ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #376

1. Title: Cardiac Autonomic Function and Multiple Metabolic Syndrome - The ARIC Study

2. Writing Group:

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3. Timeline:

Submit Proposal to Publications Committee	3/10/96
Complete Analysis	5/10/96
Sumit first draft to Publications Committee	8/10/96
Submit to Journal	12/10/96

4. Rationale:

Multiple Metablic Syndrome (MMS) has been used to describe the clustering of several inter-related metabolic disorders, and it has been found to be related to insulin resistance. Individuals with MMS are at increase risk of cardiac events. It has been hypothesized that altered autonomic function due to hyperinsulinemia is the link from insulin resistance to MMS. However, the association between autonomic function and MMS has not been reported at the population level, nor has it been studied prospectively. It has been consistently shown in the literature that beat-to-beat heart rate variability (HRV) is a simple and valid, non-invasive measure of cardiac autonomic function. Our previous work (ARIC MS#358 and MS#280) has demonstrated significant relationship of lower HRV with diabetes mellitus, fasting insulin, and with hypertension.

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 quantified fandom sample (N about 3000) of ARIC visit 1 participants. From these records, HRV high frequency and low frequency powers (frequency domain measures of HRV) and standard deviation of R-R intervals (time domain HRV index) have been calculated as measures of cardiac parasympathetic , sympathetic and sympathovagal balance. Based on this sample, several of our previous HRV manuscripts

have been published or accepted for publication.

Therefore, we propose this study to extend our investigation to the relationship of autonomic function as measured by HRV analysis, and MMS cross-sectionally and propectively.

5. Main Objectives:

Cross-sectional analysis:
   1) MMS, defined by the clustering of hypertension, diabetes mellitus, and dyslipidemias, is associated with lower HRV (both frequency and time domains).
   2) There is a dose-response relationship between the number of MMS disorders and the levels of HRV (both time and frequency domains).

Prospective analysis (case-cohort approach):
   3) To investigate the roles of baseline levels of HRV (both frequency and time domains) and fasting insulin in the development of incident MMS over three years of follow-up.

6. Data (variables, source, inclusions/exclusions):

Visit 1 variables needed: diabetes, hypertension, lipids, processed heart rate data, demographic variables, and established risk factors of CHD.
Visit 2 variables needed: diabetes, hypertension, and lipids measures. We have assembled a set of 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, 258, 280). It will be used as our population for the proposed cross-sectional analysis. This sample will also be used as the cohort component for the prospective analysis. Individuals who developed incident MMS from the entire ARIC cohort over 3 years of follow-up will be identified. This latter group will be used as the case group and their HRV data will be processed. The cohort group (free of MMS at baseline) and the case group will be combined to form the study population for the prospective analysis, employing a case-cohort approach.