ARIC Manuscript Proposal #3426

PC Reviewed: 7/9/19   **Status: _____**   **Priority: 2**
SC Reviewed: _____   **Status: _____**   **Priority: ____**

1.a. Full Title:
Association of physical activity with the incidence of atrial fibrillation among the elderly in the Atherosclerosis Risk In Communities (ARIC) cohort.

  b. Abbreviated Title (Length 26 characters): Association of physical activity with the incidence of AF

2.   Writing Group:
    Writing group members: Grace Fletcher, Faye L Norby, Lin Yee Chen, J'Neka S. Claxton, Elsayed Z. Soliman, Alvaro Alonso, others welcome

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. GEF **[please confirm with your initials electronically or in writing]**

        First author: **Grace Fletcher**
        Address: Rollins School of Public Health
                1518 Clifton RD
                Atlanta, GA 30322

                Phone: 908 487 0252
                E-mail: grace.fletcher@emory.edu

ARIC author to be contacted if there are questions about the manuscript and the first author does not respond or cannot be located (this must be an ARIC investigator).
        Name: **Alvaro Alonso**
        Address: Dept of Epidemiology, Rollins School of Public Health
                Emory University
                1518 Clifton Rd NE, CNR 3051
                Atlanta, GA 30322

                Phone: 404-727-8714
                E-mail: alvaro.alonso@emory.edu

3.   Timeline:
Analysis to be started immediately. A manuscript is expected to be drafted by May 2020.

4.   Rationale:

Atrial fibrillation (AF) is one of the more common types of cardiac arrhythmia found in developed countries.[1] 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.[2] 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.[2] Having an understanding of how physical activity, as a risk factor for atrial fibrillation, affects the elderly population will allow us to allocate proper resources in order to reduce the burden of AF on this population. Additionally, examining AF among the elderly population is important given that the prevalence of AF increases significantly with each decade of life.[3]

Although the effect of physical activity on the incidence of AF has been studied, contradictory results have been reported. 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.[4] 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.[5] 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.[5] Another source describes a reduced risk of AF among older women who exercised regularly,[6] 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.[3] 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. With this study we hope to utilize data from this elderly population in order to fill in the gaps regarding the association between physical activity and atrial fibrillation in the elderly population.

5.   Main Hypothesis/Study Questions:
The following questions will be addressed:
1.   What is the association of physical activity with the risk of atrial fibrillation among the elderly in the ARIC cohort?
2.   How does the association differ when stratified for race/ethnicity and sex?

We hypothesize that there will be a lower risk of atrial fibrillation among elderly members of the cohort that have higher levels of activity compared to those with lower levels of physical activity. We also hypothesize that there will be meaningful differences in the association between physical activity and risk of AF when stratified for race/ethnicity.

6. Design and analysis (study design, inclusion/exclusion, outcome and other variables of interest with specific reference to the time of their collection, summary of data analysis, and any anticipated methodologic limitations or challenges if present).

1. **Study Design**
   Prospective cohort starting follow up at visit 5.
2. **Inclusion/Exclusion**
   The analysis includes participants attending visit 5 and providing information on physical activity. We will exclude individuals with prevalent AF, and those from races other than white and black, and the few non-whites from the Minnesota and Washington County sites
3. **Main independent variable (physical activity)**
   Three levels of physical activity will be examined within this cohort: low, medium, and high intensity. The intensity level for each participant will be determined based on the answers given for the ARIC/Baecke questionnaire.[7] The questionnaire's three components, sports and exercise, work, and leisure will be used to assess the intensity of each observation's activity level. Levels of physical activity will be further examined for each racial/ethnic group.
4. **Outcome**
   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).[8]
5. **Other Covariates**
   Other factors will be looked at as possible confounders during analysis. Smoking and alcohol use will both be examined given that both are associated with atrial fibrillation,[9,10] and both may be associated with physical activity. We will also adjust 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 will be included as covariates in additional analyses, since they can be confounders but also could be affected by physical activity. Finally, we will evaluate physical function as a potential confounder between physical activity and AF risk, adjusting using the score in the Short Physical Performance Battery (SPPB).
6. **Statistical analysis**
   Statistical analysis will be conducted using SAS 9.4 statistical software. The elderly population within the cohort is defined as individuals age 65 or older (all participants at visit 5 were in this group). Physical activity assessed using the ARIC/Baecke questionnaire will be categorized in low, medium and high levels based on tertiles of minutes per week of moderate and vigorous physical activity. Time-to-event analysis will be performed using a Kaplan-Meier estimate. Cox

regression models will be 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 will be compared among white and black subgroups as well as among men and women. Analyses will adjust for covariates listed above. We will also conduct stratified analyses by sex and race.

7.a. Will the data be used for non-CVD analysis in this manuscript? ____ Yes   __X__ No

   b. If Yes, is the author aware that the file ICTDER03 must be used to exclude persons with a value RES_OTH = "CVD Research" for non-DNA analysis, and for DNA analysis RES_DNA = "CVD Research" would be used? ____ Yes   ____ No
   (This file ICTDER has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript? ____ Yes   _X_ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER03 must be used to exclude those with value RES_DNA = "No use/storage DNA"? ____ Yes   ____ No

9.   The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status. ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: http://www.cscc.unc.edu/aric/mantrack/maintain/search/dtSearch.html

   __X____ Yes   _____ No

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?

- "Physical activity, obesity, weight change, and risk of atrial fibrillation: the Atherosclerosis Risk in Communities study." Circ Arrhythm Electrophysiol. 2014;7(4):620-5.PubMed:24907285
- MS 2601 – Changes in physical activity and AF. This manuscript explores changes in physical activity between visits 1 and 3 and subsequent risk of AF. It does not use visit 5 data or focuses particularly on the effects of exercise in the elderly.

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? ____ Yes   ___X_ No

11.b. If yes, is the proposal

___ **A. primarily the result of an ancillary study (list number* _____)**

___ **B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* _____ _____ _____)**

*ancillary studies are listed by number at https://www2.cscc.unc.edu/aric/approved-ancillary-studies

12a. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.

12b. The NIH instituted a Public Access Policy in April, 2008 which ensures that the public has access to the published results of NIH funded research. It is **your responsibility to upload manuscripts to PubMed Central** whenever the journal does not and be in compliance with this policy. Four files about the public access policy from http://publicaccess.nih.gov/ are posted in http://www.cscc.unc.edu/aric/index.php, under Publications, Policies & Forms. http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed central.

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