Manuscript #233

1. Title:
Serum creatinine and atherosclerotic plaques of the carotid artery: The ARIC study

2. Writing Group:
(lead) Christopher Nardo, Josef Coresh, Eyal Shahar, John Eckfeldt and other interested ARIC investigators to be determined

3. Timeline:
The data for this analysis are currently available. Analysis and writing will take place over the next year.

4. Rationale:
The atherosclerotic process is thought to be a generalized, rather than a localized phenomenon, suggesting that the presence of atherosclerotic disease in one organ may indicate atherosclerosis in others. This hypothesis is supported by studies which have shown significant associations between atherosclerotic lesions in the kidney and coronary artery atherosclerosis (Kasiske, 1987; Ramirez et al., 1987; McLachlan et al., 1977). Furthermore, a number of common risk factors for cardiovascular disease (CVD), such as cigarette smoking (Black and Cooper, 1986; Mackay et al., 1979; Nicholson et al., 1983) and elevated LDL and VLDL cholesterols (Chopra et al., 1971; Jensen, 1967; Newmark et al., 1975) have been implicated in renal atherosclerotic disease. If renal atherosclerosis is a manifestation of the same factors responsible for atherosclerosis in the coronary and carotid arteries, then early detection of atherosclerotic disease of the kidney may be predictive of atherosclerotic lesions in coronary and carotid arteries, and ultimately CVD. Serum creatinine is a common laboratory measure of renal function. Previous studies have found elevated serum creatinine in patients with atherosclerotic renal disease (Mackay et al., 1979; Simon et al., 1972). Criqui et al. (1986) showed serum creatinine to be an independent predictor of coronary heart disease (CHD) among anti-hypertensive medication users. While, Shulman et al. (1989) found serum creatinine to have significant prognostic value for 8-year overall mortality in a cohort of male hypertensives. Recent reports have found serum creatinine to be an independent predictor of CHD (Heiss et al., 1993; Matts et al., 1993) in healthy men and women.

5. Main Hypothesis:
The serum level of creatinine is associated with the presence of atherosclerotic plaque in the carotid artery.

6. Design:
The study population is drawn from the Atherosclerosis Risk in Communities (ARIC) Study, a longitudinal study of cardiovascular disease, sponsored by the National Heart, Lung, and Blood Institute. The ARIC cohort was selected as a probability sample of 15,800 men and women between 45 and 64 years of age from four US communities. Details of the sampling frames and methods, and the cohort examination procedures have been described previously (The ARIC Investigators, 1989).
The proposed study will examine the cross-sectional association between serum creatinine and carotid plaque. Participants with a history of stroke or transient ischemic attack (TIA) will be excluded from the analysis. Because the presence of plaque is a qualitative determination by the ultrasound reader, participants with ultrasound exams prior to May 15, 1987 will be excluded because those exams are suspect. To investigate the relationship between serum creatinine and carotid plaque, mean serum creatinine values adjusted for age and lean body mass will be calculated for participants with and without. The best logistic regression model will be fit via backwards elimination (Kleinbaum, Kupper, and Muller, 1988) to describe the association between a one standard deviation change in serum creatinine and carotid plaque. Common cardiovascular covariates (smoking, lean body mass, diabetes, HDL cholesterol, LDL cholesterol, blood pressure, hypertension status, and anti-hypertensive medication use) will be considered in the modeling strategy. Hypertension and anti-hypertensive medication, specifically, will be tested for effect modification by including them in the model as cross product terms with creatinine.

7. Data Requirements:
Data analysis will be performed by Chris Nardo at the University of North Carolina at Chapel Hill School of Public Health. The closed Visit 1 data tape is available from the ARIC coordinating center.

REFERENCES:


