Clinical Nutrition 33 (2014) 443–447

Contents lists available at SciVerse ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Original article

Nutrient intake and peripheral artery disease in adults: Key considerations in cross-sectional studies

Asghar Z. Naqvi [a,*], Roger B. Davis [a,b,c], Kenneth J. Mukamal [a,b,d]

[a] Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, United States
[b] Harvard School of Public Health, Harvard Medical School, Boston, MA, United States

ARTICLE INFO

Article history:
Received 26 January 2013
Accepted 17 June 2013

Keywords:
Nutrients
Peripheral artery disease
Energy
Activity
Cross-sectional
Diet

SUMMARY

Background & aims: There are limited studies of nutrient intake and peripheral artery disease (PAD). Some studies have not accounted for the functional consequences of PAD, potentially leading to biased results. To determine the associations between intakes of dietary fiber, folate, vitamins A, C, E, and B6 and PAD.

Methods: Cross-sectional analysis of 6534 adults aged 40 years and older in the U.S. National Health and Nutrition Examination Survey between 1999 and 2004, including measurement of ankle-brachial index (ABI) and nutrient intake by 24-h dietary recall. Weighted multivariable logistic regression models to determine odds ratios and 95% confidence intervals.

Results: The prevalence of PAD (ABI < 0.9) was 5.3% (4.7–5.9). Inverse associations between PAD and intakes of fiber, folate, and vitamins A, B6, C, and E were statistically significant when adjusting for age, sex, hypertension, diabetes and smoking. In models further adjusted for energy intake and physical activity, these odds ratios all became null ($p \geq 0.1$).

Conclusions: In this sample, dietary fiber, folate, and vitamins B6, C, and E were not associated with PAD after accounting for energy intake and activity. Adjustment for energy and physical activity are essential to avoid bias due to reverse causation in cross-sectional studies of diet and PAD.

1. Introduction

Peripheral artery disease (PAD) is a debilitating, chronic disease characterized by atherosclerosis of the peripheral vasculature. In contrast to better studied forms of cardiovascular diseases, little is known about the role of diet in PAD. In humans, there have been few studies of PAD limited to specific nutrients often of modest sample size.[1–6] To our knowledge, there has been only one nationally representative comprehensive study of multiple nutrients and PAD, albeit cross-sectional in nature.[1]

Accounting for energy in any of several ways is standard in nutritional epidemiology to reduce variability related to general over- and under-reporting of food intake. In this manner, it improves precision, and it also changes the interpretation of derived estimates to one in which foods or nutrients are substituted rather than added (i.e., assumes an isocaloric diet). However, when total caloric intake is associated with disease, the interpretation of individual nutrient intake is complex, and the consequences of failing to account for energy intake may be far more serious.[7] To date, there are few published examples that illustrate this problem.

PAD is a particularly interesting outcome in that it commonly leads to decreased physical activity[8–13] and hence a decreased caloric intake in steady state.[1] As a result, accounting for energy in analyses of PAD is potentially of utmost import to avoid bias. Unfortunately, not all previous work relating diet to PAD has accounted for energy intake in at least some fashion.[1]

To determine how such methodologic considerations affect associations between nutrients and prevalence of PAD, we examined a series of dietary factors and their associations with PAD in a nationally representative sample of U.S. adults.

2. Methods

2.1. Study sample

This cross-sectional study used data from 6534 adults aged 40 years and older who participated in the National Health and

* Corresponding author. 1309 Beacon Street, Suite 201, Brookline, MA 02446, United States. Tel.: +1 617 667 2117/617 602 5147; fax: +1 617 667 8665.

E-mail addresses: asghar_naqvi@hms.harvard.edu, anaqvi@bidmc.harvard.edu (A.Z. Naqvi), davis@hsph.harvard.edu (R.B. Davis), kmukamal@bidmc.harvard.edu (K.J. Mukamal).

[c] Tel.: +1 617 754 1406.
[d] Tel.: +1 617 754 1401.

0261-5614/$ – see front matter © 2013 Elsevier Ltd and European Society for Clinical Nutrition and Metabolism. All rights reserved.
http://dx.doi.org/10.1016/j.clnu.2013.06.011

Nutrition Examination Survey (NHANES) between 1999 and 2004. The survey provides information on the health and nutritional status of the United States' civilian, non-institutionalized population by using a complex, stratified, multistage, probability-sampling design.[14] The NHANES includes both an initial in-home interview followed by an examination and personal interview at a mobile examination center for those who are eligible. A total of 31,126 individuals participated in the in-home interview. For this study, we excluded subjects less than 40 years of age ($n = 21{,}156$; ABI was not measured in that age group), lacking or indeterminant ABI measurement ($n = 1622$), having missing data from covariates of interest ($n = 811$), lacking physical exams ($n = 825$), not meeting minimal criteria for reliability of the dietary recall ($n = 178$), leaving 6534 for analysis. The study was exempted from continuing review by the institutional review board of Beth Israel Deaconess Medical Center.

2.2. Peripheral artery disease

PAD was assessed during the physical exam by health technicians trained in the survey examination protocol.[14] Briefly, after selecting the appropriate blood pressure cuff size and allowing a brief resting period, systolic blood pressure was measured on the right arm (brachial artery) and both ankles (posterior tibial arteries). If the participant had any condition that would interfere with accurate measurement or would cause discomfort, the left arm was used for the brachial pressure measurement. Systolic blood pressure was measured two times at each site if possible for participants aged 40–59 years and once at each site for participants aged 60 years and older. The ankle brachial blood pressure index (ABI) was calculated by dividing the mean systolic blood pressure in the right or left ankle by the mean systolic blood pressure in the arm. Since only one reading at each site for all persons 60 years and older was measured, the mean values are represented by the first recorded blood pressure reading at a site. We excluded values for ABI that were missing and those that were >1.4. We defined PAD as having an ABI <0.9.

A number of measures were taken to systematically optimize quality, including regular monitoring, periodic retraining and careful equipment maintenance. Detailed information on the NHANES lower extremity examinations for the survey periods is available elsewhere.[14]

2.3. Nutrients

Nutrient intake was assessed by a 24-h dietary recall. From 1999 to 2001, dietary intake data were collected using the NHANES computer-assisted dietary interview system (CADI). The CADI is a multiple pass recall method which provides instructions to interviewers for recording information about foods. Additional information about the CADI system is provided in the NHANES 1999–2000 Dietary Interviewers Procedures manual.[14] From 2002 to 2004, data were collected using the USDA's dietary data collection instrument, the automated multiple pass method,[15] which was found to provide valid measures of group total energy and nutrient intake in 20 highly motivated premenopausal women using doubly labeled water total energy expenditure, the Block food-frequency questionnaire, the National Cancer Institute's Diet History Questionnaire and 14-day dietary record.[16]

We examined the following specific nutrients, including fiber (gm/d), folate (μg/d), vitamins C (mg/d), E (mg/d) and B6 (mg/d) and sodium (mg/d).

2.4. Covariates

We analyzed covariates that have been found to be related to PAD or CVD in previous studies.[17] Age was modeled as a continuous variable. We assigned self-reported race-ethnicity as white, black, Mexican-American, and other. We categorized income as <$20,000, $20,000–$44,999, $45,000–$74,999, ≥$75,000, and unreported and education as <high school, high school, and some college education. Country of birth was self-reported and grouped as within the U.S., Mexico, or other locations. We categorized smoking as never, former, and current. Participants reported their general health, which we collapsed into excellent/very good, good/fair and poor. Detailed information on the collection of demographics data in NHANES for the survey periods is available elsewhere.[14]

Physical activity was assessed by questions regarding the number of episodes of vigorous activity (i.e., jogging, sports, etc. causing a substantial increase in heart rate and heavy perspiration) and moderate activity (i.e., brisk walking, dancing, etc. causing moderate increase in heart rate and perspiration) lasting for at least 10 min over the past 30 days. As in prior work,[18] we divided physical activity into 3 categories: sedentary (no moderate or vigorous activity), modest activity (at least one episode of moderate activity, but no vigorous activity), and some vigorous activity (at least one vigorous episode). As a secondary measure, we included muscle strengthening activities assessed by questions on the number of episodes (at least 10 min duration) of lifting weights, push-ups or sit-ups over the past 30 days. We categorized muscle strengthening activities based upon the median number of episodes[13] per 30 days as none, 1–13 times per month or >13 times per month. The coding algorithm for physical activity used in NHANES is described elsewhere.[19]

We defined hypertension as an average blood pressure reading >140/90 or if the subject had been told by a doctor that they have high blood pressure on two or more separate occasions and were taking medication for hypertension. Routine fasting glucose was measured as described elsewhere.[14] We defined diabetes if fasting glucose ≥126 mg/dl or if taking hypoglycemic agents or insulin to lower glucose. Cardiovascular disease included self-reported diagnoses of coronary heart disease, stroke or congestive heart failure. We categorized alcohol intake into three groups: <2 drinks/day, 2–5 drinks/day and >5 drinks/day.

2.5. Statistical analyses

We calculated descriptive statistics on the dietary intake of nutrients and other characteristics. We tested for normality of ABI using joint tests for skewness and kurtosis and histograms. To facilitate comparison with previous work,[1] we natural log-transformed all nutrients.

We first assessed and calculated odds ratios (ORs) for the relation between nutrients and PAD using four sequential multivariable logistic regression models. The first model adjusted for age, sex, hypertension, diabetes and smoking.[1] The second model additionally adjusted for total energy intake (kcal/24 h) and the third for energy and physical activity. The final model further adjusted for cardiovascular disease, race/ethnicity, education, income, self-reported health status, origin of birth, alcohol intake and other nutrients: fiber, folate, vitamins C, E and B6. We derived 6-year sampling weights, consisting of 1/3 WTMEC2YR, 1/3 WTDRD1 and 1/3 WTDRD1, to generate population-weighted effect estimates. We used SAS (v9.1, 2002, Cary, NC) SUDAAN (v10.0, 2007, Research Triangle Park, NC) to analyze dietary recall data from years 1999 to 2004.[14]

In sensitivity analyses, we tested the association of dietary sodium, which would be expected to be associated with a higher prevalence of PAD based on its effects on blood pressure,[20] with prevalence of PAD using the sequential multivariable logistic regression models in the primary analysis. For additional power, we evaluated the association of dietary sodium with ABI in sequential multivariable linear regression. In ad-hoc analyses, we examined