ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #347

1. Title: 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:

End-stage renal disease (ESRD) incidence and prevalence have been increasing relentlessly as long as national statistics have been available. In 1990, over 200,000 people received treatment for ESRD with direct costs of 7.3 billion dollars (VS Renal Data System 1993). For the past decade the incidence of ESRD has been increasing at an annual rate of 7.8% with diabetic and hypertensive patients accounting for a large proportion of this increase. Patients treated for ESRD experience a markedly higher risk of morbidity and mortality. Despite these statistics the epidemiology of ESRD is poorly understood with few large prospective studies of the progression of renal disease. MRFIT and HDFP have reported on hypertension and race as risk factors for a rise in plasma creatinine among men. However, much more information is needed.

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 relationships initially tested in the visit 1 & 2 data.

The plasma creatinine measures during visit 1 and 2 were conducted by the ARIC central laboratory using a modified kinetic Jaffe method (ARIC PROTOCOL Manual 10, version 1.0 and 2.0). The same method was used in both visits with reagents and calibration standards provided by a single manufacturer (Coulter Diagnostics). Creatinine was not measured in visit 3. During visit 4 (1996-99) creatinine will be measured using the modified kinetic Jaffe method on a Hitachi auto-analyzer. An attempt will be made to ensure that the measurement methods are as comparable as possible. Analyses will be conducted to examine for drift and the possibility of a small comparability study is being discussed.

The main endpoint in the proposed study will be incidence of hypercreatinemia 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.

The following independent variables will be explored as risk factors for the presence and progression of renal disease:

**Diabetes**: known to be associated with an increased risk of renal disease. All analyses will be done stratified on diabetes status and the possibility of interaction between diabetes and other risk factors will be examined. Power analyses (Table 2)* indicate that there will be sufficient power to study risk factors among diabetics and to study the presence of interaction is substantially lower. In addition, fasting plasma glucose and insulin will be examined.

**Blood Pressure and hypertension**: Strongly implicated in the pathophysiology of renal disease.

**Lipids**: Suspected as possible risk factors for renal disease but little data in humans is available.

**Black race**: known to be associated with a markedly increased risk of end-stage renal disease.

**Socioeconomic factos will be explores as confounders of this association.**

**Gender**: Will be used as a stratifying variable as well as possible confounder.

**Age**: Will be explored as a confounder as well as being a factor in declining renal function.

**Analgesic Use**: Particularly acetaminophen containing compounds have been associated with endstage renal disease mainly in case-control studies.

**Cigarette Smoking**: Limited evidence is available in renal disease but worth exploring given the strong association with atherosclerosis.

**Other potential confounders**: Will be explored (see data requirements).

5. Main Hypothesis/Issues to be Addressed:

Hypertension, diabetes, lipids, black race, male gender, analgesic use and cigarette smoking are associated with the presence as well as progression of decreased renal function.

The associations observed in the cross sectional and 3-year follow-up analysis will be similar to the associations in the 9-year follow-up analysis.

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.

Baseline Variables (already available): plasma creatinine and time of collection, center, age, gender, race, blood pressure, anthropometric data, 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.