

ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #278

1. Title:

Risk factors for atherosclerosis and CHD

2. Writing Group (lead person listed first):

(lead) Sharrett AR, Sorlie PD, Chambless LE, Folsom AR, Hutchinson RG, Heiss G, Szklo M

3. Timeline:

Analyses to begin with availability incident CHD. Publication to follow "hemostasis and incident CHD"

4. Rationale:

Major CHD risk factors, LDL-c, HDL-c, smoking, hypertension and fibrinogen, probably operate primarily by promoting atherosclerosis. However, some of them may relate more than others to thrombogenesis. Thus, the strength of association of these risk factors relative to each other for carotid intima-media thickness may differ from their relative strength of association for incident CHD.

One cannot compare directly a given risk factor's strength of association with carotid IMT with its strength for CHD, for several reasons. Although ultrasound imaging permits direct visualization of carotid thickening, the non-uniform arterial distribution of atherosclerotic lesions and imprecision in IMT measurement may weaken these associations. On the other hand, risk-factor-CHD associations may be attenuated by an inherent difficulty in predicting an episode of acute thrombosis. These difficulties, more to atherogenesis and fibrinogen more to athero-thrombosis, coefficients for LDL relative to those for fibrinogen, would be greater for carotid IMT than for CHD. This paper will demonstrate methods for, and the value of, this type of comparison for investigating risk factors for the atherogenic and atherothrombogenic stages of CHD.

Risk factor associations with carotid atherosclerosis will be assessed in two ways (1) by comparing their multiple linear regression coefficient with the mean of exam1 + exam2 IMT (adjusted for readers and trend) and (2) by using the category of carotid atherosclerosis "case", as defined for purpose of the lab studies. Associations of the same risk factors with incident CHD will be assessed by comparing their coefficients from survival analysis or a multiple logistic model. The study population is cohort members free of CHD at exam 1.

5. Main Hypothesis:

The pattern of association of LDL-c, HDL-c, smoking, hypertension and fibrinogen with carotid IMT differs from the pattern for incident CHD.

6. Data (variables, time frame, source, inclusions, exclusions):

Exam 1 risk factors (listed above), covariates (age, sex, race, community, exam date, medication use, medical history), endpoints (exam 1 and exam 2 ultrasound, incident CHD).