ARIC Manuscript Proposal #2732

PC Reviewed: 4/12/16  Status: A  Priority: 2
SC Reviewed: _________  Status: _____  Priority: ____

1.a. Full Title: Carotid intima-media thickness and life expectancy: the ARIC Study.

b. Abbreviated Title (Length 26 characters): Carotid IMT & life expectancy

2. Writing Group:
Writing group members: Yasuhiko Kubota, Richard F. Maclehose, Gerardo Heiss, Nicholas Roetker, B. Gwen Windham, Josef Coresh, Vijay Nambi, Aaron Folsom, others welcome

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. __YK__ [please confirm with your initials electronically or in writing]

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ARIC author to be contacted if there are questions about the manuscript and the first author does not respond or cannot be located (this must be an ARIC investigator).
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3. Timeline:
Data analysis: 1-2 months from manuscript approval date.
First draft of the manuscript: 2-3 months from manuscript approval date.

4. Rationale:
Carotid intima-media thickness (cIMT) is a biomarker of atherosclerosis and subclinical organ damage (1-3). Many studies have reported the positive association of cIMT for incident cardiovascular events, CVD mortality and even total mortality (4-6). ARIC publications on cIMT have focused on CVD (1-3), but not on total mortality.
Although the evidence on cIMT as a biomarker is being established, to the best of our knowledge, so far there has been no study on whether and how cIMT in middle age is related to life expectancy. Not only clinicians but also patients may be able to understand more easily the severity of their atherosclerosis and organ damage by estimating life expectancy or absolute risk of CVD, rather than relative risks of cardiovascular events and mortality. That is, estimates of life expectancy by cIMT may be useful for clinicians’ decision making and motivating general people to improve their lifestyle or comply with medical advice.

Here, we propose a study to investigate life expectancy according to cIMT in middle age using ARIC.

5. Main Hypothesis/Study Questions:
To estimate life expectancy according to cIMT in middle age.
We hypothesize that greater middle age cIMT is associated with lower life expectancy, and that this association is independent of CVD risk factors.

6. Design and analysis (study design, inclusion/exclusion, outcome and other variables of interest with specific reference to the time of their collection, summary of data analysis, and any anticipated methodologic limitations or challenges if present).

Design
Prospective cohort

Inclusion/exclusion criteria
Inclusion: participants whose cIMT was measured at visit 1.

Exclusion: those who had prevalent CVD (coronary heart disease and stroke) or cancer at visit 1.

Main exposure: cIMT and plaque (2)
1. cIMT: Carotid arteries were examined bilaterally at three sites: the level of the common carotid (1cm proximal to the dilatation of the carotid bulb), the carotid bifurcation (1cm proximal to the flow divider), and the internal carotid artery (1cm distal to the flow divider). The mean cIMT at the six carotid sites will be grouped into quartiles and used as a categorical variable.

2. Carotid plaque: A dichotomous variable of presence or absence of plaque will be used for the analysis.

Covariates
Age, sex, race, body mass index, diabetes, systolic blood pressure, use of anti-hypertensive medications, diabetes, LDL- and HDL cholesterol, triglycerides, use of lipid lowering medications, estimated GFR, smoking status and amount, alcohol use and amount, and education at visit 1.
Endpoints
Time to all-cause death (also CVD mortality and non-CVD mortality) using ARIC visit 1 as baseline.

Statistical analysis
We will calculate age, race-specific estimates of life expectancy by using Accelerated Failure Time model with covariates. We will also calculate crude and adjusted hazard ratios (HR) and 95% confidence intervals of all-cause mortality using Cox proportional hazards models in relation to cIMT as a supplemental data. We will also examine interactions between sex or race and main exposure.

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

b. If Yes, is the author aware that the file ICTDER03 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 ICTDER 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    ____X__ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER03 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://www.csc.c.unc.edu/ARIC/search.php
   ____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)?

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? ____X__ Yes    ____ No

11.b. If yes, is the proposal
A. primarily the result of an ancillary study (list number* 2006.16)
B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* __________ __________ __________)

*ancillary studies are listed by number at http://www.cscu.unc.edu/aric/forms/

12a. 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.

12b. The NIH instituted a Public Access Policy in April, 2008 which ensures that the public has access to the published results of NIH funded research. It is your responsibility to upload manuscripts to PUBMED Central whenever the journal does not and be in compliance with this policy. Four files about the public access policy from http://publicaccess.nih.gov/ are posted in http://www.cscu.unc.edu/aric/index.php, under Publications, Policies & Forms. http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed central.

13. Per Data Use Agreement Addendum for the Use of Linked ARIC CMS Data, approved manuscripts using linked ARIC CMS data shall be submitted by the Coordinating Center to CMS for informational purposes prior to publication. Approved manuscripts should be sent to Pingping Wu at CC, at pingping_wu@unc.edu. I will be using CMS data in my manuscript _____ Yes _____ No.

References:
5. Nambi V, Chambless L, He M, Folsom AR, Mosley T, Boerwinkle E, Ballantyne CM. Common carotid artery intima-media thickness is as good as carotid intima-media thickness of all carotid artery segments in improving prediction of coronary