ARIC Manuscript Proposal #2713

PC Reviewed: 03/08/16          Status: A          Priority: 2
SC Reviewed: __________        Status: ____        Priority: ____

1.a. Full Title: A contemporary assessment of short-term variability in conventional and novel echocardiographic measures in the elderly: A prospective, blinded, community-based study

b. Abbreviated Title (Length 26 characters):
   Echo Repeatability in ARIC

2. Writing Group:
   Writing group members: Morten Sengeløv, Kunihiro Matsushita, Dalane Kitzman, Kenneth Butler, Suma Konety, Aaron Folsom, David Couper, Scott D. Solomon, Amil M. Shah; Others welcome.

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

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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 will begin following proposal approval with anticipated manuscript completion within 6 months.
4. **Rationale:**

The short term repeatability of echocardiographic measurements may be influenced by physiological variations such as adrenergic activation, heart rate, and blood pressure,\(^1,2\) differences in image acquisition, and variability in quantitative measures. While intra- and inter-reader variability in quantitative measurements are routinely assessed and reported, limited recent data are available regarding the short-term repeatability of conventional measures of LV structure, systolic function, diastolic function, and novel measures of deformation among clinically stable elder persons in the community. Previous studies have evaluated the repeatability of M-mode based measures of LV wall thickness, chamber dimensions, and mass.\(^3,4,5\) Collins et al. found that left ventricular mass (LVM) was more reproducible on serial 2-dimensional echocardiography (2DE) than in M-mode tracings\(^6\). The repeatability of 2DE measures of LV dimensions, wall thickness, mass, and LV ejection fraction (LVEF) have subsequently been assessed in multiple studies and populations.\(^7,8,2,9,10,11\) These studies generally demonstrated good repeatability of these measures (coefficients of variation ranging from 7-19% based on study and measurement).

More limited data is available regarding Doppler-based measures of diastolic function, with some studies suggesting good overall repeatability\(^2,13\) while others reporting greater variability\(^11\). Similarly, the literature regarding the repeatability of novel speckle tracking measurements such as longitudinal strain is limited. In 2013, Thavendiranathan et al. conducted a study that included two serial measurements of LVEF, LV volumes and LV global longitudinal strain (GLS). GLS did not show a significant temporal variability, while LVEF and LV volumes showed a greater variability\(^14\). Similarly, Marwick et al demonstrated good repeatability of strain measurements in studies performed only 1 hour apart.\(^15\) Importantly, little data is available regarding the repeatability of measures of right ventricle (RV) structure and function, valvular function, and pulmonary vascular properties beyond peak pressure.

A prospectively designed repeatability study was embedded within the fifth visit of the Atherosclerosis Risk in Communities (ARIC) study. As a part of this study, 90 community-dwelling participants underwent two serial study exams at a mean time interval of 41 ± 10 days (range 28 to 83), including ARIC protocol echocardiograms. Importantly, reading centers (including the echocardiography reading center) were fully blinded to the identity of the participants undergoing the repeat visit. This study therefore is a unique and ideal opportunity for a contemporary assessment of the short-term variability in conventional echocardiographic measures of cardiac structure and function, and of novel measures of cardiac deformation.

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

Our main hypothesis is that the short-term between study variability of conventional measures of LV structure, systolic function, deformation, and RV function will be modest, while the variability of diastolic measures – particularly those reflecting LV filling pressure – will be greater.
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).

6.1. Study design:
This will be a longitudinal analysis of echocardiographic data collected on ARIC participants undergoing two visits during the Visit 5 period as part of the Visit 5 repeatability study.

6.2. Inclusion/exclusion criteria:
All participants included in the ARIC Visit 5 repeatability study who underwent echocardiography at both visits (n=90) will be included.

6.3. Key variables of interest:

1. Echocardiographic variables (visit 5 echo, both visits): (1) LV structure (LV end-diastolic and end-systolic volumes and dimensions), wall thickness, relative wall thickness, and mass); (2) LV diastolic function (E wave, A wave, E wave deceleration time, tissue Doppler imaging (TDI) E’, and left atrial volume index); (3) LV systolic function (LV ejection fraction, mid-wall fractional shortening, longitudinal strain, circumferential strain); (4) pulmonary hemodynamics (estimated pulmonary artery systolic pressure based on tricuspid regurgitation jet velocity, pulmonary vascular resistance) and right ventricular function (fractional area change, TDI tricuspid annular S’).

2. Clinical covariates (visit 5): age, gender, race/ethnicity, field center, systolic blood pressure, diastolic blood pressure, heart rate, smoking status, history of hypertension, diabetes, dyslipidemia, coronary artery disease, prior MI or revascularization procedure, prior stroke or TIA, hemoglobin, estimated glomerular filtration rate, spirometric variables (FEV1 and FVC), carotid-femoral pulse wave velocity, ankle-brachial index, measures of body fat/body fat distribution (BMI, fat mass, lean mass and % of fat mass).

6.4. Data analysis:
Repeatability for each echocardiographic measure will be assessed as the bias (mean differences between 2 time points) and the standard deviation of the bias (SD), the coefficient of variation (calculated as the SD of the bias divided by the mean value of the measure of interest), and the correlation coefficient for the measurement at the two time points. Repeatability metrics will be calculated for the repeatability study population overall, and in subgroups defined by sex and race.

6.5. Anticipated methodologic limitations:

The potential for studies to have been performed by different sonographers at each time point may be considered a limitation. We will determine whether both studies were
performed by the same or different sonographers and will also determine repeatability metrics separately for each group.

7.a. Will the data be used for non-CVD analysis in this manuscript?  ___ Yes  ___ 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  ___ No

   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/
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
