

ARIC Manuscript Proposal # 1016

PC Reviewed: 06/30/04
SC Reviewed: 07/01/04 _____

Status: A
Status: _____

Priority: 2
Priority: _____

1.a. Full Title: Dietary Factors and Risk of Venous Thrombosis: The LITE Study

b. Abbreviated Title (Length 26 characters): Diet and VTE

2. Writing Group (list individual with lead responsibility first):

Lyn M. Steffen, David R. Jacobs, Jr, Mary Cushman, Wayne Rosamond, Aaron Folsom

Lead: Lyn M. Steffen, PhD, MPH

Address: University of Minnesota School of Public Health; Division of Epidemiology, 1300 South Second St, Suite 300; Minneapolis, Minnesota 55454

Phone: 612-625-9307 Fax: 612-624-0315 E-mail: steffen@epi.umn.edu

Writing group members: David R. Jacobs, Jr (UMN), Mary Cushman (University of Vermont), Wayne Rosamond (UNC), Aaron Folsom (UMN)

3. Timeline: Analysis: 3 months; Writing the manuscript: 6 months

4. Rationale:

There is little existing information on whether diet plays a role in venous thromboembolism (VTE). In several studies, fish intake was inversely related to atherosclerotic events and sudden death (1). Fish intake is also associated with lower levels of von Willebrand factor and factor VIIIc, both strong risk factors for VTE in LITE (2). It is also known that Asian Americans who consume greater amounts of fish, have reduced VTE risk compared to Caucasians (3). Therefore, it is reasonable to hypothesize that fish intake is associated with lower risk of VTE in LITE. It is also likely that the fatty acids, EPA and DHA, are inversely related to VTE.

Many studies have shown positive associations between homocysteine and VTE, although no such association was observed in LITE. Because dietary folate intake is inversely associated with level of homocysteine (4), it seems reasonable that folate intake may be inversely associated with development of VTE. However, this has not been tested. Since whole grain foods are rich in folate, we hypothesize that whole grain intake is inversely associated with development of VTE.

Additionally, inverse associations have been observed between plasma vitamin B6 and VTE, independent of homocysteine level (5). We, therefore, hypothesize that dietary vitamin B6, as well as foods rich in B6, is inversely associated with VTE risk.

Recent evidence suggests that diets high in whole grains, fish, fruits, and vegetables, and legumes (including a Mediterranean diet and the DASH diet) may reduce risk of CHD (6-8). Two studies examining dietary patterns shown that a 'prudent' diet is related to longer survival (9) and lower risk for CHD (10). A 'prudent' diet is characterized by a diet rich in plant foods, especially whole grains, fruit, vegetables, fish, chicken, and low-fat dairy products. Conversely, a 'Western' dietary pattern, a diet rich in meat and low in fruit and

vegetables, is positively related to shorter survival and increased risk of CHD (9,10). Based on limited evidence, this dietary pattern is believed to be antithrombotic as well as antiatherogenic. There aren't any published studies about dietary patterns and risk of developing VTE.

5. Main Hypothesis/Study Questions:

1. Fish intake and individual fatty acids, EPA and DHA, are inversely related to risk of developing VTE;
2. Folate and foods rich in folate, including whole grain intake, are inversely related to risk of developing VTE;
3. Vitamin B6 and foods rich in vitamin B6 (a whole grains, nuts, legumes, and a variety of fruit and vegetables) are inversely related to risk of developing VTE;
4. A dietary pattern rich in plant foods and fish is inversely related to risk of developing VTE; while a meat-based diet is positively related to development of VTE.

6. Data (variables, time window, source, inclusions/exclusions):

Methods:

Proportional hazards regression analyses will be performed to evaluate the relation between quintiles of dietary intake and risk of developing VTE, adjusting for appropriate confounding factors. The 66-food item food frequency questionnaire (FFQ) was administered at baseline and year 6. Dietary data from visit one will be used in the analysis if an event occurred prior to year 6, while diet data from both visits will be included in the analyses if the event occurred/did not occur after year 6. To determine relations between food group intake and VTE, the following food groups will be formed: whole grain, refined grain, meat, fish, poultry, nuts, fruit, vegetables, and dairy products.

Exclusion criteria: prevalent VTE, outlying dietary intake (lower and upper 1% of distribution), missing dietary data, and baseline anticoagulant use.

Variables:

Outcome: In ARIC there are 300 cases of VTE, including incident and recurrent cases with and without cancer. The primary analysis will involve incident VTE unrelated to cancer.

Exposure variables: Nutrient intake, including n6 and n3 fatty acids, folate, vitamin B6, and food intake (frequency and serving size of all 66-food items). A dietary pattern variable(s) will be created using all the food variables.

Confounding factors: Regression models will also be adjusted for age, sex, race, center, education, smoking (status and pack-years), dietary intake (energy, protein, carbohydrate, total fat, saturated fat, vitamin C, and vitamin E), BMI, diabetes, von Willebrand factor, factor VII, and factor VIIIc.

7.a. Will the data be used for non-CVD analysis in this manuscript? Yes No

b. If Yes, is the author aware that the file ICTDER02 must be used to exclude persons with a value RES_OTH = "CVD Research" for non-DNA analysis, and for DNA analysis RES_DNA = "CVD Research" would be used? Yes No

(This file ICTDER02 has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript? Yes No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER02 must be used to exclude those with value RES_DNA = “No use/storage DNA”? Yes No

9. The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status. ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: <http://bios.unc.edu/units/csc/ARIC/stdy/studymem.html>
 Yes No

No overlap with existing publications

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?

NA

11. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.