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ORIGINAL CONTRIBUTION

Identification of change-points in the relationship between food groups in the mediterranean diet and overall mortality: an 'a posteriori' approach

Francesco Sofi · Rosanna Abbate · Gian Franco Gensini · Alessandro Casini · Antonia Trichopoulou · Christina Bamia

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Abstract
Background Adherence to Mediterranean diet has been shown to be associated with a better health and greater survival. The aim of the present study was to identify change-points in the relationship between food groups composing Mediterranean diet and overall mortality.
Methods The population of the Greek EPIC prospective cohort study (23,349 adult men and women in the Greek EPIC sample who had not previously been diagnosed as having cancer, coronary heart disease or diabetes mellitus at enrolment) was analysed. Segmented logistic regression analysis was conducted to examine the association between each of the food groups contributing to the Mediterranean diet score and overall mortality.
Results This analysis allowed the determination of the following change-points: among men: 1 change-point for vegetables, legumes, cereals, fish and seafood and dairy products and 2 change-points for fruit and nuts, meat and meat products and ethanol; among women: 1 change-point for legumes and fish and seafood and 2 change-points for the remaining food groups. These cut-off points were used to construct an 'a posteriori' score that may be better in capturing the health-promoting potential of the traditional Mediterranean diet.
Conclusion Identification of change-points in the relationship between components of the Mediterranean diet and mortality can be used to increase the discriminatory ability of a widely used Mediterranean diet score in relation to mortality.

Keywords Mediterranean diet · Adherence · Score · Food group

F. Sofi (✉) · R. Abbate · G. F. Gensini
Department of Medical and Surgical Critical Care, Thrombosis Centre, University of Florence, Viale Morgagni, 85 50134 Florence, Italy
e-mail: francescosofi@gmail.com

F. Sofi · A. Casini
Agency of Nutrition, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy

F. Sofi · G. F. Gensini
Don Carlo Gnocchi Foundation, Centro S. Maria agli Ulivi, Onlus IRCCS, Florence, Italy

A. Trichopoulou · C. Bamia
WHO Collaborating Center for Food and Nutrition Policies, Department of Hygiene, Epidemiology and Medical Statistics, University of Athens, Medical School, Athens, Greece

Introduction

Mediterranean diet has been consistently associated with better health representing a nutritional choice for the prevention of chronic diseases [1, 2]. In order to evaluate the adherence to Mediterranean diet, a score was introduced in 1995 and later modified to include fish intake [3, 4]. This score is based on the gender-specific median values of consumption of food groups, categorised as either beneficial or not beneficial for health, in line with the traditional Mediterranean diet. Recently, two meta-analyses of prospective studies demonstrated that this score can demonstrate a significant improvement in the health status [5, 6]. Nevertheless, such computational scores have inherent limitations. Firstly, the decision on the number and values of cut-off points to be used for each of their components is largely arbitrary. Secondly, the scores are not easily transferable to the daily practice. This is because researchers and physicians may struggle to calculate a person's (patient's) score since they need to relate the individual's consumption to the specific cut-offs that are used for each of the components of the Mediterranean dietary pattern in different studies.

In the last years, attempts have been made to estimate adherence to Mediterranean diet through scores that may be simpler to calculate. However, the cut-off points that were used for the calculation of these score were based either on a priori determination of the cut-offs in a beneficial diet or on dietary guidelines for the general population [7, 8].

We have undertaken this study to estimate the number and values of change-points for the consumption of each of the food groups composing the Mediterranean diet, by exploring the dose–response relationship between these food groups and overall mortality. To illustrate the methodology, we used the data of 23,349 participants from the Greek segment of the EPIC study who had not previously been diagnosed as having cancer, coronary heart disease or diabetes mellitus and who were followed up for a mean length of 8.5 years [9].

Methods

Modelling the dose–response relationship

The construction of the widely used Mediterranean Diet Score (MDS) [3, 4] implies the existence of one cut-off value (represented by the gender-specific median) for each of the food components, beyond which the effect (beneficial or detrimental) of the food group on the health outcome becomes apparent. We have relaxed this assumption by allowing for more than one cut-off point for each food component by using segmented logistic regression models that allow for piecewise linear effects of a continuous exposure on a binary outcome. With these models, we evaluated the dose–response relationship between the intakes of the foods (independent variables) comprising the Mediterranean diet score and overall mortality (dependent variable), and we estimated the number and values of change-points for each food group. Thus, the overall effect of a food component of MD on mortality is represented by two (if 1 cut-off) or more (if >1 cut-off) straight lines connected at these cut-offs referred to as change-points.

Data

We re-analysed data from the Greek segment of the EPIC study, which were recently published [9]. The sample used for the analysis consisted of 23,349 participants who, as indicated, had not previously been diagnosed as having cancer, coronary heart disease or diabetes mellitus and who were followed up for a mean length of 8.5 years. Detailed information of the study population is reported elsewhere [9].

Data of dietary intakes of the study population were assessed with the use of a validated food frequency questionnaire that includes approximately 150 food and beverages commonly consumed in Greece [9]. For this analysis, we focused on nine nutritional variables: vegetables, legumes, fruits and nuts, dairy products, cereals, meat and meat products, fish and seafood, olive oil and ethanol. We decided to use olive oil instead of lipid ratio (that is, monounsaturated to saturated lipids as reported in the original version of the adherence score) because of the greater simplicity in obtaining information for olive oil consumption than for the total lipids.

'A posteriori' adherence score to Mediterranean diet

For eight out of nine of the above-mentioned nutritional variables, we obtained the 'optimal' number of change-points as well as the actual values for these change-points. We assigned values of 0 or 2 to each of the components with one change-point and 0, or 1 or 2 to each of the components with 2 change-points. For the components presumed or indicated in the models to be beneficial, we assigned a value of 0 for the lowest category, 1 for the middle category and 2 for the highest category. In contrast, for components presumed or indicated in the models not to be beneficial for health, we assigned a value of 2 for the lowest category, 1 for the middle category and 0 for the highest category. For ethanol, we assigned value of 2 for the middle category, 1 for the lowest category and 0 for the highest category in the light of the J-shaped curve for ethanol and risk of disease reported in the literature [10]. Olive oil consumption was added as single dichotomised variable (yes/no) on the assumption that a distinct beneficial effect is obtained when olive oil is consumed in the place of other oils rather than in relation to particular increments [11]. Therefore, we calculated the 'a posteriori' score for the adherence to Mediterranean diet by summing up the values of 0, 1 and 2 for the individual components. Hence, this score takes values from 0 (minimal adherence to Mediterranean diet) to 18 (maximal adherence to Mediterranean diet).

Statistical analysis

Segmented logistic regression was performed using the CRAN R statistical software (version 8.2 for Windows; fully available at http://www.r-project.org) with the package *segmented* (available at http://cran.r-project.org/web/packages/gap/index.html). Women and men were analysed separately due to the known differences in food consumption and risk of disease. For each of the dietary components (with the exception of olive oil), we fitted an adjusted model controlled for age at enrolment (<45, 45–54, 55–64, ≥65 years: categorically), education (none, elementary school degree, university degree, secondary school, university degree or higher; categorically), smoking status (never, former and current at enrolment with cigarettes per day, 1–10, 11–20, 21–30, 31–40, ≥41; ordered), physical activity in MET-hours/day (fifths; ordered), total energy intake (fifths; ordered), waist-to-hip ratio (sex-specific fifths; ordered) and body mass index (sex-specific fifths; ordered). The number of change-points was chosen to range from a minimum of 1 to a maximum of 2 in order to obtain 2 or 3 categories of consumption for each of the food groups composing MDS. When more than 2 change-points were suggested, the 2 change-points with smaller values of the modified version of the Akaike Information Criterion (AIC), which indicates improved model fit, were taken [12]. A p value less than 0.05 was considered to indicate statistical significance.

Results

For this investigation, 23,349 study participants were included. During a mean follow-up time of 8.5 years (range, 10 days–14.2 years), 1,075 deaths from all causes occurred. Baseline demographic and clinical characteristics of the study population were previously reported [9].

In Tables 1 and 2, the numbers and values of the change-points in the relationships of each of the food groups of MDS and mortality that were identified by the segmented logistic regression models, separately for men and women, are presented. Among men, 1 change-point was estimated for vegetables, legumes, cereals, fish and seafood and dairy products, while 2 change-points were reported for fruit and nuts, meat and meat products, and ethanol. On the other hand, among women, 1 change-point was estimated only for legumes and fish and seafood, whereas for the other food groups (vegetables, fruit and nuts, cereals, dairy products, meat and meat products, as well as ethanol) 2 change-points were identified. An example of the change-points existing in the relationship between consumption of vegetables and overall mortality, among women, is depicted in Fig. 1.

The construction of a score for adherence to Mediterranean diet based on the change-points estimated from the segmented logistic regression models for men and women is shown in Figs. 2 and 3. Consumption of food groups composing the adherence score was rounded to the nearest value.

Table 1 Change-points in the relationship between food groups' consumption and overall mortality risk—Men

Food group	Change-point(s)
Vegetables	540.8
Legumes	6.4
Fruits and nuts	246.9
	477.3
Cereals	151.7
Fish and seafood	14.1
Dairy products	155.7
Meat and meat products	137.9
	150.3
Ethanol	11.6
	23.7

Change-points are reported as gram/day and are obtained by using a segmented logistic regression analysis adjusted for age at enrolment (<45, 45–54, 55–64, ≥65 years: categorically), education (none, elementary school degree, university degree, secondary school, university degree or higher; categorically), smoking status (never, former, and, current at enrolment with cigarettes per day, 1–10, 11–20, 21–30, 31–40, ≥41; ordered), MET-hours (fifths; ordered), total energy intake (fifths; ordered), waist-to-hip ratio (sex-specific fifths; ordered) and body mass index (sex-specific fifths; ordered)

Table 2 Change-points in the relationship between food groups' consumption and overall mortality risk—Women

Food group	Change-point(s)
Vegetables	370.2
	566.6
Legumes	6.7
Fruits and nuts	284.9
	335.6
Cereals	136.2
	152.6
Fish and seafood	13.1
Dairy products	106.5
	129.1
Meat and meat products	136.4
	153.8
Ethanol	5.7
	11.5

Change-points are reported as gram/day and are obtained by using a segmented logistic regression analysis adjusted for age at enrolment (<45, 45–54, 55–64, ≥65 years: categorically), education (none, elementary school degree, university degree, secondary school, university degree or higher; categorically), smoking status (never, former, and, current at enrolment with cigarettes per day, 1–10, 11–20, 21–30, 31–40, ≥41; ordered), MET-hours (fifths; ordered), total energy intake (fifths; ordered), waist-to-hip ratio (sex-specific fifths; ordered) and body mass index (sex-specific fifths; ordered)

Discussion

In this study, we used data from the large database of the Greek EPIC prospective cohort study in order to model the nature of the relationship between consumption of food

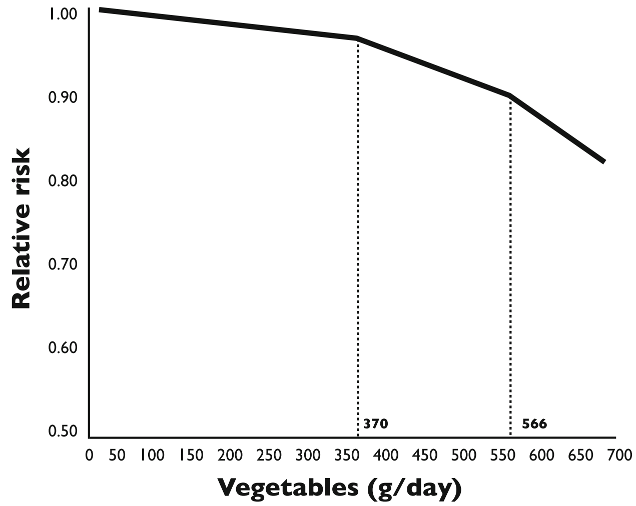

Fig. 1 Segmented regression analysis for consumption of vegetables and overall mortality risk among women. *Broken lines* represent change-points in the regression line

groups composing MDS in relation to overall mortality. With the use of segmented regression analysis, we were able to estimate, for all the food groups, the change-points existing in the relationship between diet and mortality. We were thus able to create an 'a posteriori' score for assessing the adherence to traditional Mediterranean diet with reference to specific daily intake values in grams. Such score could be helpful for physicians, nutritionists and other health professionals in their advising and counselling role.

Mediterranean diet has been recognised as a model for healthy eating and documented to have favourable effects on several chronic diseases [1, 14]. Over the last years, research efforts in the field of nutrition switched progressively to the evaluation of healthy nutrition patterns notably the Mediterranean dietary pattern, rather than to the identification of single foods or nutrients in relation to health and disease [7, 8].

Starting from 1995, when an original study by Trichopoulou et al. [3] demonstrated an association between adherence to Mediterranean diet and survival, several studies reported associations between adherence to Mediterranean diet and different health outcomes [5, 6].

Despite the great interest for the epidemiological studies, the utilisation of this adherence score in daily practice presents some limitations. Such scores [3, 4, 9] are computed on the basis of the gender-specific median values of the food groups characteristics of the Mediterranean diet, but they may not be directly applicable in daily practice, since they do not provide direct information for the amount of food and/or food groups that should be consumed to obtain a clinically significant protection against the threat of disease and death. Therefore, we decided to re-analyse the data through another statistical approach in order to establish the nature of the relationship between each of the food groups composing adherence score to Mediterranean diet and the overall mortality risk. In nutritional studies, quite often, the relationship between food consumption and the risk of disease is not linear and several change-points may exist.

Fig. 2 Novel score for estimating the adherence to Mediterranean diet according to the change-points obtained at the segmented regression analysis—*Men*. Consumption of food groups composing the adherence score were rounded to the nearest value in order to obtain categories that could be more suitable for the clinical practice

How much of the following food groups do you consume every day?

MALES

Vegetables	≤550 g [0]		>550 g [2]
Legumes	≤6 g [0]		>6 g [2]
Fruits and nuts	<250 g [0]	250-500 g [1]	>500 g [2]
Cereals	≤150 g [0]		>150 g [2]
Fish and seafood	≤15 g [0]		>15 g [2]
Dairy products	≤150 g [2]		>150 g [0]
Meat and meat products	<140 g [2]	140-150 g [1]	>150 g [0]
Ethanol	<12 g [1]	12-24 g [2]	>24 g [0]
Olive oil	Yes [2]		No [0]

Total: [ ]

Fig. 3 Novel score for estimating the adherence to Mediterranean diet, according to change-points obtained at the segmented regression analysis—*Women*. Consumption of food groups composing the adherence score were rounded to the nearest value in order to obtain categories that could be more suitable for the clinical practice

How much of the following food groups do you consume every day?

FEMALES

Food group			
Vegetables	≤350 g [0]	350-500 g [1]	>500 g [2]
Legumes	≤7 g [0]		>7 g [2]
Fruits and nuts	<300 g [0]	300-350 g [1]	>350 g [2]
Cereals	<130 g [0]	130-150 g [1]	>150 g [2]
Fish and seafood	≤10 g [0]		>10 g [2]
Dairy products	<100 g [2]	100-130 g [1]	>130 g [0]
Meat and meat products	<130 g [2]	130-150 g [1]	>150 g [0]
Ethanol	<6 g [1]	6-12 g [2]	>12 g [0]
Olive oil	Yes [2]		No [0]

Total: [ ]

We conducted a segmented regression analysis, a statistical approach that has been used for estimating the dose–response relation between a continuous measure and the risk of diseases [13, 15]. Such method provides the point(s) of exposure where the dose–response relation changes. These points, termed change-points, helped us to estimate the number and values of these points in the relationship between food groups and overall mortality. With these change-points, it is possible to create an 'a posteriori' that could be more discriminatory in assessing the association of the traditional Mediterranean diet and overall mortality.

There are several limitations to this study. The sample population is restricted to the population of the Greek EPIC cohort, i.e. to a population of adult Greeks. Moreover, Mediterranean diet is not a single diet but a complex pattern of dietary habits that may vary between countries or even within a country. Further epidemiological studies are needed to replicate these findings in other populations. Other limitations are those related to the methodology used in the study. The method used to find the cut-offs is, in fact, quite relaxed regarding the distributional assumptions. Nevertheless, the association is assumed piecewise linear, and more complex shapes for the associations are not captured. In addition, the method is based on observed mortality rates, so that different mortality rates would probably give different cut-off points. In other words, the cut-offs are 'optimal' for the specific mortality rates assuming that the piecewise shape is correct.

We have presented an approach that can be used to identify change-points in the association of food components of MDS and overall mortality using the large database of the Greek EPIC cohort. The identification of such points could improve the discriminatory ability of a widely used score towards the identification of an optimal score for the traditional Mediterranean diet.

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Conflict of interest None.

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