ARIC Manuscript Proposal # 1154

PC Reviewed: _05_/_23_/06	**Status: __D__**	**Priority: ____**
SC Reviewed: __05/24/06__	**Status: __D__**	**Priority: ____**

1.a. Full Title: Association Between Glycemic Index and the Risk of Incident Coronary Heart Disease Among Patients with Type II Diabetes: The Atherosclerosis Risk in Communities Study.

b. Abbreviated Title (Length 26 characters):

2. Writing Group:

Writing group members: Dale Hardy, Deanna Hoelscher, Mark Pereira, June Stevens, Xianglin Du, Steve Kelder, Lyn Steffan, James Pankow, and Eric Boerwinkle

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3. Timeline: February 2006 to May 2008

4. Rationale:

Coronary Heart Disease

Patients with type II diabetes are at increased risk for coronary heart disease (CHD). Heart disease rates are two to four times higher in persons with diabetes compared to non-diabetics (1-2). It has long been recognized that nutritional factors play a major role in the development of type II diabetes and subsequent CHD (3-7). Diet is a cornerstone in the treatment of type II diabetes and CHD, and has a profound role in attenuating these risks by lowering blood pressure, and normalizing lipids, and blood glucose levels. Hyperglycemia appears to be a strong risk factor in the etiology of CHD (8-14). A strong body of evidence supports the role that diet plays in controlling hyperglycemia, both in the development of type II diabetes and CHD. (15-32). These previous studies focused on foods low in fat, high in fiber, whole grains, fresh fruit and vegetables, and complex carbohydrates which are most likely to have a low glycemic index and

low glycemic load that have been shown to have a protective effect on the development of type II diabetes and subsequent CHD.

The glycemic index and glycemic load are terms used to describe the effect of food on glycemia (33). Foods low in the glycemic index and glycemic load have been found to normalize blood sugars by controlling/ preventing post-prandial spikes in the blood glucose levels which are believed to accelerate the atherosclerosis process (34-37). In addition, the glycemic index and glycemic load can decrease hyperglycemic episodes which play a deleterious role in promoting CHD (38-40).

A diet low in glycemic index contains foods that lower blood glucose levels by slowing the rate of digestion and absorption of carbohydrates consumed (41). A cross-sectional study performed by Amano on Japanese women showed that a diet both high in glycemic index and glycemic load was associated with cardiovascular disease risk factors such as HDL-c, triglycerides, and insulin (42). A 10-year prospective study by Liu et al showed that a high glycemic index diet was associated with increased risk of incident coronary heart disease (RR=1.31; 95% CI:1.02,1.68). Additionally, high dietary glycemic load from refined carbohydrates (calculated as the product of carbohydrate content per serving of food multiply by its glycemic index) increased the risk for coronary artery disease, especially in women with BMI >23 (RR=2.03; 95% CI: 1.45,2.83) (43). These aforementioned studies did not include African Americans, an ethnic group known to be at risk for CHD. To our knowledge there has been no study that addressed the association between dietary glycemic index / glycemic load and the risk of CHD in African Americans.

5. Main Hypothesis/Study Questions

We hypothesize that a high glycemic index diet, high glycemic load diet will increase the risk for CHD, especially among persons with type II diabetes.

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

All subjects in ARIC study are included. Those participants who had a history of CHD at baseline will be excluded from the analysis, as are those who report to be non-white or non-black. The three groups of study subjects (subjects with prevalent diabetes at baseline, subjects with incident diabetes detected during follow-up, and subjects without diabetes) will then be followed to identify incident CHD. Figure 1 presents the flow chart of the study inclusion and exclusion criteria.

<u>Study Variables</u>

1. Diabetes
2. CHD at baseline and at follow-up
3. Time to CHD event
4. Food variables: Glycemic index, Glycemic load, Key dietary score, Sucrose intake
5. Demographic factors: Age, Ethnicity, Gender, Educational level, Body mass index
6. Prevalent diabetes status, incident diabetes, and time to diagnosis of diabetes
7. Diabetes related variables: plasma glucose, HbA1c (hemoglobin A1c) and insulin levels
8. Hypertension
9. Lipid levels: Total cholesterol, LDL-c, HDL-c
10. Smoke cigarettes- current smoker, pack years

11. Sports activity index

Statistical Analysis

Analyses will be conducted using SAS, version 9.1 (SAS Institute Inc, Cary, NC), and STATA, version 9.2 (STATACORP, College Station, TX). The main study goal is to determine whether a low glycemic index/ glycemic load diet is protective against CHD. The exposure variable is glycemic index / glycemic load and the other variables will be considered potential confounders and / or interaction variables (see below) in evaluating the effect of glycemic index/ glycemic load on time to CHD. Descriptive statistics will be computed for each variable. Glycemic index / load will be considered both as continuous variable and as quartiles. At its most simple level, persons with incident CHD will be compared to those without CHD. Survival analysis using Cox proportional regression will be used to examine the association between CHD and glycemic index/ glycemic load. The p-value approach which requires a significance level of testing will be employed to select variables to enter into the model. Based on previous results in the literature, we will test the hypothesis of no interaction between the glycemic index/load and BMI and HbA1c as they combine to influence CHD.

We are particularly interest in whether the glycemic index / load are predictors of incident CHD among individuals with type II diabetes. For this analysis, we will use the entire data set and include prevalent diabetes as a covariate along with a diabetes-by-glycemic index interaction term. Finally, all analyses will be repeated stratifying by prevalent diabetes status.

Although difficult, we will assess the ability of the glycemic index / load to predict incident CHD in those with incident diabetes (as measured from the time of diagnosis of diabetes to the time of the first CHD event). For these analyses, person time (in years) will be calculated from half of the interval between visits in which incident type II diabetes was diagnosed or from baseline for prevalent diabetes, plus the sum of time to development to CHD.

7.a. Will the data be used for non-CVD analysis in this manuscript? ___ Yes __X__ 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 _X___ 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 _X___ 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://www.cscc.unc.edu/ARIC/search.php

____X__ Yes _____ No

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)?

Article by:

Stevens et al (2002). Dietary Fiber Intake and Glycemic Index and Incidence of Diabetes in African American and White Adults. Diabetes Care 25 (10): 1715-1721.

Steffen et al (2003). Associations of Whole Grain, Refined Grain, and Fruit and Vegetable Consumption With Risks of All-Cause Mortality and Incident Coronary Artery Disease and Ischemic Stroke: The Atherosclerosis Risk in Communities Study. Am J Clin Nutr 78: 383-390.

11. a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? ____ Yes _X___ No

11.b. If yes, is the proposal

___ A. primarily the result of an ancillary study (list number* _____)

___ B. primiarly based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* _____ _____ _____)

*ancillary studies are listed by number at http://www.cscc.unc.edu/aric/forms/

12. 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.

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