

ARIC Manuscript Proposal # 1852

PC Reviewed: 10/11/11
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Status: A
Status: _____

Priority: 2
Priority: _____

1.a. Full Title: Systolic Blood Pressure Control and incident Heart Failure: The Atherosclerosis Risk in Communities Study

b. Abbreviated Title (Length 26 characters):

2. Writing Group members: Carlos J. Rodriguez
Laura R. Loehr
Wayne Rosamond
Lynn E. Wagenknecht
Alain Bertoni

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

First author: Carlos J. Rodriguez MD, MPH
Address: Wake Forest University School of Medicine
Medical Center Blvd
Winston-Salem, N.C. 27157

Phone: 336-713-1648 (OFFICE)
E-mail: crodrigu@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: Laura Loehr
Address: 137 E. Franklin Street
Chapel Hill, 27514

Phone: 919-619-5023
E-mail: lloehr@email.unc.edu

3. Timeline: Analysis to begin after Publication Committee approval.
Manuscript anticipated for initial P&P review in March 2012.

4. Rationale:

Elevated blood pressure (BP) is an important public health concern. It is highly prevalent and it is a risk factor for several adverse health outcomes, especially coronary heart disease and heart failure. Given the high prevalence and severity of adverse outcomes, even small improvements in the treatment of elevated BP would

result in widespread benefit. The seventh report of the Joint National Committee for Detection, Evaluation, and Treatment of High Blood Pressure recommends that individuals achieve a target blood pressure of < 140 mmHg SBP and < 90 mmHg DBP. The benefit of lowering SBP to around 140 mm Hg is well accepted, but patients treated to this level of BP may still be at increased risk of BP-related adverse outcomes. Observational studies document a progressive increase in coronary heart disease risk as BP rises above 115/75 mm Hg. Such epidemiologic evidence suggests there may be substantial benefit to targeting treatment to a SBP <120 mm Hg instead of <140 mm Hg. Heart failure (HF) is a growing epidemic, with an incidence of approximately 10 per 1000 in the population age >65 years and estimated prevalence of 5.7 million Americans >20 years old. Hypertension is a major risk factor for the development of congestive heart failure. Hypertensive patients develop a spectrum of cardiac structural changes such as left ventricular hypertrophy (either concentric or eccentric), that likely lead to the development of HF. Blacks may be more susceptible to this risk given that they carry a higher burden of hypertension and appear to be more prone to cardiac structural changes. The ARIC study prospectively collected data on hospitalized incident heart failure in a biracial cohort. We will explore whether individuals with an SBP >140 or SBP 120-139 mm Hg had an increased risk of incident heart failure, relative to persons with SBP <120 mm Hg.

5. Main Hypothesis/Study Questions:

1. Among hypertensives (inclusive of treated or untreated), we will estimate HF incidence according to SBP control categories (uncontrolled >140, standard control 120-139 mm Hg, or intensive control <120).
2. Does BP control impact HF hospitalizations for recurrent hospitalization or length of hospital stay ?
3. Do the relations in 1 & 2 differ 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).

Study population: Only people who have valid blood pressure data on baseline clinical visits (visit 1, visit 2 and visit 3).

Main outcome: our primary outcome will be incident HF, defined as the first occurrence of either i) a HF hospitalization which included an International Classification of Diseases, 9th revision, discharge code of 428 (428.0 to 428.9) in any position, or ii) a death certificate with a 428 (HF) or International Classification of Diseases, 10th revision, code I50 (HF) in any position.

Analysis Plan and the Blood Pressure Control Classification:

a. Hypertensives: (includes those SBP > 140 mmHg and DBP > 90 mmHg at baseline, or with a history of hypertension, or taking antihypertensive medication) will be further divided into three groups based on BP control which will be called “Uncontrolled BP” (>140mmHg), “Standard BP Control” (120-139/80-29 mmHg), and “Intensive BP Control” (<120mmHg) groups. Contrasts of demographics and key covariates among these groups will be made. The association of SBP control with index HF hospitalization

will be assessed using survival analysis with index HF hospitalization as the event. The SBP measurement taken at the clinic visit closest to the HF event will be used to assess SBP control. To assess the effect of blood pressure control on HF incidence, survival analyses using time dependent covariates will be fit using BP data from clinic exams 1 thru 4. Models will be run separately for SBP as a continuous variable and SBP control as an ordinal variable with race and any other covariates fit as well to adjust for their effects. Additional separate modeling will be performed to see if the effects are consistent with that seen in the time dependent models. The SBP measurement taken at the clinic exam prior to HF (or SBP on the last clinic exam for those who did not have incident HF) will be used as a covariate in separate modeling looking at SBP as a continuous variable and SBP control as ordinal while adjusting for covariates. The mean SBP for all visits prior to HF (or all visits for those with no HF) will also be used as a covariate in additional survival modeling.

b. Only HF patients will be used for the purpose of a secondary analysis. Our analysis will look at time to second hospitalization (is it influenced by BP control) and number of recurrent hospitalizations over the entire follow up period. The rate of HF re-hospitalizations in adequately controlled vs. inadequately controlled will be compared as binary variables as well as SBP as a continuous variable and SBP control as ordinal as previously described. Our analysis will look at time to second hospitalization (is it influenced by BP control) and number of recurrent hospitalizations over the entire follow up period.

c. Additional analysis will stratify our results from a) and b) according to race and sex to determine any race-sex differences.

Key covariates to be adjusted for: Age, gender, diabetes, body mass index, physical activity, high cholesterol, smoking, alcohol intake, anemia.

Exclusion criteria: Prevalent cases of HF at visit 1 either by self-report, current intake of HF medication, or those with stage 3 or manifest HF by Gothenburg criteria. Missing data on blood pressure measurements or participants with missing criteria needed to define prevalent HF.

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

8.a. Will the DNA data be used in this manuscript? 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. Yes

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)? N/A

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

References

1. American Heart Association. Heart Disease and Stroke Statistics—2009 Update. *Circulation*. 2009;119:e21-e181
2. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, Jr., Jones DW, Materson BJ, Oparil S, Wright JT, Jr., Roccella EJ. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension*. 2003;42:1206-1252
3. Sega R, Corrao G, Bombelli M, Beltrame L, Facchetti R, Grassi G, Ferrario M, Mancia G. Blood pressure variability and organ damage in a general population: results from the PAMELA study (Pressioni Arteriose Monitorate E Loro Associazioni). *Hypertension*. 2002;39:710-714
4. Rywik SL, Davis CE, Pajak A, Broda G, Folsom AR, Kawalec E, Williams OD. Poland and U.S. collaborative study on cardiovascular epidemiology hypertension in the community: prevalence, awareness, treatment, and control of hypertension in the Pol-MONICA Project and the U.S. Atherosclerosis Risk in Communities Study. *Ann Epidemiol*. 1998;8:3-13
5. Arnett DK, Rautaharju P, Crow R, Folsom AR, Ekelund LG, Hutchinson R, Tyroler HA, Heiss G. Black-white differences in electrocardiographic left ventricular mass and its association with blood pressure (the ARIC study). Atherosclerosis Risk in Communities. *Am J Cardiol*. 1994;74:247-252
6. Grandi AM, Broggi R, Colombo S, Santillo R, Imperiale D, Bertolini A, Guasti L, Venco A. Left ventricular changes in isolated office hypertension: a blood pressure-matched comparison with normotension and sustained hypertension. *Arch Intern Med*. 2001;161:2677-2681