ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #304

1. Title (length 26): Lipoproteins, Apolipoproteins and PAD
   Full Title: Associations of Lipoproteins and Apolipoproteins with Lower Extremity Arterial Disease in a Middle-Aged Population: The ARIC Study

2. Writing Group:
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3. Timeline:
   Analyses are expected to be completed within 2 months; a report formatted as a draft manuscript can be presented in the writing group within 2 months after the completion of the analysis.

4. Rationale and Hypothesis:
   Associations of atherosclerotic disease with elevated plasma LDL-cholesterol, Lp(a), reduced HDL-cholesterol are well established. Studies have indicated that, although the lipid profiles are similar in individuals with preclinical atherosclerosis or clinical coronary heart disease, apolipoprotein profiles may differ in different stages of atherosclerosis. In the ARIC Study, Sharrett et al observed that individuals with preclinical carotid atherosclerosis defined by carotid wall thickness, had greater proportional elevations in LDL-cholesterol than apoB, whereas individuals with clinical CHD showed greater proportional elevation of apoB than LDL-cholesterol. These differences may be explained by the involvement of thrombosis in the later stages of atherosclerosis by impaired metabolism of triglyceride-rich lipoproteins.

   Although most clinical studies have observed increased levels of LDL-cholesterol, triglycerides, apoB, and Lp(a), and decreased levels of HDL-cholesterol in patients with symptomatic lower extremity arterial disease (LEAD), limited information from population-based epidemiologic studies is available regarding the relationship between lipoproteins/apolipoproteins and LEAD. We hypothesize that LEAD, measured by low ABI, would show univariate and independent associations with LDL-, HDL1-, and HDL2-cholesterol, triglycerides Lp(a), apoB, and apo A-I. Since a low ABI indicates changes of blood flow and pressure perfusion caused by significant arterial stenosis, we also hypothesize that the profiles of lipoproteins and apolipoproteins in individuals with LEAD would be similar to those with clinical coronary heart disease, rather than preclinical carotid atherosclerosis.

5. Data:
   The ARIC Visit 1 data will be used for analysis. The main outcome variable is PAD, defined as an ABI less than or equal to 0.9. The main independent variables include LDL-, HDL-, HDL1-, and HDL2-cholesterol, triglycerides, apo(a), apoB, and apo A-I. Covariates include age, sex, race, cigarette smoking, diabetes, hypertension, total cholesterol, and fibrinogen. Lipoprotein and apolipoprotein profiles will be compared among individuals with PAD only, with CHD only, and those without PAD and CHD.