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A high quality diet is associated with reduced systemic inflammation in middle-aged individuals

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ABSTRACT

Objective: To examine if overall diet quality is associated with cellular and soluble biomarkers of systemic inflammation in middle-aged individuals. **Methods**: A group of 667 individuals, aged 63–68 years, selected from the cardiovascular arm of the Malmö Diet and Cancer cohort, participated in this study. Baseline examinations consisted of an extensive socio-demographic questionnaire, anthropometric measurements, blood sampling and detailed dietary data. Mononuclear leukocytes frozen at baseline were thawed and analysed with flow cytometry to quantify monocyte subsets based on CD14 and CD16 expression. Plasma cytokines were measured using multiplexed immune assays. A diet quality index consisting of six components (saturated fatty acids, polyunsaturated fatty acids, fish and shellfish, dietary fibre, fruit and vegetables, and sucrose) was constructed to measure adherence to the Swedish Nutrition Recommendations/Dietary Guidelines. General linear models were used to investigate associations between index scores and several biomarkers of inflammation. **Results**: A higher percentage of women reported adherence to the nutritional recommendations and had better overall diet quality than men. Participants with higher diet quality were more likely to have a healthier lifestyle. The levels of high-sensitive CRP, S100A8/A9, TNF-α, white blood cells, neutrophils, lymphocytes and $CD14^{+}CD16^{++}$ were lower in participants with higher index scores. The associations remained significant after adjustment for potential confounders. **Conclusion**: In this cross-sectional study, we found that a high diet quality is associated with lower systemic inflammation. As the incidence of cardiovascular disease and cancer is directly correlated with the levels of inflammation, our findings might indicate a protective role of high-quality diet.

1. Introduction

Accumulating evidence points to a relationship between low-grade systemic inflammation and chronic diseases such as cardiovascular disease (CVD) [1], type 2 diabetes [2], and cancer [3]. Several biomarkers including C-reactive protein (CRP) [4], and cytokines such as IL-1β, IL-6, IL-8, or TNF-a, have been associated with the incidence of CVD and atherosclerosis [5]. Studies have also identified white blood cells (WBC), neutrophils, monocyte counts, and S100A8/A9, as independent risk factors for CVD [6–8]. Monocytes can be divided into classical ($CD14^{++}CD16^{-}$), intermediate ($CD14^{++}CD16^{+}$) and non-classical ($CD14^{+}CD16^{++}$). High circulating levels of classical monocytes have recently been shown to predict CVD [6,9]. CD16 positive monocytes (both intermediate and non-classical) have been classified as pro-inflammatory monocytes as they produce more TNF-α than the classical monocytes [9].

Lifestyle factors like physical activity (PA), diet and smoking can influence chronic inflammation [10]. Many dietary studies have previously focused on nutrients and their relationship with disease

Abbreviations: CDV, cardiovascular disease; CRP, C-reactive protein; WBC, white blood cells; $CD14^{++}CD16^{-}$, classical monocytes; $CD14^{++}CD16^{+}$, intermediate monocytes; $CD14^{+}CD16^{++}$, non-classical monocytes; DQI-SNR, diet quality index; MDC, Malmö Diet and Cancer; SNR, Swedish Nutrition Recommendations; SDG, Swedish Dietary Guidelines; SFA, saturated fatty acids; PUFA, polyunsaturated fatty acids; SD, standard deviation; IL, interleukin; TNF-α, tumour necrosis factor alpha; hsCRP, high-sensitive CRP; BMI, body mass index; PA, physical activity; GLM, general linear model.

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outcomes [11], but more recently it has been recognized that the study of dietary patterns in relation to diseases could be more fruitful [12]. A hypothesis-driven approach to food pattern studies is to construct a dietary index or score, based on dietary guidelines and/or nutritional recommendations, and use this index to rank individuals according to their dietary quality when examining associations between diet and disease [13]. A well-known and widely used index is based on the Mediterranean diet. The literature often refers to "prudent-diet" or "Mediterranean diet" as protective and "meat-based" or "Westernized" diets as inductive of an inflammatory state [14,15].

However, recognizing that Mediterranean-like diets might not be easy to achieve in other settings, Nordic countries have specific dietary guidelines/recommendations that take into consideration their own food culture [16]. Nutrition researchers argue that the health-enhancing influences observed with Mediterranean-like diets are easily achievable with traditional foods available in Northern Europe [17]. In order to evaluate the overall diet quality according to the Swedish Nutrition Recommendations and Swedish Dietary Guidelines, a diet quality index was created (DQI-SNR) [13]. The DQI-SNR has proved to be useful for ranking individuals on their reported adherence to the Swedish Nutrition Recommendations, and also to be a suitable tool for predicting overall and CVD-specific mortality [18], and CVD-incidence [19]. Nonetheless, the association between the DQI-SNR index and chronic inflammation remains to be explored. The aim of this study was to examine how diet quality is related to established cellular and soluble biomarkers of systemic inflammation in humans.

2. Methods

2.1. Study population

The Malmö Diet and Cancer (MDC) cohort is a population-based prospective study, based in Malmö, Sweden. Baseline examinations took place between 1991 and 1996, and consisted of an extensive socio-demographic self-administrated questionnaire; anthropometric measurements; non-fasting blood samples; and detailed dietary data (collected in a second visit). Its design and details have been published elsewhere [20]. Between November 1991 and February 1994, every other MDC participant was invited to participate in a sub-study with focus on the epidemiology of carotid artery disease. This sub-cohort consisted of 6103 subjects who accepted the invitation and visited the study centre a 3rd time (with a median time-lag of 7 months) to donate fasting blood samples under standardized conditions [21].

The initial population considered for the present study consisted of 700 men and women, aged 63–68 years (mean age 65 years), selected from the cardiovascular cohort of the MDC [6,22]. Of these, 33 persons were excluded due to the lack of dietary data. Analysis was performed in 667 people; 276 men and 391 women.

The Ethics Committee of Lund University approved the MDC study and all participants gave written informed consent (LU 51-90).

2.2. Dietary assessment

The MDC used a modified diet history method which consisted of a 7-day menu book (where participants recorded all cooked meals, cold beverages, drugs, natural remedies and dietary supplements) and a 168-item quantitative diet questionnaire referring to the previous year of intake (which used exact frequencies and a picture booklet to estimate portion sizes of regularly eaten food items – other than cooked meals). In addition, participants took part in a 1-h interview with the aim of excluding overlapping information derived from the different data collection tools, and also to collect detailed information on cooking practices and recipes.

From the reported food intake in the MDC Food and Nutrient Database, energy and nutrients were computed using the PC Kost2-93 from the Swedish National Food Agency [23]. The validity and reproducibility of this methodology has been published previously [24–26].

2.3. Diet quality index

A diet quality index (DQI-SNR) has been created previously within the MDC cohort in order to assess adherence to the Swedish Nutrition Recommendations (SNR–2005) and to the Swedish Dietary Guidelines (SDG) [13]. During the development process three main aspects were taken into consideration; 1) information on nutrients/dietary components had to be available in the MDC cohort database; 2) the index was constructed to reflect overall diet quality by selecting dietary components that have previously been suggested to be associated with chronic disease; and 3) included components had to be mutually independent (assessed by low correlation).

The DQI-SNR was created using the following components; 1-saturated fatty acids (SFA), 2- polyunsaturated fatty acids (PUFA), 3-fish and shellfish, 4- dietary fibre, 5- fruit and vegetables, and 6-sucrose.

The cut-offs were defined based on the recommended intake levels in the SNR and SDG [13]. The value 1 was attributed to people adhering to the recommendations on each component while 0 was attributed to the ones not adhering. The defined cut-offs were the following; SFA $\leq$14 %E (non-alcohol energy percentage), PUFA between 5 and 10%E, fish and shellfish $\geq$300 g/week, dietary fibre between 2.4 and 3.6 g/MJ, fruit and vegetables $\geq$ 400 g/day and sucrose $\leq$ 10%E.

The cut-offs for SFA, fibre and fruit and vegetables used in the DQI-SNR were slightly different from the SNR recommendations. The SFA cut-off was modified because only a small percentage of MDC participants reached the recommendations (4% in this study sample). The approach to define the new cut-off used in this study was similar to the one used by *Drake* et al. [13], adding one standard deviation (SD) of the mean intake of the population to the SNR recommended level, thus resulting in the 14%E. The cut-off for fibre was defined as described previously in the same study, using the mean recommended level of intake (between 25 and 35 g/d – approximately 3 g/MJ) and subtracting and adding one SD of the population mean. The cut-off of the fruit and vegetables component was lowered to $\geq$400 g/d as it excludes fruit juices (included in the original recommendations).

In the end, the 6 components were summed up into a total score (ranging from 0 to 6). The total index score was also categorized into low (0–1 points), medium (2 or 3 points) and high (4–6 points).

2.4. Biomarkers of inflammation

During the MDC baseline examinations, participants donated non-fasting blood samples at their first visit to the study centre. Blood components were separated and plasma and serum were stored at −80 °C while mononuclear cells (including white blood cells and monocytes) were frozen at −140 °C.

Leukocyte counts were assessed using an SYSMEX K1000 automatic counter (Sysmex Europe, Norderstedt, Germany), and expressed as total (WBC) and differential (i.e. neutrophils, lymphocytes, and mixed cells including monocytes, eosinophils and basophils).