Objectively Measured Physical Activity and the Risk of Atrial Fibrillation (from the REGARDS Study)

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The association between objectively measured physical activity and atrial fibrillation (AF) has not been examined. Therefore, we examined the association between moderate and vigorous physical activity (MVPA) with incident AF in 5,147 participants who completed accelerometer assessment for 4 to 7 consecutive days in the REasons for Geographic and Racial Differences in Stroke (REGARDS) study. MVPA was defined as >1,065 counts/minute, and daily mean time spent in MVPA was computed. Incident AF was identified during follow-up by a study-scheduled electrocardiogram and also from self-reported medical history of a physician diagnosis. Logistic regression was used to assess the relation between daily time in MVPA and incident AF. A total of 429 (8.3%) incident AF cases were detected after a median follow-up of 3.5 years following accelerometer assessment. Participants with higher daily time spent in MVPA were less likely to develop AF than those with lower MVPA achievement (Quartile 1 = 12.4%; Quartile 2 = 8.3%; Quartile 3 = 7.1%; Quartile 4 = 5.4%; p-trend <0.001). In a multivariable model adjusted for AF risk factors, the risk of AF decreased with higher levels of daily MVPA (Quartile 1: Ref; Quartile 2: hazard ratio [HR] = 0.77, 95% confidence interval [CI] 0.58 to 1.01; Quartile 3: HR = 0.72, 95% CI 0.53 to 0.98; Quartile 4: HR = 0.62, 95% CI 0.44 to 0.87; p-trend = 0.0056). In conclusion, higher levels of objectively measured daily MVPA are protective against the development of AF suggesting that promotion of MVPA should be encouraged to reduce the risk of AF. © 2020 Elsevier Inc. All rights reserved. (Am J Cardiol 2020;128:107−112)

Reports on the association between physical activity and the risk of atrial fibrillation (AF) have reached conflicting conclusions. Higher levels of physical activity have been associated with AF development,[1−3] whereas other reports have demonstrated a protective benefit.[4−7] Additionally, several reports have failed to show an association between physical activity and AF.[8−10] Explanations for these inconsistent findings have been attributed to differences in the populations examined, and the varying methods to ascertain physical activity. These studies also have relied largely on interview data to assess participants' activity levels, suggesting that the variation is related to the bias that accompanies self-reported behaviors. Therefore, to address previous shortcomings, we examined the AF risk associated with objectively measured physical activity in the REasons for Geographic and Racial Differences in Stroke (REGARDS) study.[11]

Methods

Details of REGARDS have been published previously.[12] Briefly, REGARDS is a prospective cohort study designed to identify causes of regional and black-white disparities in stroke mortality. The study oversampled blacks and persons residing in the Stroke Belt (North Carolina, South Carolina, Georgia, Alabama, Mississippi, Tennessee, Arkansas, and Louisiana) between January 2003 and October 2007. A total of 30,239 participants aged 45 years and older were recruited from a commercially available list of residents using postal mailings and telephone data. Demographic information and medical histories were obtained using a computer-assisted telephone interview that was conducted by trained interviewers. Additionally, a brief in-home physical examination was performed 3 to 4 weeks after the telephone interview. During the in-home visit, trained staff

collected information regarding medications, blood and urine samples, and a resting electrocardiogram. Participants are followed by telephone every 6 months for hospitalizations and other health outcomes.

From May 2009 to January 2013 screening and enrollment for an ancillary study collecting accelerometer data on all active members was undertaken. Usable accelerometer data were available for 8,096 participants. Of these, 6,904 completed an in-person follow-up examination similar to the baseline visit, including a 12-lead electrocardiogram. We excluded 428 with baseline AF, 687 with missing follow-up data, and 642 who were missing baseline covariate data. The final sample included 5,147 with complete data at baseline and follow-up. All participants provided written informed consent and the study was approved by all participating institutional review boards.

The characteristics of the cohort with available accelerometer data have been previously described.[11] Briefly, participants completed a log sheet daily with the date the Actical was first worn, and the time(s) put on and taken off each day. Compliant participants wore the device >10 h/day for 4 to 7 consecutive days. Nonwear periods were defined as >150 consecutive minutes of 0 activity counts. The exposure of interest was time spent in moderate or vigorous physical activity (MVPA). MVPA was defined as >1,065 counts per minute (cpm).[13] Time spent in MVPA was determined by summing the minutes in a day when the activity count met the criterion for that intensity. The average time in MVPA was computed for participants during the 4- to 7-day accelerometer wear period.

Incident AF was identified during follow-up by a study-scheduled electrocardiogram and also from self-reported medical history of a physician diagnosis during the computer-assisted telephone interview. 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?", a question that has been shown to be a reliable predictor of incident stroke events.[14]

Age, gender, race, household income, education, smoking status, and alcohol use were self-reported. Income was dichotomized at $20,000 with a separate category for those who refused to provide their income. Education was dichotomized at greater than high school graduation. Smoking was defined as never, former, or current use of cigarettes. Alcohol use was classified by the number of drinks per week reported by study participants using the following criteria: none, moderate (1 to 2 drinks/day for men and 1 drink/day for women), and heavy (>2 drinks/day for men and >1 drink/day for women). Body mass index (kg/m^2) was calculated from height and weight measured during the in-home exam. Fasting blood samples were obtained and assayed for total cholesterol and serum glucose. 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 aspirin and 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. Using electrocardiogram data, left ventricular hypertrophy was defined by the Sokolow-Lyon

Criteria.[15] Coronary heart disease was ascertained by 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. Cardiovascular disease was defined as the composite of coronary heart disease and stroke.

Baseline characteristics were compared across quartiles of MVPA. Categorical variables were reported as frequency and percentage while continuous variables were reported as mean ± standard deviation. Statistical significance for categorical variables was tested using the chi-square method and the student's t test procedure for continuous variables. Since the exact date of AF onset was unknown, multivariable logistic regression was used to compute odds ratios (OR) and 95% confidence intervals (CI) for the association between daily time in MVPA and incident AF. Multivariable models included the following covariates: Model 1 adjusted for age, gender, race, education, income, and geographic region; Model 2 included covariates in Model 1 with the addition of systolic blood pressure, high-density lipoprotein cholesterol, total cholesterol, body mass index, smoking, diabetes, antihypertensive medications, left ventricular hypertrophy, and previous cardiovascular disease. We evaluated effect modification by race and gender using a stratification technique and comparing models with and without interaction terms. Due to recent physical activity guidelines which recommend at least 150 minutes of weekly moderate physical activity (30 minutes per day over 5 days),[16] we examined the risk of AF in participants who achieved 150 minutes of MVPA during the week of accelerometer assessment. Statistical significance for all comparisons including interactions was defined as p <0.05. SAS Version 9.4 (Cary, NC) was used for all analyses.

Results

A total of 5,147 (mean age = 63 years; 54% women; 30% black) were included in this analysis. The mean daily time in MVPA was 14.6 ± 18.4 minutes. The baseline characteristics across quartiles of mean daily time in MVPA are shown in Table 1. Participants with higher mean time in MVPA were younger, and more likely to be male and white than those with lower time spent in MVPA. Additionally, those with higher values for time spent in MVPA had lower values for body mass index, systolic and diastolic blood pressures, and glucose than those with lower MVPA values.

A total of 429 (8.3%) AF cases were detected (median follow-up = 3.5 years, 25th-75th percentiles = 2.7, 4.2) after completion of the accelerometer assessment. Participants who developed AF had a mean MVPA of 10.5 ± 16.2 minutes/day compared with 15.0 ± 18.5 minutes/day in those who did not develop AF (p <0.001). Participants with higher daily MVPA were less likely to develop AF than those with lower MVPA achievement (Quartile 1 = 12.4%; Quartile 2 = 8.3%; Quartile 3 = 7.1%; Quartile 4 = 5.4%; p-trend <0.001).

In a multivariable model adjusted for AF risk factors, the risk of AF decreased with higher levels of daily MVPA (Quartile 1: Ref; Quartile 2: OR = 0.77, 95% CI 0.58, 1.01;

Table 1
Baseline characteristics of REGARDS participants by quartile of daily time spent in MVPA

Characteristic (mean ± standard deviation or %)	Daily time spent in MVPA (quartile)*				p value†
	Q1 (n = 1,326)	Q2 (n = 1,256)	Q3 (n = 1,285)	Q4 (n = 1,280)	
Age (years)	67 ± 7.8	64 ± 7.6	61 ± 7.7	60 ± 7.6	<0.001
Time in MVPA (min/day)	0.7 ± 0.6	4.4 ± 1.7	13 ± 3.9	40 ± 19	<0.001
Male	35%	44%	49%	57%	<0.001
Black	41%	33%	25%	21%	<0.001
Education ≤high school	39%	30%	22%	15%	<0.001
Income					
≥$20,000	70%	81%	84%	89%	
<$20,000	18%	10%	6%	3%	
Refused	12%	9%	10%	8%	<0.001
Body mass index (kg/m^2)	30 ± 6.0	29 ± 5.6	28 ± 5.3	27 ± 4.5	<0.001
Systolic blood pressure (mm Hg)	129 ± 16	125 ± 15	123 ± 15	121 ± 14	<0.001
Diastolic blood pressure (mm Hg)	76 ± 9.4	76 ± 9.2	76 ± 8.9	75 ± 8.8	<0.001
HDL cholesterol(mg/dl)	52 ± 16	52 ± 16	53 ± 16	55 ± 17	<0.001
Total cholesterol (mg/dl)	191 ± 38	193 ± 40	193 ± 38	196 ± 37	0.033
Glucose (mg/dl)	104 ± 34	99 ± 26	96 ± 22	94 ± 22	<0.001
Diabetes mellitus	22%	13%	9%	7%	<0.001
Smoking status					
Never	46%	49%	50%	58%	
Former	41%	40%	42%	37%	
Current	14%	11%	8%	5%	<0.001
Alcohol consumption					
None	68%	59%	47%	41%	
Moderate	29%	36%	47%	54%	
Heavy	3%	5%	6%	5%	<0.001
Aspirin	47%	41%	40%	38%	<0.001
Antihypertensive medications	47%	41%	40%	38%	<0.001
Left ventricular hypertrophy	10%	8%	6%	5%	<0.001
History of coronary heart disease	19%	13%	9%	9%	<0.001
History of stroke	6%	3%	1%	1%	<0.001

HDL = high-density lipoprotein; MVPA = moderate or vigorous physical activity.

Diabetes was defined as a fasting glucose ≥126 mg/dl (or a nonfasting glucose ≥200 mg/dl in those failing to fast) or self-reported diabetes medication use.

* Quartiles for the average daily time spent in MVPA.

† Comparisons were made between quartiles using the chi-square test for categorical variables and the analysis of variance for continuous variables.

Quartile 3: OR = 0.72, 95% CI 0.53, 0.98; Quartile 4: OR 0.62, 95% CI 0.44, 0.87; p-trend = 0.0056; Figure 1). Although not significant, MVPA ≥150 minutes per week (OR 0.77, 95% CI 0.58, 1.03) was associated with a trend for lower risk of AF. The results were similar when stratified by race (Table 2) and gender (Table 3).

Discussion

The findings of this analysis suggest that higher levels of objectively detected daily MVPA are associated with a decreased risk of AF development. The findings were similar in men and women, and in blacks compared with whites. The data reported provide insight into this important aspect of AF epidemiology, as previous reports have not examined the relation between objectively measured physical activity and AF.

Reports on association between physical activity and AF have reached varying conclusions. A higher frequency of self-reported vigorous exercise was associated with an increased risk of developing AF in young men (<50 years) and joggers in the Physician's Health Study.[1] Self-reported intense leisure-time physical activity also was shown to be associated with an increased risk of AF in men, but not
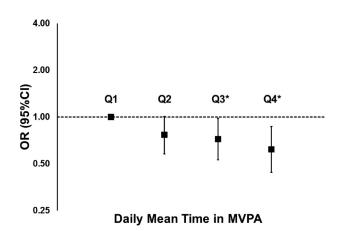

Figure 1. Association (odds ratio) between level of daily MVPA and incident AF in REGARDS participants.*

*Results of multivariable logistic regression models. Effect estimates adjusted for age, gender, race, education, income, geographic region, systolic blood pressure, high-density lipoprotein cholesterol, total cholesterol, body mass index, smoking, diabetes, antihypertensive medications, left ventricular hypertrophy, and previous cardiovascular disease. A significant trend was observed for the association between daily time spent in MVPA and AF across quartiles (p-trend = 0.0056).

AF = atrial fibrillation; MVPA = moderate or vigorous physical activity.

Table 2

Association between daily MVPA and incident AF stratified by race in REGARDS participants*

	Black participants (n = 1,544)			White participants (n = 3,603)			Interaction p value[§]
	# case/ # at risk	Model 1[†] OR (95% CI)	Model 2[‡] OR (95% CI)	# case/ # at risk	Model 1[†] OR (95% CI)	Model 2[‡] OR (95% CI)	
Daily time spent in MVPA							
Quartile 1	47/500	Ref	Ref	118/661	Ref	Ref	
Quartile 2	14/398	0.42 (0.22, 0.79)	0.45 (0.24, 0.87)	90/754	0.77 (0.57, 1.05)	0.87 (0.64, 1.20)	0.27
Quartile 3	10/313	0.39 (0.19, 0.81)	0.48 (0.22, 1.03)	81/881	0.66 (0.48, 0.92)	0.81 (0.58, 1.14)	
Quartile 4	10/252	0.49 (0.23, 1.05)	0.68 (0.30, 1.54)	59/959	0.48 (0.33, 0.69)	0.65 (0.44, 0.96)	
Weekly MVPA ≥150 minutes							
No	71/1,213	Ref	Ref	290/2,310	Ref	Ref	0.26
Yes	10/250	0.84 (0.41, 1.71)	1.11 (0.53, 2.33)	58/945	0.61 (0.45, 0.84)	0.74 (0.54, 1.02)	

MVPA= moderate or vigorous physical activity.

* Results of multivariable logistic regression models.

[†] Model 1 adjusted for age, gender, education, income, and geographic region.

[‡] Model 2 adjusted for Model 1 covariates plus systolic blood pressure, high-density lipoprotein cholesterol, total cholesterol, body mass index, smoking, diabetes, antihypertensive medications, left ventricular hypertrophy, and previous cardiovascular disease.

[§] Interactions tested using Model 2.

Table 3

Association between daily MVPA and incident AF stratified by gender in REGARDS participants*

	Male participants (n = 2,372)			Female participants (n=2,775)			Interaction p value[§]
	# case/ # at risk	Model 1[†] OR (95% CI)	Model 2[‡] OR (95% CI)	# case/ # at risk	Model 1[†] OR (95% CI)	Model 2[‡] OR (95% CI)	
Daily time spent in MVPA							
Quartile 1	79/380	Ref	Ref	86/781	Ref	Ref	
Quartile 2	61/493	0.64 (0.4, 0.92)	0.74 (0.51, 1.09)	43/659	0.75 (0.50, 1.11)	0.82 (0.55, 1.24)	0.35
Quartile 3	67/566	0.64 (0.44, 0.94)	0.83 (0.56, 1.24)	24/628	0.49 (0.30, 0.81)	0.57 (0.34, 0.94)	
Quartile 4	53/673	0.45 (0.30, 0.69)	0.66 (0.43, 1.02)	16/538	0.44 (0.24, 0.79)	0.56 (0.30, 1.03)	
Weekly MVPA ≥150 minutes							
No	208/1,444	Ref	Ref	153/2,079	Ref	Ref	0.60
Yes	52/668	0.63 (0.45, 0.88)	0.78 (0.55, 1.10)	16/527	0.61 (0.36, 1.06)	0.74 (0.42, 1.30)	

MVPA = moderate or vigorous physical activity.

* Results of multivariable logistic regression models.

[†] Model 1 adjusted for age, race, education, income, and geographic region.

[‡] Model 2 adjusted for Model 1 covariates plus systolic blood pressure, high-density lipoprotein cholesterol, total cholesterol, body mass index, smoking, diabetes, antihypertensive medications, left ventricular hypertrophy, and previous cardiovascular disease.

[§] Interactions tested using Model 2.

women, in Norway.[2] Additionally, self-reported leisure-time exercise of more than 5 hours per week at age 30 years was associated with a 19% increase in AF risk later in life.[3] In contrast, self-reported light to moderate leisure-time physical activity, assessed by the modified Minnesota Leisure-Time Activities questionnaire, was associated with a lower risk of AF in adults ≥65 years of age.[4] Similarly, higher levels of self-reported physical activity were associated with a reduced risk of AF in women.[5–7] Self-reported physical activity during working hours did not demonstrate an association with future AF risk in the Danish Diet, Cancer, and Health Study.[8] Similar null findings were reported for self-reported vigorous activity,[9,10] and self-reported total intentional exercise.[10] Meta-analyses also have reached different conclusions. One found that physical activity was associated with an increased risk of AF in men and a reduced risk in women,[17] whereas the other showed that moderate amounts of physical activity reduce the risk of AF in both men and women.[18]

The aforementioned variation in the association between physical activity and AF is largely related to the reliance on assessment of exercise habits by self-report and questionnaire. Therefore, it is not surprising that reports have demonstrated detrimental,[1–3] protective,[4–7] and null[8–10] associations between physical activity and AF. Participants also ascertained their level of physical activity using different questionnaires that were not uniform, diminishing comparability across studies. Furthermore, the study populations examined varied, with some limited to older adults and women. In contrast, the current study was able to use objectively measured physical activity to assess AF risk, as a subset of REGARDS participants completed accelerometer assessment. To our knowledge, this is the first report to examine the relation between physical activity and AF using methods to objectively ascertain physical activity levels. The objective assessment of physical activity minimized possible misclassification that is expected with physical activity ascertained by self-report. Additionally,

due to the biracial study population of men and women in REGARDS, we were able to explore if the observed associations varied by gender or race.

The mechanistic link in which higher levels of physical activity reduce AF occurrence is currently unknown. However, the maintenance of an ideal cardiovascular profile has been associated with reductions in the incidence of cardiovascular disease events and overall cardiovascular mortality.[19,20] Additionally, ideal cardiovascular health has been associated with preservation of cardiac structure and function.[21] Therefore, it is possible that greater achievement of ideal cardiovascular health, including higher levels of physical activity, likely reduces the development of subclinical changes in cardiac structure that promote the occurrence of atrial arrhythmias, such as AF. Additionally, due to the observed reductions in systemic blood pressure associated with favorable levels of physical activity,[16] it is likely that routine physical activity decreases the occurrence of AF through reductions in the development of hypertension, a well-known risk factor for AF.[22]

The promotion of healthy behaviors, including the encouragement of physical activity, has been recommended in recent guidelines due to the reported reductions in cardiovascular events.[16] The beneficial effect on cardiovascular health of routinely engaging in physical activity has been proposed to occur through favorable reductions in blood pressure and lipid levels. Accordingly, adults have been advised to engage in 3 to 4 weekly sessions of an average of 40 minutes of MVPA to observe advantageous changes in blood pressure and lipids, mirroring federal recommendations of at least 150 minutes of weekly MVPA.[16] However, these guidelines focused on overall cardiovascular health and the potential reduction in arrhythmia occurrence was not considered. The findings of the current analysis suggest that higher levels of daily MVPA, including 150 minutes of weekly MVPA, have a role in reducing the occurrence of AF. Additionally, participants in Quartile 4 achieved a mean of 40 minutes of daily MVPA, and the lowest risk of AF occurrence was observed in this group. Therefore, guidelines which promote at least 40 minutes of daily MVPA, and weekly achievement of 150 minutes of such activity, could also have an impact on the development of AF. Accordingly, our findings should be communicated to providers, patients, and strategic organizations with aims to prevent AF, as these data have important clinical implications to possibly prevent the occurrence of AF.

The findings of the current analysis should be interpreted in the context of certain limitations. It is possible that our methods of AF ascertainment missed some paroxysmal AF cases. Although several AF risk factors were included in our multivariable models, residual confounding remains a possibility. Furthermore, the data included in this analysis were limited to participants who completed the accelerometer study, and there is potential for selection bias.

Author Contribution

Study concept and design: Soliman, O'Neal
Analysis and Interpretation of data: Bennett, O'Neal, Soliman, G. Howard, Judd, Hooker
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