ARIC Manuscript Proposal #2218

PC Reviewed: 9/10/13  Status: A  Priority: 2
SC Reviewed: _________  Status: _____  Priority: ____

1.a. Full Title:

Association of Blood Pressure Burden with Cardiac Structure and Function and Incident Heart Failure in the Community

b. Abbreviated Title (Length 26 characters):

Blood pressure and echo indices

2. Writing Group:

Writing group members:

Susan Cheng, Amil Shah, Brian Claggett, Hicham Skali, Deepak Gupta, Angela Santos, Charlie Hung, Scott Solomon, and OTHERS WELCOME

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

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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:** Analyses to begin Fall 2013. A manuscript draft is expected during Spring 2014 / Summer 2014.

4. **Rationale:**

Elevated blood pressure (BP) remains the single most prevalent risk factor for heart failure (HF) for reasons that are not entirely clear. In particular, it is not well understood why some individuals with hypertension go on to develop HF whereas many others do not. Substantial data suggest that, among individuals with a predisposition for HF, the progression from hypertension to overt HF involves incremental but distinct and identifiable changes in left ventricular (LV) structure and function that occur over years to decades. Although this progression is widely believed to initially involve the development of LV hypertrophy and concentric remodeling with preserved function, followed by progressive diastolic dysfunction and then eventually eccentric LV remodeling with overt systolic dysfunction, the extent to which this proposed pathway applies to most or all individuals on the trajectory towards clinical HF is not known. Therefore, we propose to extend from the work of prior investigators and further interrogate the ways by which chronic exposure to elevated BP may lead to clinical HF through detectable alterations in cardiac structure and function in the community. Specifically, we will examine the relation of antecedent and current BP burden with conventional and advanced echocardiographic LV measures and, in turn, risk for incident HF in the bi-racial ARIC cohort.

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

Our main hypothesis is that chronic elevations in BP components, particularly increased PP, contributes to detectable changes in cardiac function with or without obvious changes in cardiac structure and, in turn, to the risk for incident HF. This hypothesis is in part based on results of our recent ARIC analysis suggesting that elevated PP may be particularly important for conferring risk of HF in the community.

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 sample will include individuals who attended the ARIC Visit 5 examination and who underwent echocardiography and were free of prevalent cardiovascular disease (history of coronary heart disease, TIA/stroke, or heart failure), valvular disease (moderate or severe), or atrial fibrillation at this visit.

**Dependent variables.** The primary dependent variables of interest will include conventional and advanced measures of LV structure and function, including: LV mass, geometry (as defined previously), ejection fraction, E’, global longitudinal strain, global circumferential strain, and torsion (in the subset of individuals with torsion measures available). In secondary analyses, the primary dependent variable will include incidence of HF.
Independent variables. The primary independent variable of interest will include BP components (SBP, DBP, PP, and MAP) measured at varying times preceding and up to the time of the echocardiogram: current BP (measured at the index Visit 5), 10-15 year antecedent BP (measured at Visit 4, so long as time interval is between 10 and 15 years), 15-20 year antecedent BP (measured at Visit 3, so long as time interval is between 15 and 20 years), 20-25 year antecedent BP (average of ≤2 measures from Visits 1 and 2, so long as time interval is between 20 and 25 years), time-averaged antecedent BP (mean of values available from Visits 1 through 4), total years with documented hypertension since Visit 1, and slope of change in antecedent BP (latest minus earliest value, divided by the time interval between measures). Multivariable analyses of all BP components will performed in models adjusting for age, sex, diabetes, smoking status, total/HDL cholesterol ratio, and eGFR.

Analytical approach. We will perform initial descriptive analyses including unadjusted analyses of the relations between each of the independent variables with the dependent variables. We will then perform multivariable adjusted regression analyses to examine the association of independent variables with measures of cardiac structure and function. Relative contributions of independent variables to variation in diastolic function will be evaluated using the partial R^2 value for each term in the model. The relative contributions of antecedent burden of elevated BP will be evaluated in separate models, with and without concurrent adjustment for current BP values.

Secondary analyses. In secondary analyses, we will use multiplicative terms to assess for effect modification by age, sex, and race and perform stratified analyses if indicated. In secondary analyses, to be performed at a later date, we will also use Cox proportional hazards models to assess the separate and joint contributions of antecedent BP components and measures of cardiac structure and function with risk for incident HF. These analyses will be performed using multivariable models adjusting for traditional cardiovascular risk factors (listed above) in addition to prior myocardial infarction and prevalent valve disease.

All analyses will be performed using STATA v11.2 (StataCorp, College Station, TX).

Limitations and challenges. Blood pressure measured at a single point in time is less precise than measured collected from ambulatory monitoring. Because all analyses will be performed using observational data, causal relationships cannot be inferred.

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)?

MS #2024 (Santos): Pre-hypertension is associated with abnormalities of cardiac structure and function

MS #2016 ( Hung): The relationship between left ventricular torsion, cardiac mechanics and geometry assessed by three-dimensional echocardiography in a community-dwelling elderly cohort: the ARIC study

MS #1953 (Shah): The relationship between concentric remodeling and left ventricular function – A preliminary analysis from the ARIC study


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/

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


