via the HEI-2015) and anti-inflammatory potential (via the DII) with RA mortality risk. Additionally, LASSO-Cox regression identified key dietary factors within mixed dietary patterns associated with reduced mortality risk in patients with RA (See Graphic Abstract).

Materials and methods

Study design and population

This observational study included participants from the National Health and Nutrition Examination Survey (NHANES) 2003–2018, encompassing eight two-year cycles with a total of 80,312 participants. NHANES is a national program designed to assess the health and nutritional status of the U.S. population and provide data that inform health policies [23]. NHANES data is publicly accessible, and written informed consent was obtained from each participant. The NHANES protocol was approved by the CDC Institutional Review Board. As a policy, our local research ethics committee does not review secondary analyses of publicly approved data.

Participants were excluded based on the following criteria: (1) age ≤ 20 years, (2) non-rheumatoid arthritis or unclear arthritis etiology, (3) lack of dietary data, (4) pregnancy, and (5) lack of mortality follow-up data. After applying these exclusion criteria, a total of 2,069 participants with self-reported rheumatoid arthritis with available data were included in this study. As required by policy, our local ethics committee ensures no further analysis of the data (Fig. 1).

Definition of rheumatoid arthritis

Rheumatoid arthritis (RA) was ascertained based on self-reported health conditions in the NHANES questionnaire. Initially, participants were asked if a healthcare professional had ever diagnosed them with arthritis. Subsequently, those who responded affirmatively were further queried about the specific type of arthritis they had been diagnosed with. Participants who indicated "Rheumatoid arthritis" were subsequently categorized as RA patients [24, 25].

Dietary assessment

The dietary interview component, known as 'What We Eat in America,' was conducted collaboratively with the United States Department of Agriculture (USDA) and the U.S. Department of Health and Human Services, utilizing the standardized Automated Multiple Pass Method (AMPM). Dietary information was evaluated based on 24-hour recall data collected prior to the interview. In this study, dietary data were assessed by averaging two dietary recalls per participant or a single recall if only one was available. Among the 2,069 participants, 193 (9.33%) had solely one day of dietary recall data.

The Healthy Eating Index-2015 (HEI-2015) is a dietary quality index established by the United States Department of Agriculture (USDA) Nutrition Policy and Promotion Center, based on the Dietary Guidelines for Americans (DGA). It assesses diet quality and healthfulness by considering the consumption of various food groups including total fruits, whole fruits, total vegetables, vegetables and legumes, whole grains, dairy products, total protein foods, seafood and plant proteins, fatty acids, refined grains, sodium intake as well as added sugars and saturated fats. Scores range from 0 to 100 with higher scores indicating healthier diets [26, 27].

The Dietary Inflammatory Index (DII) is derived from the impact of inflammatory biomarkers from different foods, including IL-1β, IL-4, IL-6, IL-10, TNF-α, and CRP. Utilizing no more than 30 food parameters effectively maintains the predictive value of DII in assessing diet-related inflammation [28]. For this study, a total of 27 food parameters were considered: energy intake, protein

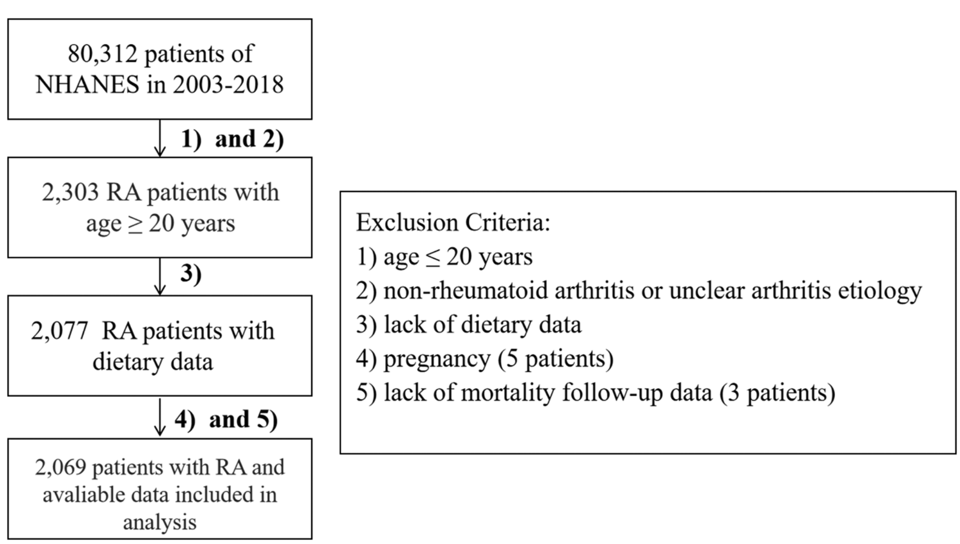


Fig. 1 Flow diagram of the selection of eligible participants

consumption, carbohydrate intake, dietary fiber content, total fat consumption, saturated fat intake, monounsaturated fatty acid (MUFA) intake levels as well as polyunsaturated fatty acid (PUFA) levels encompassing Omega-3 and Omega-6 fatty acids; cholesterol content; vitamin A concentration; β-carotene levels; vitamin B1 concentration; vitamin B2 concentration; niacin levels; vitamin B6 concentration; total folate content; vitamin B12 concentration; vitamin C level; vitamin D level; vitamin E level; magnesium content; iron content; zinc content; selenium content; caffeine consumption and alcohol consumption. Positive scores indicate pro-inflammatory potential while negative scores suggest anti-inflammatory potential. Theoretically speaking, DII scores range from −8.87 to +7.89 [29].

Ascertainment of mortality

Data on follow-up and mortality status were obtained by linking the NHANES data to the National Death Index records through December 31, 2019. All-cause mortality refers to death from any cause.

Assessment of covariates

We included several factors that could potentially affect the outcomes as covariates: sex (female, male), age (as a continuous variable), race/ethnicity (Non-Hispanic White, Non-Hispanic Black, Mexican American, others), education level (less than high school, high school, some college or above), smoking status (never smoked, former smoker, current smoker), physical activity was categorized into three groups: inactive, insufficiently active, and active. The inactive group included participants with no leisure-time physical activity. The insufficiently active group included participants who engaged in leisure-time moderate activity 1–5 times per week with MET (Metabolic Equivalent of Task) ranging from 3 to 6, or leisure-time vigorous activity 1–3 times per week with MET > 6 [30]. The active group included participants who had more leisure-time moderate or vigorous activity than the above criteria. Hypertension (yes, no), diabetes (yes, no), cardiovascular disease (yes, no), use of supplements (yes or no), body mass index (BMI) (as a continuous variable), and total calories intake (as a continuous variable). Data on physician-diagnosed history of hypertension, cardiovascular disease (including angina, myocardial infarction, heart failure, coronary heart disease, and stroke), and diabetes were self-reported.The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was used to estimate the glomerular filtration rate (eGFR) [31].

Statistical analysis

Considering the NHANES survey design, which accounts for sample weights, we used the first-day dietary recall weight divided by the number of cycles as the weight for subsequent analyses. The impact of diet on mortality risk was assessed using weighted Cox regression. For the HEI-2015 scores, we categorized them into four groups from the lowest to the highest based on quartiles: Q1 (HEI-2015 score < 41.67), Q2 (HEI-2015 score between 41.67 and 49.98), Q3 (HEI-2015 score between 49.98 and 58.75), and Q4 (HEI-2015 score > 58.75). For the DII scores, we divided them into quartiles from the highest to the lowest: Q1 (DII score > 2.84), Q2 (DII score between 1.79 and 2.84), Q3 (DII score between 0.37 and 1.79), and Q4 (DII score < 0.37). Subsequently, we integrated the two dietary patterns and classified them based on the median of HEI-2015 and DII into "relatively healthy diet" (HEI-2015 > 49.95), "relatively unhealthy diet" (HEI-2015 ≤ 49.95), "relatively pro-inflammatory diet" (DII > 1.78), and "relatively anti-inflammatory diet" (DII ≤ 1.78).Model 1 included no adjustments, Model 2 adjusted for age, sex, and race, and Model 3 further adjusted for education level, smoking status, physical activity, BMI, dietary supplement intake, total calorie intake, and medical history (self-reported diabetes, hypertension, and coronary heart disease). Covariates with missing values were imputed using the multiple imputation by chained equations method (Fig S1).

To identify dietary predictors associated with reduced mortality and mitigate collinearity among variables, We utilized the LASSO regression technique, which minimizes the coefficients of less influential variables to zero, thereby enhancing the model's predictive accuracy [32]. The LASSO model was evaluated and fine-tuned using cross-validation, where the dataset was partitioned into ten subsets. The model was then iteratively trained and evaluated on these subsets to evaluate its effectiveness and identify optimal parameter settings. During cross-validation, a plot of model performance against various lambda values is commonly created to evaluate the model's effectiveness at different settings. The "minimum deviance" represents the lambda value with the least bias identified through cross-validation, indicating the best data fit. We chose the lambda value associated with the minimum deviance as the best fit. Additionally, a nomogram for risk prediction was developed based on critical dietary factors, and its ability to forecast mortality risk was confirmed using the receiver operating characteristic (ROC) curve. Furthermore, we conducted Kaplan-Meier analysis, mediation analysis, subgroup analysis, and sensitivity analysis based on key variables linked to mortality risk in order to elucidate potential relationships. Analyses were performed using R version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria). Two-sided $P < 0.05$ was considered statistically significant.

Results

Patient characteristics

A total of 2,069 patients with RA (57.9% women, median age 59 years, IQR: 48–69 years) were enrolled and categorized based on dietary patterns, as detailed in the 'Methods' section. Patient characteristics are summarized in Table 1. Compared with those following unhealthy and pro-inflammatory diets, individuals adhering to healthier, less inflammatory diets were more likely to be male, older, have a lower body mass index (BMI), possess higher education levels, be non-smokers, engage in more physical activity, and have elevated high-density lipoprotein (HDL) levels (Table 1 and Table S1).

Table 1 Basic characteristics of participates with RA based on different dietary pattern [a]

Variables	Total (*n* = 2069)	Unhealthy and Pro -Inflammatory diet (*n* = 692)	Combined diet pattern[c] (*n* = 684)	Healthy and Anti -Inflammatory diet (*n* = 693)	*P*-value
Weighted No.	8,865,698	2,884,967	2,757,382	3,223,349	
Age, (IQR), years	59(48,69)	57(48,65)	57(48,65)	59(52,70)	< 0.001
Gender					
Male	870(42.1%)	248(33.6%)	295(42.8%)	327(49.1%)	< 0.001
Female	1199(57.9%)	444(66.4%)	389(57.2%)	366(50.9%)	
Race					
Mexican American	301(7.2%)	77(6.6%)	103(7.1%)	121(7.8%)	0.2
Non-Hispanic Black	625(17.1%)	237(20.1%)	202(17.2%)	186(14.3%)	
Non-Hispanic White	847(65.3%)	289(63.2%)	282(66.7%)	276(66.0%)	
Other[b]	296(10.4%)	89(10.2%)	97(8.9%)	110(11.9%)	
BMI, (IQR), kg/m^2	29.5(25.2,34.2)	31(26,36)	29.54(25.5,34.1)	28.4(24,32.8)	< 0.001
Education level					
Less than High school	702(24.2%)	260(26.3%)	245(28.7%)	197(18.5%)	0.001
High school	505(26.5%)	179(30.9%)	172(24.5%)	154(24.1%)	
Some College or above	859(49.3%)	252(42.8%)	267(46.8%)	340(57.4%)	
Family income to poverty ratio					
< 1.0	501(20.8%)	201(26.3%)	166(20.1%)	134(16.2%)	0.009
1.0–3.0	887(43.8%)	318(44.3%)	293(44.5%)	276(42.8%)	
> 3.0	517(35.4%)	137(29.5%)	165(35.4%)	215(41.0%)	
Smoking status					
Never	921(40.3%)	257(33.6%)	314(42.1%)	350(44.6%)	< 0.001
Former	887(43.8%)	318(44.3%)	293(44.5%)	276(42.8%)	
Current	492(26.9%)	242(38.1%)	144(24.0%)	106(19.5%)	
Use of Supplement					
Yes	1193(61.9%)	328(51.0%)	389(58.9%)	476(74.1%)	< 0.001
No	876(38.1%)	364(49.0%)	295(41.1%)	217(25.9%)	
Physical Activity					< 0.001
active	139(6.9%)	27(3.8%)	44(4.8%)	68(11.6%)	
insufficient	622(36.8%)	174(32.0%)	197(33.8%)	251(43.6%)	
no	1256(56.3%)	473(64.3%)	430(61.4%)	353(44.8%)	
Medical History					
Diabetes					
Yes	538(20.5%)	181(21.2%)	182(20.3%)	175(20.1%)	> 0.9
No	1531(79.5%)	511(78.8%)	502(79.7%)	518(79.9%)	
Hypertension					
Yes	1259(55.2%)	431(58.8%)	420(55.4%)	408(51.7%)	0.2
No	809(44.8%)	261(41.2%)	264(44.6%)	284(48.3%)	
Cardiovascular Disease					
Yes	528(24.4%)	202(27.9%)	173(24.5%)	153(21.0%)	0.11
No	1541(75.6%)	490(72.1%)	511(75.5%)	540(79.0%)	

a.All estimates accounted for complex survey designs, and all percentages are weighted

b.Other race and ethnicity includes other Hispanic, other non-Hispanic, and multirace individuals

c.Unhealthy but Anti-Inflammatory diet or Healthy but Pro-Inflammatory diet

Association between dietary patterns and mortality

Table 2 presents the associations between various dietary patterns and mortality among patients with RA. Analysis of DII and HEI-2015 indices, categorized into quartiles, indicated that lower DII scores and higher HEI-2015 scores were linked to a reduced long-term mortality risk (median hazard ratios: 0.85 and 0.74, respectively). However, these associations were not statistically significant after adjusting for confounding variables (adjusted P-values: 0.5 and 0.05; trend P-values: 0.08 and 0.05, respectively).

The combined effects of DII and HEI-2015 on mortality risk were further assessed by stratifying patients into three groups according to median DII and HEI-2015 values, as specified in the 'Methods' section. After confounder adjustment, adherence to a healthy and anti-inflammatory diet was associated with a 26% reduction in long-term mortality risk compared to an unhealthy and pro-inflammatory diet (HR: 0.70 [95% CI: 0.53–0.92], adjusted $P=0.01$; P for trend=0.02). Additionally, a diet that was relatively healthy but pro-inflammatory, or relatively anti-inflammatory but unhealthy, still demonstrated a modest reduction in long-term all-cause mortality risk compared to a fully unhealthy and pro-inflammatory diet (HR: 0.74 [0.57–0.98], adjusted $P=0.04$).

Restricted cubic splines (RCS) analysis did not reveal significant non-linear associations between DII and HEI-2015 scores and long-term mortality outcomes (Figure S2).

Subgroup analyses

Subgroup analyses were performed by stratifying by age (<60, ≥ 60 years), sex, BMI (<25; 25–29.9, ≥ 30), education level, smoking status, CVD, hypertension, diabetes, physical activity and estimated glomerular filtration rate (eGFR) to examine whether the effects of the composite dietary pattern differed across these subgroups. No significant interaction effects were observed for age, sex, education level, CVD, diabetes, or eGFR. However, in patients with RA exhibiting a normal BMI, current smokers, and those with hypertension, adherence to a low-inflammatory, healthy diet was associated with a more pronounced reduction in mortality (Table 3).

Table 2 Weighted Cox regression analysis on the association of dietary patterns and mortality among RA patients

diet pattern	Hazard Ratio (95%CI) Model 1[a]	P value	Hazard Ratio (95%CI) Model 2[b]	P value	Hazard Ratio (95%CI) Model 3[c]	P value
DII						
Q1(> 2.84)	Reference		Reference		Reference	
Q2(1.79,2.84)	1.25[0.92,1.68]	0.2	0.98[0.72,1.34]	> 0.9	1.21[0.85,1.72]	0.6
Q3(0.37,1.79)	0.78[0.56,1.11]	0.2	0.71[0.51,0.97]	0.03	0.94[0.65,1.38]	0.8
Q4(< 0.37)	0.72[0.49,1.08]	0.11	0.59[0.38,0.91]	0.02	0.85[0.53,1.35]	0.5
P for trend	0.016		0.003		0.08	
HEI-2015						
Q1(< 41.67)	Reference		Reference		Reference	
Q2(41.67,49.98)	1.09[0.79,1.52]	0.6	0.81[0.58,1.12]	0.3	0.86[0.60,1.23]	0.4
Q3(49.98,58.75)	1.09[0.81,1.47]	0.6	0.64[0.47,0.86]	0.003	0.77[0.56,1.05]	0.1
Q4(> 58.75)	1.01[0.68,1.51]	> 0.9	0.53[0.36,0.78]	0.001	0.69[0.47,1.01]	0.05
P for trend	0.9		< 0.001		0.05	
Composition effect						
Unhealthy and Pro -Inflammatory diet(DII > 1.78 and HEI-2015 < 49.95)	Reference		Reference		Reference	
Combined diet pattern[d] (DII < 1.78 and HEI-2015 < 49.95;or DII > 1.78 and HEI-2015 > 49.95)	0.86[0.63,1.17]	0.3	0.65[0.50,0.85]	0.002	0.74[0.57,0.98]	0.04
Healthy and Anti -Inflammatory diet (DII < 1.78 and HEI-2015 > 49.95)	**0.75[0.55,1.01]**	**0.06**	**0.53[0.39,0.72]**	**< 0.001**	**0.70[0.53,0.92]**	**0.01**
P for trend	0.06		< 0.001		**0.02**	

[a] The crude model did not adjust for any covariates

[b] Model 2 was adjusted for age, sex and race

[c] Further adjusted for educational levels, physical activity, smoking status, body mass index, diabetes, hypertension, cardiovasuclar disease, use of supplements, total Kal intake and eGFR

[d] Unhealthy but Anti-Inflammatory diet or Healthy but Pro-Inflammatory diet

Table 3 .Subgroup analyses of compisition diet effect and mortality risk in RA

	Hazard Ratio(95%CI)			
Characteristic	**Unhealthy and Pro -Inflammatory diet**	**Combined diet pattern[a]**	**Healthy and Anti -Inflammatory diet**	***P* for interaction**
Age, years				
< 60	Reference	0.60[0.27,1.32]	0.85[0.44,1.63]	0.8
≥ 60	Reference	0.79[0.57,1.09]	0.61[0.43,0.87]	
Gender				
Male	Reference	0.70[0.42,1.17]	0.62[0.41,0.95]	0.11
Female	Reference	0.76[0.52,1.12]	0.82[0.57,1.18]	
BMI, kg/m^2				
< 25.0	Reference	0.67[0.39,1.17]	**0.36[0.22,0.59]**	**0.003**
25.0-29.9	Reference	0.72[0.41,1.26]	0.75[0.42,1.33]	
≥ 30.0	Reference	0.87[0.52,1.46]	1.10[0.64,1.88]	
Education level				
Less than High school	Reference	0.71[0.42,1.22]	0.88[0.52,1.49]	0.8
High school	Reference	1.50[0.81,2.77]	0.71[0.38,1.34]	
Some College or above	Reference	0.47[0.29,0.78]	0.55[0.35,0.86]	
Smoking status				
Never	Reference	0.85[0.56,1.29]	0.89[0.55,1.43]	**0.03**
Former	Reference	0.90[0.54,1.50]	0.94[0.53,1.68]	
Current	Reference	0.71[0.39,1.32]	**0.32[0.16,0.65]**	
CVD				
Yes	Reference	0.73[0.45,1.18]	0.66[0.41,1.06]	0.6
No	Reference	0.84[0.58,1.21]	0.75[0.50,1.11]	
Hypertension				
Yes	Reference	0.33[0.19,0.56]	**0.35[0.21,0.57]**	**0.017**
No	Reference	0.98[0.67,1.44]	0.90[0.65,1.26]	
Diabetes				
Yes	Reference	0.81[0.47,1.37]	0.70[0.40,1.22]	0.4
No	Reference	0.74[0.52,1.06]	0.70[0.50,1.00]	
eGFR				
≤ 60	Reference	1.01[0.67,1.52]	0.74[0.46,1.17]	0.2
≥ 60	Reference	0.64[0.43,0.96]	0.70[0.49,1.02]	
Physical Activity				
No	Reference	0.77[0.54,1.10]	0.65[0.46,0.92]	0.7
Insufficient	Reference	0.47[0.25,0.89]	0.81[0.47,1.38]	
Active	Reference	6.6[1.12,14]	1.65[0.16,17.2]	

Adjusted for age, sex, race and ethnicity, educational levels, physical activity, smoking status, body mass index, diabetes, hypertension, cardiovascular disease, hypertension, use of supplements, total Kal intake and eGFR

Identification of critical dietary factors associated with mortality in patients with RA

LASSO regression, which incorporates an L1 regularization term (absolute value penalty) into ordinary least squares regression, selectively shrinks certain coefficients to zero, identifying the most critical features. This technique mitigates overfitting, enhances generalization, and facilitates feature selection, particularly useful with correlated features, thereby improving model interpretability and performance. In LASSO regression, coefficient shrinkage is achieved by minimizing the loss function combined with the L1 regularization term, driving some coefficients to zero and effectively excluding non-essential features (Fig. 2A and B).

The analysis incorporated age, sex, race, and dietary scores from HEI-2015 and DII to enhance the model's predictive accuracy. Key dietary components linked to long-term mortality risk in patients with RA included a high DII score for caffeine, indicating low caffeine intake, and low DII scores for fiber, protein, zinc (Zn), and polyunsaturated fatty acids (PUFA), indicating high intake of these nutrients (Fig. 3A). Additionally, a low HEI-2015 score for refined grains implied high refined grain consumption, while high HEI-2015 scores for saturated fats, seafood and plant proteins, fatty acids, vegetables, fruits, and whole grains indicated low intake of saturated fats and high intake of seafood, plant proteins, vegetables, and fruits. Overall, patients with RA following a diet rich

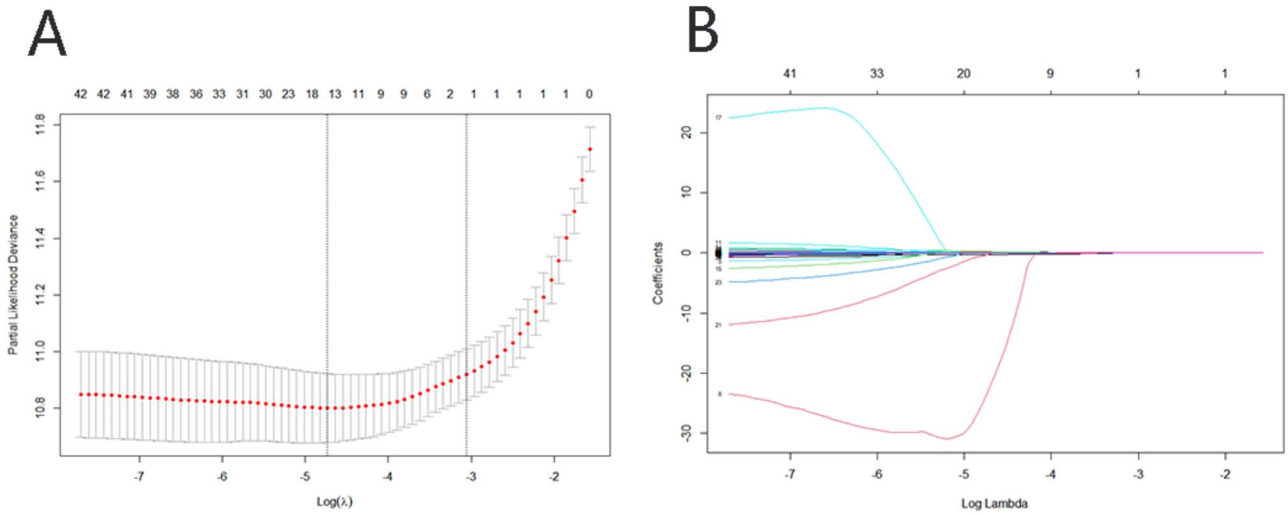


Fig. 2 LASSO penalized regression analysis used to identify key dietary factors associated with RA mortality. **A**. The coefficient shrinkage process of all 40 dietary components score and 3 covariates (gender, age, race). **B**. Ten-fold cross-validation for the LASSO regression

in caffeine, fiber, protein, zinc, and PUFA, and low in refined grains, exhibited a notably reduced risk of long-term mortality. In contrast, a diet high in saturated fats and low in seafood, plant proteins, vegetables, and fruits was associated with an elevated mortality risk. These results highlight the significance of balanced dietary patterns in managing RA and improving patient outcomes. A dietary risk score was generated for each patient, classifying them as "low-risk" if below the median and "high-risk" if above. Kaplan–Meier survival analysis demonstrated that high-risk patients faced significantly higher long-term mortality compared to low-risk counterparts (Fig. 3B). Furthermore, the predictive accuracy for all-cause mortality was robust, as reflected by the area under the receiver operating characteristic (ROC) curve (AUC): AUCs of 0.749 (0.682–0.815) for one-year, 0.763 (0.724–0.802) for three-year, 0.783 (0.749–0.802) for five-year predictions, and 0.868 (0.712–0.938) for all death events (Fig. 3C). These AUC values demonstrate strong predictive accuracy for mortality across the specified time frames.

Sensitivity analysis

In sensitivity analysis, participants who died within the first two years of follow-up were excluded. Results indicated that adherence to a healthy and anti-inflammatory diet reduced mortality risk by 29% (95% CI: 0.52–0.96, adjusted $P=0.03$, P for trend=0.03), even with adjustments for all confounding factors, underscoring the model's robustness (Table S1 and Table S2). Additionally, excluding individuals with missing data (N for analysis = 1,728; n for missing = 341) yielded similar results: patients with a healthy and anti-inflammatory diet continued to show a lower long-term mortality rate (HR: 0.72, 95% CI: 0.52–0.99, adjusted $P=0.04$, P for trend = 0.04).

Discussion

This study conducted a novel analysis of the synergistic impact of the DII and the HEI on all-cause mortality among patients with self-reported RA. Results indicated that neither index alone showed a statistically significant association with long-term all-cause mortality after adjustment for comprehensive lifestyle-related confounders. However, when both indices were integrated into a unified dietary assessment, patients with RA following a combined anti-inflammatory and health-promoting diet exhibited a 30% reduction in mortality risk ($P=0.01$; P for trend = 0.02). From a comprehensive list of 40 dietary items, 12 key items emerged as the most predictive of long-term mortality in patients with RA, including caffeine, total fat, Zn, PUFA, protein, and dietary fiber, which contribute to the DII score, along with daily intake levels of total fruits, whole grains, vegetables, refined grains, fatty acids, sea plant protein, and saturated fatty acids, components of the HEI score. By combining these essential dietary factors with demographic variables such as age and race/ethnicity, a nomogram model was developed, demonstrating strong predictive performance for long-term mortality in patients with RA.

The population was initially categorized into three groups based on adherence to DII and HEI-2015 dietary patterns: (1) Anti-inflammatory and healthy diet, (2) Pro-inflammatory and unhealthy diet, and (3) Mixed diet, situated between these extremes. Predictably, individuals with healthier, more balanced dietary habits aligned with anti-inflammatory and HEI-2015 guidelines displayed better lifestyle practices, including less smoking,

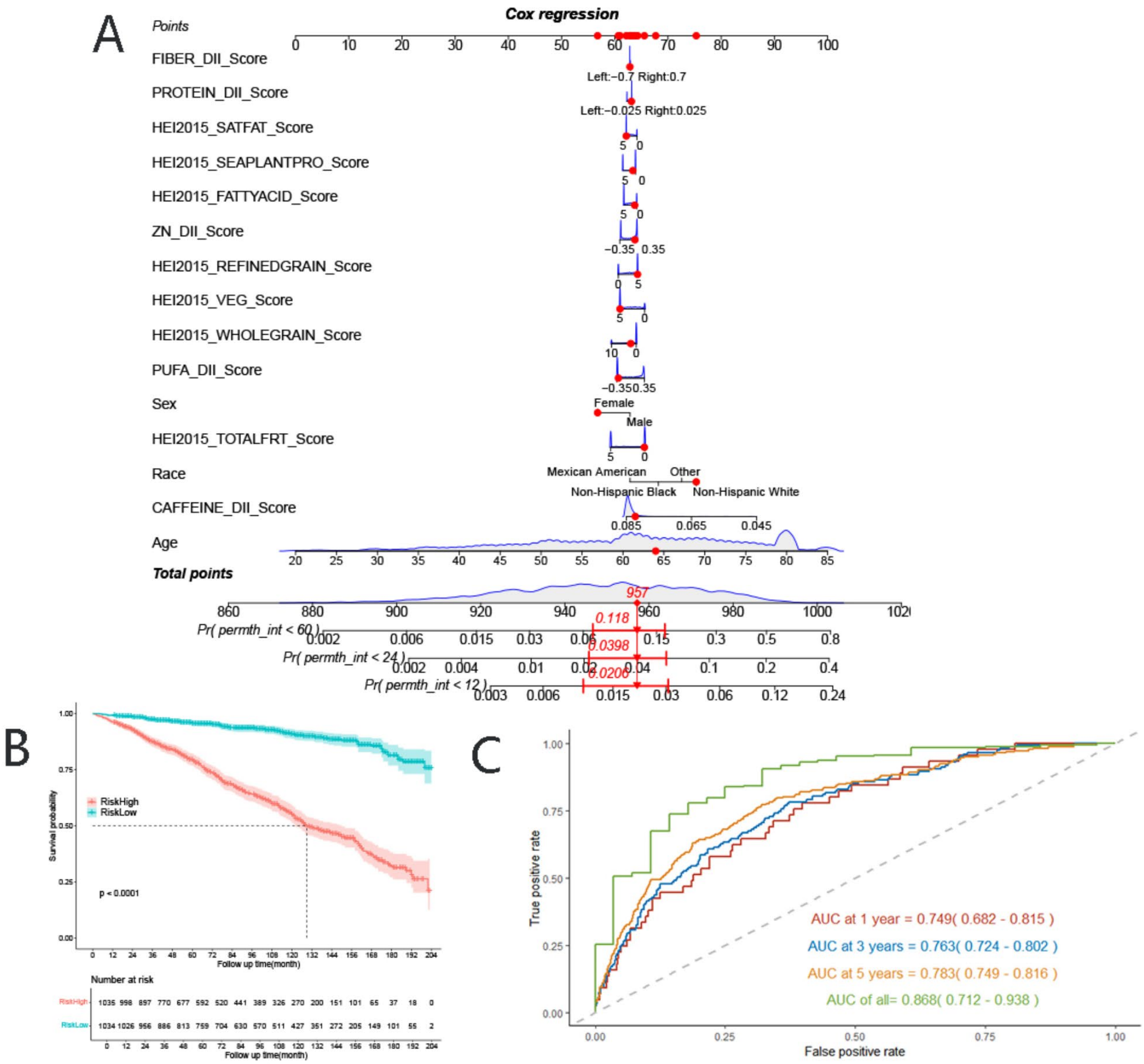


Fig. 3 Establishment and validation of the RA mortality risk model. **A**. LASSO regression nomogram based on age, race, sex, and dietary component scores. **B**. Kaplan-Meier survival analysis for high-risk and low-risk groups identified by LASSO regression. **C**.ROC curve for evaluating the predictive power for all-cause mortality among patients with RA of the nomogram model. LASSO, least absolute shrinkage and selection operator; ROC, receiver operating characteristic

regular dietary supplement use, more frequent physical activity, and healthier body weights. Unexpectedly, baseline differences emerged, with individuals following healthier diets tending to be older. Comparative studies suggest that older Mexican Americans often exhibit higher diet quality due to greater fruit and vegetable intake and reduced carbohydrate consumption compared to younger individuals [33]. Similarly, U.S. nationwide dietary surveys indicate that children and the elderly tend to have better diet quality than younger adults [34]. Additionally, in this study, males demonstrated higher diet quality than females, necessitating adjustment for these potentially influential confounders in subsequent statistical analyses.

Although low levels of the HEI and high levels of the DII have been extensively studied as independent dietary scores, with associations found between these indices and the incidence of RA in cross-sectional studies, no statistically significant correlation was observed between individual DII or HEI scores and long-term all-cause mortality in patients with RA in this study. [35–39] Unexpectedly, when both indices were assessed collectively, patients with RA exhibiting high HEI and low DII scores demonstrated significantly reduced long-term mortality

(HR: 0.70 [0.53, 0.92], adjusted $P=0.01$). This finding may reflect the multifaceted and far-reaching influence of diet on the long-term trajectory and prognosis of RA, encompassing factors such as gut microbiota composition, amino acid metabolism, and overall nutritional status [40, 41]. As previously reported, no clear relationship has been established between DII and RA progression or functional disability [42]. Moreover, several studies have suggested that the indirect effects of diet on long-term mortality in patients with RA are significant. For example, Tian et al. found that malnutrition, assessed through the Controlled Nutritional Status Score (CONUT) and the Nutritional Risk Index (NRI), significantly increases long-term mortality in patients with RA [43]. The HEI score, which broadly assesses adherence to balanced nutritional guidelines, effectively reflects the nutritional richness of a patient's diet [44]. Additionally, the triglyceride glucose (TyG) index, a reliable surrogate marker for insulin resistance (IR), has been linked to an increased risk of long-term cardiovascular events in patients with RA [45]. TyG also plays a pivotal role in mediating the effects of DII on the development and adverse prognosis of various diseases, such as COPD, chronic kidney disease, CVD, and diabetes [20, 21, 45–49]. This may suggest that, within the heterogeneous RA population, dietary components do not exhibit a simple, linear relationship with long-term prognosis. For instance, Cai et al. reported that vitamin D intake exhibits a significant nonlinear association with long-term mortality in patients with RA [50]. While a fiber-rich diet may reduce peripheral blood inflammation, excessive fiber intake could exacerbate RA severity through its effects on gut microbiota [51]. By integrating multiple dietary scores, a more holistic assessment of a patient's dietary status is possible, allowing for evaluation from different perspectives. The combined consideration of DII and HEI not only assesses the impact of dietary components on inflammatory status but also addresses the nutritional status of the patient and the overall healthiness of the diet, providing a more precise and comprehensive dietary evaluation for the long-term prognosis of patients with RA.

This study highlights specific dietary components significantly associated with comprehensive dietary patterns linked to all-cause mortality, particularly among individuals with RA. Key dietary factors identified as crucial for predicting all-cause mortality in this population include caffeine, fruits, PUFA, whole grains, vegetables, refined grains, Zn, fatty acids, sea plant protein, saturated fatty acids, protein, and fiber. These findings emphasize the pivotal role of a balanced diet in reducing the risk of all-cause mortality in patients with RA.

Contrary to initial expectations, the nomogram analysis revealed that some foods traditionally considered pro-inflammatory were linked to reduced long-term mortality, while certain foods with recognized health benefits were associated with increased long-term mortality risk. The relationship between caffeine intake and long-term prognosis is complex and remains uncertain [52]. While extensive research generally associates high caffeine consumption with lower all-cause mortality, some cross-sectional studies have identified potential links to increased cardiovascular risks and mortality, particularly in individuals with CVD or higher body weight [53, 54]. Consistent with our findings suggesting that coffee negatively affects individuals with rheumatoid disease, a meta-analysis has indicated that coffee consumption is associated with an elevated risk of developing rheumatoid arthritis [55]. Furthermore, although excessive intake of refined grains is widely acknowledged as a risk factor for various health issues, including obesity, cardiovascular diseases, increased inflammation, and gut microbiome disruption, our results suggest that moderate refined grain consumption, rather than minimal intake, may be associated with reduced long-term mortality in patients with RA.

This study identified ten key dietary components that align with expectations and may be associated with a reduced long-term mortality risk in patients with RA. These factors include high fiber intake, low protein intake, high zinc intake, and high PUFA intake (which contribute to a low DII score), as well as low intake of saturated fats, high intake of seafood and plant proteins, a high proportion of monounsaturated fatty acids, and high intake of vegetables, fruits, and whole grains (which contribute to a high HEI score). In the general population, high fiber intake is consistently associated with reduced long-term mortality [56]. Three large cross-sectional studies have indicated that a high-fiber diet correlates with a lower risk of developing rheumatoid arthritis, while two small randomized controlled trials suggest that a high-fiber diet may help alleviate disease activity in patients with RA [57–61]. The evidence linking protein intake to all-cause mortality is mixed [51, 62, 63]. Our results indicate that a low total protein diet, combined with high intake of seafood and plant proteins, may be associated with reduced all-cause mortality in patients with RA. This is consistent with findings from the general population, where consumption of seafood and plant proteins has been linked to lower all-cause and cardiovascular mortality [62, 64, 65]. The Mediterranean diet, which emphasizes plant-based and seafood proteins, adequate fruits and vegetables, whole grains, a balanced intake of unsaturated fatty acids, and low saturated fat consumption, is well-known for its potential to reduce RA incidence, decrease cardiovascular disease risk in patients with RA, improve metabolic health, and enhance long-term quality of life [66–68]. Although insufficient research exists to conclusively support the Mediterranean diet's impact on reducing long-term mortality in patients with RA, our study suggests that the components of this diet may contribute significantly to reducing long-term mortality risk in RA.

Zn is an essential mineral involved in numerous biological processes, including maintaining insulin homeostasis, modulating inflammatory responses, and participating in antioxidant defense, neuronal development, and neurogenesis [69]. Decades of research have shown that zinc levels are reduced in the blood of patients with RA [70, 71]. The relationship between dietary zinc intake and long-term all-cause mortality in patients with RA remains underexplored. However, our findings support the idea that zinc intake may be linked to a reduction in long-term mortality among patients with RA. This specific dietary pattern, consisting of 12 key dietary factors, appears to be associated with a reduced long-term mortality risk in this patient population.

The novelty of this study lies in its exploration of the combined effects of two distinct dietary patterns and their associated protective factors on all-cause mortality among individuals with RA. This research provides new insights into the specific and comprehensive dietary characteristics that may influence the long-term prognosis of patients with RA. However, several limitations of the study should be acknowledged. Firstly, the case-control design precludes the establishment of a causal relationship between diet quality and all-cause mortality. Nonetheless, the findings suggest that dietary patterns and quality are significant factors impacting the long-term prognosis of patients with RA, laying the groundwork for further causal investigations. Secondly, dietary nutrient intakes were derived from 24-hour dietary recalls, which may not fully capture long-term daily dietary exposure. However, evidence supports the validity of 24-hour recalls, showing a strong correlation with food frequency questionnaires, which are commonly used to assess long-term dietary habits. Thirdly, self-reporting, the primary method for efficiently collecting dietary intake data, introduces the potential for recall bias due to its inherent limitations [72]. For example, the reported RA prevalence of 2.8% in the NHANES sample exceeds the generally accepted prevalence of 1% or less in the United States, highlighting the need for caution in data interpretation. Fourthly, since not all food items contribute equally to dietary inflammation levels and quality, this study employed scores from the DII and the HEI-2015 in the LASSO-Cox regression, rather than considering the intake of individual food items. Thus, when interpreting the dietary component findings, it is important to account for the weighted scores of food items.

Despite these limitations, our study supports the notion that specific dietary compositions, particularly those related to inflammation and overall health, are strongly linked to the long-term mortality of patients with RA. Additionally, unmeasured confounding factors, such as environmental and genetic influences, may also play a role. As a result, further exploration and validation of these findings in cohort studies and prospective research are warranted.

Conclusions

Our findings suggest that healthy and anti-inflammatory dietary habits are associated with reduced all-cause mortality in individuals with RA. However, single assessments of healthy and anti-inflammatory diets alone did not show a significant correlation with all-cause mortality in this population. Additionally, 12 dietary components were identified as significantly linked to all-cause mortality. Future research should focus on developing comprehensive nutritional guidelines for patients with RA and investigate the potential interactive mechanisms underlying these associations.

Abbreviations

BMI	Body mass index
CI	Confidence interval
eGFR	Estimated glomerular filtration rate
HR	Hazard ratio
KM	Kaplan–Meier
NHANES	National Health and Nutrition Examination Survey
DII	Dietary Inflammation Index
HEI-2015	Health Eating Index-2015
RCS	Restricted cubic spline
RA	Rheumatoid arthritis
CVD	Cardiovascular disease

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13075-024-03462-y.

Supplementary Material 1

Acknowledgements

The authors express their gratitude to all the participants and staff of the National Health and Nutrition Examination Survey, as well as the National Center for Environmental Health, for their invaluable contributions.

Author contributions

PH W , DN W, JY S and S L collected the data and performed data analysis. PH W and YJ K wrote the manuscript. MM Z and HW L supervised and managed the study activities. All authors assisted to examine the data and statistic computation process. All authors were involved in the design of the study protocol and reviewed the manuscript. The authors read and approved the final manuscript.

Funding

This research was funded by the National Natural Science Foundation of China(grants 82070511, 82270525, 82201991) and the Natural Science Foundation of Hei longjiang Province (GA23C006).

Data availability

The data underlying this article are available in NHANES (https://www.cdc.gov/nchs/nhanes/).

Declarations

Ethics approval and consent to participate
No applicable.

Consent for publication
No applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Cardiology, The Second Affiliated Hospital of Harbin Medical University, Harbin, China
[2]Key Laboratory of Myocardial Ischemia, Ministry of Education, Harbin Medical University, Harbin, China
[3]Department of Rheumatology and Immunology, 2nd Affiliated Hospital of Harbin Medical University, Harbin 150001, PR China
[4]State Key Laboratory of Frigid Zone Cardiovascular Diseases (SKLFZCD), Harbin, China
[5]Department of Cardiology, Key Laboratory of Myocardial Ischemia, The Second Affiliated Hospital of Harbin Medical University, Chinese Ministry of Education, 246 Xuefu Road, Harbin 150086, China

Received: 16 July 2024 / Accepted: 15 December 2024
Published online: 23 December 2024

References
1. Sayah A, English JC. 3rd: rheumatoid arthritis: a review of the cutaneous manifestations. J Am Acad Dermatol. 2005;53(2):191–209. quiz 210 – 192.
2. Black RJ, Lester S, Tieu J, Sinnathurai P, Barrett C, Buchbinder R, Lassere M, March L, Proudman SM, Hill CL. Mortality estimates and excess mortality in rheumatoid arthritis. Rheumatology (Oxford). 2023;62(11):3576–83.
3. Li H, Pan X, Zhang S, Shen X, Li W, Shang W, Wen Z, Huang S, Chen L, Zhang X, et al. Association of autoimmune diseases with the occurrence and 28-day mortality of sepsis: an observational and mendelian randomization study. Crit Care. 2023;27(1):476.
4. Avci AB, Feist E, Burmester GR. Targeting IL-6 or IL-6 receptor in rheumatoid arthritis: what have we learned? BioDrugs. 2024;38(1):61–71.
5. Videm V, Liff MH, Hoff M. Relative importance of inflammation and cardio-respiratory fitness for all-cause mortality risk in persons with rheumatoid arthritis: the population-based Trondelag Health Study. RMD Open 2023, 9(3).
6. Dadoun S, Zeboulon-Ktorza N, Combescure C, Elhai M, Rozenberg S, Gossec L, Fautrel B. Mortality in rheumatoid arthritis over the last fifty years: systematic review and meta-analysis. Joint Bone Spine. 2013;80(1):29–33.
7. Anyfanti P, Gavriilaki E, Douma S, Gkaliagkousi E. Endothelial dysfunction in patients with rheumatoid arthritis: the role of hypertension. Curr Hypertens Rep. 2020;22(8):56.
8. Zhou E, Wu J, Zhou X, Yin Y. The neutrophil-lymphocyte ratio predicts all-cause and cardiovascular mortality among U.S. adults with rheumatoid arthritis: results from NHANES 1999–2020. Front Immunol. 2023;14:1309835.
9. Giugliano D, Ceriello A, Esposito K. The effects of diet on inflammation: emphasis on the metabolic syndrome. J Am Coll Cardiol. 2006;48(4):677–85.
10. Christ A, Lauterbach M, Latz E. Western Diet and the Immune System: an inflammatory connection. Immunity. 2019;51(5):794–811.
11. Hebert JR, Shivappa N, Wirth MD, Hussey JR, Hurley TG. Perspective: the Dietary Inflammatory Index (DII)-Lessons learned, improvements made, and future directions. Adv Nutr. 2019;10(2):185–95.
12. Shi H, Schweren LJS, Ter Horst R, Bloemendaal M, van Rooij D, Vasquez AA, Hartman CA, Buitelaar JK. Low-grade inflammation as mediator between diet and behavioral disinhibition: a UK Biobank study. Brain Behav Immun. 2022;106:100–10.
13. Li L, Wan Z, Geng T, Lu Q, Zhu K, Qiu Z, Zhang X, Liu Y, Tian Q, Liu L, et al. Associations of healthy dietary patterns with mortality among people with prediabetes. Eur J Nutr. 2023;62(3):1377–87.
14. Reedy J, Krebs-Smith SM, Miller PE, Liese AD, Kahle LL, Park Y, Subar AF. Higher diet quality is associated with decreased risk of all-cause, cardiovascular disease, and cancer mortality among older adults. J Nutr. 2014;144(6):881–9.
15. Hao X, Li D. The healthy eating Index-2015 and All-Cause/Cause-Specific mortality: a systematic review and dose-response Meta-analysis. Adv Nutr. 2024;15(3):100166.
16. Jayanama K, Theou O, Godin J, Cahill L, Shivappa N, Hebert JR, Wirth MD, Park YM, Fung TT, Rockwood K. Relationship between diet quality scores and the risk of frailty and mortality in adults across a wide age spectrum. BMC Med. 2021;19(1):64.
17. Pocovi-Gerardino G, Correa-Rodriguez M, Callejas-Rubio JL, Rios-Fernandez R, Martin-Amada M, Cruz-Caparros MG, Rueda-Medina B, Ortego-Centeno N. Beneficial effect of Mediterranean diet on disease activity and cardiovascular risk in systemic lupus erythematosus patients: a cross-sectional study. Rheumatology (Oxford). 2021;60(1):160–9.
18. Matsumoto Y, Shivappa N, Sugioka Y, Tada M, Okano T, Mamoto K, Inui K, Habu D, Hebert JR, Koike T. Change in dietary inflammatory index score is associated with control of long-term rheumatoid arthritis disease activity in a Japanese cohort: the TOMORROW study. Arthritis Res Ther. 2021;23(1):105.
19. Hariharan R, Odjidja EN, Scott D, Shivappa N, Hebert JR, Hodge A, de Courten B. The dietary inflammatory index, obesity, type 2 diabetes, and cardiovascular risk factors and diseases. Obes Rev. 2022;23(1):e13349.
20. Wang X, Hu J, Liu L, Zhang Y, Dang K, Cheng L, Zhang J, Xu X, Li Y. Association of Dietary Inflammatory Index and Dietary oxidative balance score with all-cause and Disease-Specific Mortality: findings of 2003–2014 National Health and Nutrition Examination Survey. Nutrients 2023, 15(14).
21. Zheng G, Cai M, Liu H, Li R, Qian Z, Howard SW, Keith AE, Zhang S, Wang X, Zhang J et al. Dietary diversity and inflammatory Diet Associated with all-cause mortality and incidence and mortality of type 2 diabetes: two prospective cohort studies. Nutrients 2023, 15(9).
22. Shan Z, Wang F, Li Y, Baden MY, Bhupathiraju SN, Wang DD, Sun Q, Rexrode KM, Rimm EB, Qi L, et al. Healthy Eating Patterns and risk of total and cause-specific mortality. JAMA Intern Med. 2023;183(2):142–53.
23. Zipf G, Chiappa M, Porter KS, Ostchega Y, Lewis BG, Dostal J. National health and nutrition examination survey: plan and operations, 1999–2010. Vital Health Stat 1. 2013;(56):1–37.
24. Chen L, Wu B, Mo L, Chen H, Zhao Y, Tan T, Chen L, Li Y, Yao P, Tang Y. Associations between biological ageing and the risk of, genetic susceptibility to, and life expectancy associated with rheumatoid arthritis: a secondary analysis of two observational studies. Lancet Healthy Longev. 2024;5(1):e45–55.
25. Liu B, Wang J, Li YY, Li KP, Zhang Q. The association between systemic immune-inflammation index and rheumatoid arthritis: evidence from NHANES 1999–2018. Arthritis Res Ther. 2023;25(1):34.
26. Reedy J, Lerman JL, Krebs-Smith SM, Kirkpatrick SI, Pannucci TE, Wilson MM, Subar AF, Kahle LL, Tooze JA. Evaluation of the healthy eating Index-2015. J Acad Nutr Diet. 2018;118(9):1622–33.
27. Krebs-Smith SM, Pannucci TE, Subar AF, Kirkpatrick SI, Lerman JL, Tooze JA, Wilson MM, Reedy J. Update of the healthy eating index: HEI-2015. J Acad Nutr Diet. 2018;118(9):1591–602.
28. Shivappa N, Steck SE, Hurley TG, Hussey JR, Ma Y, Ockene IS, Tabung F, Hebert JR. A population-based dietary inflammatory index predicts levels of C-reactive protein in the Seasonal variation of blood cholesterol study (SEASONS). Public Health Nutr. 2014;17(8):1825–33.
29. Shivappa N, Steck SE, Hurley TG, Hussey JR, Hebert JR. Designing and developing a literature-derived, population-based dietary inflammatory index. Public Health Nutr. 2014;17(8):1689–96.
30. Beddhu S, Baird BC, Zitterkoph J, Neilson J, Greene T. Physical activity and mortality in chronic kidney disease (NHANES III). Clin J Am Soc Nephrol. 2009;4(12):1901–6.
31. White SL, Polkinghorne KR, Atkins RC, Chadban SJ. Comparison of the prevalence and mortality risk of CKD in Australia using the CKD epidemiology collaboration (CKD-EPI) and modification of Diet in Renal Disease (MDRD) Study GFR estimating equations: the AusDiab (Australian diabetes, obesity and lifestyle) study. Am J Kidney Dis. 2010;55(4):660–70.
32. Rajaratnam B, Roberts S, Sparks D, Dalal O. Lasso Regression: estimation and shrinkage via the limit of Gibbs Sampling. J Royal Stat Soc Ser B: Stat Methodol. 2015;78(1):153–74.
33. Pignotti GA, Vega-Lopez S, Keller C, Belyea M, Ainsworth B, Nagle Williams A, Records K, Coonrod D, Permana P. Comparison and evaluation of dietary quality between older and younger Mexican-American women. Public Health Nutr. 2015;18(14):2615–24.
34. Hiza HA, Casavale KO, Guenther PM, Davis CA. Diet quality of americans differs by age, sex, race/ethnicity, income, and education level. J Acad Nutr Diet. 2013;113(2):297–306.

35. Berube LT, Kiely M, Yazici Y, Woolf K. Diet quality of individuals with rheumatoid arthritis using the healthy eating Index (HEI)-2010. Nutr Health. 2017;23(1):17–24.
36. Jandari S, Mosalmanzadeh N, Shadmand Foumani Moghadam MR, Soleimani D, Shivappa N, Hebert JR, Jokar M, Karamati M, Abedi SS, Malek N, et al. Dietary inflammatory index and healthy eating index-2015 are associated with rheumatoid arthritis. Public Health Nutr. 2021;24(18):6007–14.
37. Xiang S, Wang Y, Qian S, Li J, Jin Y, Ding X, Xu T. The association between dietary inflammation index and the risk of rheumatoid arthritis in americans. Clin Rheumatol. 2022;41(9):2647–58.
38. Tandorost A, Kheirouri S, Moludi J, Seyedmardani S. Association of Dietary Inflammatory Index (DII) with disease activity and inflammatory cytokines in the patients with rheumatoid arthritis. Int J Clin Pract. 2021;75(11):e14792.
39. Nikiphorou E, Philippou E. Nutrition and its role in prevention and management of rheumatoid arthritis. Autoimmun Rev. 2023;22(7):103333.
40. Dourado E, Ferro M, Sousa Guerreiro C, Fonseca JE. Diet as a modulator of intestinal microbiota in rheumatoid arthritis. Nutrients 2020, 12(11).
41. Gioia C, Lucchino B, Tarsitano MG, Iannuccelli C, Di Franco M. Dietary habits and Nutrition in Rheumatoid Arthritis: can Diet Influence Disease Development and Clinical manifestations? Nutrients 2020, 12(5).
42. Charneca S, Ferro M, Vasques J, Carolino E, Martins-Martinho J, Duarte-Monteiro AM, Dourado E, Fonseca JE, Guerreiro CS. The Mediterranean diet, and not dietary inflammatory index, is associated with rheumatoid arthritis disease activity, the impact of disease and functional disability. Eur J Nutr. 2023;62(7):2827–39.
43. Tian P, Xiong J, Wu W, Shi S, Chen A, Chen K, Chen W, Wu A, Liao Y. Impact of the malnutrition on mortality in rheumatoid arthritis patients: a cohort study from NHANES 1999–2014. Front Nutr. 2022;9:993061.
44. Panizza CE, Shvetsov YB, Harmon BE, Wilkens LR, Le Marchand L, Haiman C, Reedy J, Boushey CJ. Testing the Predictive Validity of the Healthy Eating Index-2015 in the Multiethnic Cohort: Is the Score Associated with a Reduced Risk of All-Cause and Cause-Specific Mortality? *Nutrients* 2018, 10(4).
45. Zhang J, Hou Q, Han Q, Peng X, Cao H, Wu S, Li K. Prediction of major adverse Cardiovascular events by triglyceride glucose index in predominantly male patients with rheumatoid arthritis. Rev Cardiovasc Med. 2024;25(1):28.
46. Chen C, Yang T, Wang C. The Dietary Inflammatory Index and early COPD: results from the National Health and Nutrition Examination Survey. Nutrients 2022, 14(14).
47. Tian TL, Zhi TY, Xie ML, Jiang YL, Qu XK. Dietary inflammatory index and all-cause mortality in adults with COPD: a prospective cohort study from the NHANES 1999–2018. Front Nutr. 2024;11:1421450.
48. Huang Y, Zeng M, Zhang L, Shi J, Yang Y, Liu F, Sun L, Xiao L. Dietary inflammatory potential is Associated with Sarcopenia among chronic kidney Disease Population. Front Nutr. 2022;9:856726.
49. Li Z, Xu Z, Xuan C, Xu H. Association between waist triglyceride index, body mass index, dietary inflammatory index, and triglyceride- glucose index with chronic kidney disease: the 1999–2018 cohort study from NHANES. Front Endocrinol (Lausanne). 2024;15:1390725.
50. Cai B, Zhou M, Xiao Q, Zou H, Zhu X. L-shaped association between serum 25-hydroxyvitamin D and all-cause mortality of individuals with rheumatoid arthritis. Rheumatology (Oxford). 2023;62(2):575–82.
51. Jiang L, Shang M, Yu S, Liu Y, Zhang H, Zhou Y, Wang M, Wang T, Li H, Liu Z, et al. A high-fiber diet synergizes with Prevotella copri and exacerbates rheumatoid arthritis. Cell Mol Immunol. 2022;19(12):1414–24.
52. Ingegnoli F, Cavalli S, Giudice L, Caporali R. Caffeine and rheumatoid arthritis: a complicated relationship. Autoimmun Rev. 2022;21(7):103117.
53. van Dam RM, Hu FB, Willett WC. Coffee, Caffeine, and Health. N Engl J Med. 2020;383(4):369–78.
54. Zheng H, Lin F, Xin N, Yang L, Zhu P. Association of Coffee, Tea, and Caffeine Consumption with all-cause risk and specific mortality for Cardiovascular Disease patients. Front Nutr. 2022;9:842856.
55. Asoudeh F, Dashti F, Jayedi A, Hemmati A, Fadel A, Mohammadi H. Caffeine, Coffee, Tea and Risk of Rheumatoid Arthritis: systematic review and dose-response Meta-analysis of prospective cohort studies. Front Nutr. 2022;9:822557.
56. Mirrafiei A, Jayedi A, Shab-Bidar S. Total and different dietary fiber subtypes and the risk of all-cause, cardiovascular, and cancer mortality: a dose-response meta-analysis of prospective cohort studies. Food Funct. 2023;14(24):10667–80.
57. Vadell AKE, Barebring L, Hulander E, Gjertsson I, Lindqvist HM, Winkvist A. Anti-inflammatory Diet in Rheumatoid Arthritis (ADIRA)-a randomized, controlled crossover trial indicating effects on disease activity. Am J Clin Nutr. 2020;111(6):1203–13.
58. Wan H, Zhang Y, Ning Z, Liu M, Yang S. Associations of cereal fiber intake with rheumatoid arthritis mediated by dietary inflammatory index: insights from NHANES 2011–2020. Sci Rep. 2024;14(1):2415.
59. Hager J, Bang H, Hagen M, Frech M, Trager P, Sokolova MV, Steffen U, Tascilar K, Sarter K, Schett G et al. The role of Dietary Fiber in Rheumatoid Arthritis patients: a feasibility study. Nutrients 2019, 11(10).
60. Durholz K, Hofmann J, Iljazovic A, Hager J, Lucas S, Sarter K, Strowig T, Bang H, Rech J, Schett G et al. Dietary short-term Fiber interventions in arthritis patients increase systemic SCFA levels and regulate inflammation. Nutrients 2020, 12(10).
61. Elahi N, Elahi H, Navashenaq JG, Abdollahzad H, Mahaki B, Soleimani D, Mostafaei R, Samadi M, Bagheri A, Nachvak SM. The relationship between major dietary patterns and disease activity of rheumatoid arthritis. Clin Nutr ESPEN. 2022;51:274–9.
62. Huang J, Liao LM, Weinstein SJ, Sinha R, Graubard BI, Albanes D. Association between Plant and Animal Protein Intake and overall and cause-specific mortality. JAMA Intern Med. 2020;180(9):1173–84.
63. Chen Z, Glisic M, Song M, Aliahmad HA, Zhang X, Moumdjian AC, Gonzalez-Jaramillo V, van der Schaft N, Bramer WM, Ikram MA, et al. Dietary protein intake and all-cause and cause-specific mortality: results from the Rotterdam Study and a meta-analysis of prospective cohort studies. Eur J Epidemiol. 2020;35(5):411–29.
64. Budhathoki S, Sawada N, Iwasaki M, Yamaji T, Goto A, Kotemori A, Ishihara J, Takachi R, Charvat H, Mizoue T, et al. Association of Animal and Plant Protein Intake with all-cause and cause-specific mortality in a Japanese cohort. JAMA Intern Med. 2019;179(11):1509–18.
65. Lichtenstein AH, Appel LJ, Vadiveloo M, Hu FB, Kris-Etherton PM, Rebholz CM, Sacks FM, Thorndike AN, Van Horn L, Wylie-Rosett J. 2021 Dietary Guidance to improve Cardiovascular Health: A Scientific Statement from the American Heart Association. Circulation. 2021;144(23):e472–87.
66. Johansson K, Askling J, Alfredsson L, Di Giuseppe D. Group Es: Mediterranean diet and risk of rheumatoid arthritis: a population-based case-control study. Arthritis Res Ther. 2018;20(1):175.
67. Nguyen Y, Salliot C, Gelot A, Gambaretti J, Mariette X, Boutron-Ruault MC, Seror R. Mediterranean Diet and Risk of Rheumatoid Arthritis: findings from the French E3N-EPIC Cohort Study. Arthritis Rheumatol. 2021;73(1):69–77.
68. Papandreou P, Gioxari A, Daskalou E, Grammatikopoulou MG, Skouroliakou M, Bogdanos DP. Mediterranean Diet and Physical Activity nudges versus Usual Care in Women with Rheumatoid Arthritis: results from the MADEIRA Randomized Controlled Trial. Nutrients 2023, 15(3).
69. Knez M, Stangoulis JCR. Dietary zn deficiency, the current situation and potential solutions. Nutr Res Rev. 2023;36(2):199–215.
70. Xin L, Yang X, Cai G, Fan D, Xia Q, Liu L, Hu Y, Ding N, Xu S, Wang L, et al. Serum levels of copper and zinc in patients with rheumatoid arthritis: a Meta-analysis. Biol Trace Elem Res. 2015;168(1):1–10.
71. Balogh Z, El-Ghobarey AF, Fell GS, Brown DH, Dunlop J, Dick WC. Plasma zinc and its relationship to clinical symptoms and drug treatment in rheumatoid arthritis. Ann Rheum Dis. 1980;39(4):329–32.
72. Cui Q, Xia Y, Wu Q, Chang Q, Niu K, Zhao Y. Validity of the food frequency questionnaire for adults in nutritional epidemiological studies: a systematic review and meta-analysis. Crit Rev Food Sci Nutr. 2023;63(12):1670–88.

Publisher's note