ARIC Manuscript Proposal # 1516

PC Reviewed: 5/12/09	**Status: A**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title:
Left ventricular dysfunction and risk of hospitalization for dyspnea due to noncardiac causes

b. Abbreviated Title (Length 26 characters):
LV dysfunction and dyspnea

2. Writing Group:

Writing group members:
Saul Blecker, Stuart Russell, Pete Miller, Fred Brancati, Joe Coresh
Others welcome including Herman A. Taylor, Ervin Fox – pending their approval.

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

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3. Timeline:
Analysis to begin immediately. Plan for manuscript within 6 months.

4. Rationale:
Heart failure (HF) has an estimated prevalence of over 5 million individuals in the United States.(1) The disorder is the primary diagnosis for nearly 1.1 million hospitalizations

per year, and is among the most common causes of inpatient stays in this country.(2) HF is a clinical syndrome that most commonly presents with symptoms of shortness of breath, fatigue, and edema.(3) The diagnosis of heart failure can often be difficult as symptoms of shortness of breath are nonspecific and may be due to other etiologies, especially related to diseases of the pulmonary system.(4) Unfortunately for the clinician, pulmonary disorders are also quite common; pneumonia is the most frequent cause of hospital admission other than childbirth, (5) and, together with COPD, asthma, and respiratory failure, accounts for over 2.6 million hospitalizations per year.(2) Furthermore, pulmonary comorbidities are often seen in HF, as evidenced by estimates of prevalence of COPD of 20 to 30% among the HF population.(6)

The ACC/AHA guidelines have classified heart failure as a progressive disorder, with stages A and B representing at-risk individuals, while stages C and D patients have developed symptoms of the disorder. (3) Patients with stage B heart failure have myocardial abnormalities such as left ventricular dysfunction and are at significant risk of developing symptomatic heart failure (7) although this has been less well evaluated in an African-American population. (8) Although left ventricular dysfunction has been associated with heart failure hospitalization, its relationship with other types of hospitalizations has been less well documented. A possible association between left ventricular dysfunction and hospitalizations for non-cardiac dyspnea has clinical importance as diagnostic tests for differentiating heart failure from other causes of dyspnea may not perform as well in the setting of left ventricular dysfunction.(9)The purpose of this study is to evaluate whether individuals with left ventricular dysfunction are at increased risk of hospitalization for dyspnea-related conditions other than heart failure.

5. Main Hypothesis/Study Questions:

1) Examine the association between left ventricular dysfunction and subsequent hospitalizations for dyspnea. We will plan to examine the relationship of LV dysfunction to both a composite of noncardiac hospitalizations and individual causes of dyspnea including COPD, pneumonia, pulmonary embolism, and heart failure.
2) Evaluate whether other echocardiographic abnormalities including left ventricular hypertrophy, diastolic dysfunction, and valvular abnormalities will predict future dyspnea-related hospitalizations.

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).

Study Population: Individuals from the Jackson cohort who underwent echocardiographic exam during visit 3 (1993 to 1996). We will include everyone with a valid assessment of left ventricular size and measurements from which ejection measure can be calculated. Participants will be followed from the time of echocardiogram through December 31, 2005.

Primary Exposure: Left ventricular dysfunction, as measured by abnormal ejection fraction (EF<50%)
Primary Outcome: Hospitalization from dyspnea-related cause other than heart failure, including COPD, pneumonia, asthma, pulmonary fibrosis. Hospitalization events will be obtained from the cohort annual follow through December 31, 2005.
Secondary Exposures: Left ventricular mass, diastolic dysfunction, ejection fraction, left ventricular hypertrophy
Secondary Outcomes: Hospitalizations from individual etiologies of COPD, pneumonia, asthma, and heart failure
Other Covariates: Age, gender, smoking status, education level, diabetes status, hypertension status, lipid levels, glomerular filtration rate
Statistical Analysis: In the primary analysis, hospitalization will be considered as a count variable over time. Rate ratios will be calculated to compare rates of hospitalization for those with and without left ventricular dysfunction using a negative binomial regression analysis. Cox models will be used to compared incident hospitalizations.

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 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 ____ 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)?

MP1337 – Lung function and heart failure
MP1048 ALVSD Prevalence, prognosis
MP 1475 Hypertention, LVH and Heart Failure

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/

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

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6. Le Jemtel TH, Padeletti M, Jelic S. Diagnostic and therapeutic challenges in patients with coexistent chronic obstructive pulmonary disease and chronic heart failure. J Am Coll Cardiol. 2007 Jan 16;49(2):171-80.

7. Wang TJ, Evans JC, Benjamin EJ, Levy D, LeRoy EC, Vasan RS. Natural history of asymptomatic left ventricular systolic dysfunction in the community. Circulation. 2003 Aug 26;108(8):977-82.
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