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Atrial fibrillation is a strong risk factor for ischemic stroke, and is especially frequent in the elderly. The current knowledge is based on clinically established cases; the frequency of short, often asymptomatic episodes of atrial fibrillation, which often precede the onset of sustained atrial fibrillation, is not known, and neither is their associated stroke risk. Also, the frequency of other common atrial and ventricular arrhythmias, and their potential association with stroke risk, is only partially known. A prospective community-based study is proposed on 1000 stroke-free volunteers over the age of 65 years with the following primary aims: 1. To evaluate the prevalence of undiagnosed atrial fibrillation in a multiethnic elderly cohort and describe its distribution by sex and race-ethnicity; 2. To investigate the role of cardiac subclinical disease, cardiovascular risk factors and selected biomarkers as potential predictors of undiagnosed atrial fibrillation; 3. To evaluate the prevalence of other atrial arrhythmias (supraventricular tachycardia, frequent atrial premature contractions) and ventricular arrhythmias (frequent ventricular premature contractions) possibly related to stroke; 4. To determine the risk of stroke, myocardial infarction and vascular death associated with undiagnosed atrial fibrillation and other arrhythmias in a multiethnic elderly cohort after adjusting for conventional vascular risk factors.

The study cohort will be drawn from the previously funded Cardiovascular Abnormalities and Brain Lesions (CABL) study, based on the ongoing Northern Manhattan Study (NOMAS), and from NOMAS itself. Undiagnosed atrial fibrillation and other arrhythmias will be evaluated by means of 14-day continuous recording of cardiac rhythm using a novel, validated patch-based cardiac recorder. Novel echocardiographic indicators of left ventricular systolic (LV strain) and diastolic function (by tissue Doppler) will be evaluated, in addition to LV mass and geometry. Left atrial morphology and function will be assessed on 3D echo images (LA volumes and emptying fraction) and using ECG indicators of electrical remodeling (P wave duration and dispersion). Biomarkers will be measured as predictors of atrial fibrillation that explore different pathogenic pathways: atrial distention and subclinical cardiac dysfunction (N-T pro BNP), inflammation (high-sensitivity CRP, IL-6), subclinical myocardial damage/ischemia (troponin I), thrombosis (D-dimer), atrial fibrosis (TGF ß1). Subjects will be followed by annual telephone interviews to ascertain stroke, myocardial infarction (with in-person evaluation in case of positive responses) and death. Odds ratio for putative predictors and undiagnosed atrial fibrillation will be calculated by logistic regression. Hazard ratios for atrial fibrillation/other arrhythmias and CV events will be calculated by Cox proportional hazards model, adjusting for vascular risk factors.

The present proposal will fill gaps in our knowledge on the global burden of atrial fibrillation/other arrhythmias in the elderly and their relationship with stroke and other vascular events, and will identify subjects at higher risk of developing these arrhythmias to whom preventative interventions could be addressed.