ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #348

1. Title: Dietary risk factors for 9-year incidence of decreased renal function in the ARIC Study

2. Writing Group:


Coordinating center contact - To be determined

3. Timeline:

The data for these analyses will be available as part of ARIC visits 4. We project that the analyses and writing will take place over in the year after the data is available.

4. Rationale:

ARIC provides an excellent opportunity to study risk factors for the early stages of the decline in renal function. Serum creatinine data from visit 1 and visit 2 will allow for a study of factors associated with prevalence and short term incidence of renal insufficiency (MSP# 223, 224, 225). The current proposed manuscript will focus on the 9-year incidence of renal dysfunction. This analysis will benefit from having longer follow-up and therefore will have more power to study the relationship initially tested in the visit 1 & 2 data.

The main endpoint in the proposed study will be incidence of hypercretinemia defined as in subjects with a "Normal" plasma creatinine in visit 1 (see Table 1)* who developed definite or severe hypercreatinemia by visit 4. Table 2* shows the number of prevalent cases of hypercreatinemia in visit 1 as well as the number of incident cases by visit 2 and the projected number by visit 4. In addition, the power implications of these numbers for analysis of continuous and categorical variables are shown. This table is limited to the non-diabetic members of the cohort since the analysis will be stratified on diabetes. This stratification will account for the potential for heterogeneity in the etiology of diabetic and non-diabetic renal disease.

Dietary factors to be studied are:

Dietary Protein: For more than 20 years it has been known that patients with renal disease who consume a diet severely restricted in protein have fewer uremic symptoms than those on a normal diet. The relationship of dietary protein and renal disease has been studied in many studies of subjects with advanced renal disease including the recently completed Modification of Diet in Renal Disease (MDRD) trial. It is thought that a low protein diet may decrease the progression of renal disease. However, no clear consensus exists and very little data is available on healthy populations. Study of the relationship between dietary protein intake and serum creatinine is complicated by the fact that meat products contain creatinine. Therefore, meat intake may account for a rise in plasma creatinine by increased creatinine production as well as by decreasing renal function. This limits the inferences which can be drawn from the cross-sectional analysis. However, the prospective analysis should yield valid inferences since it is unlikely that an increase in the plasma creatinine of subjects with a high protein diet is due to further increases in their dietary protein. Protein intake will be adjusted for total calorie intake.
**Antioxidant Intake:** Given the role of inflammatory cells in progressive glomerulosclerosis it is possible that a higher antioxidant intake (diet plus supplements) may protect against the oxidative component of the inflammatory damage caused by these cells. Therefore, the possibility of a protective role for antioxidants on the kidney after adjustment for dietary protein and caloric intake will be explored. Given the preliminary nature of this hypothesis both lipid soluble antioxidants (vitamin E and beta-carotene), and water soluble antioxidants (vitamin C) will be studied.

**Other dietary factors:** including cholesterol, linoleic acid, calcium and phosphorus will be explored as potential risk factors.

Potential confounding by age, gender, race & socioeconomic factors, blood pressure, hypertension, diabetes, and lipids will be controlled for. All analyses will be done stratified on diabetes and supplemented with exploratory stratification by gender, hypertension, and race to avoid overlooking.

Potential confounding by age, gender, race & socioeconomic factors, blood pressure, hypertension, diabetes, and lipids will be controlled for. All analyses will be done stratified on diabetes and supplemented with exploratory stratification by gender, hypertension, and race to avoid overlooking potential interactions.

Subjects who report being on a special diet other than for weight loss, low salt, low cholesterol, weight gain, or diabetes will be excluded from this analysis (Dietary Intake Form Q81 answer F=Other). Subjects with a plasma creatinine above 2.0 mg/dl will be excluded as well since they may have been told to restrict their protein intake if their marked renal insufficiency has been diagnosed.

5. Main Hypothesis/Issues to be Addressed:

High protein intake is a risk factor for the decline in renal function.

Low antioxidant intake is a risk factor for the incidence of decreased renal function after controlling for protein and caloric intake.

6. Data Requirements:

Data analysis will be performed by Dr. J. Coresh at Johns Hopkins School of Hygiene & Public Health in collaboration with Dr. J. Nieto

Variables needed: plasma creatinine and time of collection, center, age, gender, race, blood pressure, anthropometric data, dietary data, dietary antioxidants, lipids, lipoproteins and apolipoproteins, medical history data (diabetes), risk factor questions (smoking, alcohol consumption).

Visit 4 variables (not yet available): plasma creatinine & anthropometric data.

*Note: For a copy of the manuscript with the tables, please contact the ARIC Student Assistant at Collaborative Studies Coordinating Center, Department of Biostatistics, UNC-Chapel Hill. Contact by phone: (919) 962-3268 or fax: (919) 962-3265.*