ARIC Manuscript Proposal #1920

PC Reviewed: 3/20/2012 **Status: A** **Priority: 2**
SC Reviewed: _____ **Status: _____** **Priority: ____**

1.a. Full Title:

Mortality Risk Associated with Bundle Branch Blocks and Associated Repolarization Abnormalities: Gender Differences in the Atherosclerosis Risk in Communities Study (ARIC)

1.B. Abbreviated Title (Length 26 characters):
Bundle Blocks and Mortality

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. ZMZ **[please confirm with your initials electronically or in writing]**

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3. Timeline:

Start analyses: upon receipt of data from the coordinating centre
Submission for publication: December 2012

4. Rationale:

The presence of electrocardiographic (ECG) depolarization and repolarization abnormalities have both been shown to contain valuable independent information on the risk of coronary heart disease (CHD) and all-cause mortality.[1-5] Mortality risk data for left and right bundle branch block (LBBB and RBBB, respectively) in general populations are conflicting.[6-14] There are only limited data available with comparative evaluation of the predictive value of different types of bundle branch block for fatal and nonfatal cardiac events and total mortality.

According to a recent analysis from the Women's Health Study (WHI), prevalent LBBB in CVD-free women and LBBB and RBBB in women with CVD are significant independent predictors of CHD death. Further, in women with LBBB, ST depression in aVL was a further strong independent predictor of CHD death, but not in those with RBBB and CHD –free at the study baseline. Because the WHI study involved only women, the question of gender differences in the risk associated with BBB and whether these finding are the generalizable to men remains open and will require attention in future investigations.

5. Main Hypothesis/Study Questions:

<u>This study aims to</u>:

(1) To evaluate CHD and all-cause mortality risk associated with RBBB and LBBB in both men and women in the ARIC study.

(2) To evaluate if repolarization abnormalities in RBBB and LBBB contain additional prognostic information, and if such prognostic significance differ by gender.

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).

<u>Sample Size</u>

All ARIC participants with good quality baseline ECG data as well as information on relevant risk factor variables and outcome variables of CHD deaths and all-cause mortality during ARIC follow-up will be eligible for inclusion in this analysis. Participants with artificial pacemaker, or Wolf Parkinson White Syndrome will be excluded. From the total of 15,571 ARIC participants at baseline we expect to have approximately 450 ECGs with BBB.

<u>The Variables:</u>

<u>ECG variables needed to fulfill the aim of the study will be:</u>

Complete Minnesota codes[16-17] for all ECGs at baseline and follow up visits, which will include specifically,

- Complete left bundle branch block (MC-7.1)
- Complete right bundle branch block (MC-7.2)
- Combination of RBBB and left anterior fascicular block (MC-7.8)
- Intraventricular conduction defect, QRS $\geq$ 120ms (MC-7.4).
- ECG- Myocardical infarction/Ischemia -- MC 1, MC 4, MC 5, MC 92 --Q/QS wave, ST segment, T wave amplitude.
- Frontal QRS axis and T axis, QRS/T angles (spatial and frontal)
- Continuos measurements of the duration and amplitude of Q-R-S-T waves by leads.
- Presence of arrhythmias and ectopic beat including atrial and ventricular ectopic beats and atrial fibrillation.

Non-ECG variables:

Non-ECG variables include demographic and clinical data, and outcome measures, which are summarized in below:

(1) The key demographic and clinical variables -- age, race, gender, body mass index, education, smoking status, alcohol use, hypertension, diabetes mellitus, previous stroke, history of cardiovascular disease, family history of coronary heart disease, HDL cholesterol, LDL cholesterol, total triglycerides, total cholesterol, systolic blood pressure, diastolic blood pressure, baseline fasting blood glucose.

(2) The outcomes include updated incident fatal CHD event and all-cause mortality confirmed by the endpoints committee. (update to the end of 2006)

FATCHD06	Fatal CHD by end of year 2006
DEAD06	Dead by end of year 2006

Data Analysis:

First, frequency distributions of all ECG and non-ECG variables will be inspected to rule out anomalies and outliers possibly due to measurement artifacts.

Time dependent Cox regression analysis will be used to examine the risk of mortality and the association with each pattern of BBB (LBBB, RBBB, and IVCD) as predictors for CHD death and total mortality.

Models will be initially adjusted for demographic (age, sex, race), then further adjusted for clinical characteristics (which are the variables mentioned as non-ECG variables above). Similar analysis will be conducted for QRS duration, QRS/T angle (spatial and frontal), amplitude of Q-R-S by leads, magnitude of ST segment elevation or depression in leads with predominantly positive or negative QRS complexes (discordant or concordant of QRS complex and ST segment), magnitude of T wave change in leads with predominantly positive or negative QRS complexes (discordant or concordant of

QRS complex and T wave), separately and combined with BBB patterns. Interaction by sex, race, and history of CVD will be examined and models will be stratified accordingly.

The proportional hazards assumption of the Cox regression model will be checked graphically for each of the candidate variables. All analyses will be performed with the SAS software, version 9.2.

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)?

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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