1.a. Full Title: Body Fat Distribution and Left Ventricular Structure and Function in African Americans: the Atherosclerosis Risk in Communities Study

b. Abbreviated Title (Length 26 characters): Body Fat & LV Structure & Function

2. Writing Group:
   Writing group members: Ervin Fox, Herman Taylor, Alan Penman, Kenneth Butler, William Johnson and Robert Garrison

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

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3. Timeline: Complete Analysis
   November 2006
   Submit first draft to publications committee  January 2007
4. Rationale:

Obesity is a major cause of mortality and morbidity through the development of insulin resistance, dyslipidemia, and hypertension leading to cardiovascular diseases (CVD). A strong relationship between obesity and development of CVD, diabetes and dyslipidemia in men and women and in diverse race/ethnic groups has been established in epidemiological studies (1-4). A recent analysis of data from the Jackson Heart Study showed a high prevalence of abdominal obesity, hypertension and low HDL-C concentration which are central features of the metabolic syndrome (data not published), which may contribute to higher mortality and morbidity from CVD in African Americans. Many mechanisms have been postulated for obesity, but they remain speculative.

Obesity is defined by a body mass index (BMI) value ≥ 30 kg/m², an indicator of total body fat that refers to the excess body weight compared with height. Waist circumference (WC) is an index of body fat distribution that refers to excess body fat accumulation in abdominal areas. Several studies have suggested that body fat distribution (defined by WC) rather than total body fat (BMI) is a better predictor and more strongly associated with increased risk for CVD (5-6), diabetes (7) and other health problems (8). Recent guidelines recommend WC over BMI as a predictor of obesity-related diseases as WC is simple to measure and interpret and is highly correlated with visceral fat as measured by computed tomography (9). Yet, WC is also highly associated with BMI and thus also reflects general, as well as abdominal, obesity.

There is supportive evidence that abdominal obesity is an important risk factor for subclinical cardiac abnormalities and subsequent heart failure (5-8). A recent study showed that African-Americans have a higher prevalence of left ventricular hypertrophy than European Americans (10). However, it is unclear whether the higher prevalence of abdominal obesity (with or without metabolic syndrome) in African-Americans is a major risk factor leading to changes in LV structure and function. Also, there are few data available to demonstrate whether abdominal obesity can synergize the other risk factors to cause changes in LV structure and function. One possibility is an interrelation between body fat distribution, especially in the abdominal area, and left ventricle geometric pattern, which might help to explain the excess risk associated with abdominal obesity. Therefore, it is important to understand the effect of body fat distribution on LV structure and function and to determine the relation between body fat distribution patterns and left ventricular LV structure and function in the ARIC study population.

REFERENCES


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

1. What is the distribution of BMI in African Americans in the Jackson cohort; what are the most prevalent obesity patterns (according to the table of definitions below) - overweight, obesity class I, II, III (regular vs. abdominal obesity) - in African Americans?

2. What is the association between LV structure and function and obesity patterns?

3. What is the role of abdominal obesity in the interaction of various CVD risk factors in causing LV structure and function? How does abdominal obesity modify the association between traditional CVD risk factors and LV structure and function?

**Definition of Overweight and Obesity (10):**

<table>
<thead>
<tr>
<th>Overweight and Obesity (Body Mass Index)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt; 18.5</td>
</tr>
<tr>
<td>Normal</td>
<td>18.5-24.9</td>
</tr>
<tr>
<td>Overweight</td>
<td>25.0-29.9</td>
</tr>
<tr>
<td>Obesity, class</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>30.0-34.9</td>
</tr>
<tr>
<td>II</td>
<td>35.5-39.9</td>
</tr>
<tr>
<td>III (extreme obesity)</td>
<td>≥ 40.0</td>
</tr>
<tr>
<td>Visceral (Abdominal) Obesity (Waist Circumference)</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>≥102 cm</td>
</tr>
<tr>
<td>Women</td>
<td>≥ 88 cm</td>
</tr>
</tbody>
</table>
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).

The study population will include African-American participants of the Jackson ARIC cohort (all African-American) who have undergone 2D and M-mode echocardiographic exams (N=2,445). Those with missing values for individual parameters will be excluded.

Demographic variables will include age, sex, and education. Clinical variables that will need to be adjusted for in the regression model include total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, smoking and drinking status, hypertension status, systolic and diastolic blood pressures measured over multiple visits, diabetes status, and physical activity.

Echocardiographic variables that will be measured or calculated include LV internal diameter, septal wall thickness, posterior wall thickness, relative wall thickness, LVMI, LV systolic function, and LV diastolic function. (LV relative wall thickness and LV mass – and hence LV geometric pattern - will be calculated from LV internal diameter, LV septal thickness, and LV posterior wall thickness.)

This will be a descriptive / cross-sectional analysis to determine:
1. The prevalence of overweight / obesity classes (both general and abdominal obesity) in the ARIC study population;
2. The associations between these classes and LV geometric patterns (normal, concentric remodeling, concentric LVH, and eccentric LVH);
3. The associations between these classes and LV systolic and diastolic dysfunction, LV ejection fraction, LV fractional shortening, and LV regional wall motion.

To assess the independent associations of obesity class / abdominal obesity with LV geometric patterns, covariate-adjusted prevalence ORs and 95% CIs will be calculated from regression models using SAS Proc Logistic. For continuous variables, covariate-adjusted mean values and SDs will be calculated using SAS Proc GLM. The following covariates will be adjusted for: age, sex, hypertension, diabetes, smoking, drinking, physical activity, total cholesterol, HDL, and LDL. (Covariates were measured at the time of the echo exam.) In all analyses, obesity class and abdominal obesity status will be evaluated both separately and together (that is, cross-classified).

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
____ 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
couraged to contact lead authors of these proposals for comments on the new
proposal or collaboration)?

1. Correlates of body fat distribution - variation across categories of race, sex and
   body mass in the Atherosclerosis Risk in Communities Study (MS#059A)
2. Reliability of body fat distribution measurements: The ARIC Study. (MS#058)
3. Prospective associations of fasting insulin, body fat distribution, and diabetes with
   risk of ischemic stroke (MS#445)

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/ 

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.