ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #280

1. Title:
Cardiac Autonomic Function Assessed by Heart Rate Variability and Hypertension: The Population Based ARIC Study

2. Writing Group:
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4. Timeline:

Submit Proposal to Publications Committee	8/31/94
Complete analysis	12/20/94
Submit first draft to Publications Committee	3/20/95
Submit to Journal	5/20/95

5. Rationale:
As consistently shown in the literature, beat-to-beat heart rate variability (HRV) is a simple and valid, non-invasive measurement of cardiac autonomic function. In clinical studies, it has been found that essential hypertensives have an enhanced sympathetic activity and a reduced vagal activity, measured by spectral analysis of short-term HRV. Biologically, it is plausible that such alteration of sympatho-vagal balance may lead to reduced responsiveness of neural regulatory mechanisms in hypertensives, and therefore increase the risk of ventricular dysrrhythmias and sudden cardiac death. The association of autonomic cardiac function and whole spectrum of blood pressure has not been well studied. None of the studies published in this area is population based. On the other hand, it has been proposed that the alteration of autonomic cardiac function is associated with increased risk of hypertension, but this hypothesis has not been tested at the population level.

In ARIC Visit 1, two-minute resting, beat-to-beat heart rate data were collected according to a standard protocol. Utilizing Fast Fourier Transformation, spectral analysis was applied to the heart rate data for a stratified random sample (N about 3000) of ARIC visit 1 participants. From these records, HRV high frequency power (HF), HRV low frequency power (LF) and the ratio of HF/LF were calculated as a marker of cardiac parasympathetic activity, a measurement of sympathetic function influenced by vagal activity, and a measurement of vagal-sympathetic balance respectively. From our previous work, it can be shown that our procedure to estimate HRV has high operator repeatability (with intra and inter operator reliability coefficients for all three HRV indices greater than 0.95). Also, our ARIC manuscripts in this area of research (MS#130, 131, 258) found a significant association of HRV with age, race and sex; a significant, inverse association between HRV-HF and prevalent MI; a significant, inverse association between HRV-HF and diabetes mellitus, serum insulin and glucose. These findings are consistent with the clinical literature, and thus, indirectly support the validity of HF, LF and HF/LF ratio estimated from 2 minute beat-to-beat heart rate records in the ARIC study.

Therefore, we propose this analysis to investigate the association between cardiac autonomic function as

measured by HRV and hypertension in the ARIC study using a cross-sectional and a cohort design.

6. Main alternative hypotheses:
(1) Prevalent hypertensives have a lower HRV-HF (lower vagal function);
(2) Prevalent hypertensives have a higher HRV-LF (higher sympathetic activity);
(3) Prevalent hypertensives have a lower HRV HF/LF ratio (sympatho-vagal imbalance);
(4) In normotensives, blood pressure is associated with HRV-HF (negatively), HRV-LF (positively) and HF/LF ratio
(negatively);
(5) Lower HRV-HF, higher HRV-LF, and/or lower HF/LF ratio are associated with increased risk of hypertension over three
years of follow-up
Hypothesis (1) - (4) will be tested in a cross-sectional analysis. Hypothesis (5) will be tested using 3 years of follow-up data.

7. Data (variables, source, inclusion/exclusion):
We have assembled a set of about 3000 ARIC visit 1 participants, a stratified random sample of the ARIC cohort, which was used as the study population for our previous manuscripts (MS #130, 131, and 258). It will serve as the study population for this proposed study. Study design: cross-sectional and prospective analysis, accounting for the sampling strategy. Major variables include hypertension status at visit 1 and visit 2, systolic and diastolic blood pressure, anti-hypertensive medication usage, ß-blocker medication usage, processed heart rate data, demographic variables, education level, and established risk factors of CVD. The effects of anti-hypertensive medication and ß-blocker medication on the proposed HRV and hypertension relationship will be examined in the analysis.