ARIC Manuscript Proposal # 1048

1.a. Full Title: Prevalence and Prognosis of Asymptomatic Left Ventricular Systolic Dysfunction (ALVSD) in African Americans: the ARIC study

b. Abbreviated Title (Length 26 characters): ALVSD Prevalence, Prognosis

2. Writing Group (list individual with lead responsibility first):

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3. Timeline:
   Statistical Analyses                                          Start Immediately
   First Draft of manuscript        by Dec 2005

4. Rationale:
   In developed countries, numerous findings have demonstrated that left ventricular systolic dysfunction is the most common cause of heart failure.\textsuperscript{2, 5, 10} It is a disease that afflicts nearly 5 million people and is the cause of nearly a quarter of a million deaths in the United States annually.\textsuperscript{10} In a study by McDonagh et al, on participants of the Glasgow MONICA coronary-risk-factor survey, asymptomatic left ventricular systolic dysfunction was found to be at least as common as congestive heart failure.\textsuperscript{2} Detection and treatment of symptomatic or asymptomatic left ventricular systolic dysfunction may be crucial to reduce the substantial risks of mortality and morbidity associated with heart failure.\textsuperscript{6} There is limited information present regarding the rates of progression to congestive heart failure and death in those individuals that have asymptomatic left ventricular systolic dysfunction.\textsuperscript{1, 3}

   Although widespread screening may be unnecessary, in certain subpopulations (e.g. those with hypertension, left ventricular hypertrophy), echocardiography use could prove invaluable in early detection of asymptomatic left ventricular systolic dysfunction (ASLVD).\textsuperscript{4} Based on the
study performed by Dries et al, black patients are at increased risk for progression of LVSD, whether asymptomatic or symptomatic as compared with similarly treated white patients. The reasons for these observations are presently unknown. The SOLVD trial has shown the efficacy of ACE inhibitors in the prevention and treatment of heart failure, but it has also shown that African Americans are less likely to benefit from the use of ACE inhibitors than their Caucasian counterparts.

The data from the echocardiographic component of the ARIC study on African Americans at the Jackson site will be an excellent resource as to finding the subjects with asymptomatic left ventricular systolic dysfunction, and following their progression to determine what their prognosis could be. These subjects will also include patients with diabetes mellitus, hypertension, alcoholic and other comorbid factors.

5. Main Hypothesis/Study Questions:

1) Examine the prevalence of asymptomatic left ventricular systolic dysfunction (ASLVD) in the middle aged African American ARIC cohort, examined at the Jackson site. Prevalence of the ASLVD by gender and age decades will be looked at. Also the cardiovascular risk factor profiles for patients with or without ASLVD will be examined.

2) Examine the prognosis of patients with asymptomatic left ventricular systolic dysfunction within the African American population of ARIC cohort. The specific outcomes are CVD (CHD + stroke), all-cause mortality, and CVD mortality, admissions for congestive heart failure and the development of heart failure symptoms.

6. Data (variables, time window, source, inclusions/exclusions):

Study population:
These will include participants from the third ARIC study who underwent the echocardiographic exam in exam 3 (1993-1996) and had the valid measurement on ejection fraction. Only African Americans from the Jackson site of the ARIC study were involved in this arm of the study (N = 4000).

Exclusions: 1) Patients who has been hospitalized as having the diagnosis of “congestive heart failure” on their discharge code (ICD-9 code 428 and other related codes). 2) For the prospective analysis, participants who have the endpoints (Incident CVD, All-cause mortality, CHD mortality) before the echocardiogram exam. We will also exclude patients with aortic stenosis condition.

Components of interest from Echocardiogram:
The definition of asymptomatic LVSD is “depressed left ventricular systolic function without signs or symptoms of congestive heart failure”. In the ARIC echocardiographic study, LV ejection fraction was measured semi-quantitatively by an experienced cardiologist, and was categorized as normal (≥ 50%), mildly depressed (≥ 40% and < 50%), moderately depressed (≥ 30% and < 40%) or severely depressed (< 30%).

In the analyses, asymptomatic LVSD will first be examined by the echocardiographic categories as described above, without the patient reported symptom of cardiac dyspnoea (shortness of breath). Further, the existing categories will be collapsed into two dichotomous variables as indicated by the recent clinical guidelines, EF ≥ 50% vs < 50%.
Other Echocardiogram components of interest include LVMI (g/m²), PWT diastole, IVST diastole, LV diameter in diastole, relative wall thickness defined as (PWT + IVST)÷LVDD, left atrial size. Also within our interest are variables indicating valvular heart disease, the severity of mitral regurgitation, aortic regurgitation and aortic stenosis. Different geometric types of left ventricular hypertrophy will also be examined. LV geometry may be classified into the following four mutually exclusive groups on the basis of LVM and relative wall thickness: concentric hypertrophy (increased mass and increased relative wall thickness), eccentric hypertrophy (increased mass and normal relative wall thickness), concentric remodeling (normal mass and increased relative wall thickness) and normal geometry (normal mass and normal relative wall thickness).

**Other Covariates of Interest:** gender, age, BMI, hypertension status, diabetic status, smoking status, alcohol consumption, renal function based on serum creatinine, total cholesterol, LDL and HDL, selective medications (digoxin, nitrates, ACE inhibitors, beta blockers medications, diuretics).

**Statistical Model:** Descriptive data will be reviewed for the prevalence of ASLVD by gender and age decades. Multiple logistic regression analysis will be used to examine the relationship between binary EF categories and selective cardiovascular risk factors. For the prospective analysis, Cox proportional hazard model will be used. Time-to-endpoint is available in surveillance file (up to 2001).

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:

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)?  

N/A
11. 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.

REFERENCE LIST


