ARIC Manuscript Proposal # 2921

PC Reviewed: 01/10/2017   **Status:** _____   **Priority: 2**
SC Reviewed: _____   **Status:** _____   **Priority:** ____

1. a. Full Title:

Silent myocardial infarction and Risk of Heart of Failure in the Atherosclerosis Risk in Communities Study (ARIC)

  b. Abbreviated Title (Length 26 characters):

HF and silent MI

2.   Writing Group:
Writing group members:

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I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. <u>WTQ</u>

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3. **Timeline:**
   Start analyses: within a month of approval of the proposal
   Submission for publication: Within 6 months of the approval of the proposal.

4. **Rationale**:

Heart failure (HF) is a frequent complication of myocardial infarction (MI).[1-4] Improvements in the management of acute MI together with ageing population have contributed to a growing burden of HF.[5] Each year more than 1 million hospitalizations occur due to HF in United States.[6] Several factors, such as recurrent MI, infarct size, ventricular remodeling, stunned myocardium, mechanical MI complications, and hibernating myocardium lead to HF after MI.[7-9] These conditions might not be clinically apparent and may go unnoticed for a long time. Electrocardiogram (ECG) may serve as a potential screening tool to identify individuals at risk of HF.

Silent MI (SMI), defined as ECG-evidence of MI in the absence of history of MI, accounts for about half of the total number of MIs.[9] Previous reports from different populations including a recent report from the ARIC study have shown that silent MI is associated with poor prognosis as is clinically documented MI (CMI).[9, 10] However, whether silent MI is associated with HF similar to CMI is currently unclear. It is also unclear if there is effect modification of the race and gender on the association between MI (silent and clinical) with HF. Therefore, the aim of this proposed study is to examine and compare the associations between SMI and CMI, separately, with HF in the ARIC study, and to examine the consistency of these associations in sex and race subgroups. The ARIC study with its high quality digital ECG data and corresponding clinical data represents a unique opportunity to answer and address this aim.

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

This study aims to:

• Examine and compare the association between SMI and CMI (versus no MI) with incident HF in the ARIC study.

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).

Sample Size

All ARIC participants with good quality ECG data at baseline as well as information on all relevant risk factors and HF events during study's long term follow-up will be eligible for inclusion in this analysis.
Partcipants with pevalent MI (by ECG or past medical hisotry) as well as HF at baseline and between baseline until visit 4will be excluded.

Variables:

Outcomes:
- Incident heart failure events after ARIC visit 4.

Main exposure variables:
- **Silent MI** will be defined as ECG evidence of MI based on Minnesota code in the absence of clinically detected in the same period (visit 1 to visit 4).
- **Clinical MI** will be defined as definite or probable adjudicated MI occurring in the period from ARIC visit 1 to ARIC visit 4.
  The definitions of silent and clinical MIs will be similar to the definitions used in our recent ARIC report on racial and sex differences silent and clinical MIs (10)

Other Variables
- All ECG Minnesota codes at the first 4 ARIC visits.
- Key demographic and clinical variables -- age, race, gender, body mass index, education, smoking status, hypertension, diabetes mellitus, family history of coronary heart disease, HDL cholesterol, LDL cholesterol, total triglycerides, total cholesterol, systolic blood pressure, diastolic blood pressure, fasting blood glucose, use of blood pressure lowering medications, aspirin use, use of lipid lowering medications and creatinine.

Data analysis:

Baseline participant characteristics will be stratified and compared according to the MI status (silent MI, clinical MI, no MI) that occurred between visit 1 to visit 4.

Incidence of HF occurring after visit 4 will be calculated per 1000 person years and compared among ARIC participants according to the MI status (silent MI, clinical MI, no MI) that occurred between visit 1 to visit 4.

Cox proportional hazard analysis will be used to examine the association between clinical MI and silent MI (versus no MI) with incident HF in models adjusted as follows: Model 1 adjusted for age, sex, race; Model 2 adjusted for variables in model 1 plus study field center, education, body mass index, smoking status, systolic blood pressure, blood pressure lowering medications, diabetes mellitus, ratio of total cholesterol/high density lipoprotein, use of cholesterol lowering medications, use of aspirin, family history of coronary heart disease and serum creatinine.

Subgroup analysis by sex and race as well as key risk factors know to be associated with heart failure (i.e. components to the Framingham HF risk score) will be examined in similar models. Interaction terms will be examined in model 2.

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 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.cscc.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)?
MS#2075- Zhang: Race and sex differences in the incidence and prognostic significance
of silent myocardial infarction in the atherosclerosis risk in communities (ARIC) study.
The lead and senior authors are presented in the proposal
11. a. Is this manuscript proposal associated with any ARIC ancillary studies or use
any ancillary study data? _____ Yes **X 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.cscc.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:

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