ARIC Manuscript Proposal # 948

PC Reviewed: 07/01/03	**Status: __A__**	**Priority: __2__**
SC Reviewed: 07/18/03	**Status: __A__**	**Priority: __2__**

1.a. Full Title: Predictive Value of Mitral Early to Late Diastolic Velocity Ratio to Incident CHD Events and Mortality

b. Abbreviated Title (Length 26 characters): **Mitral Velocity Ratio and CHD, Mortality**

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

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Timeline:

Complete analysis	Winter, 2003
Submit first draft to publications committee	Spring, 2004
Submit to Journal	Summer, 2004

3. Rationale:

Abnormalities of diastolic filling are increasingly recognized as causes of symptoms and predictors of outcome in patients with heart disease. Impaired diastolic filling often indicates a poor prognosis in heart failure (Aurigemma 2001), and the presence of LV diastolic dysfunction with preserved systolic dysfunction is associated with increased morbidity and mortality following acute MI (Poulsen 2001).

Diastolic dysfunction is also an indicator of cardiac damage in patients with diabetes, hypertension, or kidney disease. Schannwell *et al* found that left ventricular diastolic dysfunction was an early manifestation of diabetic cardiomyopathy. From the 11th year follow up data of a prospective follow-up study of essential hypertension patients (PIUMA study), Schillaci *et al* found that impaired LV early diastolic relaxation identified hypertensive patients at increased cardiovascular risk. In a hospital setting of hypertensive and normtensive patients, Simone *et al* found that diastolic abnormalities occured in the presence of normal ejection fraction or systolic fractional shortening.

However, the predictive power of diastolic filling in a normal population is still not clear. There are only a few cohort studies available addressing this issue. Aurigemma *et al* investigated the predictive value of systolic and diastolic function in an aged cohort (the

Cardiovascular Health Study), and found that subclinical contractile dysfunction and diastolic filling abnormalities were both predictive of subsequent congestive heart failure. Bella JN *et al* found that mitral ratio of peak early to late diastolic filling velocity was a predictor of mortality in a cohort of American Indians (the Strong Heart Study).

The Jackson cohort of ARIC study has gone through a thorough echocardiographic evaluation at their third visit. These participants have been followed for another 4 to 7 years and enough incident cardiovascular events have occurred in this cohort, thus providing us an excellent opportunity to address this question and to compare our findings with other cohort study findings mentioned above.

5. Main Hypothesis/Study Questions:

Our main purpose is to investigate whether diastolic dysfunction has predictive value for incident cardiovascular events, all cause mortality, or cardiovascular related mortality.

We will also describe the prevalence and associations of abnormal LV filling patterns in a normal population free of cardiac diseases at baseline. The relationship between different patterns of diastolic dysfunction to left ventricular hypertrophy, and to indicators of systolic cardiac function will also be addressed.

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

Echocardiograph variables: Flow velocity-derived variables including early diastolic filling, atrial filling, early/atrial mitral flow velocity ratio. Echo M-mode or 2-D derived measurements including LV mass, left ventricular hypertrophy, left ventricular geometry, ejection fraction, ejection shortening.

Key covariates to be adjusted for: Age, gender, race, smoking, hypertension, diabetes, body mass index, serum LDL, serum HDL, serum total cholesterol, ejection fraction, left ventricular hypertrophy, etc.

Outcome variables from surveillance: Incident CHD, all cause mortality, CHD mortality, time of follow up.

Exclusion criteria: Prevalent CHD, missing data on echocardiograph measurements, aortic stenosis, mitral stenosis, severe aortic regurgitation, severe mitral regurgitation.

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://bios.unc.edu/units/cscc/ARIC/stdy/studymem.html

____ Yes __X_ 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)?

The most related proposal is a withdrawn proposal: MS # 614, Left ventricular geometry, systolic function and diastolic filling in African Americans. Besides, the main focus in MS 614 is to compare systolic function and diastolic filling parameters in different patterns of left ventricular hypertrophy, which is not the same from our hypothesis.

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.

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