ARIC Manuscript Proposal # 3111

1.a. Full Title: Heart Failure and Venous Thromboembolism (VTE)

  b. Abbreviated Title (Length 26 characters): Heart Failure and VTE

2.   Writing Group:

Writing group members: Christina Fanola, Aaron Folsom, Pam Lutsey, Patty Chang, Faye Norby, Amil Shah, Wayne Rosamond, Mary Cushman

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

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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).

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3.   Timeline: Summer 2018

4.   Rationale:

Heart failure (HF) hospitalization places patients at increased risk of VTE. A meta-analysis suggested the risk is 1.5 fold (PMID 26765646), but there was considerable heterogeneity among studies. In general population or unselected patients (11 studies), the RR was 1.36 (95%CI:1.22-

1.51). Confounding adjustment in these studies was generally limited to hospital-based confounders.

The LITE study has recently updated VTE occurrence in ARIC through 2015 and can therefore examine the association of HF with VTE with better control for confounding and less likelihood of selection bias.

5.   **Main Hypothesis/Study Questions**:

Main hypothesis: Incident HF hospitalization (time dependent) is associated with increased short-term and long-term VTE risk. This association may differ between blacks and whites.

Exploratory: We are also interested in looking at Visit 5 echo findings in relation to VTE, but there would be too few VTEs between Visit 5 and the 2015 end of VTE follow-up. So, this analysis, if done, would probably be cross-sectional, relating past VTE to V5 echo findings.

Note: if there is an interesting association, we may seek to replicate it in the Cardiovascular Health Study (CHS), but this is not currently proposed.

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).

Main design: Prospective
Exposure: incident HF hospitalization (time dependent). If there are enough events after 2005, we will examine HFpEF separately from HFrEF.
Outcome: time to VTE occurrence
Exclusions: baseline HF, cancer, VTE, and anticoagulant use
Potential fixed confounders: sex, race (after first examining for interaction)
Potential time-dependent confounders: age, BMI, anticoagulant use, CKD or cancer diagnosis and number of hospitalizations during follow-up. Possibly a few other co-morbidities.
Analysis: Calculate age and sex-adjusted incidence rates using Poisson and multivariably adjusted HRs for HF diagnosis (yes, no) and Cox models, respectively. Test multiplicative interaction by race using a cross-product term.

The exploratory cross-sectional analysis of VTE history will examine echo findings potentially related to HF or risk (reduced systolic function (low EF), diastolic dysfunction, LVH, pulmonary hypertension, elevated pulmonary vascular resistance).

7.a. Will the data be used for non-CVD analysis in this manuscript? ____ Yes   _xx___ 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   __xx__ 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

___xx___ 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)?**

None

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

11.b. If yes, is the proposal
**_xx__ A. primarily the result of an ancillary study (list number* ___2001.16
LITE__)**
**___   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.