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Association of proinflammatory diet with low-grade inflammation: results from the Moli-sani study

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ABSTRACT

Objectives: The association between diet and inflammation is well documented. Yet, no evidence exists on the relationship between the inflammatory potential of the diet and low-grade inflammation (LGI) as measured by a composite score of plasma and cellular biomarkers. The aim of this study was to assess the association between the Dietary Inflammatory Index (DII®) and LGI in a large population-based cohort. *Methods:* Cross-sectional analyses were conducted on data from 20 823 adults (age ≥35 y; 48% male) without acute inflammation, who were recruited within the general population of the Moli-sani study from 2005 to 2010. LGI was measured by using a composite score (INFLA-score) including platelet and leukocyte counts, the granulocyte to lymphocyte ratio, and C-reactive protein. DII scores were computed based on dietary intake assessed by the EPIC food frequency questionnaire. Multivariable linear regression models were fit to produce adjusted regression coefficients and 95% confidence intervals (CIs). *Results:* Higher DII scores were associated with increased LGI (β = 0.131; 95% CI, 0.089–0.174 for the highest versus lowest quintile of DII) after adjusting for age, sex, lifestyle, prevalence of chronic diseases, and health conditions. A higher DII score also was positively associated with each single biomarker of inflammation included in the INFLA-score, unhealthy behaviors (smoking, sedentary lifestyle), and insulin. *Conclusions:* Higher DII scores, indicating greater inflammatory potential of the diet, were directly associated with LGI, as measured by a composite score of plasma and cellular biomarkers of inflammation. These findings are consistent with the contributing role of diet-mediated inflammation in increasing risk for inflammation-related chronic diseases.

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Introduction

It has been shown that dietary components are associated with a variety of chronic conditions ranging from cardiovascular diseases (CVDs) to cancer and mental disorders [1–4]. Acute inflammatory response is the process of the body's natural reaction to injury or infection to heal wounds and promote tissue regeneration [5,6]. Chronic, low-grade (or subclinical) systemic inflammation is associated with numerous chronic conditions [7,8] and the ironic inability to mount a competent immune response to injury or infection [9]. A number of biomarkers, both circulating (i.e., C-reactive protein [CRP]) and cellular (i.e., leukocyte count) have been associated with the onset of major chronic diseases, such as CVDs [10,11] and cancer (8, 9) and, more recently, with higher risk for death [12].

The Mediterranean dietary pattern, which is high in fruits, vegetables, olive oil, whole grains, and fish, and low in red meat and butter, with moderate alcohol intake, has been associated with lower levels of inflammation [13]. By contrast, the Western-type diet, which is high in red meat, high-fat dairy products, and refined grains, has been associated with higher levels of CRP, interleukin (IL)-6, and fibrinogen [14]. Specific nutrients also have consistently been associated with lower levels of inflammation. These include ω-3 poly-unsaturated fatty acids [15], fiber [16], vitamin E [17], and β-carotene [18].

The Dietary Inflammatory Index (DII®) was developed by researchers at the University of South Carolina to estimate the overall inflammatory potential of the diet [19]. The DII is based on an extensive literature search incorporating cell culture, laboratory animal, and epidemiologic studies of the effects of diet on inflammation. Previously, the DII was shown to be associated with single markers of inflammation, including CRP, IL-6, and tumor necrosis factor-α levels [20–28]. Specifically, it has been observed in Italy that the DII is associated with several cancers and myocardial infarction [29–36]. To our knowledge, no work has yet been conducted to validate the DII with low-grade inflammation (LGI), as measured by a composite score of plasma and cellular biomarkers [12]. The aim of the present study was to conduct a cross-sectional analysis to examine the association between DII scores and LGI in the general adult population of the Moli-sani study.

Materials and methods

Study population

Data presented here are from the Moli-sani study, a large population-based cohort study that recruited 24 325 men and women ≥35 y of age from the general population of the Molise region, in central-southern Italy from 2005 to 2010 [37].

For the purpose of the present analyses, we excluded individuals with implausible energy intakes (<800 kcal/d in men and <500 kcal/d in women or >4000 kcal/d in men and >3500 kcal/d in women; 3.2%), missing data on dietary habits (0.4%) or on markers of LGI (3.3%), CRP levels ≥10 mg/L (4%), unreliable medical or dietary questionnaires (1% and 3.9%, respectively), and missing data on main covariates (4.5%).

The final sample consisted of 20 823 individuals. The Moli-sani study complies with the Declaration of Helsinki and was approved by the ethical committee of the Catholic University in Rome, Italy. All participants provided written informed consent.

Inflammatory biomarkers and INFLA-score

Blood samples were obtained from participants who had fasted overnight and had refrained from smoking for ≥6 h. A full description of biomarkers measurement is given elsewhere [38].

LGI was assessed by an INFLA-score, which has already been defined and used within the Moli-sani cohort [39] and includes CRP (mg/L), leukocyte (white blood cells, $\times 10^9$/L) and platelet counts ($\times 10^9$/L), and the ratio of granulocyte to lymphocyte (G/L ratio). For all four components, being in the highest deciles (7–10) was scored from +1 to +4; whereas being in the lowest deciles (1–4) was negatively scored from –4 to –1. The mid-deciles (5 or 6) were assigned a score of zero. The INFLA-score, which is sum of the four components, ranged between –16 and +16. Higher scores represented greater LGI. For analytical purposes, the INFLA-score was rescaled to have a mean of 0 and an SD of 1.

Assessment of risk factors

History of CVD included documented angina, myocardial infarction, revascularization procedures, and cerebrovascular events. History of cancer included self-reported diagnosis of the disease. Hypertension was defined as systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg or treatment for hypertension. Hypercholesterolemia was defined if total cholesterol ≥240 mg/dL or by use of specific medication. Diabetes was defined as fasting blood glucose ≥126 mg/dL, or on the basis of specific pharmacologic treatment.

Socioeconomic variables

Education was based on the highest qualification attained and was categorized as up to lower secondary school (≤8 y of study), up to higher secondary school (8–13 y of study), and postgraduate (>13 y of study). Household income, expressed as earned euros per year, was a five-level variable (<10 000; 10 000–25 000; 25, 000–40 000; >40 000 with missing values collapsed into a non-respondent category). Occupational social class was based on the Registrar General's occupation-based classification scheme but, differently from the original UK classification, the social class for women was obtained as done for men [40].

Dietary information

Food intake during the year before enrollment was assessed by the validated Italian EPIC food frequency questionnaire (FFQ) [41]. Adherence to the Mediterranean diet (MD) was defined according to the Mediterranean Diet Score (MDS) [42], with score ranging from 0 to 9.

Food antioxidant content was appraised by a score determining the content in antioxidant vitamins and phytochemicals of each food group and ranged from –99 to 99 with higher values indicating increased consumption of foods rich in antioxidants [43]. The polyphenol content of diet was measured by a polyphenol antioxidant content score calculated as in Pounis et al. [43].

Variety of fruit and vegetable intake was assessed by a Diet Diversity Score [44] derived from the total number of individual vegetable and fruit items eaten at least once in a 2-wk period (range 0–37). FFQ-derived dietary information was used to calculate DII scores for all participants, as described elsewhere [19]. Briefly, the dietary data for each study participant were first linked to the regionally representative global database that provided a robust estimate of a mean and SD for each of the food parameters (i.e., foods, nutrients, and other food components such as flavonoids) considered. A *z*-score was derived by subtracting the "standard global mean" from the amount reported and then dividing this value by the SD. To minimize the effect of "right skewing" (a common occurrence with dietary data), this value was then converted to a centered proportion, which was then multiplied by the respective food parameter inflammatory effect score (derived from a literature review and scoring of 1943 "qualified" articles) to obtain the individual's food parameter–specific DII score. All of the food parameter–specific DII scores were summed to create the overall DII score for every participant. For the present study, data were available for 34 food parameters (carbohydrate, protein, total fat, alcohol, fiber, cholesterol, saturated fat, monounsaturated fat, polyunsaturated fat, ω-3, ω-6 fatty acid, niacin, thiamin, riboflavin, vitamin B_{12}, vitamin B_6, iron, magnesium, zinc, vitamin A, vitamin C, vitamin D, vitamin E, folic acid, β-carotene, anthocyanidins, flavan-3-ol, flavones, flavonols, flavonones, isoflavones, garlic, onion, and tea). A description of validation work of the DII score, based on both dietary recalls and the 7-d dietary recall, a structured questionnaire similar in terms of its layout to an FFQ, is available elsewhere [23].

Risk factor assessment

Leisure-time physical activity (LTPA) was expressed as daily energy expenditure in metabolic equivalent task-hours. Body mass index (BMI) was calculated as weight (kg)/height $(m)^2$ and then grouped into three categories as normal (≤25 kg/m^2), overweight (>25 to <30 kg/m^2) or obese (≥30 kg/m^2). Abdominal obesity was defined as waist-to-hip ratio ≥0.85 or ≥0.90 for women and men, respectively [45]. Participants were classified as never-smokers, current smokers, or ex-smokers (quitting from ≥1 y).