

**ARIC Manuscript Proposal #2561**

**PC Reviewed:** 6/9/15  
**SC Reviewed:** \_\_\_\_\_

**Status:** A  
**Status:** \_\_\_\_\_

**Priority:** 2  
**Priority:** \_\_\_\_\_

**1.a. Full Title:** The Electrocardiographic J-Wave and Cardiovascular Outcomes in the General Population.

**b. Abbreviated Title (Length 26 characters):** J-wave and Outcomes

**2. Writing Group:**

Writing group members: Wesley T. O'Neal, MD, MPH  
Yi (Grace) Wang, PhD  
Hau-Tieng Wu, MD, PhD  
Zhu-Ming Zhang MD, MPH  
Yabing Li MD  
Larisa Tereshchenko MD, PhD  
E. Harvey Estes MD  
Ingrid Daubechies PhD  
Elsayed Z. Soliman, MD, MSc, MS

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. [WO]

**First author:** **Wesley T. O'Neal**  
Address: Department of Internal Medicine  
Wake Forest School of Medicine  
Medical Center Blvd  
Winston-Salem, NC 27157

Phone: 919-288-4616  
E-mail: woneal@wakehealth.edu

**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).

Name: **Elsayed Z. Soliman, MD, MSc, MS**  
Address: EPICARE Center, Wake Forest School of Medicine  
Medical Center Blvd  
Winston-Salem, NC 27157-1063

Phone: 336-716-8632  
E-mail: esoliman@wakehealth.edu

### **3. Timeline:**

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

### **4. Rationale:**

Early repolarization, a common finding on the 12-lead electrocardiogram, has been traditionally considered a benign entity.<sup>1-3</sup> However, several reports have implicated early repolarization as a marker for adverse cardiovascular outcomes.<sup>4,5</sup> Inherent in the definition of early repolarization are slurs and notches at the terminal portion of the QRS complex which are collectively known as the “J-wave.” Hence, the prognostic significance of the J-wave has become of great interest to clinical researchers. While some reports have shown that the J-wave is a benign finding,<sup>6</sup> others shown the opposite.<sup>7-9</sup> Inconsistencies in the observed findings possibly have stemmed from the different methods used to measure the J-wave which have consisted of manual and partially automated techniques.

Recently, a purely automated technique has been developed to detect the presence of the J-wave.<sup>10</sup> The application of an entirely automated method to measure this hallmark component of early repolarization eliminates bias and error, and enables researchers to appropriately compare the prognostic significance of this pattern between epidemiological cohorts. Therefore, the purpose of this analysis is to examine the association between the J-wave, detected by an automated method, and adverse outcomes in the Atherosclerosis Risk in Communities (ARIC) study.

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

The J-wave is associated with an increased risk of sudden cardiac death, coronary heart disease (CHD) death, and all-cause death in ARIC

### **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:* Retrospective cohort study using prospectively collected data.

*Inclusion/Exclusion Criteria:* We will include all participants with good quality baseline electrocardiogram data and follow-up data. The following groups of participants will be excluded: 1) Participants with major ventricular conduction abnormalities (e.g. complete left or right bundle branch blocks), pacemakers, Wolf-Parkinson–White Syndrome or QRS duration  $\geq 120$  ms; 2) the few ARIC participants with race other than black or white will be excluded; 3) Participants with history of cardiovascular disease.

*Outcomes:* The outcomes of interest will be sudden cardiac death, CHD death, and all-cause death.

*Variables:* Baseline electrocardiogram data will be used to detect the J-wave using the automated method described by Wang et al.<sup>10</sup> Follow-up electrocardiograms will be used in additional analysis to examine J-wave as time-dependent variable. Other electrocardiographic variables will include heart rate, electrocardiographic left ventricular hypertrophy (ECG-LVH), and ST-elevation defined by Minnesota code 9.2 (which is part of the definition of early repolarization).

Other variable needed from the baseline study visit will include the following: socio-demographics (age, sex, race, income, education, and study site), cardiovascular disease risk factors (systolic blood pressure, HDL-cholesterol, total cholesterol, body mass index, smoking, diabetes), ECG-LVH, and baseline medication use (blood pressure lowering drugs, statins and other lipid-lowering therapies, and aspirin).

*Statistics:* Baseline characteristics for study participants will be stratified by the presence of the J-wave. Categorical variables will be reported as frequency and percentage while continuous variables will be recorded as mean  $\pm$  standard deviation. Follow-up will be defined by the time between the baseline visit until the outcome of interest, loss to follow-up, or end of follow-up. Kaplan-Meier estimates will be used to examine the cumulative incidence of each outcome by the presence of the J-wave. Cox proportional hazard models will be used to compute hazard ratios (HR) and 95% confidence intervals (CI) for the association between the J-wave and each outcome. Multivariable models will be constructed as follows: Model 1 adjusted for age, sex, race, income, and education; Model 2 adjusted for Model 1 covariates plus smoking, systolic blood pressure, heart rate, diabetes, body mass index, total cholesterol, HDL-cholesterol, ECG-LVH, ST-elevation, antihypertensive medication use, lipid-lowering medication use, and aspirin use. Subgroup analyses by age, sex, and ST-elevation will be performed and tests for interaction will be examined using 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 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.csc.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.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](http://publicaccess.nih.gov/submit_process_journals.htm) shows you which journals automatically upload articles to Pubmed central.

## References

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