

## ARIC Manuscript Proposal #2281

PC Reviewed: 1/14/14  
SC Reviewed: \_\_\_\_\_

Status: A  
Status: \_\_\_\_\_

Priority: 2  
Priority: \_\_\_\_\_

**1.a. Full Title:** Race and Gender Differences in Heart Failure with Preserved Ejection Fraction: Morbidity, Case Fatality, and their Determinants

**b. Abbreviated Title (Length 26 characters)**  
Race and HFpEF Case Fatality

### 2. Writing Group:

Writing group members (**alphabetical**):

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Others welcome

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

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### 3. Timeline:

The study analysis is to begin immediately with the plan for manuscript submission within 12 months.

#### **4. Rationale:**

Of the estimated 6.6 million patients with heart failure in the United States, up to 38-60% of these patients have preserved left ventricular systolic function, or heart failure with preserved ejection fraction (HFpEF).<sup>1</sup> The morbidity and mortality of this population is on par with that seen in heart failure with reduced ejection fraction (HFrEF).<sup>2-3</sup> The clinical syndrome of HFpEF has traditionally been described in elderly, predominantly female, Caucasian patients, with associated hypertension and atrial fibrillation.<sup>2-3</sup> In our experience, the HFpEF patients from an inner-city population are younger, nearly half male, with an African American (AA) predominance and higher rates of hypertension, obesity, and chronic kidney disease. In addition, these patients have a high incidence of acute kidney injury (AKI) during hospitalizations for acute decompensated heart failure (ADHF). We have found race to be independently associated with hypertension, the development of AKI during admission for (ADHF) admission, and hospital length of stay in patients with HFpEF.

Gender differences in HF patients – from co-morbidities to outcomes – are well-established in patients with reduced systolic function. Although women with HF have a higher survival rate than men, they are less likely to be on standard HF therapies, have higher readmission rates, and are less likely to undergo invasive procedures.<sup>1,4</sup> Our rationale for this study is to examine the relationships between race and gender with co-morbidities, inpatient morbidity, and case fatality in the HFpEF population within the ARIC HF surveillance to determine if similar relationships exist on a larger scale.

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

We hypothesize that HFpEF patients in the ARIC HF surveillance population will be a younger, with more men and African Americans, and higher rates of co-morbidities including hypertension, diabetes, obesity, and chronic kidney disease. We predict gender and race are associated with differences in in-hospital morbidity and one year case fatality rates in HFpEF patients.

Our study questions are as follows:

1. To describe the co-morbidities and clinical care in HFpEF patients with particular interest in age, gender, and race differences.
2. To explore if there are gender and racial differences in in-hospital morbidity among HFpEF patients
3. To explore if there are gender and racial differences in one year case fatality among HFpEF patients

If gender and/or racial differences are found in any of the above, we intend to study the determinants of these differences including socio-demographics, comorbidity burden, and clinical care.

**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 methodological limitations or challenges if present).**

**Study design:**

*Study sample*

This study will include hospitalized patients age  $\geq 55$  years with HFpEF. HFpEF will be defined as ADHF hospitalizations (definite or probable, classified as “A” or “B” by ARIC panel) where left ventricular ejection fraction is  $\geq 50\%$ . We will restrict to those who never had a reduced EF  $<50\%$  (i.e., though currently a patient may have an EF  $\geq 50\%$ , if there was ever HFrEF then we don’t consider them as HFpEF). Those with HFpEF will be included in this study.

***Outcomes***

- Length of stay
- One year case fatality

*Other variables of Interest*

Hospital type (teaching vs. non-teaching),

ARIC community,

Whether echocardiogram was measured during this hospitalization,

Prevalent CHD,

Atrial Fibrillation,

Sleep Apnea,

Diabetes,

Pulmonary hypertension,

Hypertension,

Use of statins, beta blockers, digoxin, ACEI/ARB,

Serum sodium,

Renal function and staging,

BNP or NT-proBNP,

Body Mass Index,

Significant valvular heart disease

Worst eGFR, discharge eGFR, (for 2011 admission creatinine will be available thus to compare AKI rates too).

**Analysis plan:**

For aim 1, we will use descriptive statistics to examine differences in HFpEF patients by race group, gender, and age categories (age 55 to  $<65$  vs.  $\geq 65$  years). We will use t-tests and Chi-square tests for comparison.

For aim 2, we will compare the health care characteristics (length of stay), in-hospital mortality, and one year case fatality by race, gender, and age categories as above.

For aim 3, if we find differences in outcomes by race, gender, or age categories:

- a). we will examine if the similar differences are seen with HFrEF.
- b). we will examine whether inclusion of covariates can drive the observed association (race, gender) go towards null by examining %change in log (odds ratio) with addition of each variable in the order of their univariate association with the outcome.

**Limitations:**

Though, %change method may give some indication of unbalanced race groups in terms of other measured confounders/mediators that will be balanced by statistically adjustment, there is no clear method to uncover potential mediators/confounders.

EF may be missing in about 10-15% of the hospitalizations.

As ARIC communities include multiple hospitals – generalization to general hospitalized HFpEF patients is expected to be high but can't be guaranteed.

The variables abstracted in the charts were retrospective and their absence could indicated lack of measurement rather than true absence and thus define hospital characteristics or quality of care and may be inaccurately ascribed to a characteristics.

**7.a. Will the data be used for non-CVD analysis in this manuscript? No**

**8.a. Will the DNA data be used in this manuscript? 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.**

**Yes**

**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)?**

Ms. # 1551: Characteristics and outcomes of patients with HFpEF

**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.csc.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.**

1. Roger VL, Go AS, Lloyd-Jones DM, et al. Heart disease and stroke statistics--2012 update: a report from the American Heart Association. *Circulation*. Jan 3 2012;125(1):e2-e220.
2. Bhatia RS, Tu JV, Lee DS, et al. Outcome of heart failure with preserved ejection fraction in a population-based study. *N Engl J Med*. Jul 20 2006;355(3):260-269.
3. Owan TE, Hodge DO, Herges RM, Jacobsen SJ, Roger VL, Redfield MM. Trends in prevalence and outcome of heart failure with preserved ejection fraction. *N Engl J Med*. Jul 20 2006;355(3):251-259.
4. Ross JS, Chen J, Lin Z, et al. Recent national trends in readmission rates after heart failure hospitalization. *Circ Heart Fail*. Jan 2010;3(1):97-103.