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A Mediterranean diet and risk of myocardial infarction, heart failure and stroke: A population-based cohort study

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ABSTRACT

Background and aims: The Mediterranean diet, which is palatable and easily achievable, has been associated with lower all-cause and cardiovascular disease (CVD) incidence and mortality. Data on heart failure (HF) and stroke types are lacking. The aim was to examine a Mediterranean diet in relation to incidence of myocardial infarction (MI), HF and stroke types in a Swedish prospective cohort.

Methods: In a population-based cohort of 32,921 women, diet was assessed through a self-administered questionnaire. The modified Mediterranean diet (mMED) score was created based on high consumption of vegetables, fruits, legumes, nuts, whole grains, fermented dairy products, fish and monounsaturated fat, moderate intakes of alcohol and low consumption of red meat, on a 0–8 scale. Relative risks (RR) with 95% confidence intervals (CI), adjusted for potential confounders, were estimated by Cox proportional hazards regression models.

Results: During 10 y of follow-up (1998–2008), 1109 MIs, 1648 HFs, 1270 ischemic strokes and 262 total hemorrhagic strokes were ascertained. A high adherence to the mMED score (6–8), compared to low, was associated with a lower risk of MI (RR: 0.74, 95% CI: 0.61–0.90, $p = 0.003$), HF (RR: 0.79, 95% CI: 0.68–0.93, $p = 0.004$) and ischemic stroke (RR: 0.78, 95% CI: 0.65–0.93, $p = 0.007$), but not hemorrhagic stroke (RR: 0.88, 95% CI: 0.61–1.29, $p = 0.53$).

Conclusions: Better adherence to a Mediterranean diet was associated with lower risk of MI, HF and ischemic stroke. The Mediterranean diet is most likely to be beneficial in primary prevention of all major types of atherosclerosis-related CVD.

1. Introduction

Cardiovascular disease (CVD) is the leading cause of morbidity and death worldwide [1,2]. The costs for health care and medications related to CVD surpass €200 and $300 billion in Europe and the U.S., respectively [2]. Lifestyle including a healthy diet can reduce CVD mortality by 50% [3,4]. The Mediterranean diet is palatable and easily achievable. Therefore, this diet has gained popularity also in non-Mediterranean countries [5]. It is characterized by high intakes of vegetables, fruits, legumes, nuts, whole grains, monounsaturated fat, moderate intakes of dairy products (mainly cheese and yogurt), fish and alcohol and low intakes of red and processed meat [6]. It has been consistently observed that the Mediterranean diet is associated with lower all-cause and CVD mortality in prospective studies [7–14], as well as with lower incidence of myocardial infarction (MI)/coronary heart disease and stroke [7,14–19]. Furthermore, high adherence to the Mediterranean diet has been associated with improvement in clinical risk factors of CVD in clinical trials [20–23]. However, data is scarce on the relationship between the Mediterranean diet and incidence of heart failure (HF) [24] and stroke types [14,17,19,25]. Moreover, most previous studies have assessed the association between a Mediterranean diet and risk of either total CVD or only MI or stroke. Hence, the aim of this study was to determine the association between the adherence to a Mediterranean diet, as indicated by a

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modified Mediterranean diet (mMED) score, and incidence of MI, HF and stroke types, during a 10-year follow up of a large Swedish population.

2. Subjects and methods

2.1. Study population

The population-based, prospective Swedish Mammography Cohort provided data for the present study. In the late autumn of 1997, 39,227 women who were born between 1914 and 1948, were residents of Uppsala and Västmanland counties of central Sweden, and had already participated in the Swedish Mammography Cohort-study 10 years earlier, completed a 350-item questionnaire about diet and lifestyle (participation rate 70%). Women with a missing or an erroneous National Registration Number were omitted. We also excluded those with cancer (n = 1803) and cardiovascular disease (ischemic heart disease, HF and stroke, n = 2495) at baseline and those with implausible energy intakes (i.e., 3 SDs from the $\log_e$-transformed mean total energy intake; n = 404). Furthermore, women with missing values of the components of the mMED score were excluded (n = 1319). After these exclusions, 32,921 women (aged 48–83 years) remained for the analysis. Informed consent was obtained from each participant and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the Regional Ethical Review Board at Karolinska Institutet in Stockholm, Sweden.

2.2. Baseline assessment of covariates and diet

We obtained information on education, body weight and height, tobacco smoking, aspirin use, prevalence of hypertension, hypercholesterolemia, family history of MI before 60 years of age, alcohol consumption, physical activity and diet through a self-administered questionnaire. We calculated body mass index by dividing the weight in kilograms by the square of height in meter. Data on diabetes were available through the National Diabetes Register, the National Patient Register at the National Board of Health and Welfare, and was also self-reported in the questionnaire.

The food frequency questionnaire (FFQ) reflected the habitual average consumption of 96 different foods/food items and beverages during the previous year. The FFQ included open-ended questions with predefined serving sizes (1 glass, 1 cup, teaspoon, tablespoon, slice) for commonly consumed foods (e.g. dairy products and bread) and 8 predetermined categories of food frequency (range from never to >3 times/day) for other food items, including vegetables, fruits, legumes, nuts, grains, fish, red and processed meat and alcoholic beverages. Reported frequencies of consumption of specific alcoholic beverages (wine, beer, and liquor) were multiplied by the reported amount, consumed at each occasion, resulting in an average total alcohol intake [26]. The question about the quality of fat intake was “what type of fat do you usually use on sandwiches and in dressing and cooking?” We calculated totally energy intake by multiplying the frequency of intake of each food item by the energy content of age-specific portion sizes, using composition values from the Swedish Food Administration Database [27]. The FFQ used in the present study has been validated for foods and nutrients by comparison with the mean of multiple 24-h recall interviews distributed over a year [28]. The Spearman correlation coefficients between estimates from the FFQ and the mean of fourteen 24-h recall interviews ranged from 0.44 (protein) to 0.81 (alcohol) for macronutrients, with a mean value of 0.65 [28].

2.3. Modified Mediterranean diet (mMED) score

The mMED score indicating the degree of relative adherence to the traditional Mediterranean diet was adapted from the Mediterranean diet scale by Trichopoulou et al. [8,9]. The mMED score included: 1) vegetables and fruits (excluding fruit juices and potatoes), 2) legumes and nuts, 3) non-refined/high fiber grains (whole meal bread, crisp bread, oatmeal and bran of wheat), 4) fermented dairy products (cultured milk, yogurt, and cheese), 5) fish, 6) red and processed meat, 7) use of olive oil and/or rapeseed oil and 8) alcohol. Participants with an intake above the median intake received 1 point for the presumed beneficial components: vegetables and fruits, legumes and nuts, non-refined/high fiber grains, fermented dairy products, and fish; for intake below the median intake they received 0 points. For red and processed meat, the reverse was applied. For alcohol, a value of 1 was assigned to women who consumed on average between 5 and 15 g of ethanol per day, otherwise 0 points. For the quality of fat, 1 point was assigned to women who used olive oil and/or rapeseed oil as a main source of fat for cooking or as dressing, otherwise 0 points. The total mMED score ranged from 0 (low adherence) to 8 (high adherence to Mediterranean diet).

2.4. Case ascertainment and follow-up

Primary incident cases of MI, HF (including HF event listed either as the primary diagnosis or at any diagnosis position) and stroke that occurred in the cohort during follow-up were ascertained by linkage of the study cohort to the Swedish Inpatient Register and the Swedish Cause of Death Register. We used the International Classification of Diseases, 10th revision, codes to classify the cardiovascular events as MI (I21), HF (I11 and I50), ischemic stroke (I63) and hemorrhagic stroke (I60 [subarachnoid hemorrhage] and I61 [intracerebral hemorrhage]).

2.5. Statistical analysis

Participants accumulated follow-up time from 1 January 1998 until the date of diagnosis of MI, HF, or stroke, date of death (the Swedish Cause of Death Register), or end of follow-up (31 December 2008), whichever came first. We categorized women into quartiles of the mMED score (slightly larger 1st quartile). We also analyzed mMED score as a continuous variable per 1-point increment. Relative risks (RR) with corresponding 95% confidence intervals (CIs) of MI, HF, ischemic stroke and hemorrhagic stroke were estimated by using Cox proportional hazards regression models with age as the time scale. All multivariable models were also adjusted for education level (≤12 years, >12 years) and established risk factors for cardiovascular disease, including family history of MI before 60 year of age (yes or no), cigarette smoking (current, former, never), physical activity as following: >40 min walking and/or cycling per day (yes or no), >1 h of exercise per week (yes or no), body mass index (<20, 20–24.9, 25–29.9, ≥30 kg/m^2), history of hypertension (yes or no), history of hypercholesterolemia (yes or no), history of diabetes (yes or no), aspirin use (never, 1–6 tablets/week, ≥7 tablets/week) and total energy intake (continuous, kcal/day). Missing values were treated as a separate “missing category” in the models and were few (<2%), with the exception of physical activity (<10%).

In order to determine whether associations could be described by a single component, we also tested single components of the mMED score separately as variables above/below the median (while mutually adjusted for all other components and risk factors). We also ran a sensitivity analysis after excluding alcohol from the mMED score. For HF, we performed a sensitivity analysis including