1.a. Full Title: The relationship between aortic valve sclerosis, subclinical cerebral abnormalities, and cardiovascular morbidity and mortality in middle aged African-Americans: The Atherosclerosis Risk in Communities Study

b. Abbreviated Title (Length 26 characters): AVS and SCA in AA

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

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3. Timeline:

Submit proposal: April 2003
Complete analysis: June 2003
Submit manuscript to ARIC publications committee: August 2003

4. Rationale:

Aortic valve sclerosis (AVS) has been associated with a number of adverse cardiovascular events, including stroke. With MR imaging it is now possible to determine whether cardiovascular risk factors such as AVS, are associated with earlier, subclinical markers of cerebrovascular disease. The association between AVS and subclinical cerebral abnormalities SCA (encompasses white matter lesions (WML) and silent brain infarction (SBI) ) has not been examined in previous studies.

The prevalence of AVS and SCA in population studies is similar, although greater variation exists in the occurrence of WML (Aronow, Otto, Stewart, Liao 1996, Wong, Longstreth 1996, Bernick, Kobayashi, Price). The two processes also share many of the same risk factors. AVS and SBI are associated with increasing age, hypertension, diabetes mellitus, smoking, and lipid abnormalities (Kobayashi, Masuda, Otto, Stewart). Increasing age, hypertension, and smoking are also associated with WML (Wong, Liao 1996, Longstreth 1996, Liao 1997).

These conditions are also associated with significant risk for subsequent cardiovascular events. In several large, prospective studies, each condition was associated with increased risk for death, MI, and/or stroke (Wong, Longstreth 2001, Bernick, Otto).

Their comparable prevalences, common risk factors, and similar associated risks raise the possibility that a relationship exists between AVS and SCA. The proposed analysis seeks to
elucidate such a relationship, which could further aid in risk stratification and guide further diagnostic testing in those individuals with cardiovascular risk factors but without overt disease.

5. Main Hypothesis/Study Questions:

Aortic valve sclerosis is independently associated with subclinical cerebral abnormalities.

The prevalence of cardiovascular morbidity and mortality in middle-aged African-Americans is higher in those with AVS and SCA than in those with either or neither condition.

Participants with AVS and SBI have a greater number of and, where applicable, greater abnormality in traditional risk factors for cardiovascular events than those with either or neither condition.

WML and SBI are distinct, but related, entities that when present together, engender greater risk for subsequent cardiovascular and cerebrovascular events than either condition alone.

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

The prevalence of AVS and SCA will be determined based on echocardiographic and cerebral MRI studies obtained during the third ARIC visit. The diagnosis of AVS is based on evidence of valve leaflet thickening of the aortic valve in the parasternal long and short axis views. The MRI images have been characterized previously as have the definitions of WML and SBI (Bryan, Liao 1996, Liao 1997, Wong). Incident cardiovascular events and mortality as well as the elapsed time between the third visit and those events, available from ARIC surveillance, will be used for longitudinal analysis. Associated data regarding cardiovascular status at the time of the third visit (smoking history, blood pressure, lipid status, family history, diabetes control, ten-year Framingham risk) will be used to evaluate the relationship of AVS and SCA to risk factors and morbid events.
REFERENCES


Longstreth WT, P Diehr, NJ Beauchamp, and TA Manolio. Patterns on cranial magnetic resonance imaging in elderly people and vascular disease outcomes. *Archives of Neurology* 2001; 58: 2074.


7.a. Will the data be used for non-CVD analysis in this manuscript?  ____ Yes  ____ No

b. If Yes, is the author aware that the file ICTDER02 must be used to exclude persons with a value RES_OTH = “CVD Research” for non-DNA analysis, and for DNA analysis RES_DNA = “CVD Research” would be used?  ____ Yes  ____ No
(This file ICTDER02 has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript?  ____ Yes  ____ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER02 must be used to exclude those with value RES_DNA = “No use/storage DNA”?  ____ Yes  ____ No

9. The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status. ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: http://bios.unc.edu/units/cscc/ARIC/stdy/studymem.html

____ x ____ Yes  _______ No

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?

307 - Prevalence and anatomic characteristics of infarct-like lesions on MR images of middle-aged adults: The Atherosclerosis Risk in Communities Study

308 - The prevalence and severity of white matter lesions, their relationship with age, ethnicity, gender, and cardiovascular disease risk factors

309 - White matter lesions are associated with cardio- and cerebral vascular disease risk factors

336 - Presence and severity of cerebral white matter lesions and hypertension, its treatment, and its control

369 - Cigarette smoking and other risk factors for silent cerebral infarction in the general population

371 - Silent cerebral infarction and cognitive function

396 - Lower pulmonary function and cerebral subclinical abnormalities detected by MRI

435 - Association of hemostatic variables with MRI-detected cerebral abnormalities

464 - The relationship between prevalent clinical disease with MRI-defined cerebral infarction and white matter disease

753 - Cerebral white matter lesions, retinopathy, and incident clinical stroke

790 - Aortic valve sclerosis as a marker for cardiovascular morbidity and mortality in the African-American cohort: The Atherosclerosis Risk in Communities Study
11. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.