ARIC Manuscript Proposal #2400

PC Reviewed: 8/12/14  Status: A  Priority: 2
SC Reviewed: _________  Status: _____  Priority: ____

1.a. Full Title: Longitudinal Tracking of Left Ventricular Mass and Systolic Function over the Adult Life Course in African Americans

b. Abbreviated Title: Clinical Correlates of Left Ventricular Mass in Blacks

2. Writing Group:

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3. **Timeline:**

4. **Rationale:**

Recent research in white cohorts suggests that cardiac remodeling evolves over the life course and antedates CHF. Furthermore, it is likely that diet, systemic inflammation, neurohormonal activation, oxidative stress and kidney function may operate in concert with standard risk factors to influence both left ventricular (LV) remodeling and the pathogenesis of CHF. However, no prior study has comprehensively evaluated the conjoint contributions of these risk factors with cardiac and vascular remodeling in African-Americans (AA). The current application will bridge this gap using data from the ARIC and Jackson Heart Study (JHS).

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

Specific Aim. To relate risk factors to longitudinal changes in echocardiographic indices of LV mass and LV systolic function in approximately 735 ARIC-JHS participants with serial echocardiography ~10-years apart as well as in participants with serial echocardiography over approximately 20 years (i.e. long-term tracking).
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).

**Eligible Subjects:** All JHS participants with serial echo data at exam 0 (conducted as part of ARIC exam 3; 1993-1995) and 1 (2000-2004) and ARIC exam 5 (2010-2013) will be eligible for these analyses.

We will examine longitudinal change of LV Mass as a continuous variable (absolute change, percentage change) both on short- and long-term follow-up. LV systolic function on the other hand, due to its binary nature, will be represented both in the short- and long-terms as incidence of LV systolic function/dysfunction. Individuals with a normal LV ejection fraction at JHS exam 0 (EF≥0.50 and FS ≥0.29) will be followed up to exam 1 and the incidence of LV systolic dysfunction (EF<0.50 or FS<0.29). LV mass will be naturally-log-transformed to normalize and stabilize sex-specific variance. This will allow for sex-pooled analyses. The risk factors will include: traditional (e.g. age, sex, blood pressure, lipids, diabetes, smoking) and novel (eGFR, BNP).

**Statistical Analyses:** We will assess the relation of key risk factors with short and long-term changes in LV mass and LV systolic function. Long term LV mass changes will be analyzed using multi-level statistical modeling, where event participants with missing data in any of the three visits can still be accommodated in the analyses. Initially, analyses will be sex-pooled unless there is evidence of effect modification by gender (which will be tested by modeling appropriate interaction terms. Logistic regression models will be constructed for incidence of LV systolic dysfunction adjusting for traditional and novel risk factors (see above).

We will also estimate growth curves for LV mass using multi-level modeling (SAS PROC MIXED; using compound symmetry matrix) and elucidate the associations of LV mass with clinical covariates, using a direct entry procedure. The examination cycle will be included in the analysis to adjust for variation in LV mass across examinations due to variation in the instrumentation used. Random intercepts will also be fitted for all models to reflect a different starting value of LV mass for each participant.

**Power:** We expect to have good power (≥0.80) to detect factors with intermediate influence on progression of LV mass and systolic function (OR 1.57 per 1-SD increment). Furthermore, we expect excellent power in the full sample, and sufficient power in smaller sub-samples, to detect risk factors with large effects (OR ~2.0).

10. **References:** (Maximum 15)


(7) Barnes PM SC. Trends in adults receiving a recommendation for exercise or other physical activity from a physician or other health professional. 2012. National Center for Health Statistics, Hyattsville, MD. Ref Type: Pamphlet


Diagnosis and Management of Heart Failure in Adults. Circulation 2009;119:e391-e479.


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.cscs.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)?

There are currently no existing proposals examining lifestyle factors and longitudinal change in LV mass in African Americans
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
___x___ A. primarily the result of an ancillary study (list number* 2013.24  
“The impact of lifestyle and clinical factors on cardiac remodeling in African Americans.”  
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.