1. Title:
Lower Extremity Arterial Disease as an Independent Predictor of Incident Coronary Heart Disease

2. Working Group:
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3. Timeline:
April - June, 1995: Initiation and completion of statistical analyses
July - August, 1995: Preparation of manuscript

4. Rationale:
The presence of lower extremity arterial disease (LEAD) has been shown in several studies to be a sentinel for total and cardiovascular mortality. Intermittent claudication (IC), the symptomatic expression of lower extremity arterial disease, is associated with a twofold to fourfold increase in mortality risk (1-8) and in incidence of fatal and non-fatal stroke (9). In studies using non-invasive methods to measure presence of pre-clinical LEAD, such as those Using low ankle-brachial index (ABI) or venous occlusion plethysmography, relative risks between 2.5 and 6.6 have been reported for all-cause and coronary heart disease mortality (2,10-16). There is less information available on risk of CHD morbidity, though in a preliminary report describing hypertensive men and women, low ABI was associated with a doubling in risk in incident coronary heart disease morbidity and mortality, and a relative risk of 2.5 in cardiovascular fatal and nonfatal events (13).

Because many of the studies above were comprised of highly selected participants, such as persons referred to non-invasive laboratories for testing for LEAD (10,12,15), hypertensives (13), and women 65 years of age or older (11), the generalizability of these results to middle-aged populations is at issue.

5. Purpose:
The purposes of this study are to: (1) determine whether there is an association between baseline LEAD, defined by low ABI, and incident (fatal and non-fatal) CHD in the ARIC population; (2) explore the LEAD-incident CHD association using ABI values on an interval or continuous scale; and (3) determine whether LEAD is associated with all-cause mortality, and if so, describe the association in relation to the incident CHD mortality/LEAD association.

6. Data:
a) Exposure variable: Visit 1 ankle-brachial index
b) Outcome variables: Incident fatal and non-fatal coronary heart disease; all-cause mortality; incident cases of symptomatic CHD, such as angioplasty, coronary artery bypass graft surgery, or Rose Questionnaire angina
c) Co-variables as possible confounders or effect modifiers, also at Visit 1: Gender, race, center, triglycerides, waist-to-hip ratio, measures of socio-economic status
d) Risk factors common to both CHD and LEAD: age, smoking, hypertension, cholesterol, diabetes, body mass index
7. **Analysis Strategy:**
Survival, using life table and/or Kaplan-Meier methodology, to compare those with and without baseline LEAD, using ABI as a marker of LEAD. Examine the survival experience along the range of low ABI, from very low, indicating severe disease, to values indicating moderate and mild disease. If the assumption of proportional hazards is met, Cox models will be constructed to consider covariates.

8. **Feasibility:**
An issue may be whether there are currently enough incident, fatal and non-fatal, CHD events. The formula below comparing two binomial proportions from two independent sample can be used to estimate power.

**To request tables and formulas, please contact (919) 962-2073 or the ARIC Student Assistant at (919) 962-3268**

**REFERENCES**


