Nut consumption and incidence of hypertension: The SUN prospective cohort

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Abstract  Background and aims: The consumption of tree nuts could reduce the risk of hypertension, but scarce research has been done to evaluate this potential association. We assessed the association between nut consumption and the incidence of hypertension among 9919 Spanish university graduates followed-up biennially for a median of 4.3 years.

Methods and results: Food habits were assessed with a validated 136-item food-frequency questionnaire. Nut consumption was classified into four categories: rarely/never, 1–3/month, 1/week, and 2+/week. A participant was classified as an incident case of hypertension when, being free of hypertension at baseline, he/she subsequently reported a physician-made diagnosis of hypertension in at least one of the follow-up questionnaires. The incidence of hypertension was 12.4 per 1000 person-years. We found no association between nut consumption and incidence of hypertension after adjusting for sex, age and other dietary and non-dietary potential confounders (hazard ratio [HR] for those in the highest vs. lowest nut consumption category 0.77 [IC 95%: 0.46–1.30] p = 0.795). Results were not modified when we stratified the analyses according to sex or to body mass index.

Conclusion: Our data do not provide evidence for an inverse association between nut consumption and incident hypertension in our cohort. Further results from cohorts and trials with a higher baseline risk of hypertension should be obtained to test this relationship.

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Abbreviations: CVD, cardiovascular disease; IHD, ischemic heart disease; BP, blood pressure; PHS, Physicians Health Study; SUN Project, Seguimiento Universidad de Navarra; BMI, body mass index; HR, hazard ratio; MET, metabolic equivalent index; DASH, Dietary Approaches to Stop Hypertension; MDP, Mediterranean dietary pattern.

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Introduction

Hypertension is a major public health problem, affecting approximately 1 billion individuals,[1] causing 7.6 million premature deaths and 6% of all cases of disability-adjusted life years worldwide [2]. In European countries hypertension prevalence is increasing [3]. Ischemic heart disease (IHD) and stroke are the two main cardiovascular causes of mortality around the world, and hypertension explains 47% and 54% of deaths by IHD and stroke, respectively [2].

Lifestyle modification may lower blood pressure (BP) [4,5] and reduce the incidence of hypertension. Lifestyle modification includes weight loss among overweight/obese individuals [4,5] increased physical activity [4]; reduced alcohol consumption [4,5]; adoption of a diet rich in fresh fruit, vegetables, [5,6] potassium [5] and a reduced sodium content [4,5,7]. For instance, the DASH diet (Dietary Approaches to Stop Hypertension) has similar BP lowering effects to a single drug therapy [7]. In addition, a DASH-type diet has been shown to be associated with a lower cardiovascular risk in the Nurses Health Study [8].

As is known, nuts are an integral part of the Mediterranean Dietary Pattern (MDP) [9]. MDP has been shown to be protective against age-related changes in blood pressure [10]. Results from the PREDIMED randomized trial showed that a Mediterranean diet enriched with mixed nuts was able to reduce BP levels to a larger extent than a low-fat diet during a 3-month follow-up [11]. Moreover, during a 1-year follow-up of the PREDIMED trial the arm of the trial allocated to the Mediterranean diet plus free provision of nuts exhibited a significant reduction in the prevalence of the metabolic syndrome, with a small reduction in hypertension prevalence after 1 year. However, in that trial most participants initially had hypertension at baseline [12]. Also, recently the Physicians Health Study (PHS) reported a lower risk of hypertension for those who consume nuts on a daily basis [13]. This is plausible since raw nuts have a high content of magnesium, potassium and unsaturated fatty acids, and only small amounts of sodium. However, with the exception of the PREDIMED trial [11] and the PHS cohort [13] there is scarce information about the ability of a nut-rich diet to prevent the incidence of hypertension.

The aim of our study was to assess the association between the consumption of tree nuts and the incidence of hypertension in a large prospective cohort of university graduates in Spain.

Methods

Subjects

The SUN project (Seguimiento Universidad de Navarra) is a dynamic cohort comprised exclusively of Spanish university graduates. The recruitment of participants started in December 1999 and it is permanently open. Information is collected using self-administered questionnaires mailed every 2 years. The objectives and methods of this project have been detailed elsewhere [14].

By April 2008, 19,519 participants were recruited and had answered the baseline questionnaire. Those participants who completed the baseline assessment before July 2005 were eligible for longitudinal analyses for either 2-, 4- or 6-year follow-up (n = 13,740). The overall follow-up rate was approximately 88%.

Participants who had one or more of the following characteristics were excluded from the analysis (n = 3821): prevalent hypertension (n = 1495); those who reported extremely low or high values for total energy intake (less than 800 kcal/day in men and 500 kcal/day in women or more than 4000 kcal/day in men and 3500 kcal/day in women) (n = 1220); pregnant women at baseline (n = 41); those without information about nut consumption (n = 274); those who reported at baseline a history of CVD (n = 360), diabetes mellitus (n = 114), or cancer (n = 317). Finally, data from 9919 participants remained available for the analysis.

The Human Research Ethical Committee from the University of Navarra approved the study. Voluntary completion of the first questionnaire was considered as informed consent.

Dietary assessment

The baseline questionnaire included a 136-item semi-quantitative food-frequency questionnaire that was previously validated in Spain, it also included open-label questions for information about use of dietary supplements [15]. The questionnaire was adapted from the Willett’s questionnaire and it was based on typical portion sizes. Participants selected one of 9 options for the frequency of intake in the previous year for each food item (rarely/never, 1–3/month, 1/week, 2–4/week, 5–6/week, daily, 2–3/day, 4–6/day, 6+/day). We asked the participants how often, on average, they had consumed nuts during the previous year. Information on nut consumption was collected in a single disaggregated question, which included walnuts, almonds, hazelnuts or peanuts. These varieties represent a single disaggregated question, which included walnuts, almonds, hazelnuts or peanuts. These varieties represent more than 95% of the total nut consumption in the Spanish population [16]. Due to the small number of subjects in the categories corresponding to a higher frequency of nut consumption, we merged the upper categories to obtain more stable estimates as has been previously reported in similar studies [17,18]. Thus, in all our analyses, we classified nut consumption into four categories: rarely/never, 1–3/month, 1/week, and 2+/week.

The food-frequency questionnaire was also used to obtain information on other nutrients that could act as potential confounders. Nutrient intake scores were computed using an ad hoc computer program. A trained dietitian updated the nutrient data bank using the most up-to-date food composition tables for Spain [19,20]. We calculated the amount of each of these nutrients without taking into account the share allocated to nut consumption, and adjusted the estimates for these new variables.

The intakes of foods and nutrients (other than nut consumption) were adjusted for total energy intake applying the residual method, and separate regression models were run to obtain the residuals for men and women [21].

Assessment of other covariates

The baseline questionnaire included questions about a wide array of characteristics: socio-demographic (e.g. sex, age, ...
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Statistical analysis

For each participant we computed person-time of follow-up from the date of return of the baseline questionnaire to the date of return of the last follow-up questionnaire or to the date of the physician-made diagnosis of hypertension, whichever occurred first.

Hazard ratios (HRs) for the three upper categories of nut consumption and their 95% CIs were estimated with Cox proportional hazard models, adjusting for potential confounders and taking as the reference category those subjects who consumed nuts never or rarely.

The initial model included only age and sex as covariates (model 1). We fitted an additional model adding universally accepted risk factors for hypertension (family history of hypertension [yes, no] and hypercholesterolemia [yes, no]) and variables closely associated with lifestyle and health-related habits (smoking [never, past, current, not specified], educational level [degree 1: 3 years of university study, degree 2: 4–5 years of university study, degree 3: 6–9 years of university study], and physical activity [MET hour/week, continuous]) (model 2). To assess the possibility of confounding by other dietary variables, we fitted an additional model adding several dietary factors that have been related to the risk of hypertension in some studies (total energy intake, alcohol intake, the intake of polyunsaturated fatty acids, monounsaturated fatty acids, saturated fatty acids, proteins, carbohydrates, sodium, magnesium, potassium, calcium, folic acid, vitamin E, mineral supplements, caffeine intake, and fiber intake) (model 3). Finally, we fitted a last model adding BMI (body mass index) at baseline, and weight change during follow-up [lost, gain, equal] (model 4).

We also included a separate model adjusting for other food groups instead of macro and micronutrients to avoid the possibility of over-adjustment bias of a model including total energy intake and all energy providing macronutrients in the same model (model 5).

To assess whether a multiplicative interaction existed between nut consumption and sex, we introduced a product-term (nut × sex) in the fully adjusted model. We also assessed interaction between nut consumption and overweight status (nut × BMI), dichotomizing BMI (<25 or ≥25 kg/m²) and nut consumption (never or ever). To assess multiplicative interactions, we introduced interaction terms and then compared both models, the one with and the one without the product-term using the likelihood ratio test.

Analyses were performed with SPSS version 15.0 (SPSS Inc, Chicago, IL). All p values are 2-tailed. Statistical significance was set at p < 0.05.

Results

We observed five hundred and forty two new cases of hypertension (341 men and 201 women) during a median follow-up of 4.3 years (mean = 4.5 years). The incidence of hypertension in our population was 12.4 per 1000 person-years.

Table 1 shows the non-dietary and dietary characteristics of participants according to their categories of nut consumption at baseline.
consumption. Participants belonging to the highest category of nut consumption were more likely to be men, older, non-smokers, physically more active and reported a higher frequency of hypercholesterolemia. Among participants in the lowest category of nut consumption, we identified more women and a higher proportion of current smokers. Participants belonging to the highest category of nut consumption had a higher intake of total energy, alcohol, monounsaturated fatty acids, polyunsaturated fatty acids, fiber, magnesium, potassium, folic acid, and vitamin E but lower intakes of sodium, protein, carbohydrate, saturated fats, and caffeine. Nut consumption was positively related to fruit, vegetable and fish intakes and inversely related to dairy and meat intake.

Table 2 shows the association between nut consumption and the incidence of hypertension. We found no association between nut consumption and incidence of hypertension after adjusting for sex, age and other dietary and non-dietary potential confounders.

No statistically significant interaction was found either for sex (p for interaction = 0.82) or BMI (p for interaction = 0.75).
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Discussion

In this prospective cohort study, we found no evidence for an inverse association between nut consumption and incident hypertension. These results are in agreement with a clinical trial that evaluated the effects of nut consumption on selected markers of the metabolic syndrome, and found that mean blood-pressure values only slightly decreased, but the observed changes were not statistically significant [26].

On the other hand, in the PREMED randomized trial, a reduction in mean BP was observed in both intervention groups using either a nut-enriched or an olive oil-enriched Mediterranean diet [11]. In the group allocated to a Mediterranean diet plus free provision of tree nuts, the PREMED trial participants received 30 g/d of raw tree nuts (15 g/d of walnuts, 7.5 g/d of hazelnuts and 7.5 g/d of almonds). In addition to its experimental design (different from the observational nature of the present cohort), the PREMED trial differs methodologically from the SUN cohort. First of all, subjects in the PREMED trial consumed more nuts than those belonging to the highest category of nut consumption in the SUN cohort; in addition, the PREMED trial only included participants at high cardiovascular risk and many participants were taking antihypertensive drug treatment. Any potential synergism between lifestyle factors and pharmacological agents for management of hypertension would have contributed to a stronger effect [27]. The PREMED trial did not evaluate nut consumption separately from the overall intervention with a Mediterranean-type dietary pattern. Moreover, the tree nuts provided to the corresponding intervention group in the PREMED trial were raw nuts, i.e. non-salted nuts. However, nuts are usually consumed with salt in Spain. In fact, according to Datamonitor, nuts and seeds represent the first source (38.5%) of the savory snacks market in Spain [28]. Nuts in Spain are seldom consumed as raw products, except for walnuts and pine nuts. They are more frequently consumed toasted, grilled, fried, or salted [16]. Salted nuts can contain important amounts of sodium. The effect of sodium to increase BP is well known [7].

The Physicians Health Study (PHS) has recently shown that nut consumption is associated with a lower risk of hypertension [13]. The protective effect on hypertension (adjusted hazard ratio = 0.82 [0.71–0.94]) reported in that study is similar in magnitude to the point estimates we have found. However, the statistical power of the PHS with more than 8000 new cases of hypertension is considerably higher, rendering narrower confidence intervals than our estimates. However, the protective effect reported in the PHS was restricted only to lean participants, limiting the generalisability of their findings.

A potential protection against hypertension for raw nuts is plausible because they contain a high proportion of mono and polyunsaturated fatty acids, but are low in saturated fatty acids. They are also good sources of fiber, protein (arginine), and minerals (magnesium, potassium, and calcium) and all these nutrients are potentially beneficial against hypertension [16].

Our results demonstrate that participants belonging to the highest category of nut consumption had a higher intake of monounsaturated fatty acids, polyunsaturated fatty acids, fiber, magnesium, potassium, folate and vitamin E, but a lower intake of carbohydrate and saturated fatty acids.

In Spain the varieties of nuts most widely consumed are peanuts, walnuts, hazelnuts and almonds [16]. The last two are rich in oleic acid that offers a lowering effect on BP as has already been reported [11]. Walnuts are rich in \( \alpha -\)
linolenic acid, and its anti-inflammatory properties are being evaluated. This feature could prevent the progression of atherosclerosis, which is an important risk factor for hypertension [29]. Fiber intake could protect against hypertension through weight reduction due to the influence on satiety and energy intake [30]. Potassium [5] also offers a lowering effect on BP.

Other explanations make it also likely that a high nut consumption might be able to reduce BP, but this BP lowering effect may be insufficient to prevent the development of hypertension in our study. This fact could be occurring because: (1) nut consumption might have been underestimated since we did not compute the amount included in sauces, cheeses, cereals, and desserts [16]; (2) information about nut consumption was collected only in the baseline questionnaire and we were not able to assess changes in nut consumption during follow-up; (3) we were not able to isolate the role of each specific type of nut; so if only some kind of nut were protective against the development of hypertension, the aggregation of consumption data in a single question would very probably underestimate its specific effect; (4) we could not examine the influence of the preparation method (salted, roasted or raw nuts) on the risk of hypertension; (5) the case ascertainment for hypertension was based on self-reported data and it is well known that about one third of hypertensive individuals are not aware of their status [1]; however, we have shown an adequate validity of this self-report of a physician-made diagnosis of hypertension in this highly educated cohort [25]; (6) and, especially, because the incidence of hypertension was relatively low in our cohort and this scarcity in the number of observed new cases could hinder the finding of a statistically significant association between nut consumption and hypertension. We acknowledge that our statistical power might be too low to detect an association of small magnitude. We observed 542 cases of hypertension over 9919 subjects. Assuming an alpha error (bilateral) equal 0.05, a power of 0.80 and a relative risk of 0.75 for a dichotomized exposure, we would need 3947 exposed and 3947 unexposed subjects to detect a protective effect at that level.

The strengths of this study are the large sample size, longer duration of follow-up (4.3 years median), its prospective design that could avoid inverse causation bias, and the control for a wide variety of potential confounders. Additionally, both dietary exposure and outcome were ascertained through standardized and validated questionnaires [15,25].

In conclusion, though our estimated confidence intervals are compatible with some degree of protection of nut consumption against hypertension, our data do not support an inverse association between nut consumption and incidence of hypertension in this cohort of Spanish university graduates. Larger cohorts and trials including participants initially free of hypertension and with greater statistical power and ability to differentiate between raw nuts and salted nuts would contribute to clarifying this association.

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References


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