Manuscript #500

1.a. Full Title Carotid Artery Plaque with and without acoustic shadowing as a predictor of incident CHD and stroke.

   b. Abbreviated Title (Length 26:) Calcified plaque & events

2. Writing Group (list individual with lead responsibility first):

   Lead: Kelly Hunt
   Address: UNC-Chapel Hill, School of Public Health
   Dept.of Epid 27599-7400
   Phone: (919) 966-1949
   Electronic Mail Address: KELLY_HUNT@UNC.EDU
   A. Folsom, C. Tegeler
   R. Sharrett
   A. Brown
   L.E. Chambless

   Fax: (919) 966-9800

3. Timeline:
Analyses to begin following publications committee approval. Ms. anticipated in July 1998.

4. Rationale:
Until recently, vascular mineralization was seen as a late (or secondary) development in the process of complicated atherosclerotic plaque formation. Recent evidence suggests that mineralization not only occurs early in the development of atherosclerotic plaques, but is a regulated process similar to bone growth. While mineralization is seen in complicated plaques and is a marker of advanced atherosclerosis, it is unclear whether it plays a protective or destructive role.
Arguments for a protective role include its ability to stabilize soft lipid plaques; while arguments for a destructive role include loss of distensibility, loss of compensatory enlargement, and a weakening at the interface between the arterial wall and fibrous material.
Coronary calcification is reported to be associated with an increased CVD risk profile; however, the association between coronary calcification and CVD events has not been studied. Further, we expect that extracoronary (carotid, abdominal, femoral) calcification is associated with coronary calcification.
The ARIC cohort provides the opportunity to relate information on carotid plaques with and without acoustic shadowing (a surrogate of mineralization) to incident coronary and cerebrovascular events.

ARIC Manuscript and Analysis Procedures June 1996

Because acoustic shadowing may draw attention to a plaque, plaques with and without shadowing may be recognized differentially. Using ARIC quality assurance data, Li et al examined the combined reproducibility of carotid atherosclerotic lesions (with and without shadowing) during the first and second ARIC examination; however, the reproducibility of measuring shadowing was not addressed. This will be done as part of this manuscript proposal.

Further, because plaques with mineralization are not expected to regress, an analysis of the information obtained during the second exam on individuals with mineralization at the baseline examination will provide information on the reproducibility of measuring acoustic shadowing. These analyses will identify false positives--individuals who exhibited signs of mineralization during the first ARIC but failed to show shadowing during the second ARIC exam. However, the ability to identify false negatives would be hindered by the expected progression of mineralization over the three-year period.

5. Main Hypothesis:

1) Carotid artery plaques are a predictor of CHD events and of CVA events after adjustment for IMT.
2) Acoustic shadowing is an effect modifying element in the prediction of CHD and CVA events from carotid artery plaque.

If acoustic shadowing is not shown to have a modifying effect on the association between plaques and incident events, power calculations will be done to determine the smallest detectable association in our data.

6. Data (variables, time window, source, inclusions/exclusions):
exposure: carotid artery plaque(n=4491)
outcome: CVA & CHD events (events data set)
effect modifier: plaque with shadowing(n=858) vs. plaque w/out shadowing
time window: MIC baseline exam will serve as time zero and the events data set will provide the endpoints (CHD & CVA events).
Covariates: baseline IMT, LDL, HDL, total cholesterol, smoking, hypertension, fibrinogen, age, gender, race, center

References:
quantity of coronary artery calcification to identify new risk factors for asymptomatic atherosclerosis. AJE 144 (10):943-953.

