ARIC Manuscript Proposal #2018

PC Reviewed: 10/9/12  Status: A  Priority: 2
SC Reviewed: _________  Status: _____  Priority: _____

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

b. Abbreviated Title (Length 26 characters): Blood pressure control and AF

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

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

4. Rationale:

Atrial fibrillation, the most common cardiac arrhythmia, currently affects nearly 2.5 million people in the United States, and is associated with increased stroke and cardiovascular morbidity and mortality\(^1\). Approximately 10\(^\%\) of people over the age of 65 years carry this diagnosis\(^2\), and as the geriatric population in the United States grows, is expected to increase by 2.5 fold over the next 50 years\(^3\).
Hypertension is another chronic highly prevalent pandemic which is one of the most well known and accepted risk factors for multiple adverse health outcomes, including coronary heart disease, stroke, and heart failure. In addition, hypertension is a very well established risk factor for the development of atrial fibrillation. 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. However, observational studies demonstrate a linear increase in risk for the development of ischemic heart disease and stroke starting at blood pressures as low as 115 mmHg systolic and 75 mmHg diastolic. The Framingham Heart Study demonstrated blood pressures of 130-139/85-89 were associated with a more than 2-fold increased risk for the development of cardiovascular disease compared to those with optimal blood pressures. These findings suggest high normal blood pressures may be associated with cardiovascular pathophysiologic changes.

The ARIC study prospectively collected data on incident atrial fibrillation using study scheduled ECGs and hospital discharge ICD codes or death certificates. Among ARIC participants with hypertension, we will explore whether individuals with a follow-up SBP > 140 or SBP 120-139 mm Hg had an increased risk of incident atrial fibrillation, relative to persons with SBP < 120 mm Hg. This will shed light on the impact of achieving different levels of SBP control among hypertensive individuals on incident AF.

5. Main Hypothesis/Study Questions:
1. Among ARIC participants with hypertension (inclusive of treated or untreated), we will estimate and compare atrial fibrillation incidence across different SBP categories during follow up (uncontrolled >140, standard control 120-139 mm Hg, or intensive control <120).

2. We will evaluate whether the outcomes in hypothesis #1 differ by race or gender.

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 from at least one of three clinical visits (visit 1, visit 2 and visit 3) and who are hypertensive at visit 1 (includes those with SBP > 140 mmHg and DBP > 90 mmHg, or with a history of hypertension, or taking antihypertensive medication). Individuals without an ECG or who had diagnosed AF or atrial flutter at baseline will be excluded from analyses.

**Main outcome:** Independent variables in our analysis include blood pressure control categories. The dependent variable is incident AF.

a. Incident cases of atrial fibrillation will be identified through hospital discharge codes (ICD-9 code 427.31 and 427.32), death certificates (underlying cause of death ICD-9 code I48 or 427.3), and ECGs performed during follow-up visits. Individuals who develop both atrial flutter and AF during follow-up will be considered as having an event, and follow-up will be censored at the first occurrence of either AF or atrial flutter. Those that develop atrial flutter only will not be considered as having an event, and will be censored at the date of diagnosed atrial flutter.
b. 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 follow-up SBP levels which will be called “Uncontrolled BP” (>140mmHg), “Standard BP Control” (120-139/80-90 mmHg), and “Intensive BP Control” (<120mmHg) groups. Contrasts of demographics and key covariates among these groups will be made.

Analysis Plan:
The association of SBP control with incident atrial fibrillation will be assessed using survival analysis with incident AF as the event. The SBP measurement taken at the clinic visit closest to the AF event will be used to assess SBP control. To assess the effect of blood pressure control on AF 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 AF (or SBP on the last clinic exam for those who did not have incident AF) 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 AF (or all visits for those with no AF) will also be used as a covariate in additional survival modeling. The associations will be adjusted for age, sex, race, field center, education, drinking status and amount of alcohol consumed, body mass index, diabetes, ECG-defined left ventricular hypertrophy, and presence of CHD and heart failure at baseline. Interaction tests by race and sex will be conducted, and analyses will be reported separately by race and/or sex if evidence of heterogeneity by these variables is present.

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)?
The analytical approach in this proposal is similar to approved paper proposal # 1852-Rodriguez in which SBP control among hypertensives is considered as a predictor of incident heart failure. We will be using a similar modeling strategy.

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

References: