1.a. Full Title: Associations between arterial wall and lumen dimensions

b. Abbreviated Title (Length 26 characters): Wall size and lumen

2. Writing Group:
   Writing group members: Wasserman B, Coresh J, Youngblood M, Sharrett AR

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

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3. Timeline: Analysis to begin with currently available interpreted carotid MRI scans and be completed by Oct06

4. Rationale: Arterial compensatory remodeling, specifically outer wall expansion accommodating the lumen, was studied by pathologic examination of the left main coronary artery by Glagov\(^1\). He concluded that functionally important stenosis occurred in the coronaries only after an atherosclerotic lesion occupied more than 40% of the area surrounded by the internal elastic lamina. Ultrasound imaging, though extending this investigation to population-based samples, has permitted only a more limited investigation of the association of lumen diameter with inter-adventitial diameter. In ARIC, compensatory remodeling as assessed by this technique was seen for the common carotid artery, but remodeling appeared to be quite limited for the internal carotid\(^2\). The common carotid lumen diameter was preserved until far wall IMT attained 1.2 mm, but greater IMT was associated with substantial lumen diameter reduction. In the internal carotid, however, even minimal IM thickening was associated with lumen reduction. Preserved lumen in the presence of greater IMT has been confirmed for the common carotid in several studies\(^3\)\(^-\)\(^10\) with one exception\(^11\), and the studies which also assessed the internal carotid\(^3\)\(^,\)\(^5\) confirmed the finding in ARIC that there is much less compensatory remodeling in the internal carotid.
Area measurements, as in Glagov’s pathological studies, are expected to describe remodeling much better than those based on the single, one-dimensional diameters permitted by ultrasound imaging of only the near and far walls. The circumferential view of the wall and lumen acquired in the ARIC carotid MRI exam will permit evaluation of remodeling phenomena at several sites along the long axis of the common and internal carotid. This will add to our knowledge of the extent to which the wall at each site accommodates atherosclerotic expansion without compromising the lumen and of the threshold, if any, where the lumen is reduced in the presence of further arterial wall expansion. Since different cardiovascular risk factors are known to affect IMT and lumen diameter in different ways, this knowledge may inform subsequent studies of risk factors and clinically important aspects of atherosclerosis.

5. Main Hypothesis/Study Questions:

1. The common carotid artery will show a little or no cross-sectional association between MRI-measured wall area and lumen area until the wall area exceeds a threshold, after which the lumen area will be reduced. While a threshold has been reported for coronary arteries, its existence and location remains to be established for the carotid arteries by the current analysis.

2. The internal carotid artery will show a negative association between MRI-measured wall area and lumen area. If there is any threshold (as described in hypothesis #1), it will occur at less wall area in the internal carotid than in the common carotid artery - i.e. “sooner” in atherosclerotic development.

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).

All ARIC MRI participants with wall and lumen area measurements at 3 sites (defined below) will be included. No exclusions are expected on the basis of participant characteristics.

Outer wall area, lumen area, and (by subtraction) wall area will be assessed at 3 locations: the common carotid, at the flow divider, and 3 MRI slices above the flow divider. The study will relate each to age, race, sex, and height. The association of lumen area with wall area will be studied using both graphic and non-linear modeling methods. Evidence will be sought for a threshold where greater wall area begins to be associated with reduced lumen.

Alternative analyses, comparable to the available ultrasound literature, will examine the dependence of lumen on wall using wall thickness and lumen diameter.

Though this manuscript will be based on incomplete recruitment available at the time of the analysis, an attempt will be made to better represent the ARIC population eligible for the MRI study by applying the sample weights used for the earlier phases of selection.
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 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  
_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 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://www.csec.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)?

ARIC ms# 132 and 132A (Crouse et al.) are published. 2,12

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

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.  Understood
References


