



Brief Original Report

Greater frequency of nut consumption is associated with lower prevalence of peripheral arterial disease



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ABSTRACT

Nut consumption has been associated with lower risk of coronary heart disease and all-cause mortality. The association between nut intake and peripheral arterial disease (PAD) is uncertain.

Objective. We sought to investigate the association between nut consumption and presence of prevalent PAD in a large cross-sectional sample.

Methods. Self-referred participants at >20,000 US sites who completed a medical and lifestyle questionnaire were evaluated by screening ankle brachial indices for PAD. Multivariable logistic regression analysis was used to estimate odds of PAD in different nut consumption categories.

Results. Among 3,312,403 individuals, mean age was 63.6 ± 10.6 years and 62.8% were female. There were 219,527 cases of PAD. After multivariable adjustment there was an inverse association of nut intake with PAD. Compared to subjects with consumption of nuts < once/month, daily nut consumption was associated with a 21% (95% CI 20%–23%) lower odds of having PAD.

Conclusion. These observations suggest the need for more rigorous testing evaluating the role of nuts in PAD prevention.

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Introduction

The role of diet in the development and progression of atherosclerosis has been recognized for nearly a half-century, with dietary modification a cornerstone of primary and secondary prevention (Eckel et al., 2014). Epidemiologic studies on which lifestyle guidelines are based have largely assessed coronary heart disease (CHD) and ischemic stroke endpoints. Nut consumption improves lipid profile (Sabate et al., 2010) and measures of endothelial function (Casas-Agustench et al., 2011), has been associated with lower levels of inflammatory markers (Jiang et al., 2006), and may reduce development of diabetes (Salas-Salvado et al., 2011). Increasing frequency of nut intake has been associated with lower incidence of CHD (Kris-Etherton et al., 2008), myocardial infarction (Fraser et al., 1992), and fatal CHD events (Fraser et al., 1992), as well as all-cause and cardiovascular mortality (Ellsworth et al., 2001;

Bao et al., 2013). However, such a protective effect has not been consistently seen in stroke (Bao et al., 2013).

Data supporting dietary composition specifically in the prevention of peripheral artery disease (PAD) is remarkably scant and has led to calls for assessment of dietary components as they relate specifically to PAD (Brostow et al., 2012). Indeed, a recent exploratory analysis of the PREDIMED trial suggested that a Mediterranean diet supplemented with nuts may reduce incidence of symptomatic PAD (Ruiz-Canela et al., 2014). Our study sought to investigate the association between dietary nut consumption and presence of diagnosed PAD in a large cross-sectional sample.

Methods

The study was based on data provided by Life Line Screening Inc. (Independence, OH) for research purposes. The data was provided without any financial considerations, and without any editorial control over analyses or resulting publications. The study population consisted of self-referred individuals who underwent vascular screening tests at more than 20,000 sites throughout the United States between 2003 and 2008. Screening sites were generally stationed for short periods in public places (community centers, shopping malls, etc.) and advertised ankle-brachial index (ABI), carotid Doppler and abdominal aorta ultrasound, as well as bone density screening services for a small fee. Before undergoing anthropometric measures, individuals completed an extensive questionnaire regarding demographics, risk factors, medical history, dietary intake

Abbreviations: PAD, peripheral arterial disease; ABI, ankle brachial index; CHD, coronary heart disease.

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and physical activity. As a part of the questionnaire, participants were asked, “how often do you eat a serving of nuts?” Subjects were given five options for their response: “less than once a month,” “between once a week and once a month,” “2–3 times a week,” “4–5 times per week,” or “daily.” Serving size was interpreted by the subject.

For the diagnosis of PAD, systolic blood pressure was measured in both arms and both ankles by trained staff. Left and right ankle-brachial index (ABI) measurements were obtained by dividing the ankle systolic blood pressure (measured in the posterior tibial artery or dorsalis pedis artery if a posterior tibial artery Doppler signal was inaudible) by the highest of the two systolic blood pressures in the left or right arm (brachial artery), as previously described (Berger et al., 2013). PAD was defined as an ABI < 0.90 in either leg or prior lower extremity revascularization.

Hyperlipidemia was defined by reported physician diagnosis or medication use. Diabetes was defined by reported physician diagnosis or medication use. Hypertension was defined by reported physician diagnosis or anti-hypertensive medication use at the time of screening. Subjects reporting less than once weekly engagement in vigorous leisure time activity were considered to have a sedentary lifestyle. Obesity was defined as a body mass index (BMI) of ≥ 30 kg/m².

Multivariable logistic regression models were used to determine the association between nut intake and PAD. Models were adjusted for age (as a continuous variable), sex, self-reported race/ethnicity, smoking status, sedentary lifestyle, diabetes, hypertension, hyperlipidemia, obesity, income, family history of cardiovascular disease, and consumption of fruits and vegetables, red meat and fish. Additional adjusted analyses with stratification by BMI, race/ethnicity and sex were also performed. The Cochran–Armitage test was used to assess for trend.

All statistical analyses were performed with PASW (version 18.0, SPSS Inc., Chicago, Illinois), SAS (version 9.12, SAS Institute Inc.), and the R package (R Development Core Team).

Results

Among 3,312,403 unique individuals, mean age was 63.6 ± 10.6 years, 62.8% were female and 86.2% were Caucasian. There were 219,527 cases of PAD. The geographic distribution of the sample was similar to that of the overall population of the United States. The sample also included a broad representation of socioeconomic status, as represented by participant zip-code (Shah et al., 2014). As we have published previously, the prevalence of different cardiovascular risk factors in this population database was similar to those of the general US adult population (Savji et al., 2013). Characteristics of the population by category of reported nut consumption frequency appear in Table 1. Nearly half of the population consumed a serving of nuts less than once weekly (Table 1). Relative to individuals who reported less than once monthly consumption, there was a significant reduction in the odds of prevalent

PAD in individuals reporting consumption of a serving of nuts at any frequency greater than once monthly (OR's 0.74–0.77, Table 2). After multivariable adjustment, a significant inverse association remained between any nut intake and the prevalence of PAD, with a trend toward further lower odds of prevalent PAD with more frequent nut intake (Supplementary Figure, *P* for trend < 0.001). Compared to subjects with the lowest consumption of nuts, daily nut consumption was associated with a 21% lower odds of PAD (OR 0.79, 95% CI 0.77–0.80). The association between reported nut ingestion and PAD was robust across different baseline demographics (Table 2).

Discussion

We present data from a large, self-referred, cross-sectional sample, in which nut consumption exhibited an inverse association with prevalence of PAD. Our unadjusted analysis indicated a monotonic reduction in odds ratio for PAD for any consumption of nuts versus no consumption. After adjustment for multiple confounders and established risk factors for atherosclerosis, an inverse association remained, with a trend toward lower odds of PAD with increasing nut consumption.

The 21% lower multivariable adjusted odds of PAD in participants reporting daily nut consumption is smaller than the protective association of nut intake with incident fatal and non-fatal CHD in several large, prospective cohorts (Kris-Etherton et al., 2008), but similar to the protection from death from cardiovascular disease in the combined Nurses' Health and Health Professionals Follow-Up Study cohorts (Bao et al., 2013). The association is also more modest than the reduction in incident PAD observed in participants consuming a Mediterranean diet supplemented with nuts (Ruiz-Canela et al., 2014) in the PREDIMED trial, although reported nut consumption was greater in our sample than in the PREDIMED control group (Estruch et al., 2013). Furthermore, our observations of monotonically lower odds with any consumption of nuts in unadjusted analyses, with a majority of odds lowering with infrequent nut consumption and modestly lower odds with increased intake frequency, are comparable to the association seen between nut intake and cardiovascular disease in other cohorts (Bao et al., 2013).

Limitations of our study include the assessment of self-referred individuals, which potentially allows for selection bias. This bias may affect findings in diametrical ways, as persons who are aware of risky health behaviors may be more likely to seek vascular screening, while individuals who are particularly concerned about their overall health, adhere to healthy lifestyles and actively seek ways to reduce their risk, may also seek screening exams. Likewise, the fee associated with the screening exam, although modest, may have introduced further selection bias by underrepresenting individuals with low socioeconomic

Table 1
Characteristics of study population undergoing vascular screening exams at over 20,000 US sites between 2003 and 2008 categorized by reported frequency of consumption of a serving of nuts.

	Less than once/month	Once/week–once/month	2–3 times/week	4–5 times/week	Daily
<i>n</i> =	663,118 (20.1%)	951,329 (28.7%)	763,522 (23.0%)	448,606 (13.5%)	485,828 (14.7%)
Age (years) \pm SD	63.7 \pm 11.1	62.3 \pm 10.6	63.4 \pm 10.4	64.4 \pm 10.1	65.7 \pm 10.0
Male	36.0%	37.7%	37.3%	34.8%	31.1%
Race/Ethnicity					
White	86.7%	90.0%	89.6%	90.0%	90.1%
Black	3.6%	2.9%	3.1%	3.1%	2.5%
Hispanic	2.9%	2.3%	2.4%	2.2%	2.1%
Asian	2.2%	1.8%	2.0%	1.8%	1.8%
Native American	3.9%	2.5%	2.5%	2.3%	2.4%
BMI (kg/m ²) \pm SD	28.1 \pm 6.1	28.2 \pm 5.9	27.8 \pm 5.6	27.4 \pm 5.5	26.7 \pm 5.2
Hypertension	50.8%	48.1%	47.9%	47.0%	45.6%
Diabetes	11.3%	10.4%	10.8%	11.0%	11.1%
Hypercholesterolemia	53.4%	53.5%	54.1%	54.3%	53.6%
Family history of CVD	26.2%	26.0%	25.2%	25.0%	24.5%
Current smokers	28.0%	26.1%	24.6%	22.9%	21.5%
Sedentary lifestyle	47.8%	41.2%	34.3%	30.8%	26.2%

BMI—body mass index; CVD—cardiovascular disease; SD—standard deviation.

Nut consumption exhibited significant bivariate interactions with all characteristics listed above (*p* < 0.0001).

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