Project Title	Lifespan Determinants of Early Myocardial Dysfunction in Young Adults.
Investigators	Camilo Fernandez A, Dianjianyi Sun, Rupert Barshop, Shengxu Li, Wei Chen and Gerald S. Berenson
Affiliation	Department of Epidemiology Tulane School of Public Health and Tropical Medicine New Orleans, LA
Collaborative Site	Cardiac Imaging Core Laboratory Brigham and Women's Hospital Boston, MA Contacts: Scott D. Solomon, MD / Susan Cheng, MD

PROJECT OUTLINE

I. Background

Clinical evidence of adult cardiac structure and function abnormalities --due to cardiovascular risk factors exposure during the lifespan-- generally does not begin until the 4th decade of life. Conventional echocardiography is a clinically useful tool to document the nature of these abnormalities, as it provides considerable amount of diagnostic information –aiding in the detection of both, clinical and subclinical disease.

Although broadly used to assess myocardial contractile function, conventional echocardiography possess noticeable limitations with regard to evaluating active/passive movement of myocardial segments, as well as high intraobserver and interobserver variability –since visual estimation of the regional wall motion is very subjective and thus, operator dependent. During the recent years, "deformation imaging" (strain imaging) has emerged as a valuable tool for a more comprehensive and reliable echocardiographic assessment of myocardial function, allowing clear and objective discrimination between active and passive myocardial tissue movement.

Echocardiograms were originally recorded beginning in 2001 in a Bogalusa Heart Study (BHS) cross-sectional survey, and are now being repeated in each survey as a routine part of the research. Some 1-3 examinations have been conducted on subjects over serial screenings leading to a considerable body of data, which provides a unique opportunity to perform cross-sectional and longitudinal comparative and predictive analyses on myocardial contractile function (as measured by conventional and strain imaging) --in addition to document its changes over time-- in a biracial (black-white) community-based cohort.

II. Specific Aims and Hypotheses

a. To estimate adult myocardial contractile function by conventional and strain echocardiography imaging, and assess its racial (black-white) / gender differences in the BHS cohort.

   Hypothesis: racial (black-white) and gender differences exist in myocardial contractile function – measured by conventional and strain echocardiography imaging- in young adults.

b. To evaluate longitudinal changes in adult myocardial contractile function over time, as well as its racial (black-white) /gender divergence.

   Hypothesis: racial (black-white) and gender differences exist in the decline of adult myocardial contractile function over time.

c. To determine general and race/gender specific associations between myocardial contractile function and CV risk factors measured serially since childhood.

   Hypothesis: racial (black-white) and gender differences exist in the association between cardiovascular (CV) risk factors --measured cross-sectionally, longitudinally and cumulatively since childhood-- and myocardial contractile function assessed by conventional and strain echocardiography imaging in young adults

III. Methods

a. **Study population**
   Participants with available echocardiographic images in the BHS cohort

b. **Materials required**
   Echocardiographic images stored in Compact Discs (CD) and VHS Tapes

c. **Data required**
   Outcome:
   Left ventricular myocardial contractile function estimated by conventional and strain echocardiographic imaging, considered as categorical (decreased contractile function vs. normal) and continuous.

   Predictor Variables:

   Longitudinal/Cumulative: systolic blood pressure (SBP), diastolic blood pressure (DBP), body mass index (BMI), waist-to-height ratio (Wt/Ht), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), glucose, triglycerides, insulin and high sensitivity C-reactive protein (hsCRP).

   Cross-sectional (one time point): SBP, DBP, BMI, HDL-C, LDL-C, triglycerides, glucose, hsCRP, F2-Isoprostane and adiponectin.

   Covariates: age, race and gender (for general models), self-reported current smoking status (yes vs. no), self-reported alcohol drinking (yes vs. no), self-reported treatment for hypertension (yes vs.no), self-reported treatment for high cholesterol (yes vs. no), self-report level of physical activity (low, moderate, high) and self-reported family history of cardiovascular disease.

d. **General Logistics and Analysis Plan**

Echocardiographic images will be transferred to the collaborative site to perform measurements of the different components required to calculate the outcome variables. Image resolution correction will be performed prior to conducting the measurement, using a pixel deinterlacing refinement (PDR) technique for better assessment of the final image –especially for those images stored in VHS format (analog media). Upon completing the image processing, all image storage media will be returned to Tulane School of Public Health and Tropical Medicine. Since all images have a built-in name stamp that cannot be removed, all procedures pertaining to protection of subject privacy will be applied prior to transferring research materials to the collaborative center. Also, compliance with all data and materials transfer dispositions will be ensured at all times.

The estimated number of available echocardiographic images by study is depicted in Table 1. Echocardiographic observations by study participants are listed in Table 2. Two-dimensional (2D) images will be used to evaluate regional wall motion of each ventricular segment for velocity and displacement (conventional method), generating wall motion scores and classifying wall motion as: normal, hypokinetic, akinetic and dyskinetic (see figure 1). Tissue velocity imaging (TVI)-derived images will be employed to obtain myocardial deformation components form the different axes (radial, circumferential and longitudinal), for later estimation of myocardial strain (deformation). Myocardial strain will expressed in percentage (%) and defined as “positive” (thickening %) and “negative” (shortening %) –see figure 2.

Descriptive statistics will be utilized to list cohort characteristics across race-gender groups, as well as by adult contractile function estimation method (conventional vs strain imaging). Race/Gender group comparisons will be performed through Analyses of Co-variance (ANCOVA), controlling for covariates where necessary. Multiple regression and structured equation modeling analyses will be conducted to assess the determinants of early myocardial dysfunction, controlling for covariates as required. Interaction terms for race and gender will be included in the models. Analyses will be performed using SAS 9.3 for Windows (SAS Institute, Cary, North Carolina).

APPENDIX

Table 1: physically available echocardiographic image storage media by BHS survey

Study Name	Y110	Y310	Y315	Y610
Images Media Inventory (n)	1179	1072	196	914
Study Years	2001-2002	2003-2007	2007-2008	2008-2012
Image Format	VHS	VHS	Digital-CD	Digital-CD

Table 2: available echocardiographic observations by participant

At least 1 (n)	At least 2 (n)	At least 3 (n)	4 (n)
1562	1037	683	79

Figure 1: wall-motion scores by myocardial segment number for conventional estimation of contractile function

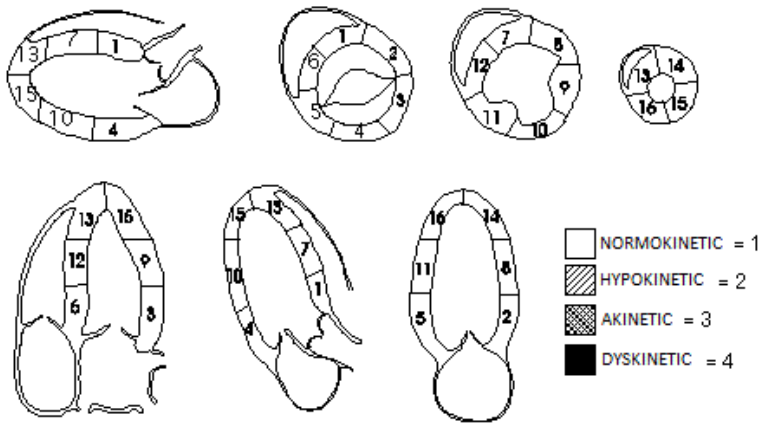

Figure 2: tissue velocity derived left ventricular myocardial strain