1.a. Full Title: Depression and incident heart failure: A prospective analysis from the ARIC Study

b. Abbreviated Title (Length 26 characters): Depression and heart failure

2. Writing Group:
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3. Timeline: Analyses will begin immediately upon approval by the Publications/Steering Committee.

Analyses completed - November 2013
Manuscript completed - January 2014
Submit manuscript to journal - March 2014
4. Rationale:

Heart failure, a serious and debilitating condition, is a rapidly growing public health problem. According to statistics provided by the American Heart Association, approximately 5,700,000 million people in the United States have this disease (1). Increasingly, researchers are investigating psychological factors for their contribution to the development and progression of this disease. Depression is most frequently examined as its co-morbidity with heart failure is common (2). Results from the most recent National Health and Nutrition Examination Survey (2005 – 2008) indicate a 6.8% prevalence of moderate to severe depression among adults in the general population (3). In contrast, the prevalence of depression in heart failure patients is substantially higher, as estimates upward to 60% have been reported (4). Depression may be linked to heart failure through biological (i.e., neurohormonal dysregulation and inflammation) and behavioral (i.e., maladaptive health behaviors) mechanisms (5).

Epidemiologic studies have consistently shown a positive association between depression and cardiovascular disease (CVD). It precedes new cardiac events (6) and is a factor in disease progression among patients with established CVD (7). A similar impact of depression on heart failure has been reported (2, 8). The clinical trajectory of people with heart failure and depression is poor. In a recent meta-analysis, the authors reported that heart failure patients with depression were more than twice as likely to visit the hospital emergency department compared to their non-depressed counterparts (2). Heart failure re-hospitalization rates among them were significantly elevated, ranging from 25 – 54.8% among depressed compared to 16.1 – 35.7% among non-depressed patients. The authors also reported an overall relative risk of death as 2.1 in depressed versus non-depressed heart failure patients.

There are few epidemiologic studies examining the role of depression in new-onset heart failure, and even fewer that are population-based. Only a handful of published studies exist. Among elderly, hypertensive patients, ages 60 years and older, depressive symptoms were associated with more than double the risk of heart failure after an average of 4.5 years of follow-up (9). The results from a second prospective study indicated that depression was an independent risk factor for heart failure in elderly (65 years and older) women but not in men (10). Using data from the Carotid MRI and Brain MRI ancillary studies in ARIC, the current analyses among middle-aged men and women in the ARIC Study are intended to add to the existing research on depression and heart failure by examining this question in a bi-racial population-based cohort.

5. Main Hypothesis/Study Questions:

Main Hypothesis: Participants who are depressed (i.e., total CES-D scores ranging from 16 to 60) will have significantly increased risk for incident heart failure compared to their non-depressed counterparts.

5a. Statistical Analyses
**Descriptive:** One-way analyses of variance or chi-square tests of association will be used to assess differences in means (for continuous variables) and percentages (for categorical variables), respectively, for the baseline HF risk factors.

**Inferential:** Cox proportional hazards regression analysis will be used to assess the association between depressive symptoms and incident HF.

Cumulative probabilities of incident HF over time will be estimated by the Kaplan-Meier product-limit method and will be compared between depressed and non-depressed participants using the log rank test. Statistical significance will be set at an alpha level of 0.05.

6. **Data (variables, time window, source, inclusions/exclusions):**
   Carotid MRI Visit Variables: individual CES-D variables, total CES-D, date of CES-D, incident heart failure, date of incident heart failure, diabetes status, cigarette years, hypertensive status, BMI, age, center, race/ethnicity, gender, prevalent heart failure, antidepressive medication use.

   Excluded will be participants with:
   1) a racial/ethnic identity other than black or white.
   2) incomplete responses on the CES-D

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 ICTDER02 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 ICTDER02 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 ICTDER02 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:  
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)?

ARIC MS #1276: Vital exhaustion and incident heart failure

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

11.b. If yes, is the proposal
   __ X__ A. primarily the result of an ancillary study (list number* ARIC Carotid MRI and Brain MRI)
   ___   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.cscu.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


