

# Healthy Diets Rich in Vegetables and Systemic Inflammation in Older Adults <sup>†</sup>

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<sup>†</sup> Presented at the 2nd International Electronic Conference on Nutrients, 15–31 March 2022; Available online: <https://iecn2022.sciforum.net/>.

**Abstract:** The aim of the present study was to explore links between dietary habits and biomarkers of systemic inflammation in older adults. In a sample of 233 community-dwelling older adults (65–70 years), dietary habits were assessed by food frequency questionnaire. Physical activity and sedentary time were assessed using accelerometry. Inflammatory biomarkers were assessed from blood samples. The results showed that intake of vegetables was inversely related to levels of systemic inflammation ( $p < 0.05$ ), independently of physical activity level. The present study strengthens public health efforts to promote vegetable-rich diets in older adults to mitigate age-related systemic inflammation.

**Keywords:** aging; dietary patterns; inflammatory biomarkers; abdominal obesity; nutrition; sedentary time; physical activity

## 1. Introduction

Aging is connected with an elevated risk of several cardiometabolic abnormalities, while a chronic inflammatory state characterized by slight elevations in circulating levels of pro-inflammatory biomarkers has been implicated in the pathogenesis of various age-related diseases [1]. In this respect, the potential of dietary habits to mitigate age-related chronic systemic inflammation has received a particular attention [2,3]. However, previous compilations of observational studies have shown conflicting results, where associations between specific food groups, such as fruit and vegetables, and inflammatory biomarkers have been demonstrated in some but not all reviewed studies [2,3]. Importantly, in order to determine the actual role of dietary habits on levels of systemic inflammation it is necessary to consider the potential confounding impacts of physical activity behaviors. Indeed, more time spent in moderate-to-vigorous physical activity (MVPA) and less time spent in sedentary behaviors have been related to reduced levels of systemic inflammation in older adults [4,5]. Although low FV intakes are commonly reported in aging populations [6], there is relatively few studies specifically targeting older adults when depicting the role of FV on systemic inflammation. Therefore, the aim of the present study was to explore the links between dietary habits and selected biomarkers of systemic inflammation in older adults, while considering objectively assessed physical activity behaviors.

## 2. Materials and Methods

### 2.1. Participants

Two-hundred-and-fifty-two community-dwelling older adults were recruited through local advertisement. For inclusion in the study, participants were 65 to 70 years

**Citation:** Papaioannou, K.-G.; Nilsson, A.; Kadi, F. Healthy Diets Rich in Vegetables and Systemic Inflammation in Older Adults. *2022*, *69*, x. <https://doi.org/10.3390/xxxxx>

Academic Editor(s): David Nieman

Received: 21 February 2022

Accepted: 24 February 2022

Published: 14 March 2022

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old, free from overt diseases such as diabetes mellitus, coronary heart disease, had no mobility disabilities and reported no anti-inflammatory treatment. Written informed consent was obtained from all participants and all research procedures were performed according to the principles set by the Declaration of Helsinki. The study was approved by the Swedish Ethical Review Authority.

## 2.2. Assessment of Dietary Intake

Dietary data were collected using a 90-items food-frequency questionnaire (FFQ) and The Healthy Diet Score (HDS) was derived on the basis of reported intakes of favorable (fish, fruits (except juices), vegetables (except potatoes) and whole grains) and unfavorable (red or processed meats, desserts and sweets, sugar-sweetened beverages and fried potatoes) food groups as previously described [7]. Based on HDS, participants were divided into sex-specific tertiles reflecting adherence to a healthy diet (Low, Moderate and High). In addition, two questions were used to assess number of fruit and vegetable servings per day as previously reported [8]. Participants were categorized into groups based on reporting at least 2 daily servings of fruits (yes/no) or vegetables (yes/no) and reporting at least 4 daily servings of fruits and vegetables combined (yes/no).

## 2.3. Assessment of Inflammatory Biomarkers

Blood samples were collected by venipuncture after an overnight fast. High-sensitivity C-reactive protein (CRP) was assessed using fully automated immunoturbidimetric assay. Fibrinogen was assessed using an automated immunoassay method with a polyclonal rabbit anti-human antibody (Dako, Glostrup, Denmark). Interleukin-6 (IL-6), IL-18, and Tumor Necrosis Factor- $\alpha$  (TNF- $\alpha$ ) were analyzed using the Olink Proseek Multiplex Inflammation panel (Olink, Uppsala, Sweden) as previously described [5].

## 2.4. Assessment of Covariates

Waist circumference (WC) was measured to the nearest 0.1 cm at the midpoint between the iliac crest and lower costal margin using measuring tape. Physical activity behaviors were assessed by accelerometry (Actigraph GT3x, Pensacola, FL, USA), as previously described [5]. An average of 22 min of MVPA per day (approximating 150 min per week) was used to classify participants as meeting the MVPA guideline. Time spent sedentary was expressed in relation to total registered time per day. Information about prescribed medication use, education level (university/college, high-school, secondary school) and tobacco use (current, past, never) were retrieved by self-report.

## 2.5. Statistical Analysis

Differences in categorical data across tertiles of HDS were analyzed by chi-square ( $\chi^2$ ) test. Differences in biomarkers of systemic inflammation across groups of HDS (tertiles) or between groups of fruit and vegetable intake (above or below a given intake) was investigated by analysis of covariance (ANCOVA), with the inflammatory biomarker set as dependent and the dietary variable set as a fixed factor. Models were adjusted by sex, total energy intake, adherence to MVPA guideline (yes/no), daily sedentary time and waist circumference. The potential influence of age, medication use, tobacco use, and education level were determined prior to the final analysis. As none of these variables significantly impacted on the model outcomes, they were left out of final models in order to retain statistical power. Statistical significance was set to  $p < 0.05$ . All statistical analyses were performed using SPSS version 27.0 (IBM Corp., Armonk, NY, USA).

## 3. Results

Data on diet, inflammation and other covariates were collected in a total of 86 men ( $67 \pm 1.5$  yrs;  $179 \pm 7$  cm;  $81 \pm 11$  kg) and 147 women ( $67 \pm 1.6$  yrs;  $164 \pm 6$  cm; and  $64 \pm 10$  kg). Total energy intake was  $1747 \pm 573$  kcal (men:  $2099 \pm 586$  kcal; women:  $1542 \pm 455$

kcal). Information on medication use, tobacco use, education level, and proportions of participants with abdominal obesity and being physical active in according to the MVPA guideline are shown in Table 1. Proportions of participants with abdominal obesity differed significantly ( $p < 0.05$ ) between diet groups, with higher proportions by lower adherence to a healthy diet (Table 1).

**Table 1.** Participant characteristics across tertiles of adherence to a healthy diet (n = 233).

	Low Adherence (n = 73)	Moderate Adherence (n = 74)	High Adherence (n = 86)
Medication use (%)	55	42	41
Abdominal obesity (%)	63	47	41*
Physically active (%)	75	85	86
<u>Tobacco use (%)</u>			
Never	49	54	47
Former	41	41	51
Current	10	5	2
<u>Education level (%)</u>			
University/College	63	57	71
High school	25	35	21
Secondary school	12	8	8

\* significant difference between groups ( $p < 0.05$ ).

Levels of inflammatory biomarkers across tertiles of adherence to a healthy diet are shown in Table 2. No significant between-group differences were observed for any inflammatory biomarker (Table 2).

**Table 2.** Levels of inflammatory biomarkers across tertiles of adherence to a healthy diet (n = 233).

Inflammatory Biomarkers	Low Adherence (n = 73)	Moderate Adherence (n = 74)	High Adherence (n = 86)
CRP (mg/L) <sup>a</sup>	1.31 ± 2.0	0.98 ± 1.66	0.98 ± 2.43
Fibrinogen (mg/L)	3.27 ± 0.52	3.10 ± 0.53	3.15 ± 0.59
IL-6 (au)	3.36 ± 0.53	3.30 ± 0.54	3.32 ± 0.67
IL-18 (au)	8.14 ± 0.49	8.04 ± 0.58	7.98 ± 0.51
TNF- $\alpha$ (au)	3.20 ± 0.41	3.07 ± 0.30	3.17 ± 0.38

<sup>a</sup> geometric mean, au = arbitrary units.

A total of 50% and 56% of the participants had at least two servings of vegetables and fruits per day, respectively. Forty-one percent reported at least four servings per day of fruit and vegetables combined. Our analysis revealed that participants with a vegetable intake of at least 2 servings per day had a 9% lower average level of the pro-inflammatory biomarker IL-6 compared to those with less servings ( $p < 0.05$ ). Importantly, this significant difference remained evident after adjustment for sex, total energy intake, adherence to MVPA guideline, sedentary time and waist circumference. No corresponding differences in levels of inflammatory biomarkers were observed between groups of fruit intake alone (<2 vs.  $\geq 2$  servings/day) or when combining total intake of fruits and vegetables (<4 vs.  $\geq 4$  servings/day).

#### 4. Discussion

While significant associations between healthy dietary patterns and biomarkers of systemic inflammation have been previously reported [9,10], the present study did not reveal any significant differences in levels of systemic inflammation across levels of adherence to an overall healthy diet comprising several different food groups. However,

older adults with a vegetable intake of at least 2 servings or more per day had a significantly lower level of the pro-inflammatory biomarker IL-6 compared to those with fewer daily servings, which adds to the body of evidence suggesting a vegetable intake of 2–3 servings per day for general health benefits [11]. This finding is also in line with recent data indicating inverse associations between vegetable intake and biomarkers of inflammation in older adults [12]. Our finding is further strengthened by the consideration of time spent in MVPA and in sedentary behaviors, as well as variations in waist circumference, which have shown potential to modulate the systemic inflammatory environment [4,5,13]. Therefore, our results indicate that vegetables can influence on the systemic inflammation through pathways independent of PA behaviors and adiposity level.

Given that no corresponding benefits from fruit intake was observed, it may be hypothesized that the relatively higher amount of fructose in fruits compared to vegetables may mitigate their protective health effects [14]. However, further studies are warranted in order to clarify the general role of fruits and the proposed impact of their fructose content. The following should be considered when interpreting our data: causality cannot be determined as it is based on a cross-sectional analysis; due to characteristics of the study sample, caution should be taken when generalizing the findings to broader populations of older adults; although impacts of several covariates were considered, residual confounding from additional variables may still be present.

## 5. Conclusions

In conclusion, the present study demonstrates that a higher intake of vegetables is related to lower levels of the pro-inflammatory biomarker IL-6 regardless of physical activity behaviors and adiposity level in older adults. Our finding strengthens public health efforts to promote vegetable-rich diets in older adults to mitigate age-related systemic inflammation.

**Author Contributions:** Conceptualization, K.-G.P., A.N. and F.K.; methodology, K.-G.P., A.N. and F.K.; formal analysis, K.-G.P., A.N. and F.K.; investigation, K.-G.P., A.N. and F.K.; writing—original draft preparation, K.-G.P.; writing—review and editing, K.-G.P., A.N. and F.K.; project administration, A.N. and F.K.; supervision, A.N. and F.K., funding acquisition, F.K. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research was funded by the EU HORIZON 2020 Research and Innovation Programme (European Joint Programming Initiative “A healthy diet for a healthy life” “JPI HDHL” and the ERA-NET co-fund HDHL-INTIMIC) GA no. 727565.

**Institutional Review Board Statement:** The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by Swedish Ethical Review Authority (2017/511).

**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** Data supporting reported results are available upon reasonable request and in accordance with the ethical principles.

**Acknowledgments:** The authors would like to express their sincere appreciation to Oscar Bergens for his valuable assistance in participant recruitment and collection of data, together with other colleagues involved in the research project. We thank the European Commission through the Marie Skłodowska-Curie Actions, Cofounding of Regional, National and International Programs (MSCA COFUND) for supporting KGP.

**Conflicts of Interest:** The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

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