ARIC Manuscript Proposal #817

PC Reviewed: 08/23/01  Status: __A__  Priority: __1__
SC Reviewed: 09/06/01  Status: __A__  Priority: __1__

1.a. Full Title: “Cardiovascular Events and Cognitive Changes.”

b. Abbreviated Title (Length 26 characters): CVD and Cognitive Changes

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

Lead: Suzana Alves de Moraes
Address: Department of Epidemiology, School of Hygiene and Public Health- The Johns Hopkins University- Baltimore, MD.
Phone: 410-9553462
Fax:410-9558086
e-mail: smoraes@jhsph.edu

Writing group members
Moyses Szklo: Department of Epidemiology, School of Hygiene and Public Health- The Johns Hopkins University- Baltimore, MD.
Phone: 410-9553462
e-mail: hszklo@jhsph.edu

Kate Tilling: Department of Public Health Sciences, King's College, London, U.K.
Phone: 020-7848 6629
e-mail: kate.tilling@kcl.ac.uk

Reiko Sato: Department of Epidemiology, School of Hygiene and Public Health-The Johns Hopkins University- Baltimore, MD.
Phone: 410-2430883
e-mail: rsato@jhsph.edu

David Knopman: Department of Neurology, Mayo Clinic, Rochester, MN.
Phone: +1 612-625-9900
e-mail: knopman@mayo.edu

3. Timeline: The first manuscript is expected in 6 months.

4. Rationale:

Some epidemiological studies have shown that cardiovascular events are related to a lower cognitive function, although most of these studies have been restricted to older populations in which co-morbidities may confound the relationship (1-7). Only few epidemiological studies have focused on cognitive function or cognitive decline in middle-age populations (8,9). It is, in addition, unclear
whether the cognitive decline seen after a cardiovascular event is merely the continuation of a decline trend that started before the event (10,11), rather than a result from the event.

Several clinical and epidemiological studies have suggested a relationship between coronary artery bypass and cognitive decline as well as the long-term persistence of such a relationship (12,13). Results from pooled analyses based on 12 cohort studies and 11 intervention studies have suggested that coronary artery bypass surgery can promote cognitive decline (14), with some authors hypothesizing that such decline could result from microembolization and/or hypoperfusion following cardiopulmonary bypass (15,16).

The role of life events such as marital status changes, vital exhaustion, occupation, or income has not been explored in relation to cognitive decline in younger cohorts; neither have these factors been evaluated as confounding variables pertaining to the relationship between cardiovascular disease and cognitive changes over time (17-22).

The purpose of the present study is to explore whether cardiovascular events (MI and stroke), or procedures such as bypass surgery or angioplasty occurring between the ARIC visits 2nd and 4th may accelerate the age-related cognitive decline, after adjustment for known and potential confounders.

5. Main Hypothesis/Study Questions:

The analyses aim at evaluating whether stroke, MI or specific procedures are associated with cognitive changes over time, taking into account, a) whether the event is an incident or a recurrent acute event; and b) the lag-time between the event and the cognitive tests.

The data will be adjusted for confounding variables such as demographic characteristics, cardiovascular risk factors and behavioral correlates.

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

ARIC visits 2 and 4 data are necessary to examine the cognitive changes (outcome). Data on procedures, stroke and MI will be based on the updated data-set available through 1997 (or through the end of V4, if available). Definite, probable and possible ischaemic or hemorrhagic strokes, and definite and probable MI will be considered.

Covariates:
Social demographic variables: Age, gender, education level, race-center, income, occupation, marital status and perceived health status. Marital status will take into account the possible loss of a partner between visits 2 and 4.
Cardiovascular risk factors: Diabetes, hypertension, fasting plasma fibrinogen, cholesterol and triglycerides, Body Mass Index, Carotid intimal medial thickness and vital exhaustion. Previous myocardial infarction will be based on past medical history and/or ECG evidence. Previous stroke will be based on clinical history.
Behavioral factors: Smoking, drinking and sports index.
People with missing values for cognitive tests in either or both visits and those reporting CNS medications will be excluded.

Statistical analysis:

Linear regression modeling will be done using STATA software, Version 7.0 (23). Those diagnosed as an incident/recurrent cardiovascular event will be compared to event-free subjects.

Dummy variables will be created for categorical variables.

All variables that show associations with cognitive changes at a p value \( \leq 0.25 \) will be considered for inclusion in the multivariate models. For the multivariate models, a variable will be kept in subsequent models if it changes the estimates by more than 10% (24). The predicted values for the
outcome (adjusted between-visit mean change) will be estimated from the final models for each cognitive function test.

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  
   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](http://bios.unc.edu/units/cscc/ARIC/stdy/studymem.html)  
   ____ Yes  ____ No

References:


4. Kuller LH; Lynn S; Manolio T; Haan M; Fried L; Bryan N; Burke GL; Tracy R; Bhadelia R. Relationship between Apo E, MRI findings, and cognitive function in the Cardiovascular Health Study. Stroke 1998; 29: 388-98.


8. Knopman D; Boland L; Mosley T; Howard G; Liao D; Szklo M; Mc Govern P; Folsom AR. Cardiovascular risk factors and cognitive decline in middle-aged adults: The Atherosclerosis Risk in Communities (ARIC) Study Investigators. Neurology 2001; 56: 42-8.


