

ARIC Manuscript Proposal # 1461

PC Reviewed: 12/09/08
SC Reviewed: _____

Status: A
Status: _____

Priority: 2
Priority: _____

1.a. Full Title: The association of arterial stiffness with incident cardiovascular disease – an analysis from the ARIC study

b. Abbreviated Title (Length 26 characters): Arterial stiffness and incident CVD

2. Writing Group:

Writing group members:

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Others are welcome.

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. __EY/VN__ **[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: Analysis is to start as soon as approval is obtained. Manuscript is to be prepared as soon as analysis is available. We hope that the manuscript will be prepared within one year from approval of the analysis.

4. Rationale:

Arterial stiffness has been measured in the ARIC study during Visits 1 and 2. The methods have been previously described.¹ Prior manuscript proposals have described several associations between traditional risk factors for atherosclerosis and arterial stiffness (see section 10). Several other observational studies have also been published examining vascular mechanics (distensibility, Young's modulus) and their relation to various cardiovascular (CV) risk factors.²⁻⁴ A strong relationship between carotid stiffness and CV risk factors has been established.

However, while there are some studies that have investigated the association between arterial stiffness and incident CVD, none have a long term follow up. In the ARIC study there was a proposal in 1997⁵ that aimed at evaluating the association of stiffness and incident CHD and another on its association with incident stroke but there has been no publication associated with this. Given the longer term follow up that is now available we propose to investigate if there is any association between arterial stiffness and incident CVD in the ARIC study.

This analysis will be important as it will provide us with information as to whether arterial stiffness is associated with incident CVD over a long period of follow up. Further, given that improvements in ultrasound technology now allow direct strain analyses in echocardiography which can be performed using automated speckle tracking systems a renewed interest in using carotid stiffness as a risk predictor has resulted.

5. Main Hypothesis/Study Questions:

- a) Increased arterial stiffness is significantly associated with higher incidence of cardiovascular events.
- b) Increased arterial stiffness is significantly associated with higher incidence of recurrent cardiovascular events in those individuals with prevalent CVD
- c) This relationship will persist after adjustment for a traditional cardiovascular 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).

The analysis will be done by the coordinating center

1. After standard ARIC exclusions, participants in ARIC visit 1 and 2 who had carotid ultrasounds done will be eligible.
2. All subjects with prevalent cardiovascular disease (strokes, coronary heart disease) at the time of carotid ultrasonography or absent arterial stiffness data will be excluded for the incident CVD analysis (please see point #6 below).

3. Arterial stiffness will be modeled both as a continuous variable and as quartiles.
4. Association of arterial stiffness and incident CHD, incident stroke (all strokes and then classified as hemorrhagic and ischemic) and incident CVD (all strokes + coronary heart disease and then ischemic strokes + coronary heart disease) will be tested using Cox-proportional hazards model.

Kaplan-Meier survival analysis will also be performed.

5. Models will be constructed with and without adjustment for different variables will be applied using logistic regression models. Adjustments will include demographics, anthropometric measurements, and cardiovascular risk factors from Visits 1 or 2 (whichever visit the arterial stiffness was estimated in).
 - a. Demographic variables will include age, sex, and study center.
 - b. Anthropometric measurements will include baseline height and weight.
 - c. Cardiovascular risk factors will include traditional CV risk factors
6. Additional analysis will be performed in those with prevalent CHD and stroke who were excluded for the incident CVD analysis. In these individuals with prevalent CVD those who have ultrasound data and stiffness data will be included. Then whether arterial stiffness predicts recurrent CVD events (stroke, CHD) will be evaluated as described in 4,5 above

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 ICTDER03 has been distributed to ARIC PIs, and 0contains 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

8.c. If yes, is the author aware that the participants with RES_DNA = 'not for profit' restriction must be excluded if the data are used by a for profit group?

___ 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.unc.edu/ARIC/search.php>

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)?

MS #003A – Relationship of arterial stiffness and CVD risk factors

MS #003B – Variation of CCA elasticity with IMT

MS #003C – Association of distensibility and carotid wall thickness in healthy middle-aged adults

MS #003D – Hypertension and arterial wall stiffness

MS #003E – Type 2 diabetes mellitus, fasting glucose, insulin concentrations associated with arterial stiffness

MS #087 – Arterial wall thickness, distensibility, prevalent disease

MS #462 – Carotid artery size, stiffness versus incident events

MS #510 – Multiple metabolic syndrome (disorder) and arterial stiffness

MS #513 – Association of arterial stiffness and cerebrovascular diseases

MS #723 – Association of ethnicity and vascular stiffness

MS #928 – Vascular capacity and multiple metabolic syndrome

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

11.b. If yes, is the proposal

A. primarily the result of an ancillary study (list number* _____)

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.csc.c.unc.edu/aric/forms/>

12. 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.

References

1. Arnett DK, Evans GW, Riley WA. Arterial stiffness: a new cardiovascular risk factor? *Am J Epidemiol.* Oct 15 1994;140(8):669-682.
2. Urbina EM, Srinivasan SR, Kieltyka RL, et al. Correlates of carotid artery stiffness in young adults: The Bogalusa Heart Study. *Atherosclerosis.* Sep 2004;176(1):157-164.
3. Simons PC, Algra A, Bots ML, Grobbee DE, van der Graaf Y. Common carotid intima-media thickness and arterial stiffness: indicators of cardiovascular risk in high-risk patients. The SMART Study (Second Manifestations of ARterial disease). *Circulation.* Aug 31 1999;100(9):951-957.
4. Gosling RG, Budge MM. Terminology for describing the elastic behavior of arteries. *Hypertension.* Jun 2003;41(6):1180-1182.
5. Evans GW. Carotid Artery Size and Stiffness vs. Incident Events. In: *ARIC Manuscript Proposal Database* [Internet]. March 19, 2003; <http://www.csc.unc.edu/aric/mantrack/maintain/manuscript/MP462.pdf>. Accessed November 27, 2008. MP#462.