Relation Between Estimated Cardiorespiratory Fitness and Atrial Fibrillation (from the Reasons for Geographic and Racial Differences in Stroke Study)

Abhishek Bose, MD[a], Wesley T. O'Neal, MD[b], Aleena Bennett, MS[c], Suzanne E. Judd, PhD[c], Waqas T. Qureshi, MD, MS[d], Xuemei Sui, MD, PhD[e], Virginia J. Howard, PhD[f], George Howard, DrPH[c], and Elsayed Z. Soliman, MD[d,g,*]

Estimated cardiorespiratory fitness (e-CRF) based on readily available clinical and self-reported data is a promising alternative to the costly traditional assessment of CRF using exercise equipment, but its role as a predictor for incident atrial fibrillation (AF) is unclear. This study included 10,126 participants (54.5% women, 35% African-American, mean age 63.2 years) from the Reasons for Geographic and Racial Differences in Stroke study who were free of AF at baseline. Baseline (2003 to 2007) e-CRF was determined using a previously validated nonexercise algorithm. Incident AF cases were identified at a follow-up examination by electrocardiogram and self-reported medical history of previous physician diagnosis. After a median follow-up of 9.4 years, 906 participants (8.9%) developed AF. In a multivariable logistic regression model adjusted for sociodemographics and baseline cardiovascular disease risk factors as well as incident coronary heart disease, heart failure, and stroke, each 1-metabolic equivalent of task increase in e-CRF was associated with a 5% lower risk of AF development (odds ratio [95% CI] 0.95 [0.92 to 0.99]; p = 0.0129). This association was stronger in women (OR [95% CI] 0.85 (0.79, 0.92) than in men (OR (95% CI) 0.88 (0.84, 0.93), interaction p value = 0.05. No significant interactions by age, race, history of cardiovascular disease, or physical limitations were observed. In conclusion, e-CRF using a nonexercise algorithm is a useful predictor of incident AF, which is consistent with previous reports using traditional CRF. This suggests that e-CRF using nonexercise algorithms may serve as a useful alternative to CRF measured by costly and time-consuming exercise testing. **(Am J Cardiol 2017;119:1776−1780)**

Poor cardiorespiratory fitness (CRF) measured in metabolic equivalent of task (MET) is a strong predictor of cardiovascular disease (CVD) including AF.[1−5] However, the need for specialized exercise equipment and trained personnel have been obstacles for wide use of CRF in risk stratification and identifying subjects at risk for poor outcomes. A novel method for estimating CRF using readily available clinical and self-reported data including age, gender, body mass index (BMI), heart rate, physical activity, waist circumference, and smoking status has recently been developed.[6] Estimated CRF (e-CRF) is a promising alternative to the need for expensive exercise testing, but its role as a predictor of incident AF is unclear. Therefore, we examined the association between e-CRF and AF in the Reasons for Geographic and Racial Differences in Stroke (REGARDS), one of the largest biracial population studies in the United States.

Methods

The methods and design for the REGARDS study have been published previously.[7] The primary aim of the REGARDS study was to elucidate the mechanisms behind black-white and regional differences in stroke mortality. Participants were recruited from the continental United States with oversampling from blacks and the stroke belt (North Carolina, South Carolina, Georgia, Alabama, Mississippi, Tennessee, Arkansas, and Louisiana) between January 2003 to October 2007 using commercially available postal and telephone records. After verbal consent, the initial assessment involved computer-assisted telephone

[a]Section of Hospital Medicine, Department of Medicine, [d]Section of Cardiology, Department of Medicine, and [g]Department of Epidemiology and Prevention, Epidemiological Cardiology Research Center, Wake Forest School of Medicine, Winston-Salem, North Carolina; [b]Division of Cardiology, Department of Medicine, Emory University School of Medicine, Atlanta, Georgia; Departments of [c]Biostatistics and [f]Epidemiology, School of Public Health, University of Alabama at Birmingham, Birmingham, Alabama; and [e]Department of Exercise Science, Arnold School of Public Health, University of South Carolina, Columbia, South Carolina. Manuscript received January 24, 2017; revised manuscript received and accepted March 1, 2017.

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*Corresponding author: Tel: (366) 716 8632; fax: (336) 716 0834.
E-mail address: esoliman@wakehelath.edu (E.Z. Soliman).

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interview followed by an in-home physical examination. During the telephone interview, demographic information and medical history were obtained, whereas during the in-home examination, blood and urine sample collection, an electrocardiogram, medication information, height and weight measurements, and blood pressure recording were performed. All participants provided written informed consent, and the study was approved by the institutional review boards of all participating universities.

The final cohort included 30,239 participants with baseline data. Approximately, 10 years after the baseline assessment, 15,521 participants completed a second examination similar to the baseline visit. Of those who completed the second assessment visit, we excluded participants with baseline AF, BMI <18.5 and missing variables for e-CRF calculation or covariates leaving a final sample of 10,126 participants.

A nonexercise-based gender-specific algorithm was used to calculate e-CRF as follows: e-CRF (women) = 14.17873 + (age × 0.1159) − (age^2 × 0.0017) − (body mass index × 0.1534) − (waist circumference × 0.0085) − (resting heart rate × 0.0364) + (active × 0.5987) − (smoker × 0.2994) or e-CRF (men) = 21.2870 + (age × 0.1654) − (age^2 × 0.0023) − (body mass index × 0.2318) − (waist circumference × 0.0337) − (resting heart rate × 0.0390) + (active × 0.6351) − (smoker × 0.4263).[6] Active was defined as someone who exercises 4 times or more per week based on a previous REGARDS study.[8] Smoker was defined based on self-reported current use of cigarettes.

Details regarding the identification of AF have been previously published.[9] Incident AF was identified by the study electrocardiogram and also from a self-reported medical history of a physician diagnosis during the computer-assisted telephone interview surveys. The electrocardiograms were read and coded at a central reading center (Epidemiological Cardiology Research Center, Wake Forest School of Medicine, Winston-Salem, North Carolina) by analysts who were masked to other REGARDS data. Self-reported AF was defined as an affirmative response to the following question: “Has a physician or a health professional ever told you that you had atrial fibrillation?”

Age, gender, race, education, household income, and smoking status were self-reported. Physical limitation was defined as self-reported inability to climb stairs or to perform moderate physical activities. Fasting blood samples were obtained and assayed for total cholesterol, high-density lipoprotein, and serum glucose. Hyperlipidemia was defined as total cholesterol ≥ 240 mg/dl or low-density lipoprotein ≥ 160 mg/dl or high-density lipoprotein ≤ 40 mg/dl or on cholesterol-lowering medication. Diabetes was defined as a fasting glucose ≥126 mg/dl (or a nonfasting glucose ≥200 mg/dl among those failing to fast) or self-reported diabetes medication use. The current use of antihypertensive medications was self-reported. After the participant rested for 5 minutes in a seated position, blood pressure was measured using a sphygmomanometer. Two values were obtained following a standardized protocol and averaged. Hypertension was defined as systolic blood pressure ≥140 mm Hg or a diastolic blood pressure ≥90 mm Hg, or by the self-reported use of antihypertensive medications. Coronary heart disease was ascertained by a self-reported history of myocardial infarction, coronary artery bypass grafting, coronary angioplasty or stenting, or if evidence of previous myocardial infarction was present on the baseline electrocardiogram. Previous stroke was ascertained by participant self-reported history. The history of CVD was defined as the composite of coronary heart disease, stroke, peripheral vascular disease, or aortic aneurysm. BMI was calculated using the height and weight collected during the in-home visit. Coronary heart disease, heart failure, and stroke events that occurred during follow-up were ascertained from medical records by an adjudication committee.

Baseline characteristics were compared between those who developed and did not develop AF. Categorical variables were reported as frequency and percentage, whereas continuous variables were reported as mean ± SD. Statistical significance for categorical variables was tested using the chi-square method and the Student’s *t* test procedure for continuous variables. Multivariable logistic regression was used to calculate the odds ratios (ORs) and 95% CIs for the association between baseline e-CRF (per 1-MET increase) and incident AF. The multivariable models were adjusted as follows: model 1 is adjusted for baseline race, region, education, and income; model 2 is further adjusted for systolic blood pressure, blood pressure−lowering medications, diabetes, hypercholesterolemia, history of CVD, and presence of physical limitations; and model 3: further adjustment for coronary heart disease, stroke, and heart failure occurring during follow-up. To test for the consistency of the results across, we conducted subgroup analysis stratified by age (median), gender, and race/ethnicity and examined interactions. Statistically significant results were defined by a p value of <0.05. Statistical analysis for this study was performed by SAS, version 9.3 (SAS, Cary, North Carolina).

Results

A total of 10,126 (54% women, 35% African-American, mean age 63.2 years) were included in the final analysis. The baseline e-CRF was 8.7 ± 2.1 METs. After a median follow-up of 9.4 years, 906 (8.9%) participants developed AF. Table 1 lists the baseline characteristics of the participants stratified by occurrence of AF during follow-up. As shown, baseline e-CRF was lower in those who developed AF versus those who did not (p <0.01). In addition, study participants who developed AF were more likely to have risk factors such as hypertension, diabetes, and history of CVD (Table 1).

In multivariable analysis adjusted for sociodemographics, every 1-MET increase in e-CRF decreased the risk of AF by 9% (p <0.001). On further adjusting for CVD risk factors and presence of physical limitations, the risk of AF was still reduced by 5% (p <0.007), which did not change after further adjustment for incident coronary heart disease, heart failure, and stroke (Table 2). This association was stronger in women than men (interaction p value = 0.05), but no differences were observed in the participant subgroups stratified by age, race, history of CVD, or physical limitations (Figure 1).

Discussion

In this analysis from the REGARDS study, we showed that better e-CRF, estimated from readily available clinical