ARIC Manuscript Proposal #2563

PC Reviewed: 6/09/15   **Status: A**   **Priority: 2**
SC Reviewed: _____   **Status: _____**   **Priority: ____**

1.a. Full Title: Electrocardiographic Interatrial Block and Atrial Fibrillation Risk in the General Population

  b. Abbreviated Title (Length 26 characters): Atrial Block and Arrhythmia

2.   Writing Group:
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I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. WTO

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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:

Analysis to begin after Publication Committee approval. Manuscript anticipated for initial P&P review 3 months after proposal approval.

4.   Rationale:

Interatrial block (IAB) exists when a delay of conduction occurs over the Bachmann bundle.[1] Although IAB is an established electrocardiographic phenotype, its prevalence, incidence and prognostic significance in the general population are unclear.

The presence of IAB was shown to be an independent predictor of new-onset AF in patients with congestive heart failure undergoing cardiac resynchronization therapy and among patients who received cavotricuspid isthmus ablation for typical atrial flutter.[2,3] Additionally, IAB has been associated with a higher risk of AF recurrence after pharmacological cardioversion to normal sinus rhythm.[4] To date, the association between IAB and AF has not been examined in prospective population-based studies.

The ARIC Electrocardiogram (ECG) Reading center (EPICARE) has recently derived IAB from the ARIC study ECGs using the current consensus report on this ECG phenotype.[1] This provides a unique opportunity to determine the prevalence and incidence of IAB in the general population and to examine its association with AF in the ARIC.

5.   Main Hypothesis/Study Questions:

The aims of this study are:
1) Determine the prevalence and incidence of IAB in the ARIC cohort study.
2) Examine the association between IAB (as time-dependent variable) with incident AF.

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).

Design: Secondary data analysis from prospective cohort.

Inclusion/Exclusion Criteria: We will include all participants with baseline ECG data. Participants with baseline AF will be excluded. The few ARIC participants with race other than black or white will also be excluded, including the small number of black participants from Washington County and Minneapolis.

Outcomes: The outcome of interest will be AF determined by subsequent ARIC visits and ICD-9 codes from hospitalization data.

Variables: IAB as derived by the ARIC ECG Reading Center (EPICARE). Other variables needed from the baseline study visit will include the following: socio-demographics (age, sex, race/ethnicity, income, education, and study site), cardiovascular disease risk factors (systolic

blood pressure, HDL-cholesterol, total cholesterol, body mass index, smoking, diabetes), and baseline medication use (blood pressure lowering drugs, statins and other lipid-lowering therapies, and aspirin).

Statistics: Baseline characteristics will be examined by stratifying participants by the presence of IAB at baseline. Categorical variables will be reported as frequency and percentage while continuous variables will be recorded as mean ± standard deviation. Incident IAB will be defined as first occurrence of IAB in ARIC participants who do not have IAB at baseline. Incidence rates of IAB per 1000-person years will be calculated for all participants and stratified by race and sex

For the AF analysis, follow-up will be defined as the time between IAB detection until AF development, loss to follow-up, or end of follow-up. Subsequent study visit ECGs will be used to identify more IAB cases due to the limited number of cases present in the baseline study visit. The period between the baseline visit and IAB diagnosis will be considered as non-IAB follow-up. Kaplan-Meier estimates will be used to examine the cumulative incidence of AF by the presence of IAB as time-dependent variable. Cox regression will be used to compute hazard ratios (HR) and 95% confidence intervals (CI) for the association between IAB as time-dependent variable and AF. Multivariable models will be constructed as follows: Model 1 adjusted for age, sex, race/ethnicity, income, and education; Model 2 adjusted for Model 1 covariates plus smoking, systolic blood pressure, diabetes, body mass index, total cholesterol, HDL-cholesterol, antihypertensive medication use, heart rate, lipid-lowering medication use, and aspirin use. The variables included in the multivariable models will be from the initial study visit. A sensitivity analysis will be performed with further adjustment for incident coronary heart disease and heart failure events, separately.

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 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   __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)?

    None.

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/

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.cscc.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.

References

1. Bayes de Luna A, Platonov P, Cosio FG, et al. Interatrial blocks. A separate entity from left atrial enlargement: a consensus report. *J Electrocardiol.* 2012;45(5):445-451.
2. Enriquez A, Sarrias A, Villuendas R, et al. New-onset atrial fibrillation after cavotricuspid isthmus ablation: identification of advanced interatrial block is key. *Europace.* 2015.
3. Sadiq Ali F, Enriquez A, Conde D, et al. Advanced Interatrial Block Predicts New Onset Atrial Fibrillation in Patients with Severe Heart Failure and Cardiac Resynchronization Therapy. *Ann Noninvasive Electrocardiol.* 2015.
4. Enriquez A, Conde D, Hopman W, et al. Advanced interatrial block is associated with recurrence of atrial fibrillation post pharmacological cardioversion. *Cardiovasc Ther.* 2014;32(2):52-56.