ARIC Manuscript Proposal #2667

PC Reviewed: 11/10/15  Status: A  Priority: 2
SC Reviewed: _________  Status: _____  Priority: ____

1a. Full Title: Incidence and Risk Factors for Incident Premature Ventricular Complexes: the Atherosclerosis Research in Communities (ARIC) Study.

b. Abbreviated Title (Length 26 characters): Predictors of Premature Ventricular Complexes

Writing Group:
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I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. [AM]

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3. Timeline: Analysis to begin after P&P approval. Manuscript anticipated for initial P & P review 6 months after approval.
4. Rationale

Premature Ventricular Complexes (PVCs) are common findings on electrocardiography in healthy individuals [1]. The clinical presentation of PVCs might range from asymptomatic to an impairment of left ventricular systolic function leading to congestive heart failure (CHF). The presence of PVCs has been associated with a poor prognosis in the setting of acute myocardial infarction, but the significance of PVCs in the absence of structural heart disease remains less understood [2]. A meta-analysis by Ataklte et al observed a significantly increased risk of sudden cardiac death (SCD) in patients with frequent PVCs [3]. From a mechanistic standpoint, PVCs may act as potential triggers for fatal cardiac arrhythmias. Data from the MADIT-II trial revealed that 77% of the total episodes of ventricular fibrillation were preceded by PVCs [4].

In addition to the increased risk of SCD, PVCs have also been implicated in the development of cardiomyopathy over a course of time [5]. Presence of at least one PVC on a 2-minute rhythm strip was associated with increased risk of the development of CHF in the ARIC study [6]. These results are further supported by recent data from the Cardiovascular Health Study (CHS) showing that a greater frequency of PVCs (ascertained on 24 hour Holter monitor) was associated with a subsequent decline in left ventricular ejection fraction (LVEF) [7].

Despite the importance of PVCs as a potential marker for increased risk for poor cardiovascular outcomes, its incidence and determinates in a racially diverse general population free of cardiovascular disease are not well established. Therefore, we propose to investigate the incidence and risk factors for premature ventricular complexes in the ARIC study.

5. Main Hypothesis/Study Questions:

The aims of this study are:
(a): To examine and compare race and sex differences in the incidence of PVCs detected from 10-second standard 12-lead ECG during ARIC follow up examinations.

(b): To identify independent risk factors and predictors of developing incident PVCs during ARIC follow up.

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 methodological limitations or challenges if present).

Inclusion/Exclusion Criteria

We intend to include all ARIC participants who have 12-lead electrocardiogram at baseline and in at least one follow up visit. Participants with history of cardiovascular disease (CHD, heart failure) at baseline will be excluded.

Outcome:

The primary outcome will be the occurrence of at least one PVC detected on the 12-lead ECG during the ARIC follow-up examinations (visit 2 to visit 5). Last EKG was recorded at visit 5 (2011-2013).

Variables

At baseline: Age, race, smoking status, body mass index, diabetes mellitus, systolic and diastolic blood pressure, hypertension, total cholesterol, HDL-cholesterol, LDL-cholesterol, hyperlipidemia, the use of antihypertensive medication(s), ECG-based left ventricular hypertrophy.

Follow up variable: Incident CHD and incident heart failure (Updated to the year of 2009).

Statistical analysis

Participants’ characteristics at baseline will be compared in those with and without PVCs (detected during follow up) using Wilcoxon rank sum tests for quantitative variables and Chi-
Square tests for categorical variables. Age adjusted incidence rates of PVCs will be calculated per 1000 person years in all ARIC participants as well as stratified by age, sex and race/ethnicity. Cox proportional hazard models will be used to examine the association between participants’ characteristics at baseline with incident PVCs. Models will initially include each baseline factor with adjustment for age, sex, and race (demographic models). Variables with significant association in the demographic model will be then entered in a multivariate risk factor models. We will also perform a multivariable analysis using a model which will include potential predictors based on their physiological and a potentially confounding role in the occurrence of PVCs. Variables with significant associations in the multivariate risk factor model will be entered in an additional model where incident heart failure and incident coronary heart disease will be included. This is to examine whether the observed associations of the PVCs predictors are mediated by heart failure and coronary heart disease.

In addition, longitudinal data analysis will be performed. Multilevel mixed-effects Poisson regression will be used. The number of PVCs on each visit (including baseline visit 1, and subsequent visits 2-5) 12-lead ECG (time-series variable) will serve as an outcome. Predictors will be included in the model as fixed factor variables (e.g. sex, race), fixed continuous variables (e.g. age), time-updated variables (incident heart failure and CHD), and time-series variables (e.g. time-series BMI, time-series systolic/diastolic blood pressure, time-series cholesterol, etc).

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/search.php

___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)?


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 http://www.cscc.unc.edu/aric/forms/

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.
References


