

**ARIC Manuscript Proposal #2116**

**PC Reviewed: 4/9/13**

**Status: A**

**Priority: 2**

**SC Reviewed: \_\_\_\_\_**

**Status: \_\_\_\_\_**

**Priority: \_\_\_\_\_**

**1.a. Full Title:** Exploring the value of cardiac troponin T in various blood pressure categories

**b. Abbreviated Title (Length 26 characters):** blood pressure, cardiac troponin T

**2. Writing Group:**

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

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**3. Timeline:** Analysis to start as soon as approval is obtained. Manuscript is to be prepared as soon as analyses are available. The analysis and manuscript preparation will take place within 1 year from approval of the proposal.

**4. Rationale:** Cardiac troponin T (cTnT) is emerging as a marker that is strongly associated with incident cardiovascular end points including coronary heart disease, heart failure, stroke, and, death.

Elevated blood pressure is cardiovascular risk factor and has been shown in several studies to be associated with all the above mentioned adverse cardiovascular events. Reductions in blood pressure have in general been associated with improved cardiovascular outcomes. However, there are some blood pressure ranges (and age groups) where epidemiological data suggests increasing cardiovascular risk with increasing blood pressure and yet therapy to lower blood pressure is not associated with a decrease in clinical end points. Examples include systolic blood pressure <140 mmHg where “aggressive treatment” to systolic blood pressures <120 mmHg have failed to show benefit even in higher risk groups such as individuals with diabetes as seen in the ACCORD study (N Engl J Med. 2010 Apr 29;362(17):1575-85); for the elderly there is controversy even in the systolic blood pressure range of 140-150 mmHg where it is unclear if treatment will be of benefit (Krause T BMJ 211; 343, d4891, Aronow WS Circ 2011; 123: 2434, Pimenta E Nat Rev Cardiol 2012; 9: 286). While there are potential explanations for the lack of benefit (example hypotension induced by medications, effect on diastolic blood pressures etc) the clinical equipoise suggests that some individuals may benefit from therapy while others may not. Therefore an improved risk assessment of these individuals may be of clinical value. We propose to examine the value of troponin T in the various blood pressure categories (measures would include systolic, diastolic BPs and pulse pressure) and across various age ranges and describe its association with adverse cardiovascular events across these categories

## **5. Main Hypothesis/Study Questions:**

### **Hypothesis:**

1. Cardiac troponin T measured with a high sensitivity assay will be associated with adverse cardiovascular events (includes CHD events, stroke, heart failure and cardiac mortality) across various systolic and diastolic blood pressure, and, pulse pressure ranges
2. Cardiac troponin T will help identify subjects at higher and lower cardiovascular risk across these blood pressure measures and categories

**Study questions:**

1. Describe the distribution of troponin T across the various blood pressure categories (further stratified by age, anti-hypertensive medication use and cardiovascular disease status)
2. Describe the association of troponin T with adverse cardiovascular events across various systolic and diastolic blood pressure values (continuous and categories)
3. Describe the association of troponin T with adverse cardiovascular events across various pulse pressure values (continuous and categories)

**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 methodological limitations or challenges if present).**

Standard ARIC exclusions (race/ center) will be applied

All other individuals with available troponin T and blood pressure measures at the 4<sup>th</sup> ARIC visit will be eligible. Additional stratified analysis will be performed among those with/ without prevalent cardiovascular disease and among those on/ not on anti-hypertensive medications.

Systolic blood pressure will be categorized as <120, 120-129, 130-139, 140-149, 150-159 and  $\geq 160$  mmHg. If adequate numbers (especially when events are considered) are not available in some of the bins they may be combined. Diastolic blood pressure will similarly be categorized into <70, 70-79, 80-89, 90-99 and  $\geq 100$  mmHg. Finally pulse pressure categories will be described as well (<30, 30-39, 40-49, 50-59 and  $\geq 60$  mmHg).

Distribution of troponin in these various blood pressure categories will be described with and without stratification by anti-hypertensive medication use and CVD status. Linear splines will be used to further evaluate the relationship of the blood pressure categories with troponin T. Finally the cumulative blood pressure (over ARIC visits) and its association with troponin will be evaluated as well.

Using Cox-proportional hazards model, the association between troponin and adverse cardiovascular events (defined as myocardial infarction (silent or manifest), death from coronary heart disease, revascularization), stroke (all types), heart failure hospitalization and death from cardiovascular causes) will be reported initially using minimally adjusted models (age/ race in gender specific models) and then after adjustment for other variables including anti-hypertensive medication use, renal function (eGFR), diabetes, fasting glucose, total/HDL cholesterol, BMI, cigarette smoking and CVD status for the various blood pressure groups/ categories.

Stratified analysis will be pursued by hypertension status and by CVD status

Additional analysis will be pursued modelling blood pressure as a continuous variable. The interaction between blood pressure and troponin T levels will be examined

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 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  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.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 1808, 1757, 1759, 1564

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\* 2008-10)

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.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.csc.unc.edu/aric/index.php>, under Publications, Policies & Forms. [http://publicaccess.nih.gov/submit\\_process\\_journals.htm](http://publicaccess.nih.gov/submit_process_journals.htm) shows you which journals automatically upload articles to Pubmed central.