

ARIC Manuscript Proposal #2909

PC Reviewed: 12/13/16

Status: _____

Priority: 2

SC Reviewed: _____

Status: _____

Priority: _____

1.a. Full Title: High-sensitivity cardiac troponin T and natriuretic peptide at middle age and prognosis after myocardial infarction at later life

b. Abbreviated Title (Length 26 characters): V2/4 TnT/BNP & events after MI

2. Writing Group:

Writing group members: Yejin Mok, Yingying Sang, Shoshana Ballew, Ron C. Hoogeveen, Christie M. Ballantyne, Wayne Rosamond, Josef Coresh, Elizabeth Selvin, Kunihiro Matsushita; others welcome

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. __YM_ [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: Analyses and manuscript preparation will be performed over the next 6 months.

4. Rationale:

Cardiac troponin T (cTnT) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) are diagnostic biomarkers for myocardial infarction and heart failure, respectively. Furthermore, higher levels of these cardiac markers in patients with coronary heart disease or heart failure are related to poor prognosis[7-15]. Of interest, those cardiac markers are identified in some individuals without clinical cardiovascular disease and predict cardiovascular disease events particularly cardiovascular death and heart failure [1-6].

However, whether such a subclinical elevation of cardiac biomarkers in the general population is related to prognosis after the development of clinical cardiovascular disease is unknown. Such an investigation will provide us a few implications. If these cardiac markers at in middle-age free of clinical cardiovascular disease predict prognosis after a

cardiovascular disease event in later life in addition to the development of cardiac disease, that would further support the usefulness of these markers to identify at high cardiovascular risk and emphasize the importance of prevention approach at earlier stage of life. Therefore, using data from the Atherosclerosis Risk in Communities (ARIC) study, we will examine the associations of hs-cTnT and NT-proBNP levels at middle-age (visits 2 and 4) with the risk of adverse outcomes after MI at later life.

5. Main Hypothesis/Study Questions:

We hypothesize that levels of hs-cTnT and NT-proBNP in middle-age among persons without a history of cardiovascular disease will be associated with poor prognosis after incident MI at later life beyond covariates assessed at the development of MI.

6. Design and analysis

Design: Prospective cohort study.

We will quantify the associations of hs-cTnT and NT-proBNP at Visits 2 or 4 with the risk of adverse outcomes (All-cause mortality, cardiovascular mortality, recurrent MI, heart failure, and stroke) after incident MI independently of potential confounders at MI occurrence. As detailed below, we will use covariates at MI occurrence using data from other visits and the medical record prior to incident MI. Since it will allow us to explore a larger number of incident MI cases, we will use visit 2 data of hs-cTnT and NT-proBNP for primary analysis and repeat the analysis using visit 4 hs-cTnT and NT-proBNP to confirm the robustness of our findings.

Inclusions: All black and white ARIC subjects who developed MI after Visits 2 or 4

Exclusions:

1. Race other than black and white
2. Individuals with missing data on hs-cTnT and NT-proBNP at visits 2 and 4 or outcomes described below
3. Participants who had a history of MI prior to visit 2 (or visit 4 for the analysis of visit 4 hs-cTnT and NT-proBNP) based on self-report or electrocardiogram (ECG) at visit 1 or adjudicated MI prior to visit 2 (or visit 4).

Exposures:

Covariates at MI occurrence: Age, gender, race/ethnicity, weight, blood pressure, history of hypertension, diabetes, current and former smoking status, prior heart failure, prior stroke, prior peripheral artery disease, revascularization procedure, prior kidney disease, troponin and natriuretic peptide at admission and calendar years.

Outcomes:

All-cause mortality, cardiovascular mortality, recurrent MI, heart failure, and stroke after incident MI.

Statistical Analysis:

1. Hs-cTnT will be categorized into five categories (<3, 3-5, 6-8, 9-13 and 13+ ng/L) and NT-proBNP will be categorized into five categories corresponding to the same percentiles of each category of hs-cTnT. [16] We will summarize basic characteristics according to the 5 categories of hs-cTnT and NT-proBNP.
2. We will first quantify the association of hs-cTnT and NT-proBNP with the risk of adverse events (all-cause mortality, cardiovascular mortality, recurrent MI, heart

failure, and stroke) after incident MI, using Kaplan-Meier method as well as Cox proportional hazards regression models accounting for potential confounders.

3. We will conduct a few sensitivity analyses:
 - a. We will repeat analysis in several subgroups by race and gender.
 - b. Since those with higher levels of hs-cTnT and NT-proBNP were likely to develop MI earlier than those with lower levels, leading to longer follow-up after MI to capture adverse outcomes, we will restrict our analysis to 1, 3, or 5 years after MI as sensitivity analysis.

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)?

MP #965: Characteristics and Outcome of Troponin Elevation in the Absence of Other Criteria for Myocardial Infarction

MP #725: Prognosis of hospitalized myocardial infarction according to degree of myocardial injury assessed by biochemical markers and other risk indicators

MP #2319: Does cardiac troponin T help identify subjects with metabolic syndrome at higher risk of cardiovascular events? An analysis from the ARIC study

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.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 shows you which journals automatically upload articles to PubMed central.

13. Per Data Use Agreement Addendum, approved manuscripts using 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

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