Association of Diet Quality with Risk of Incident Rheumatoid Arthritis in the Women's Health Initiative

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INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease impacting about 1.3 million Americans, with women much more likely to be affected than men. Various foods and nutrients are associated with inflammatory biomarkers, and thus have been linked with increased or decreased risk of RA. However, these associations between individual food groups and RA risk have been inconsistent across studies. Conversely, overall dietary patterns and diet quality as measured by the Healthy Eating Index-2015 (HEI-2015) may reveal stronger, more consistent relationships with RA risk. Specifically, the HEI-2015 consists of 13 foods and nutrients that have all been associated with chronic disease risk and fall into healthy or unhealthy categories. Therefore, our study will further investigate both overall diet quality and individual dietary components from a large, ethnically diverse prospective study of postmenopausal women.

OBJECTIVES

Given the relationship between nutrition and chronic disease, our primary objective was to evaluate the prospective relationship between long-term dietary quality, as measured by the HEI-2015, with the development of incident RA in postmenopausal women.

METHODS

❖ **Design: Prospective cohort study**

❖ **Participants:** 109,591 participants in the Women's Health Initiative (WHI) were included in our analytic sample. The participants did not have baseline RA or medical conditions with a predictive survival time of less than 3 years, and were not active in other randomized controlled clinical trials. They also had reliable food frequency questionnaire (FFQ) data.

❖ **Exposure**: Baseline habitual diet was assessed using a validated semiquantitative FFQ. Participants were asked to recall their diet over the past 3 months and report their usual frequency of intake and portion size of 122 food and beverage items. All the specific nutrients and foods from the HEI-2015 are given a score which measures compliance with a different aspect of standard dietary guidelines. Using the WHI FFQ, a cumulative HEI score was calculated by summing the individual scores for each HEI nutrient.

❖**Outcomes**: Incident RA was based on self-reported physician diagnosed RA up through 2005. Specifically, participants were asked, "Has a doctor told you for the first time that you have any of the following specific conditions… Rheumatoid Arthritis (not including rheumatism)."

❖**Statistical Analysis**: Baseline characteristics of the study population were examined by HEI-2015 quartiles using means with standard deviations or frequency with group percentages. Differences across quartiles for categorical variables used chi-square and for continuous variables used ANOVA. Cox proportional hazards models examined the incidence of RA by HEI quartile. Incident RA was also examined by quartiles of the individual food groups and nutrients of HEI-2015.

RESULTS

Table 1: Associations between baseline HEI-2015 and RA risk in the Women's Health Initiative

	HEI Quartile				
	Q1	Q2	Q3	Q4	
N	24203	25937	28172	31279	
# of RA cases	1612	1510	1360	1341	
Person-years	185981	202265	221756	247516	
Crude RA Incidence Rate (#/1,000 person-years)	8.67 (8.63, 8.71)	7.47 (7.43, 7.50)	6.13 (6.11, 6.16)	5.42 (5.40, 5.44)	
Age-adjusted RA Incidence Rates (#/1,000 person-years)	8.68 (8.61, 8.75)	7.48 (7.43, 7.54)	6.15 (6.11, 6.20)	5.43 (5.40, 5.47)	
Cox Model Hazards Ratio (95% CI)					p-trend
Age-adjusted	(ref)	0.86 (0.80, 0.92)	0.70 (0.65, 0.75)	0.61 (0.57, 0.66)	<0.001
Model 1	(ref)	0.95 (0.89, 1.02)	0.84 (0.78, 0.91)	0.77 (0.72, 0.83)	<0.001
Model 2	(ref)	0.92 (0.85, 0.99)	0.79 (0.73, 0.85)	0.72 (0.67, 0.78)	<0.001
Model 3	(ref)	0.86 (0.80, 0.92)	0.73 (0.67, 0.78)	0.64 (0.59, 0.69)	<0.001
Model 4	(ref)	0.97 (0.90, 1.04)	0.87 (0.81, 0.94)	0.82 (0.76, 0.88)	<0.001
Model 5	(ref)	0.97 (0.90, 1.05)	0.88 (0.81, 0.95)	0.82 (0.75, 0.89)	<0.001

Table 2: Associations between HEI-2015 individual component scores and RA risk in the Women's Health Initiative

Individual HEI 2015 Component	**Q1**	**Q2**	**Q3**	**Q4**	**p-trend**
Total Fruits					
Median servings/day (range)	0.97 (0.00-1.57)	2.02 (1.57-2.65)	3.36 (2.65-4.16)	5.33 (4.16-17.64)	
n	24239	26515	28354	30483	
# incident RA cases	1470	1471	1401	1481	
Age & total calorie adjusted model	(ref)	0.88 (0.82, 0.95)	0.77 (0.72, 0.83)	0.74 (0.69, 0.80)	<.0001
Model 4*	(ref)	0.97 (0.90, 1.04)	0.93 (0.86, 1.01)	0.90 (0.84, 0.98)	0.0061
Whole Fruits					
Median servings/day (range)	0.47 (0.00-0.87)	1.27 (0.87-1.60)	1.97 (1.60-3.25)	4.20 (3.25-12.01)	
n	24418	26608	28133	30432	
# incident RA cases	1543	1461	1412	1407	
Age & total calorie adjusted model	(ref)	0.84 (0.78, 0.90)	0.75 (0.70, 0.81)	0.69 (0.64, 0.74)	<.0001
Model 4*	(ref)	0.94 (0.88, 1.01)	0.92 (0.86, 0.99)	0.86 (0.80, 0.92)	<.0001
Total Vegetables					
Median servings/day (range)	1.48 (0.00-1.98)	2.42 (1.98-2.86)	3.35 (2.86-3.96)	4.87 (3.96-51.35)	
n	25416	27457	27981	28737	
# incident RA cases	1572	1461	1400	1390	
Age & total calorie adjusted model	(ref)	0.80 (0.75, 0.86)	0.73 (0.67, 0.78)	0.66 (0.61, 0.71)	<.0001
Model 4*	(ref)	0.96 (0.89, 1.03)	0.93 (0.86, 1.01)	0.89 (0.82, 0.96)	0.004
Dark Green Vegetables					
Median servings/day (range)	0.08 (0.00-0.14)	0.19 (0.14-0.25)	0.33 (0.25-0.45)	0.66 (0.45-10.94)	
n	26011	26771	27529	29280	
# incident RA cases	1507	1485	1424	1407	
Age & total calorie adjusted model	(ref)	0.93 (0.87, 1.00)	0.86 (0.80, 0.92)	0.78 (0.72, 0.84)	<.0001
Model 4*	(ref)	0.98 (0.91, 1.06)	0.94 (0.88, 1.02)	0.86 (0.80, 0.93)	<.0001
Whole Grains					
Median ounce equivalents/day (range)	0.25 (0.00-0.47)	0.70 (0.47-0.95)	1.22 (0.95-1.59)	2.14 (1.59-13.58)	
n	24850	27243	28449	29049	
# incident RA cases	1542	1457	1365	1459	
Age & total calorie adjusted model	(ref)	0.83 (0.77, 0.89)	0.71 (0.66, 0.77)	0.71 (0.66, 0.77)	<.0001
Model 4*	(ref)	0.94 (0.87, 1.01)	0.87 (0.80, 0.93)	0.89 (0.83, 0.97)	0.004
Refined Grains					
Median ounce equivalents/day (range)	1.63 (0.00-2.23)	2.76 (2.23-3.30)	3.91 (3.30-4.73)	6.13 (4.73-62.55)	
n	26576	28702	27865	26448	
# incident RA cases	1398	1434	1422	1569	
Age & total calorie adjusted model	(ref)	0.93 (0.86, 1.01)	0.93 (0.86, 1.01)	1.08 (0.98, 1.19)	0.0446
Model 4*	(ref)	0.96 (0.89, 1.04)	0.95 (0.87, 1.03)	0.99 (0.89, 1.09)	0.908
Total Dairy					
Median servings/day (range)	0.50 (0.00-0.80)	1.09 (0.80-1.39)	1.73 (1.39-2.21)	3.07 (2.21-20.54)	
n	25536	27732	27989	28334	
# incident RA cases	1552	1513	1346	1412	
Age & total calorie adjusted model	(ref)	0.84 (0.78, 0.91)	0.70 (0.65, 0.76)	0.67 (0.61, 0.73)	<.0001
Model 4*	(ref)	0.98 (0.91, 1.05)	0.87 (0.81, 0.95)	0.89 (0.81, 0.97)	0.004
Total Protein					
Median servings/day (range)	0.51 (0.00-0.70)	0.87 (0.70-1.04)	1.22 (1.04-1.45)	1.82 (1.45-27.93)	
n	27374	29017	27718	25482	
# incident RA cases	1408	1494	1413	1508	
Age & total calorie adjusted model	(ref)	0.99 (0.91, 1.06)	0.97 (0.90, 1.05)	1.13 (1.02, 1.24)	0.013
Model 4*	(ref)	1.02 (0.95, 1.10)	1.01 (0.93, 1.10)	1.05 (0.95, 1.15)	0.405
Seafood/Plant Protein					
Median servings/day (range)	0.10 (0.00-0.16)	0.22 (0.16-0.28)	0.35 (0.28-0.44)	0.61 (0.44-11.70)	
n	1532	1451	1457	1383	
# incident RA cases	25954	27701	28040	27896	
Age & total calorie adjusted model	(ref)	0.86 (0.80, 0.92)	0.83 (0.77, 0.90)	0.75 (0.70, 0.82)	<.0001
Model 4*	(ref)	0.96 (0.89, 1.03)	0.98 (0.91, 1.06)	0.90 (0.83, 0.98)	0.015
Percent Saturated fat					
Median % daily caloric intake (range)	6.99 (1.25-8.55)	9.75 (8.55-10.81)	11.84 (10.81-12.98)	14.57 (12.98-43.34)	
n	32815	28364	24650	23762	
# incident RA cases	1512	1453	1388	1470	
Age & total calorie adjusted model	(ref)	1.12 (1.04, 1.21)	1.24 (1.15, 1.33)	1.37 (1.27, 1.47)	<.0001
Model 4*	(ref)	1.04 (0.96, 1.11)	1.06 (0.98, 1.15)	1.14 (1.06, 1.23)	0.001
Fatty Acid Ratio					
Median ratio (range)	1.38 (0.61-1.54)	1.67 (1.54-1.79)	1.91 (1.79-2.07)	2.31 (2.07-6.41)	
n	26993	27451	27558	27589	
# incident RA cases	1413	1430	1475	1505	
Age & total calorie adjusted model	(ref)	1.00 (0.93, 1.07)	1.03 (0.96, 1.11)	1.06 (0.98, 1.14)	0.0948
Model 4*	(ref)	0.97 (0.90, 1.04)	0.96 (0.90, 1.04)	0.98 (0.91, 1.05)	0.6
Percent Added Sugars					
Median % daily caloric intake (range)	4.85 (0.00-6.23)	7.38 (6.23-8.52)	9.78 (8.52-11.39)	13.98 (11.39-74.90)	
n	27057	27443	27789	27302	
# incident RA cases	1410	1386	1398	1629	
Age & total calorie adjusted model	(ref)	0.94 (0.87, 1.01)	0.94 (0.87, 1.01)	1.12 (1.04, 1.20)	0.0002
Model 4*	(ref)	0.97 (0.90, 1.05)	0.96 (0.89, 1.03)	1.03 (0.96, 1.11)	0.333
Sodium					
Median mg/day (range)	1481 (2-1880)	2203 (1881-2525)	2876 (2525-3316)	4006 (3316-51565)	
n	26366	28876	28081	26268	
# incident RA cases	1455	1466	1377	1525	
Age & total calorie adjusted model	(ref)	0.86 (0.80, 0.93)	0.79 (0.72, 0.86)	0.86 (0.76, 0.97)	0.011
Model 4*	(ref)	1.00 (0.92, 1.08)	0.96 (0.88, 1.05)	1.04 (0.92, 1.17)	0.671

Model 1: Age + Sociodemographic covariates (race, education status, income, marital status)
Model 2: Age + Lifestyle covariates (smoking status, alcohol consumption, total caloric intake, physical activity, multivitamin use, BMI class)
Model 3: Age + Medical/Women's Health covariates (Diabetes, hypertension, dyslipidemia, hysterectomy/oophorectomy status, postmenopausal hormone use, menarche before age 12, breastfeeding, parity)
*Model 4 (main model): Age + Sociodemographic covariates (race, education status, income) + BMI
Model 5: Age + All covariates (Models 1-3)

STRENGTHS

Firstly, the study cohort was comprised of a large, geographically and ethnically diverse group of postmenopausal women who were followed for on average 9 years. Additionally, with 109,591 participants and 5,823 incident RA cases, there is adequate statistical power to examine both diet quality overall and food groups as well. Furthermore, the study controlled for multiple potential confounding variables.

LIMITATIONS

Firstly, it relied on FFQs which are known to have some limitations regarding inaccuracy of absolute nutrient values and lack of detail for specific foods. However, these measurement error limitations apply more so for nutrient density rather than diet quality, and it has been found that the WHI FFQ produced nutrient estimates that were similar to those obtained from short-term dietary recall and recording methods. Furthermore, RA status was also a self-report of a physician diagnosis. Self-reported diet and RA status may be prone to potential measurement error. Still, our results are unlikely to be explained by this bias alone. Additionally, the self-reported RA was based on a physician diagnosis, which lends credibility to the RA status classification. Likewise, this cohort does not include any premenopausal women or men.

NEXT STEPS

Future studies may benefit from measuring specific biomarkers associated with RA to have a more objective measurement of RA status. Further studies are also warranted to see if our findings are consistent across other cohorts.

CONCLUSIONS

- **Long term adherence to a healthy diet may be associated with lower risk of incident RA.**
- **Higher intake of total fruits, whole fruits, total vegetables, dark green vegetables, whole grain, total dairy, and seafood/plant protein was associated with lower risk of RA.**
- **Higher intake of percent saturated fat was associated with higher risk of RA.**
- **The results of this study should be reviewed with caution because it relies on self-report of diet and self-report of a physician diagnosis of RA.**

No authors have professional or financial affiliations that would bias this work.