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Association of Physical Activity with the Incidence of Atrial Fibrillation among the  
Elderly in the Atherosclerosis Risk In Communities (ARIC) Cohort

By

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Master of Public Health

Epidemiology

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Bachelor of Science

Rutgers the State University of New Jersey

2018

Faculty Thesis Advisor: Alvaro Alonso, MD, PhD

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Rollins School of Public Health of Emory University

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## Abstract

Association of Physical Activity with the Incidence of Atrial Fibrillation among the Elderly in the Atherosclerosis Risk In Communities (ARIC) Cohort

By Grace Fletcher

**Background:** The relationship between physical activity (PA) and atrial fibrillation (AF) remains unclear, especially among the elderly population.

**Methods:** We studied 4,719 participants of the Atherosclerosis Risk in Communities (ARIC) cohort that took part in its visit 5 (2011-2013), were free of AF and had complete information on all variables. The exposure for this study was weekly MET-minutes of moderate to vigorous physical activity (MVPA), categorized in tertiles. The outcome was incident AF between the beginning of visit 5 to the end of 2017, ascertained from hospital discharges and death certificates. Time-to-event analysis was used to generate hazard ratios for AF by levels of physical activity adjusting for potential confounders.

**Results:** The mean (SD) age for the sample was 80.9 (4.9) years, 59% were female and 22% were black. Mean (SD) follow-up time was 5.2 (1.3) years. Compared to those with low weekly MVPA, individuals with moderate weekly MVPA showed a 21% reduction in the hazard of AF (HR= 0.79; 95% CI: 0.63, 0.93) while those with high MVPA showed a smaller 7% reduction in the hazard of AF (HR= 0.93; 95% CI: 0.73, 1.17) when adjusted for all covariates. There was no evidence of heterogeneity when stratified by race and sex.

**Conclusion:** This analysis suggests that being involved in moderate or high levels of MVPA was associated with reduced hazard of AF, particularly at moderate levels. There was no evidence of increased risk of AF in those with higher levels of MVPA.

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**Association of Physical Activity with the Incidence of Atrial Fibrillation among the Elderly in the Atherosclerosis Risk In Communities (ARIC) Cohort**

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**ABSTRACT**

**Background:** The relationship between physical activity (PA) and atrial fibrillation (AF) remains unclear, especially among the elderly population.

**Methods:** We studied 4,719 participants of the Atherosclerosis Risk in Communities (ARIC) cohort that took part in its visit 5 (2011-2013), were free of AF and had complete information on all variables. The exposure for this study was weekly MET-minutes of moderate to vigorous physical activity (MVPA), categorized in tertiles. The outcome was incident AF between the beginning of visit 5 to the end of 2017, ascertained from hospital discharges and death certificates. Time-to-event analysis was used to generate hazard ratios for AF by levels of physical activity adjusting for potential confounders.

**Results:** The mean (SD) age for the sample was 80.9 (4.9) years, 59% were female and 22% were black. Mean (SD) follow-up time was 5.2 (1.3) years. Compared to those with low weekly MVPA, individuals with moderate weekly MVPA showed a 21% reduction in the hazard of AF (HR= 0.79; 95% CI: 0.63, 0.93) while those with high MVPA showed a smaller 7% reduction in the hazard of AF (HR= 0.93; 95% CI: 0.73, 1.17) when adjusted for all covariates. There was no evidence of heterogeneity when stratified by race and sex.



**Conclusion:** This analysis suggests that being involved in moderate or high levels of MVPA was associated with reduced hazard of AF, particularly at moderate levels. There was no evidence of increased risk of AF in those with higher levels of MVPA.

## INTRODUCTION

Atrial fibrillation (AF) is one of the more common types of cardiac arrhythmia found in developed countries.<sup>1</sup> In addition to an aging population, the high prevalence of AF in the United States could be linked to the high prevalence of conditions such as hypertension, elevated blood glucose levels, obesity, and physical inactivity found within the country.<sup>2</sup> The relationship between physical activity (PA) and AF is less clear when compared to other risk factors, especially in elderly populations. The treatment of elderly patients with AF must be well-managed since older people are at higher risk for comorbid conditions such as stroke and heart failure.<sup>2</sup> Having an understanding of how physical activity, as a risk factor for atrial fibrillation, will allow us to have evidence to properly inform the elderly population of appropriate lifestyle recommendations. Additionally, examining AF among the elderly population is important given that the prevalence of AF increases significantly with each decade of life.<sup>3</sup>

Although the effect of physical activity on the incidence of AF has been studied, contradictory results have been reported. In younger and middle age individuals, high levels of PA, such as those observed among elite athletes, could increase the risk of AF. This observation does not seem to apply to older individuals and those engaging in more moderate levels of PA<sup>4</sup>. Such discrepancies may reflect the different effects of various types of PA upon AF, as well as gender interactions. Moreover, studies of the association between PA and AF in a community-based setting are limited in elderly populations. Physical activity has been shown to reduce the burden of AF.<sup>5</sup> In an older cohort, low to moderate PA has been associated with a lower incidence of AF compared to no exercise, but high-intensity PA was not significantly associated with a lower incidence of AF.<sup>6</sup> It is

possible that PA can reduce the risk of AF since it has been established that exercise is able to reduce obesity and hypertension which are known risk factors of AF. However, there is no clear answer as to how physical activity and AF are related. The association is likely a non-linear relationship.<sup>6</sup> Another source describes a reduced risk of AF among older women who exercised regularly,<sup>7</sup> but it is unknown whether the same effect will be present in a male cohort. Further research of this association is especially crucial given that the elderly population has the greatest risk of AF.<sup>3</sup> The results of this study can be utilized by public health organizations to develop lifestyle guidelines for elderly people and other groups who are deemed at-risk for AF.

It is well-known that social factors tied to race and ethnicity can contribute to the overall health of a demographic group, and analyzing race-stratified measures of the association between physical activity and AF risk may help characterize racial differences in cardiovascular health. Moreover, having an understanding of how PA is associated with AF among different racial and ethnic groups will aid professionals in the creation of health information materials that are specific to these groups. In this analysis, we used data from a community-based cohort to fill in the gaps regarding the association between physical activity and atrial fibrillation in the elderly population.

## **METHODS**

### **Study Population**

Data was taken from the Atherosclerosis Risk In Communities (ARIC) cohort. The ARIC study is a prospective cohort study in which people between ages 45-64 were recruited from 4 communities in the United States: Forsyth County, North Carolina, Jackson, Mississippi, Washington County, Maryland and some suburbs of Minneapolis, Minnesota. For this particular analysis, follow up started in 2011-2013, when participants attended the fifth study exam, and ended at the end of 2017. Participants were excluded from analysis if they had prevalent AF before visit 5 and were races other than white or black, due to small sample size.

The analysis includes participants attending visit 5 and providing information on physical activity. Those with missing information pertaining to survival time, incident atrial fibrillation, or any of the other covariates that were to be included in the analyses were removed from the study population. At the end of the inclusion/exclusion process the study population consisted of 4,719 individuals.

### **Assessment of Physical Activity**

The primary exposure in this study is the number of MET-minutes of moderate to vigorous physical activity (MVPA) per week. Three levels of physical activity were examined within this cohort: none, moderate, and high amount. The levels for each participant were determined based on the answers given for the ARIC/Baecke questionnaire.<sup>8</sup> The classification of each level was determined by approximate tertile cutpoints of MVPA. Those with greater than zero but less than 944.327 MET-

minutes/week of MVPA were classified as having moderate MVPA, and those with at least 944.327 MET-minutes/week of MVPA were classified as having high MVPA. The questionnaire's three components, sports and exercise, work, and leisure were used to assess the intensity of each observation's activity level.

### **Ascertainment of Incident Atrial Fibrillation**

The main outcome was incident AF between visit 5 and end of 2017. Incident AF is defined according to standard ARIC criteria between visit 5 and the end of 2017. Specifically, AF was identified from hospital discharge codes ICD9CM 427.3x and ICD10CM I48.x not occurring in the context of cardiac surgery, and from death certificates with AF as underlying or contributing cause of death (ICD10 I48).<sup>9</sup> Those with an AF diagnosis at the start of visit 5 were considered prevalent cases and dropped from the study population. Incident AF cases were those who were diagnosed after the start of visit 5 and before the end of 2017.

### **Other Covariates**

Other factors were considered as possible confounders during analysis. Smoking and alcohol use were examined given that both are associated with atrial fibrillation,<sup>10,11</sup> and both may be associated with physical activity. We also adjusted for age, sex, race/center, and education. Risk factors such as systolic and diastolic blood pressure, diabetes, prior history of cardiovascular disease (coronary heart disease, heart failure, stroke), and body mass index are included as covariates in additional analyses, since they can be confounders but also could be affected by physical activity. Finally, we evaluated

physical function as a potential confounder between physical activity and AF risk, adjusting using the score in the Short Physical Performance Battery (SPPB).

### **Statistical Analysis**

Statistical analyses were conducted using SAS 9.4 statistical software. Physical activity assessed using the ARIC/Baecke questionnaire was categorized in low, medium and high levels based on tertiles of MET-minutes/ week of moderate and vigorous physical activity. Time-to-event analysis were performed using a Kaplan-Meier estimate. Cox regression models were used to calculate hazard ratios and 95% confidence intervals for medium compared to low-intensity activity and high compared to low-intensity activity. Moreover, hazard ratios are compared among white and black subgroups as well as among men and women. An initial model adjusted for age, sex, research center, and race. A subsequent analysis adjusted additionally for hypertension defined as at least 90 diastolic and/or at least 140 systolic or use of antihypertensive medications, diabetes defined as a fasting blood glucose  $\geq 126$  mg/dL, a random blood glucose  $\geq 200$  mg/dL, use of antidiabetic medication, or self-reported diagnosis of diabetes, BMI, prevalent CHD, education level, current drinking, current smoking, and physical function score.

## RESULTS

Among 4,719 eligible participants at visit 5, there were 487 incident AF cases through the end of 2017. **Table 1** presents patient characteristics by physical activity level. The three groups are comparable overall by mean age, prevalent CHD, and current smoking. Other demographic and clinical factors varied by physical activity levels, with participants in the highest activity group being more likely to be white, male, more educated, and less likely to have diabetes or hypertension.

**Table 2** shows the hazard ratios for each of the three activity levels. Model 1 adjusted for age, sex, research center and race. Model 2 is adjusted for age, sex, race, hypertension defined as at least 90 diastolic and/or at least 140 systolic or use of antihypertensive medications, diabetes defined as a fasting blood glucose  $\geq 126$  mg/dL, a random blood glucose  $\geq 200$  mg/dL, use of antidiabetic medication, or self-reported diagnosis of diabetes, BMI, prevalent CHD and research center. Model 3 was adjusted for all previous covariates in addition to education level, current drinking, current smoking, and physical function score.

The hazard ratios (HRs) and confidence intervals (CIs) of the total population (N=4,719) are depicted in Table 2. Compared to having 0 MET-minutes of MVPA per week those who had moderate weekly MVPA had a lower hazard of AF when adjusted for age, sex, center, and race, and this finding was statistically significant (HR=0.70, 95% CI: 0.56, 0.89; p= 0.002). Compared to having 0 MET-minutes of MVPA per week those who had high weekly MVPA had a lower hazard of AF when adjusted for age, sex, center and race, and this finding was statistically significant (HR=0.76, 95% CI: 0.61, 0.95; p=

0.02). Once adjusted for risk factors of cardiovascular disease those with moderate MVPA had a lower hazard of AF compared to those with none (HR=0.77, 95% CI: 0.61, 0.96; p=0.02). Those with high MVPA displayed a lower hazard of AF compared to those with no MVPA, but this association was not statistically significant (HR=0.88, 95% CI: 0.70, 1.12; p=0.30). Model 3 included the most covariates. Those with moderate MVPA had a lower hazard of AF compared to those with no MVPA (HR=0.79, 95% CI: 0.63, 0.99; p=0.04). Participants with high MVPA had a lower hazard of AF compared to those with no MVPA, but this association was not statistically significant (HR=0.93, 95% CI: 0.73, 1.17; p=0.53). The results suggest an approximate 10-20% reduction in the hazard of AF in this population when there is at least some MVPA each week.

There appears to be some minor differences with the HRs when the population is stratified by race, as seen in **Table 3**. When adjusted for age, sex, and center, black individuals with moderate MVPA saw a statistically significant reduction in the hazard of AF (HR=0.55, 95% CI: 0.31, 0.96; p=0.03). Black individuals with high MVPA saw a statistically significant reduction in the hazard of AF (HR=0.40, 95% CI: 0.19, 0.83; p=0.01) when adjusted for the same variables, and this association is even stronger compared to what was seen among black individuals with moderated MVPA. A reduction in the hazard of AF in black individuals was seen in all three models for both moderate and high MVPA, but only the associations from model 1 were statistically significant.

When adjusted for sex, age, and research center, white individuals showed a statistically significant reduction in the hazard of AF (HR=0.74, 95% CI: 0.59, 0.95; p=0.02), but only for model 1 (Table 3). When tested for interaction between race and physical activity, there was no evidence of heterogeneity (p=0.22).



**Table 4** displays the HRs for moderate and high MVPA when stratified by sex. For both males and females, only moderate MVPA displayed in model 1 showed a significant decrease in the hazard of AF. This association appears to be more pronounced among females (HR=0.67, 95% CI: 0.47, 0.94; p=0.03). For males and females all three models showed a decrease in the hazard of AF, but only moderate MVPA in model 1 was statistically significant. When tested for interaction, there was no evidence of heterogeneity by sex (p= 0.97).

## DISCUSSION

In this large, community-based prospective study of elderly individuals, we found an inverse association between physical activity and the risk of AF. Compared to individuals not engaged in MVPA, those who had at least some amount of moderate-vigorous physical activity per week appeared to have a lower hazard of atrial fibrillation. In the overall study population, this association was only statistically significant for those with moderate and high MVPA in the minimally adjusted model and those with moderate MVPA in multivariable models. While it appeared that black individuals had a lower reduction in the hazard of AF compared to whites, there was no evidence of heterogeneity by race ( $p= 0.22$ ). Men and women appeared to have comparable reductions in the hazard of AF at the moderate MVPA level. While it appears that for that the hazard for AF at the high MVPA level may be higher in females compared to males, no evidence of heterogeneity was found by sex ( $p= 0.97$ ).

In the total population and when stratified by sex and race, the minimally adjusted model consistently yielded the strongest inverse associations, with attenuated associations after adjusting for lifestyle and clinical factors. This observation may suggest that these factors may be confounding the association between physical activity and AF risk, and adjustment for them provides less biased estimates. Alternatively, some of the covariates included in the model could be mediators rather than confounders. Hypertension and diabetes are seen as risk factors for cardiovascular disease, but it could be possible that being aware of having these conditions may affect individuals' likelihood to engage in regular physical activity.

Regarding the relationship between physical activity and AF in an elderly cohort, there appears to be a U-shaped relationship except among black individuals. In most cases the hazard is highest among those with no MVPA, lowest among those with moderate MVPA, and slightly higher than moderate MVPA in those with high MVPA. This trend suggests that engaging in moderate weekly MVPA is the ideal amount to prevent AF in white, elderly adults. Black individuals were the only people examined in this study to consistently show high MVPA as being the most protective level of physical activity. While only the minimally adjusted model yielded a statistically significant association for moderate (HR=0.55, 95% CI: 0.31, 0.96; p=0.03) and high (HR=0.40, 95% CI: 0.19, 0.83; p=0.01) MVPA, reductions in the hazard of AF were seen in every model and appeared to be strongest in the high MVPA group for blacks. Point estimates for the HRs for AF were the most protective among the black population. This could reflect differing levels of socioeconomic status. Blacks may have lower access to healthcare in which AF would be diagnosed, and therefore have smaller number of individuals diagnosed with the condition. It should also be considered that out of all the stratified populations that were analyzed, the black population had the smallest number of people (N=1,059). It is plausible that this could explain why this group showed a trend differing from the other groups. In fact, a test for race interaction was not significant, which may be explained by the limited number of AF events among blacks.

This study has several limitations. This sample of the ARIC population is very selective, since it includes individuals who had been part of a cohort study for almost 25 years. All individuals who self-reported race other than white or black were removed from this population (due to small numbers). Those with missing data were also excluded from the study population. Both of these reasons could limit the generalizability of this study to larger populations or other races and ethnicities. Data for the exposure, physical activity level, was self-reported, and we did not have information on the validity of this information. There is also the possibility that some of

the covariates included in the analyses were mismeasured, and this in turn could have affected our results by leading to residual confounding. Moreover, the data for incident AF cases are limited to those who were diagnosed in the context of a hospitalization, which may have led to missing asymptomatic cases and those managed exclusively in an outpatient setting.

There are also some important strengths, such as the relatively large sample size, the inclusion of two racial groups, and the availability of information on multiple covariates, including lifestyle factors, clinical variables and physical function status.

## **CONCLUSION**

There appears to be an inverse association between physical activity and incident AF in an elderly population. In most of the subgroups studied moderate MVPA is most strongly correlated with a reduction in the hazard of AF. There are not many studies that examine the association between PA and AF in an elderly cohort, and perhaps more research needs to be done with this population. More specifically, future research should focus on a more racially and ethnically diverse population in order to have a greater understanding of how PA will affect AF within those populations.

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## TABLES

**Table 1. Demographic Characteristics of Study Participants**

	<b>No MVPA</b> (N = 1545)		<b>Moderate MVPA</b> (N=1518)		<b>High MVPA</b> (N=1656)	
	N	%	N	%	N	%
<b>MVPA</b>						
Mean METS-min-wk (SD)	0 (0)		530.2 (256.8)		1694.3 (693.1)	
<b>Race</b>						
White	1068	69%	1169	77%	1423	86%
Black	477	31%	349	23%	233	14%
<b>Sex</b>						
Male	513	33%	591	39%	823	50%
Female	1032	67%	927	61%	833	50%
<b>Age</b>						
Mean years (SD)	75.7 (5.2)		75.3 (5.0)		74.7 (4.8)	
<b>Hypertension</b>						
Yes	1259	81%	1121	74%	1103	67%
No	286	19%	397	26%	553	33%
<b>Diabetes</b>						
Yes	608	39%	491	32%	376	23%
No	937	61%	1027	68%	1280	77%
<b>BMI</b>						
Mean (SD)	30.0 (6.3)		28.5 (5.3)		27.4 (4.7)	
<b>Prevalent CHD</b>						
Yes	214	14%	185	12%	226	14%
No	1331	86%	1333	88%	1430	86%
<b>Education (years)</b>						
11 or less	323	21%	191	13%	81	5%
12 to 16	709	46%	656	43%	614	37%
17 to 21	513	33%	671	44%	961	58%
<b>Current Drinking</b>						
Yes	583	38%	785	48%	1051	63%
No	962	62%	733	52%	605	37%
<b>Current Smoking</b>						
Yes	114	7%	78	5%	81	5%
No	141	93%	1440	95%	1575	95%
<b>Physical Function Score</b>						
Mean Score (SD)	8.56 (2.7)		9.4 (2.3)		10.2 (1.9)	



**Table 2. Hazard Ratios (HRs) and Confidence Intervals (CIs) in the Overall Population for the Association between Physical Activity and Atrial Fibrillation**

	No MVPA	Mod MVPA		High MVPA	
N. events	189	134		164	
Person-Years	7,864.18	7,857.26		8,640.54	
Incidence rate	24 events per 1000 person-years	17 events per 1000 person-years		19 events per 1000 person-years	
	HR (95%CI)				
Model 1	1 (Ref)	0.70	(0.56, 0.89)	0.76	(0.61, 0.95)
Model 2	1 (Ref)	0.77	(0.61, 0.96)	0.88	(0.70, 1.12)
Model 3	1 (Ref)	0.79	(0.63, 0.99)	0.93	(0.73, 1.17)

**Table 3. Hazard Ratios (HRs) and Confidence Intervals (CIs) Stratified by Race for the Association between Physical Activity and Atrial Fibrillation**

**Black**

	No MVPA	Mod MVPA		High MVPA	
N. events	42	28		9	
Person-Years	2445.06	1841.32		1244.34	
Incidence rate	17 events per 1000 person-years	15 events per 1000 person-years		7 events per 1000 person-years	
	HR (95%CI)				
Model 1	1 (Ref)	0.55	(0.31, 0.96)	0.40	(0.19, 0.83)
Model 2	1 (Ref)	0.59	(0.33, 1.05)	0.48	(0.22, 1.04)
Model 3	1 (Ref)	0.63	(0.35, 1.13)	0.50	(0.23, 1.09)

**White**

	No MVPA	Mod MVPA		High MVPA	
N. events	147	116		155	
Person-Years	5419.12	6,015.94		7,396.20	
Incidence rate	27 events per 1000 person-years	19 events per 1000 person-years		21 events per 1000 person-years	
	HR (95%CI)				
Model 1	1 (Ref)	0.74	(0.59, 0.95)	0.83	(0.66, 1.06)
Model 2	1 (Ref)	0.81	(0.64, 1.05)	0.96	(0.75, 1.23)
Model 3	1 (Ref)	0.84	(0.65, 1.08)	1.02	(0.79, 1.32)

**Table 4. Hazard Ratios (HRs) and Confidence Intervals (CIs) in Stratified by Sex for the Association between Physical Activity and Atrial Fibrillation**

**Male**

	No MVPA	Mod MVPA		High MVPA	
N. events	75	59		97	
Person-Years	2587.41	2,963.70		4,256.56	
Incidence rate	29 events per 1000 person-years	20 events per 1000 person-years		23 events per 1000 person-years	
	HR (95%CI)				
Model 1	1 (Ref)	0.73	(0.54, 0.98)	0.76	(0.55, 1.04)
Model 2	1 (Ref)	0.77	(0.57, 1.04)	0.85	(0.61, 1.18)
Model 3	1 (Ref)	0.79	(0.58, 1.06)	0.89	(0.64, 1.24)

**Female**

	No MVPA	Mod MVPA		High MVPA	
N. events	114	75		67	
Person-Years	5,276.77	4,893.56		4,383.98	
Incidence rate	22 events per 1000 person-years	15 events per 1000 person-years		15 events per 1000 person-years	
	HR (95%CI)				
Model 1	1 (Ref)	0.67	(0.47, 0.94)	0.75	(0.54, 1.03)
Model 2	1 (Ref)	0.75	(0.53, 1.08)	0.92	(0.66, 1.30)
Model 3	1 (Ref)	0.76	(0.54, 1.12)	0.94	(0.70, 1.33)