ARIC Manuscript Proposal # 1889

PC Reviewed: 1/10/12 Status: A Priority: 2
SC Reviewed: _________ Status: _____ Priority: ____

1.a. Full Title: Height and Sudden Cardiac Death

b. Abbreviated Title (Length 26 characters):

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

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3. Timeline: 1-2 months: data analysis
4. **Rationale:**
The association of sudden cardiac death (SCD), which is primarily caused by ventricular fibrillation, with increased left ventricular mass has been well established\(^1,^2\). Left ventricular mass increases with increased body size, although the specific manner in which adjustment for body size should be performed remains to be determined\(^3\). An increased risk of sudden cardiac death has been linked with increased body mass index in certain populations\(^4\), although the relationship is complex\(^5\), which suggests an importance of both weight and height, although no formal studies have demonstrated an association with height alone. Although height might be expected to increase risk of SCD via increase in left ventricular mass, it has generally been associated with lower risk of coronary heart disease. As a result, it remains unclear whether height is positively or negatively associated with risk of SCD.

We have an approved proposal to examine the association of height with risk of SCD in the Cardiovascular Health Study. In this proposal, we propose to further examine this association in a similar but younger cohort.

5. **Main Hypothesis/Study Questions:**
Increased height is positively associated with the incidence of sudden cardiac death.

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).**

A longitudinal design will be used with variables obtained on study enrollment (baseline). The analysis will consider development of SCD, with the follow-up time being that from baseline until first episode of SCD or end of follow-up (censorship). In order to perform survival analysis, we will include definite and probable/possible SCD as ‘SCD’ and none or unclassifiable SCD as ‘no SCD,’ and will try to only include outpatient SCD, if this information is available. We plan to examine these variables qualitatively beforehand to ensure no significant bias with this grouping scheme.

We plan to examine three models for the impact of height on SCD. The first will consist of an unadjusted Cox proportional hazards model, stratified by gender, with particular attention to the strength of association of height and SCD, as well as the linearity of the association. To examine non-linear associations, we plan to use flexible methods such as spline or fractional polynomial analysis. The second model we will examine will be a multivariable Cox proportional hazards model, stratified by gender, with adjustment for race, BMI, clinic site, education and age. The association of SCD with age, which has been shown in other diseases such as atrial fibrillation to
be nonlinear, will be analyzed using spline modeling, with the appropriate association method used for the multivariate model. The third model, which we will employ if there is a significant association of height and SCD in the two previous models, will be a multivariable model including all the covariates from the second model, as well as incremental inclusion of potential mediators of height on SCD, including LV mass, which will be examined separately for association with SCD and included as indicated by relevance and significance of association, and then included in a model with height to examine effect attenuation. We may also consider stratification based on prevalent CHD (based on history of MI, CABG surgery, or angiography) or incident non-fatal CHD (defined by the above criteria, except that SCD could not occur at the time of CHD incidence).

We plan to include all patients with and without a history of SCD who underwent measurement for height.

In addition to height and SCD, we plan to examine the following co-variates as outlined in the analysis plan if available in a sufficient number of participants:
- Age, gender, race, education, history of HTN or HTN medications, prevalent DM, smoking status, prevalent CHD based on history of MI, CABG surgery, or angiography, prevalent adjudicated CHF, prevalent adjudicated stroke or TIA, LV mass based on ECG.

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 ___x__ No

(This file ICTDER03 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 ___x__ 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.cscce.unc.edu/ARIC/search.php
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)? There is a pending proposal to examine BMI; we have confirmed that this does not address height.

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? Yes ___ 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/](http://www.cscc.unc.edu/aric/forms/)

12. 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.

References: