1. Title:
Case-control study of the association between cardiovascular autonomic function and unrecognized myocardial infarction (UMI)

2. Writing Group:
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3. Timeline:

4. Rationale:
Age, diabetes, and hypertension are associated with UMI in the 34 year follow-up of the Framingham cohort (Kannel et al, 1990). They are also associated with cardiovascular autonomic dysfunction (Ori et al, 1992). Although the associations between age, diabetes, hypertension, and UMI may be partially attributable to cardiovascular autonomic dysfunction, prior epidemiologic investigations have not specifically addressed this possibility.

5. Main Hypothesis:
The associations between age, diabetes, hypertension, and UMI are partially attributable to cardiovascular autonomic dysfunction.

6. Analysis:
Interior myocardial infarctions (as defined in ARIC Protocol Manual 5: Electrocardiography) will be classified as unrecognized if there is no self- or physician-reported history of myocardial infarction during annual follow-up, interim hospitalization, and subsequent cohort visit. Cases of unrecognized and recognized myocardial infarction, and a random sample of non-cases matched for exposure time, will form the comparison groups. Cases and controls will be stratified by presence of CHD at baseline. Indices of cardiovascular autonomic function (heart rate; postural change in heart rate and blood pressure; linearly-corrected QT interval; heart rate variability) will be determined. The 3-minute supine resting heart rate records will be processed by trained and certified individuals blind to case-control status. Baseline heart rate variability will be measured from the processed records using time and frequency domain analysis. The putative association between indices of cardiovascular autonomic function and UMI will be measured. Effect modification by age, diabetes, and hypertension will be
considered. In addition, influences of obesity, renal function, and the use of alcohol, cardioactive medication, or nicotine-containing products will be considered because these variables also may influence cardiovascular autonomic function. Associations between indices of cardiovascular autonomic function and unrecognized myocardial infarction will be analyzed together with the covariables listed below.

7. Data:
For Visit 1, demographic variables, sitting blood pressure, blood pressure and heart rate during postural change, glycemic control (glucose; insulin), medication, renal function (creatinine; electrolytes), ECG composite, ECG 2-minute rhythm, home interview, derived variables (disease prevalence; hypertension; smoking; medication use; alcohol use; obesity), and covariables (social status; lipids; hematology; hemostasis; TIA/stroke; reproductive history), all in cases and controls. For Visits I and II and for the Annual Follow-ups, responses to interview questions (chest pain on effort; possible infarctions; hospitalization) and ECG measures (serial change; Q and QS patterns of incident infarctions).