ARIC Manuscript Proposal #1946

PC Reviewed: 5/29/12	**Status: A**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Prevalence and outcomes of anemia in acute decompensated heart failure: ARIC Community Surveillance

b. Abbreviated Title (Length 26 characters):

2. Writing Group:

Writing group members:
Melissa Caughey, Laura Loehr, Hanyu Ni, Brad Astor, Kuni Matsushita, Lisa Wruck, Wayne Rosamond
Others are invited to join

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

First author: **Melissa Caughey, MPH**
Address: Division of Cardiology, CB #7075
160 Dental Circle, 6th floor Burnette-Womack Bldg
The University of North Carolina at Chapel Hill
Chapel Hill, NC 27599

Phone: (919) 843-0757 Fax: (919) 966-1743
E-mail: caughey@med.unc.edu

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).

Name: **Laura Loehr**
Address: 137 E. Franklin Street, Ste 306
Chapel Hill, NC 27514

Phone: 919-966-8275 Fax: 919-966-9800
E-mail: lloehr@email.unc.edu

3. Timeline: Analysis to begin summer 2012, with abstract to be completed by October 1, 2012, and manuscript by fall 2013.

4. Rationale:

Anemia is a common comorbidity of heart failure, and has been associated with increased mortality in cohort studies[1,2], clinical trials[3,4], administrative claims analyses[5], and hospital-selected registries[6,7]. However, it remains unclear if the prevalence and outcomes of anemia in heart failure patients differ by demographic subgroup and type of heart failure. Understanding these disparities may help management of anemia and improve outcomes for heart failure patients.

The surveillance of hospitalized HF events in the ARIC Communities provides a unique opportunity to study population prevalence and outcomes of anemia in hospitalized heart failure patients. This mitigates the possibility of selection bias that may occur with alternate study designs, such as bias by hospital catchment, clinical trial inclusion criteria, and consent to participation. Most heart failure cases captured by ARIC Surveillance were validated, decreasing the likelihood of misclassification bias that may occur when defining heart failure by administrative claims records.

We propose to describe the prevalence of anemia with systolic and diastolic heart failure, and examine associations with age, race, and gender. We will also examine heart failure management trends, as indicated by persistent, transient and new onset anemia at the time of hospitalization, and associations with demographic variables. Finally, we will assess the impact of anemia on progression of heart failure by examining the associations of anemia with length of hospital stay, and mortality, defined as in-hospital, 28-day and 1 year mortality.

5. Main Hypothesis/Study Questions:

1. What is the prevalence of anemia in systolic and diastolic heart failure, and does the prevalence differ by gender, age, and race?
2. Among those with hospitalized HF, what proportion of anemia is persistent, as compared to new-onset, and how is this associated with gender, age, and race?
3. Among those with hospitalized HF, does presence of anemia influence hospital length of stay, in-hospital mortality, and 1 year mortality, and are the outcomes influenced by gender, age, and race?

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).

Data abstracted from heart failure medical records from 2005-onward from the ARIC Community Surveillance will be used. Heart failure events that were classified as definite or possible acute decompensated heart failure with linkage to the National Death Index (for case fatality) index will be used. Demographic and clinical variables will

include age, gender, race, heart failure type (HFpEF or HFrEF), length of hospital stay, in-hospital, 28-day and 1 year mortality, anemia history, hospitalized hematocrit and hemoglobin (worst and last), height, weight, creatinine (worst), history of renal disease (dialysis), smoking, COPD, blood pressure, diabetes, history of coronary disease, ejection fraction, medicines, edema, smoking, and health insurance status.

All analyses will be weighted by sampling fractions specific to each of the ARIC Communities, accounting for population size, gender, and race.

Anemia will be defined by WHO guidelines (hemoglobin < 12 g/dL for women and < 13 g/dL for men, using the "worst" hemoglobin value from the hospitalization record. Anemia will be categorized as "persistent" if the presence of anemia is determined by both the worst and last hemoglobin values, and there is a positive history of anemia. Anemia will be categorized as "transient" if the presence of anemia is determined by the worst, but not the last hospitalized hemoglobin value. Anemia will be classified as "new-onset" if the presence of anemia is determined by both the worst and last hemoglobin values, and there is a negative history of anemia.

Continuous hemoglobin values will be stratified by covariates of interest (HF type, gender, race, edema, kidney disease, smoking, and medication use) and mean values compared by t testing (or Wilcoxon testing). The continuous relation between hemoglobin and age, and hemoglobin and eGFR will be analyzed by simple regression. After examining trends between continuous hemoglobin and covariates of interest, further analyses of anemia severity and outcomes may be considered.

Hemoglobin will be categorized as either anemia or not anemia, and prevalence odds ratios by HF type, gender, and race will be calculated. Anemia prevalence may be stratified by covariates of interest, and compared by chi square testing. Next, anemia will be categorized as either persistent, transient, or new onset, and prevalence odds ratios by HF type, gender, and race will be calculated. Persistent anemia prevalence may be stratified by covariates of interest, and compared by chi square testing.

Associations between anemia among HF patients and in-hospital mortality will be examined by logistic regression, after controlling for factors thought to cause both the exposure (anemia) and the outcome (mortality). Age, gender, race, and eGFR (calculated from the worst creatinine and CKD-Epi formula) will be entered into the model, along with medications, smoking, edema, other covariates previously cited in the literature. Associations between anemia among HF patients and 28-day and 1 year mortality will be examined by logistic regression, after controlling for confounders. Associations between anemia and length of stay will be analyzed with linear regression, after controlling for confounders.

Additional statistical analyses may be conducted, as needed.

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)?
#952 Brad Astor et al, Anemia and kidney dysfunction as predictors of cardiovascular disease.

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

1. Dunlay S, Weston S, Redfield M, et al. Anemia and heart failure: A community study. Am J Med. 2008 Aug; 121(8) 726-32.
2. Tang W, Tong W, Jain A. Evaluation and long-term prognosis of new-onset, transient, and persistent anemia in ambulatory patients with chronic heart failure. J Am Coll Cardiol. 2008 Feb 5; 51(5): 569-76.
3. O'Meara E, Clayton T, McEntegart M, et al. Clinical correlates and consequences of anemia in a broad spectrum of patients with heart failure: Results of the Candesartan in Heart Failure: Assessment in Reduction in Mortality and Morbidity (CHARM) Program. Circulation. 2006 Feb 21; 113(7): 986-94.
4. Komajda M, Anker S, Charlesworth A, et al. The impact of new onset anaemia on morbidity and mortality in chronic heart failure: results from COMET. Eur Heart J. 2006 Jun;27(12): 1440-6.
5. Go A, Yang J, Ackerson L, et al. Hemoglobin level, chronic kidney disease, and risk of death and hospitalization in adults with chronic heart failure: The Anemia in Chronic Heart Failure: Outcomes and Resource Utilization (ANCHOR) study. Circulation. 2006 Jun 13; 113(23): 2713-23.
6. Young J, Abraham W, Albert N, et al. Relation of low hemoglobin and anemia to morbidity and mortality in patients hospitalized with heart failure (insight from the OPTIMIZE-HF Registry). Am J Cardiol. 2008 Jan 15; 101(2): 223-30.
7. Adams K, Patterson J, Oren R. Prospective assessment of the occurance of anemia in patients with heart failure: results from the Study of Anemia in Heart Failure Population (STAMINA-HFP) Registry. Am Heart J. 2009 May; 157(5): 926-32.
8. von Haehling S, Anker M, Jankowska. Anemia in chronic heart failure: Can we treat? What to treat? Heart Fail Rev. 2012 Mar; 17(2): 203-10.