ARIC Manuscript Proposal # 1601

PC Reviewed: 1/12/10	**Status: 2**	**Priority: A**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title:
Prevalence and Long-Term Prognosis of J-point Elevation in a Large Biracial Cohort.

b. Abbreviated Title (Length 26 characters):
J-point Elevation Prognosis

2. Writing Group:
Writing Group members: Wayne Rosamond, Richard Crow, Elsayed Z. Soliman, Anthony Viera, Kristoff Olson, others welcome

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

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3. Timeline:
The manuscript will be complete by July 2010.

4. Rationale:

In electrocardiography, the J-point is the common name for the junction between the QRS complex and the ST segment.[1,2] J-point elevation above the baseline is a common ECG finding that is seen in 1-5% of people.[3] J-point elevation has traditionally been viewed as a benign finding, especially in young healthy adults. However, an association between J-point elevation and idiopathic ventricular fibrillation has been suggested by several recent studies.[3-5]

J-point elevation may in fact be a marker of underlying electrical vulnerability that increases the risk of fatal arrhythmias. A recent study conducted by Tikkanen and colleagues showed that J-point elevation was associated with increased risk of death from cardiac causes and with increased risk of death from arrhythmia.[6] The Tikkanen study is the only cohort study on the topic that we are aware of. In the study, the authors used visual measurements of J-point and did not have quantitative measures like those available in ARIC. In addition, the study was conducted in Finland and its findings may not be generalizable to U.S. adults. For example, the Finnish cohort likely had few Blacks in the sample, though this was not discussed explicitly. This is an important point, because Blacks have a higher prevalence of J-point elevation. Experts have called for investigation of the significance of these junctional changes the groups that are at higher risk for them.[1] In addition, there is speculation that J-point elevation could be linked to a genetic defect in cardiac ion channels.[7]

Using ARIC data, we aim to (1) estimate the prevalence of J-point elevation in a biracial cohort of US adults, and (2) examine the association of J-point elevation with cardiac events and whether prognostic significance of the finding varies by race. The serial ECG data available on ARIC cohort members will also enable us to examine progression and stability of J-point elevation over time. Finally, we will use ARIC's extensive family history information to examine whether J-point elevation is associated with a family history of cardiac events.

REFERENCES

1. Wellens HJ. Early repolarization revisited. *N Engl J Med*. 2008;358(19):2063-2065.
2. Wang K, Asinger RW, Marriott HJ. ST-segment elevation in conditions other than acute myocardial infarction. *N Engl J Med*. 2003;349(22):2128-2135
3. Haissaguerre M, Derval N, Sacher F, et al. Sudden cardiac arrest associated with early repolarization. *N Engl J Med*. 2008;358(19):2016-2023.
4. Nam GB, Kim YH, Antzelevitch C. Augmentation of J waves and electrical storms in patients with early repolarization. *N Engl J Med*. 2008;358(19):2078-2079.
5. Rosso R, Kogan E, Belhassen B, et al. J-point elevation in survivors of primary ventricular fibrillation and matched control subjects: Incidence and clinical significance. *J Am Coll Cardiol*. 2008;52(15):1231-1238.
6. Tikkanen JT, Anttonen O, Junttila MJ, et al. Long-term outcome associated with early repolarization on electrocardiography. *N Engl J Med*. 2009.
7. Boineau JP. The early repolarization variant--normal or a marker of heart disease in certain subjects. *J Electrocardiol*. 2007;40(1):3.e11-3.e16.

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5. Main Hypothesis/Study Questions:

The purpose of the proposed study is to estimate the prevalence of J-point elevation on ECG in the ARIC cohort and to investigate whether it is related to long term risk of cardiac events (including fatal/non-fatal MI, hospitalization for arrhythmia or death with arrhythmia code on death certificate) and all-cause mortality. We will also assess whether prevalence and prognosis of J-point elevation vary by race.

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).

The study will utilize ARIC cohort data. Included will be all ARIC cohort members for whom J-point elevation data on baseline ECG is available. We will exclude any individuals for whom J-point data is missing or incomplete. The variable for J-point in the ARIC database is called "STJ" and is measured in each of the 12-ECG leads separately.

Primary endpoints will be sudden cardiac death and CHD death. Secondary endpoints will include fatal/non-fatal MI, all-cause mortality, and the soft composite endpoint of hospitalization for arrhythmia or death with arrhythmia code on death certificate.

We will use Cox proportional-hazards models to calculate hazard ratios for all outcomes. Bivariate analysis will be used to examine relationships between J-point elevation and potential covariates. Variables with a known association with cardiovascular disease will be examined and controlled for as necessary. Variables examined for inclusion in the model will likely include age, sex, systolic blood pressure, heart rate, BMI, smoking status, presence of coronary artery disease by history, left ventricular hypertrophy by ECG, carotid intima-media thickness, peripheral arterial disease, blood lipids, fasting plasma glucose, lifestyle factors, and family history of CHD. We will also control for the use of beta-blockers and other medications that have the potential to cause changes in cardiac repolarization.

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)?
MP #776, Man #482, Man #897

11. a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? **__X__ Yes ____ No**

11.b. If yes, is the proposal
___ A. primarily the result of an ancillary study (list number* _____)
_X__ B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)*
2004.03

*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.