Dietary patterns and total mortality in a Mediterranean cohort: the SUN project

ABSTRACT

Background: Different dietary patterns have been associated with several health outcomes, including morbidity and mortality. There is little evidence on the association between empirically-derived dietary patterns and all cause mortality in Southern European populations.

Objective: the aim of this study was to prospectively evaluate the association between an empirically-derived dietary pattern and all-cause mortality.

Design: The SUN Project is an ongoing, multipurpose, prospective and dynamic Spanish cohort.

Participants/setting: a prospective cohort of 16,008 middle-aged Spanish adults. All of them were former university graduates (alumni) (59.6 percent women, mean age: 38 years). Usual diet was assessed at baseline with a validated semiquantitative food-frequency questionnaire.

Main outcome measures: Deaths were confirmed by review of medical records and of the National Death Index.

Statistical analyses performed: Dietary patterns were ascertained through a factor (principal component) analysis based on 30 predefined food groups. Participants were classified according to tertiles of adherence to the three main dietary patterns identified with factor analysis. Cox regression models were fitted to estimate multivariable-adjusted hazard ratios (HR) and 95% confidence intervals (CI) for mortality.

Results: Three major dietary patterns were identified: they were labelled Western dietary pattern (WDP) (rich in red and processed meat, potatoes and fast food), Mediterranean dietary pattern (MDP) (rich in vegetables, fish and seafood, fruits, and olive oil) and Alcoholic beverages dietary pattern (ABDP). During follow-up, 148 deaths were reported (mean age at death: 54.5 years). After adjustment for potential confounders, the lowest risk of all-cause mortality was found in the tertile of highest adherence to the MDP (adjusted HR for third vs. first tertile: 0.53; 95% CI: 0.34-0.84) (p for trend <0.01). The WDP and ABDP showed no significant association with mortality.

Conclusions: Greater adherence to an empirically-derived dietary pattern approaching the traditional Mediterranean diet was associated with a reduction in the risk of all-cause mortality among middle-aged Mediterranean adults.

INTRODUCTION

Dietary habits play an important role as determinants of health status. The promotion of healthy dietary patterns can be especially useful for health promotion and for the prevention of major chronic diseases, such as cancer or cardiovascular diseases, which are the main global causes of mortality (1).

The study of food patterns offers a broader view of food and nutrient consumption, and could better predict disease risk than the study of single nutrients or foods (2,3,4). In the last decade, nutritional epidemiologists have focused on this new way of assessing exposure to diet which overcomes the methodological limitations related to the complex interactions that can exist among foods and nutrients (5).

There are two methods to characterize dietary patterns: the a priori approach consists of calculating a score of the overall quality of a diet based on compliance with current dietary guidance and plausible hypotheses, whereas the a posteriori approach empirically derives combinations of foods or nutrients through several statistical techniques (for example factor or cluster analysis) that explain a sizeable amount of total variability in food intake (6,7).

Several studies (8-15), have evaluated the effect of different dietary patterns as defined by healthy a priori scores and certain health outcomes, including total mortality (12-15). Most of them have reported an inverse association between adherence to healthy dietary patterns defined a priori and overall mortality. This inverse association with total mortality has been especially consistent for a priori defined scores which include the typical components of the traditional Mediterranean diet (2,9-10,16-17).

However, to our knowledge, there is still limited evidence on the association between the adherence to empirically-derived dietary patterns and all-cause mortality (8,18-21) in Mediterranean populations (22).

In the present study, we investigated the association between empirically-derived dietary patterns and total mortality in a cohort of university graduates conducted in Spain (the SUN project).

SUBJECTS AND METHODS

Study population

The SUN project is an ongoing, multipurpose, prospective and dynamic Spanish cohort of university graduates designed to investigate associations between several sociodemographic, nutritional and lifestyle characteristics and the occurrence of major chronic diseases (23). The study protocol was approved by the Institutional Review Board of the University of Navarra. Voluntary completion of the first questionnaire was considered to imply informed consent.

The study methods have been published in detail elsewhere (24-25). In short, the recruitment of participants started in December 1999 and it is permanently open. Participants are contacted every 2 years through mailed or web-based questionnaires. Non respondents receive up to 5 additional mailings requesting their follow–up questionnaire. To assure a minimum follow-up of two years, 21,353 participants recruited before September 2009 were considered as candidates for this analysis. We excluded 5,345 participants because one or more of the following criteria: 1,294 participants reported prevalent cancer, cardiovascular disease or diabetes at baseline, 1,924 participants showed total energy intake out of predefined (26) and, finally, 2,126 participants did not respond to the follow-up questionnaires. Therefore, the final sample comprised 16,008 participants.

Assessment of dietary exposure

Usual diet was assessed at baseline with a semiquantitative 136-item food-frequency questionnaire (FFQ). This FFQ has been previously validated in Spain (27), recently re-evaluated (28) and extensively used in large Spanish studies of nutritional epidemiology (30-31). Each item included a typical portion size, and consumption frequencies were gathered in nine categories that ranged from “never or almost never” to “≥ 6 times/day”. Daily food consumption was estimated by multiplying the portion size of each food item by its consumption frequency. Trained dietitians derived food and nutrient intakes using a computer program based on available information in Spanish food composition tables (32-33). Participants out of predefined limits for total energy intake (<500 or > 3500 kcal/day in women, or <800 or > 4000 kcal/day in men) were excluded from the main analyses.

Assessment of other variables

The baseline questionnaire also included questions about diverse characteristics: socio-demographic (sex, age, marital status, college degree and employment), and anthropometric (weight, height and weight change in the last 5 years) variables, lifestyle and health-related habits (consumption of alcohol, smoking status, time spent watching TV or physical activity), family history of major diseases, obstetric history for women (pregnancy) and medical history variables (medication use, prevalence of chronic diseases and lipid or blood pressure levels).

Body mass index (BMI) was calculated directly by measuring weight (kilograms) and height (meters) and dividing weight by the square of height.

Information on physical activity was collected at baseline through a previously validated questionnaire (34), which contained time spent in 17 different activities and showed a fair correlation with objectively measured energy expenditure. The time spent in each activity was multiplied by a multiple of the resting metabolic rate (MET score) in conformity with previously published guidelines (35).

The validity of self-reported weight, BMI and hypertension in the SUN cohort has been previously documented (36-37).

Assessment of the outcome

If participants did not answer any of the up to five mailings with the follow-up questionnaires, they were contacted by email or phone. Most deaths (>85%) were reported to the project team by the participants´ relatives, work associates and postal authorities. For participants lost to follow-up, the National Death Index was checked every six months to identify deceased cohort members. Taking into account all these sources of information, we considered that follow-up ascertainment for the deceased participant was complete.

The follow-up for each participant was calculated from the date of returning the baseline questionnaire to the date of death or to the date of returning the last follow-up questionnaire of June 2012, whichever came first.

Assessment of dietary patterns

The 136 food items included in the food-frequency questionnaire were grouped into 30 predefined food groups. The grouping scheme was based on the similarity of nutrients profile or the typical culinary usage for each of the foods. To identify major dietary patterns of participants we performed a principal component analysis. In determining the number of factors to retain, we considered the Scree test, eigenvalues >1 and the interpretability of the factors (See supplemental material). Factors were then rotated with an orthogonal rotation procedure (varimax rotation), so noncorrelated factors were derived and results were more easily interpretable. Absolute factor group loadings ≥ 0.30 were considered relevant components of the dietary patterns (Table 1).

According to the observed factor loadings of the food groups, we labelled the first factor as “Western dietary pattern” (WDP), the second pattern as “Mediterranean dietary pattern” (MDP), and the third pattern as “Alcoholic beverage dietary pattern” (ABDP). The score for each participant was calculated by summing the standardized consumption of each food group weighted by the coefficient of each factor score. The obtained quantitative score was then categorized into tertiles.

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Statistical analysis

We used Cox regression models with the length of follow-up as the primary time variable, to test the following hypotheses: a) the current diet in this Spanish population is exhibiting a departure from the traditional MDP and adopting instead a WDP; b) a departure from the traditional MDP and a consequent higher adherence to a Western-type dietary pattern is associated with higher risk of mortality in this Mediterranean cohort; c) there is an inverse association between a higher adherence of the MDP and risk of death; and d) the MDP is associated with less risk of mortality also among younger subjects.

Hazard ratios (HR) with 95 % confidence intervals (CI) for the two upper tertiles were calculated using the lowest tertile of adherence to each dietary pattern as the reference category.

In the multivariable models, potential confounders included as covariates were age (20 categories), sex, total energy intake (Kcal/day, continuous), total alcohol intake (g/day, continuous), smoking status (3 categories), baseline BMI (kg/m2, continuous), physical activity during leisure time (2 categories), self-reported hypertension, self-reported hypercholesterolemia, self-reported depression, years of university education (4 categories), prescription of a special diet at baseline and daily hours of television watching (continuous).

Additionally, tests of linear trend across successive tertiles of adherence were conducted assigning the median value to each tertile category and treating the variable as continuous.

We performed the following sensitivity analyses to assess the robustness of our findings: a) including only men or only women, b) including only health professionals or only non-health professionals, c) excluding participants with hypertension or hypercholesterolemia at baseline, d) adopting different allowed limits for total energy intake (27): percentiles 5 to 95 or percentiles 1 to 99, e) including participants with prevalent diabetes, CVD and cancer at baseline, f) excluding participants who died early during follow-up (within the two first years of follow-up), g) including only participants with age at recruitment less than 55 years, h) including participants with premature death (occurring less than 60 years or 65 years), i) excluding participants with special diets at baseline, j) excluding participants with nine or more missing values in the baseline food-frequency questionnaire, k) imputing deaths to all those participants who were untracked during follow-up and had three or more cardiovascular risk factors at baseline, l) adopting the following criteria to compute additional follow-up times: participants who did not respond to any follow-up questionnaire, were imputed a follow-up time equal to the median follow-up time of the rest of the sample and a random term taken from a uniform distribution in the range of minus/plus the standard deviation of observed follow-up times, and m) additionally adjusting the results for incident new cases of CVD (n=172), or cancer (n=476) or diabetes (n=165) occurring during the follow-up period.

We used SPSS version 15.0 (SPSS Inc., Chicago, Illinois, USA) for all analyses.

RESULTS

The main analysis

The mean (SD) age of the 16,008 participants was 38.1 (12.3) years. The 25th and 75th percentiles of age were 18 and 91. The median follow-up of participants was 6.96 years, with a minimum and maximum follow-up of 0.10 and 12.9 years respectively. During this period 148 deaths were registered. The main causes of death were cancer (36.9 %), cardiovascular disease (18.1 %), accidents (8.1 %) and other causes (36 %). The median age at recruitment for deceased participants was 54.5.

Three major dietary patterns, explaining 19.7 % of the total variance in the consumption of the 30 food groups, were identified in the factor analysis procedure. Absolute factor loadings greater than or equal to 0.30 for each dietary pattern are presented in Table 1. The first factor, WDP, was characterized by a high consumption of red meat, processed meats, potatoes, processed meals, fast food, whole-fat dairy products, sauces, commercial bakery, eggs, sugar-sweetened sodas, refined grains and sugary products, and by a low consumption of low-fat dairy products. The second factor, MDP, was characterized by a high consumption of vegetables, fish and seafood, fruits, olive oil, low-fat dairy products, poultry, whole-wheat bread, nuts, juices and legumes. The third factor, ABDP, was characterized by a high alcohol intake (wine, beer and other alcoholic beverages).

Baseline characteristics of participants according to the first and last tertile of the three dietary patterns are shown in Table 2. Subjects with the highest adherence to the WDP were more likely to be men, younger, current smokers and less physically active. Their higher intake of total energy and fat (13.6% of saturated fat) was probably related to higher intakes of unprocessed red meat, processed meats, fast-food, processed meals, whole-fat dairy products and alcohol. On the other hand, participants with the highest adherence to the MDP were more likely women, older, ex- smokers, more physically active and more likely to have hypertension at baseline. This pattern was characterized by a lower intake of total fat (11.2 % of saturated fat). Finally, subjects in the third tertile of adherence to the ABDP were more likely men, older, smokers, more physically active and also with a higher prevalence of hypertension at baseline.

HR and 95% CI for total mortality according to baseline adherence to the three dietary patterns are shown in Table 3. No association between the highest tertile of adherence to the WDP or ABDP and total mortality was apparent in the multivariable model (HR 0.79; 95% CI: 0.45, 1.38 and HR 0.78; 95% CI: 0.48, 1.27 respectively). Also, no statistically significant trend was evident (P for trend= 0.40 and P for trend= 0.27 respectively).

In contrast, the MDP showed a strong inverse association with total mortality when we compared the highest tertile of adherence versus the lowest tertile (HR 0.53; 95% CI: 0.34, 0.84, P for trend = 0.01) after adjusting for age, sex and other potential confounders.

The sensitivity analysis

We conducted several sensitivity analyses to verify our findings. Tables 4, 5 and 6 show the HR and 95% CI of mortality for the comparisons between the highest vs the lowest thirds of adherence to each of the three dietary patterns. In general, the main results did not change substantially. Thus, the inverse association between the MDP and risk of death was robust and remained statistically significant in most sensitivity analyses (Table 4). Finally, no association between a higher adherence to the WDP or the ABDP and mortality was observed after sensitivity analyses were carried out (Tables 5 and 6).

DISCUSSION

In this large cohort of middle-aged Spanish university graduates three major dietary patterns were found using a principal component analysis: the WDP, MDP and the ABDP.

Although dietary patterns could be discerned in our sample, these patterns explained only a reduced proportion (20%) of total variability in dietary intake. A highest adherence to the MDP, characterized mainly by a high intake of vegetables, fish and seafood, fruits and virgin olive oil, was associated with a significant 47% reduction in the risk of all-cause mortality. However, a greater adherence to the WDP or ABDP did not present any apparent association with mortality in our Mediterranean cohort.

The finding of a prominent Western-type dietary pattern in this Mediterranean cohort of highly educated middle-aged adults is surprising. Our results show a dangerous departure in Spain from the traditional Mediterranean diet, mainly among younger individuals, who seem to be more likely to adopt “Western- type” diets. However, the MDP was the second pattern identified. These data are in agreement with previous studies in Spain and in other Mediterranean countries bordering the Mediterranean Sea

(22, 38-41). A possible explanation could be that highly educated people are more likely to work in activities which very often may also condition their dietary pattern (38).

Our findings were obtained using a principal component analysis, a method that might involve some degree of subjectivity and that identified three specific dietary patterns, which do not necessarily reflect the traditional MDP and WDP (41). Thus, for example, processed meat or unprocessed red meat consumption was higher in the upper tertile of adherence to MDP than in the lowest tertile.

However, in spite of these differences and the methodological limitations inherent to the use of principal component analysis and that must be taken into account (e.g. the number of components extracted of empirically-derived patterns or the establishment of predefined food groups), we found a strong inverse association between a Mediterranean-style diet and total mortality.

Moreover, our results are in line with previous findings that have investigated the association between healthy overall dietary patterns and all-cause mortality using factor analysis, although these previous analyses did not always identify a MDP. Thus, in a previous study in USA, empirically derived dietary patterns (that were also in concordance with food- based dietary guidelines) were associated with a lower risk of all-cause mortality (12). In the Nurses' Health Study, women with a higher adherence to the "Prudent" dietary pattern had a lower risk of total and cardiovascular mortality (21). Contrarily, women with a higher adherence to the WDP showed a higher risk of all-cause, cardiovascular and cancer mortality. In a cohort study of 74,942 Chinese women, a fruit–rich diet was related to a lower probability of premature death, whereas a meat-rich dietary pattern appeared to increase the risk of mortality (8). On the other hand, a dietary pattern rich in olive oil and raw vegetables was associated with lower overall mortality in Italian elderly subjects (23). However, these results are not directly comparable with ours, because the participants of that study were aged 60 or older. In a Danish prospective study with 3,698 men and 3,618 women aged 30-70 years, a prudent pattern was inversely associated with all-cause and cardiovascular mortality, while a WDP was not significantly associated with mortality (20).

Finally, it is noteworthy that, except for the study conducted in Italy (23) and a previous study in the Spanish EPIC-cohort which assessed coronary heart disease as the outcome, but not total mortality (22), most studies using this approach have been conducted outside the Mediterranean setting.

In contrast to the empirically-derived (or post hoc) approach, several previous studies have ascertained the association between a priori defined dietary patterns and survival among middle-aged and elderly subjects in different European countries (10-11,16-17,43) and in the USA (18). Most of them (10-11,16-18,43) have reported inverse associations between an a priori defined Mediterranean-type diet or dietary patterns similar to the traditional Mediterranean diet and overall mortality. However, different country-specific dietary patterns have been described in Mediterranean populations and these results should be interpreted with caution.

Several mechanisms have been proposed to explain the reported inverse association between better adherence to a MDP and mortality. First, several studies have demonstrated that its higher content of vitamins, minerals, antioxidants, fibre, omega-3 fatty acids (from fish) and monounsaturated fatty acids (from olive oil) have beneficial effects on health (44). In fact, individuals with a higher adherence to this dietary pattern had a better nutrient profile and lower total fat and saturated fatty acid intake than those with the lowest adherence. Besides, a previous study in the SUN cohort showed that in subjects following a MDP the prevalence of inadequate intakes of micronutrients was considerably lower (13). Second, food groups of dietary pattern present interactions and synergistic effects that could have a protective role for the primary prevention of major chronic diseases, which are the main causes of mortality in developed countries (2,6).

We split the sample into non-health or health professionals, although we did not find a statistical interaction (p=0.816). The association between a better adherence to MDP and lower mortality was only present among health professionals. However we acknowledge that no statistically significant differences in HRs between the health professionals and the non-health professionals were found. It seems plausible to think that health professionals are more likely to complete the questionnaires more accurately and thus to provide an information with reduced measurement error (45). On the other hand, it is possible that the protective effect of MDP observed only in men, might be due to the fewer deaths observed within women (n=47). Finally, when we excluded participants with poorer dietary assessment, because they left nine or more missing values in the FFQ, the results did not change. This finding does not support a potential misclassification bias in our results.

Several explanations are possible to the unexpected lack of association between the WDP or ABDP and total mortality found in all our analyses. It is possible that unmeasured or uncontrolled residual confounders that were not considered in our analyses could explain this association. Another explanation is that the WDP in our cohort differs in several aspects from the usual Western dietary pattern found in other large cohorts outside the Mediterranean setting. Thus, our participants with higher adherence to WDP had also higher consumption of some potentially beneficial foods, such as olive oil, poultry and fish (46-47). Besides, it is possible that in order to reduce mortality risk, it is more important to increase the number and variety of healthy foods than to reduce the consumption of unhealthy foods regularly consumed. In fact, a cohort study conducted in Sweden with 59,038 women, found that for each additional healthy food added to the diet, total mortality was lowered by 5% (15). However, this interpretation has to be made cautiously. Finally, some frequently consumed foods in the WDP, for example potatoes or sauces, are customarily combined with olive oil, the main culinary fat in the Mediterranean cuisine. Finally, we acknowledge that some healthy eating habits common in the Mediterranean area were not fully collected in the FFQ, such as some aromatic herbs or carefully prepared and minimally processed dishes with a variety of plant-derived ingredients (48). Thus, participants with higher adherence to WDP might be consuming also some of these healthy dishes.

Our study has several strengths, including a large sample of participants, a high retention rate, the control for a wide number of potential confounders, the long-term follow-up and the prospective design which avoids the possibility of reverse causation in the reported associations. Other strength is the existence of published validation studies for most of the measurements including dietary assessment (36-37,28,29). Moreover, the high educational level of this cohort allows a higher accuracy in their self-reported data and a better retention in the cohort. Finally, the robustness of findings in multiple sensitivity analyses is another strength of our study.

There are some limitations in our study. First, our participants do not constitute a representative sample of the general Spanish population (a young cohort formed entirely by university graduates). However, we consider that our study has a strong internal validity because of the good retention rate and the high quality of the self-reported information. This may compensate for the limitations that selecting a highly educated cohort may impose to generalizability or external validity. Second, residual confounding might have not been totally excluded. However, we performed the analyses adjusting for the main known risk factors for mortality. Therefore, we do not consider residual confounding as the most likely explanation for the observed results. Finally, we acknowledge the limitation related to the small number of deaths which precludes sub-analyses according to specific causes of mortality.

In conclusion, our data suggest that greater adherence to the MDP is associated with improved survival and with a reduced risk of all-cause mortality in a Mediterranean population of young adults. Although further research is required to confirm the present findings in other Mediterranean and non-Mediterranean settings, last Dietary Guidelines for Americans 2010 confirm that a healthy dietary pattern should be rich in nutrient-dense foods and beverages such as vegetables, fruits, whole grains, fat-free or low-fat milk and milk products, seafood, lean meats and poultry, eggs, beans and peas, nuts and seeds (49-50). Most of these foods are typical of the traditional Mediterranean diet.

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