Heart failure (HF) is a progressive disorder afflicting 5 million Americans, with >80% of HF hospitalizations occurring in persons >65 years of age. Up to half of HF cases occur in the setting of preserved left ventricular (LV) ejection fraction (EF), a syndrome for which there are currently no proven therapies. Within the aging population, women and blacks are critically understudied populations. Limited normative and prognostic data exist on measures of cardiac structure, diastolic function, and novel measures of systolic deformation in older adults living in the community.

Background—Heart failure is an important public health concern, particularly among persons >65 years of age. Women and blacks are critically understudied populations that carry a sizeable portion of the heart failure burden. Limited normative and prognostic data exist on measures of cardiac structure, diastolic function, and novel measures of systolic deformation in older adults living in the community.

Methods and Results—The Atherosclerosis Risk in Communities (ARIC) study is a large, predominantly biracial, National Heart, Lung, and Blood Institute–sponsored epidemiological cohort study. Between 2011 and 2013, ∼6000 surviving participants, now in their seventh to ninth decade of life, are expected to return for a fifth study visit during which comprehensive 2-dimensional, Doppler, tissue Doppler, and speckle-tracking echocardiography will be performed uniformly in all cohort clinic visit participants. The following objectives will be addressed: (1) to characterize cardiac structural and functional abnormalities among the elderly and to determine how they differ by sex and race/ethnicity, (2) to determine the relationship between ventricular and vascular abnormalities, and (3) to prospectively examine the extent to which these noninvasive measures associate with incident heart failure.

Conclusions—We describe the design, imaging acquisition and analysis methods, and quality assurance metrics for echocardiography in visit 5 of the ARIC cohort. A better understanding of the differences in cardiac structure and function through the spectrum of heart failure stages in elderly persons generally, and between sexes and racial/ethnic groups specifically, will deepen our understanding of the pathophysiology driving heart failure progression in these at-risk populations and may inform novel prevention or therapeutic strategies. (Circ Cardiovasc Imaging, 2014;7:173-181.)

Key Words: aging ■ echocardiography ■ epidemiology
populations and may inform novel preventive and therapeutic strategies.

The National Heart, Lung, and Blood Institute’s (NHLBI’s) Atherosclerosis Risk in Communities (ARIC) study was initiated in 1985 in 4 communities in the United States and follows 15,792 individuals, 27% of whom are black. Participants are now in their seventh to ninth decade of life, during which the prevalence of HF increases dramatically. More than 6,000 participants are expected to attend the fifth visit cycle (visit 5) occurring from July 2011 to September 2013. The incorporation of comprehensive echocardiography (echo) into ARIC, therefore, presents a unique opportunity to examine cardiac structure and function in a biracial elderly cohort and to investigate alterations in cardiac structure and function across the spectrum of HF stages, their relationship to clinical outcomes, and whether they vary in these critically understudied populations.

We describe the design, imaging acquisition and analysis methods, and quality assurance metrics for echocardiography in visit 5 of the ARIC cohort.

Methods

The ARIC study design and methods have been previously described in detail. ARIC is a prospective epidemiological cohort study that, between 1987 and 1989, enrolled 15,792 middle-aged subjects in 4 US communities: Forsyth County, NC; Jackson, MS; suburban Minneapolis, MN; and Washington County, MD. Cohort participants underwent 4 examination visits between 1987 and 1998. Between 2011 and 2013, ≈6,000 surviving participants are expected to return for a fifth study visit. Institutional review committee approval was obtained for all field centers, and participants provided informed consent. ARIC participants undergo surveillance for cardiovascular events, including HF, incident coronary heart disease, and all-cause mortality as previously described. Incident HF is based on ARIC Mortality and Morbidity Classification Committee–adjudicated HF hospitalization (performed since 2005), including data on LVEF assessment during hospitalization, as previously published.

Visit 5 is the first examination in which echocardiography is being performed in all 4 ARIC field centers. Echocardiographic imaging and analysis protocol, the sonographer training and certification process, the quality assurance plan, and statistical methodologies were initially designed by investigators at the Echocardiography Reading Center (ERC; Brigham and Women’s Hospital, Boston, MA) in response to a Request for Proposals from the NHLBI. These methods were then modified, finalized, and implemented in collaboration with investigators from the ARIC field centers, coordinating center, and steering committee.

Echocardiography in ARIC visit 5 is designed to address 3 specific aims. The first is to characterize the abnormalities of cardiac structure and function in a community-based sample of elderly individuals and to assess how these abnormalities vary by sex and race/ethnicity. The study uses standard and novel echocardiographic techniques to characterize 5 specific domains of cardiac performance: LV structure and geometry; LV systolic function assessed by novel 2-dimensional (2D) speckle-tracking–based deformation imaging; LV diastolic function; left atrial (LA) structure; and pulmonary vascular resistance and systolic pressure and right ventricular (RV) function. These data will be used to define the population distribution of these measures and to determine their relationship with cardiovascular risk factors, including hypertension, diabetes mellitus, coronary disease, renal insufficiency, and prognostically relevant biomarkers such as N-terminal pro-brain natriuretic peptide and high-sensitivity troponin T. The second aim is to characterize the cross-sectional relationship of ventricular with vascular abnormalities in the community setting and to determine how these associations vary by sex and race/ethnicity. The study will investigate ventricular-arterial coupling in addition to the association of cardiac structure and function with arterial stiffness assessed by contemporaneous carotid-femoral pulse wave velocity, aortic morphology, and ankle-brachial index. The third aim is to prospectively examine the extent to which these noninvasive measures associate with incident HF and to determine the degree to which these associations vary by sex and race/ethnicity. This study will assess the incremental value of LV deformation, pulmonary pressure and vascular resistance, and RV function in predicting risk of HF beyond LV structure and conventional measures of systolic and diastolic function. In accomplishing these objectives, this study is developing an echocardiographic imaging database that will facilitate future investigations to compare these echocardiographic measures both with studies previously performed in the ARIC Jackson cohort (1993–1995) and with studies in complementary cohorts and to evaluate novel strain-based and 3-dimensional (3D) measures of cardiac function, including the LA and the RV.

Echocardiography Timeline

Development of the imaging and analysis protocol. *End date for visit 5 is approximate.


<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Protocol Developent</td>
<td>• Echo protocol development</td>
<td>Field Center Preparation</td>
</tr>
<tr>
<td></td>
<td>• ERC and FC manual of operations development</td>
<td></td>
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</tbody>
</table>

Throughput during Visit 5 Period (6/2011 – 9/2013*)

- Participant Visit at FC
  - Sonographer performs echo & completes eCRF
  - Same-day transfer to digital images to ERC via VPN connection
- Image Analysis at ERC
  - Modular analysis of 2D, Doppler, and speckle-tracking echo by dedicated and trained analysts
  - Data automatically inputted into study database (no manual entry)
- Cardiologist Over-Reading at ERC
  - Over-reading of key quantitative measures on all studies by staff echocardiographers at ERC
  - Over-reader approval of study data analysis
- Data Transfer from ERC to CC
  - Incremental weekly electronic data transfers to ARIC Data Coordinating Center

Figure 1. Outline of the overall design of the Atherosclerosis Risk in Communities (ARIC) echocardiographic study. 2D indicates 2-dimensional; CC, Coordinating Center; eCRF, electronic case report form; ERC, Echocardiography Reading Center; FC, field center; and VPN, virtual private network. *End date for visit 5 is approximate.
of Operations, hiring of field center sonographers, and purchase of uniform field center echocardiographic imaging equipment occurred between November 2010 and April 2011 (Figure 1). Training and certification of sonographers occurred in April 2011. Pilot testing occurred from May to June 2011, followed by the initiation of ARIC visit 5 in June 2011, which was expected to continue until September 2013.

Data Recording and Transmission
All echocardiograms were performed using dedicated Philips iE33 Ultrasound systems with Vision 2011 and X5-1 xMatrix transducer for 2D, Doppler, and 3D data acquisition, purchased specifically for use in the ARIC study. Machines at all field centers were set to acquisition defaults as detailed in Table 1. Image acquisition was performed using a preprogrammed acquisition protocol, which guided sonographers through each protocol required view as outlined in Table 2. All studies were acquired and stored digitally on a local PAC and transferred from field centers to a secure server at the ERC on the same day via a dedicated VPN connection, along with an electronic case report form containing information on demographics, anthropomorphic measures, and blood pressure at the time of echocardiography.

Image Acquisition Protocol and Techniques
The ARIC echocardiographic imaging protocol is detailed in Table 2. Participant blood pressure was taken <30 minutes of starting the echocardiographic exam and after the subject had been resting for 5 minutes. ECG leads were placed on the subject before imaging, and sonographers were instructed to ensure adequate ECG signal with a clearly identifiable QRS complex throughout the examination duration. All echocardiograms were obtained in a manner most consistent with good subject care.

For patients in sinus rhythm, ≥3 full cardiac cycles were recorded for each view, with recording beginning once the view was optimized. For subjects in atrial fibrillation, 1 or more 5-second acquisitions per view were recorded. Sonographers did not record measurements on the images because all measurements were performed centrally at the ERC.

For 2D imaging, sonographers were instructed to continuously optimize both imaging depth and sector width to maintain a frame rate of 50 to 80 frames per second. Because optimal visualization of endocardial borders was essential for quantitative analysis, sonographers were instructed to increase 2D gain if necessary to optimally demonstrate LV endocardial borders, particularly in the apical views, and to use harmonic imaging except in the unusual situation when this would worsen endocardial border definition.

For all color Doppler imaging, the color Doppler Nyquist limit was set at 64 cm/s. Color Doppler gain was set just below the level at which random background noise was seen. Sonographers were proscribed from altering the color Doppler gain and the Nyquist limit from the ARIC protocol defaults: sweep speed, 100 cm/s; and sample volume length, 5 mm; and filter setting, 100 Hz.

For 3D echocardiography, a full-volume ECG-gated 3D data set of both the LV/LA and RV/right atrium was acquired from the apical position with the matrix-array 3D transducer. During breath hold,
depth and sector width were adjusted to optimize spatial and temporal resolution within the sample volume. In the tissue harmonic mode, 4 wedge-shaped subvolumes were acquired over 4 consecutive cardiac cycles and automatically integrated into a wide-angle pyramidal data set with the highest frame rate achievable (20–26 Hz in our study).

Measurement Protocol
All conventional echocardiographic measures were performed using proprietary validated echocardiographic analysis software, which directly inputs and tracks measurement data into an automated database system, with each measurement linked to a JPEG image of the associated tracing for later review by cardiologist over-readers. Myocardial deformation analysis was performed using the TomTec Cardiac Performance Analysis package (Munich, Germany), a validated vendor-independent software package for echocardiographic speckle-tracking analyses of strain and strain rate. All quantitative measures were performed in a modular fashion by 4 analysts (Figure 2), so that for any given measure, the same analyst performed that measure for all echocardiographic studies. All measurements were performed in triplicate.

As outlined in Table 3, LV dimensions, wall thickness, anterior-posterior LA dimension, and outflow tract diameter were measured from the parasternal long-axis view according to the recommendations of the American Society of Echocardiography (ASE). LV mass was calculated from LV linear dimensions and indexed to body surface area as recommended by ASE guidelines. LV hypertrophy was defined as LV mass indexed to body surface area (LV mass index) >115 g/m² in men or >95 g/m² in women. Relative wall thickness was calculated from LV end-diastolic dimension and posterior wall thickness. LV volumes were calculated by the modified Simpson method using the apical 4- and 2-chamber views, and LVEF was derived from volumes in the standard manner.

LA volume was measured by the method of disks using apical 4- and 2-chamber views at an end-systolic frame preceding mitral valve opening and was indexed to body surface area to derive LA volume index. Mitral regurgitation was categorized by tracing the jet area (obtained with color Doppler imaging) occupying the left atrium in 4- and 2-chamber views and was expressed as a proportion of the LA area. The presence of an eccentric jet raised the grade of mitral regurgitation by 1 degree. Early transmitral velocity (E-wave) was measured by pulsed-wave Doppler from the apical 4-chamber view with the sample volume positioned at the tip of the mitral leaflets.

Peak lateral and septal mitral annular relaxation velocities (e') were assessed using tissue Doppler imaging. The E/e' ratio was calculated as the E the wave divided by e'.

In accordance with ASE guidelines, RV function was assessed using the tricuspid annular peak systolic velocity measured from the lateral tricuspid annulus, and RV fractional area change was calculated as the percent change in cavity area from end-diastolic to end-systolic tracings of the RV cavity in the apical 4-chamber view. From the parasternal short-axis view at the level of the aortic valve, the RV outflow tract time-velocity integral by pulsed-wave Doppler was measured as a correlate of RV stroke volume. Peak tricuspid regurgitation velocity was measured and peak RV-to-right atrial systolic gradient was calculated as 4×(peak tricuspid regurgitation velocity). Pulmonary vascular resistance was calculated using the RV outflow tract time-velocity integral/tricuspid regurgitation velocity ratio, as previously published.

To assess ventricular-arterial coupling, effective arterial elastance was estimated as end-systolic pressure divided by stroke volume, determined using the Simpson method of disks and indexed to body surface area. LV end-systolic pressure was estimated as 0.9 multiplied by brachial systolic blood pressure measured at the time of echocardiography. LV end-systolic elastance was estimated from the modified single-beat method using brachial pressures, stroke volume calculated from LV volumes, pre-ejection and total ejection times measured from spectral Doppler tracings, LVEF, and an estimated normalized ventricular elastance at arterial end diastole and indexed to body surface area.

Deformation analysis was performed using the TomTec Cardiac Performance Analysis package, which has been validated against MRI and sonomicrometry. Analysis was performed on 2D images acquired at a frame rate of 50 to 80 frames per second. Longitudinal strain was measured by tracing the endocardial borders in the apical 4-chamber and 2-chamber views, whereas circumferential strain and radial strain were measured by tracing endocardial and epicardial borders from the parasternal short-axis view at the level of the midpapillary muscle. Studies with inadequate image quality were not measured and defined as studies with >1 segment dropout or significant foreshortening of the LV. Endocardial border was traced at an end-diastolic frame in apical views, where end diastole was defined as the frame after mitral valve closure, and at an end-systolic frame in short-axis views. The software tracked speckles along the endocardial and epicardial borders throughout the cardiac cycle. Peak longitudinal and circumferential strain and strain rate were computed.

Figure 2. Illustration of the modular analysis approach used in the Atherosclerosis Risk in Communities echocardiographic study and the timing of serial analyst variability testing during the visit 5 period. *End date for visit 5 is approximate. LAV indicates left atrial volume; LV, left ventricle; LVEDD, left ventricular end-diastolic dimension; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESD, left-ventricular end-systolic dimension; LVESV, left ventricular end-systolic volume; RVFAC, right ventricular fractional area change; TDI, tissue Doppler imaging; and TR, tricuspid regurgitation.
Table 3. Atherosclerosis Risk in Communities Echocardiographic Study Primary and Derived Measures

<table>
<thead>
<tr>
<th>Primary Measures</th>
<th>Derived Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV structure</td>
<td>LV end-diastolic dimension (PLAX)</td>
</tr>
<tr>
<td></td>
<td>LV end-systolic dimension (PLAX)</td>
</tr>
<tr>
<td></td>
<td>LV wall thickness (PLAX)</td>
</tr>
<tr>
<td></td>
<td>LV end-diastolic volume (A4C, A2C)</td>
</tr>
<tr>
<td></td>
<td>LV end-systolic volume (A4C, A2C)</td>
</tr>
<tr>
<td></td>
<td>LV end-diastolic volume (3D)</td>
</tr>
<tr>
<td></td>
<td>LV end-systolic volume (3D)</td>
</tr>
<tr>
<td>LV systolic function</td>
<td>TDI s’ (A4C)</td>
</tr>
<tr>
<td></td>
<td>Longitudinal S, SR (A4C, A2C)</td>
</tr>
<tr>
<td></td>
<td>Radial and circumferential S, SR (PSAX)</td>
</tr>
<tr>
<td>LV diastolic function</td>
<td>Mitral annular TDI e’ (A4C)</td>
</tr>
<tr>
<td></td>
<td>E-wave, A-wave, DT (A4C)</td>
</tr>
<tr>
<td>Ventricular-arterial interaction</td>
<td>Arterial elastance (Ea) = (SBP×0.9)/SV</td>
</tr>
<tr>
<td></td>
<td>LV end-systolic elastance (Ees) = (DBP−(Ees×SBP×0.9))/[SBP×Ees], where Ees = 0.0275−0.165×EF+0.3656×(DBP/SBP)+0.515×Ees_avg, and Ees_avg = ( \frac{n}{\sum_{i=0}^{7} a_i} ), where n = onset/R−end, and a_i are (0.35695, −7.2266, 74.249, −307.39, 684.54, −856.92, 571.95, −159.1) for i=0 to 7</td>
</tr>
<tr>
<td></td>
<td>Peak RV–RA gradient (mm Hg) = 4*(peak TR velocity)^2</td>
</tr>
<tr>
<td></td>
<td>Pulmonary vascular resistance (Wood units) = 0.1618+10.006*(peak TR velocity/ RVOT VTI)</td>
</tr>
<tr>
<td>Valvular function</td>
<td>Aortic valve: LVOT VTI, aortic valve peak velocity, mean gradient, and VTI (A5C)</td>
</tr>
<tr>
<td></td>
<td>Mitral valve: MR jet area (A4C)</td>
</tr>
<tr>
<td>LA structure and function</td>
<td>LA A-P dimension (PLAX)</td>
</tr>
<tr>
<td></td>
<td>LA volume (A4C, A2C)</td>
</tr>
<tr>
<td></td>
<td>LA area (A4C, A2C)</td>
</tr>
<tr>
<td>Pulmonary vascular measures</td>
<td>TR velocity (A4C)</td>
</tr>
<tr>
<td></td>
<td>RVOT VTI (PSAX)</td>
</tr>
<tr>
<td>RV systolic function</td>
<td>RV end-diastolic area (A4C)</td>
</tr>
<tr>
<td></td>
<td>RV end-systolic area (A4C)</td>
</tr>
<tr>
<td></td>
<td>Tricuspid annular TDI s’ (A4C)</td>
</tr>
</tbody>
</table>

Speckle-tracking analysis was performed on images acquired at 50 to 80 frames per second. 3D indicates 3-dimensional; A2C, apical 2-chamber view; A4C, apical 4-chamber view; A-P, anterior-posterior; ASWT, interseptal wall thickness; BSA, body surface area; DBP, diastolic blood pressure; DT, deceleration time; e’, peak early diastolic mitral annular velocity; LA, left atrial; LV, left ventricular; LVEDD, left ventricular end-diastolic dimension; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVOT, left ventricular outflow tract; MR, mitral regurgitation; PLAX, parasternal long-axis view; PSAX, parasternal short-axis view; PW, posterior wall thickness; RA, right atrial; RV, right ventricular; RVEDA, right ventricular end-diastolic area; RVEF, regional wall motion abnormality; RVEFA, right ventricular ejection fraction; RVOT, right ventricular outflow tract; s’, peak systolic mitral annular velocity; S, strain; SBP, systolic blood pressure; SR, strain rate; SV, stroke volume; TDI, tissue Doppler imaging; TR, tricuspid regurgitation; and VTI, velocity-time integral.

Over-reading

All ECGs were over-read by a staff cardiologist at the Brigham and Women’s Hospital with COCATS level 3 advanced training in echocardiography or ASE Board Certification in Comprehensive Adult Echocardiography. Over-readers were presented with the following key quantitative measurements made by technicians: LV end-diastolic dimension, wall thickness, end-systolic volume, end-systolic volume, LVEF, LA volume index, RV fractional area change, ratio of mitral regurgitation jet area to LA area aortic valve peak antegrade velocity, and tricuspid regurgitation velocity. Over-readers reviewed echocardiograms to confirm the accuracy of these measurements and to identify clinically important findings not otherwise represented by the technical measurements. Such clinically important findings included significant aortic insufficiency, mitral stenosis, pulmonary hypertension, and RV enlargement. Over-readers had to approve analysis for each study before study data are finalized for transfer to the ARIC coordinating center.

After data transfer, the ARIC coordinating center incorporated LVEF, LV end-diastolic dimension, and LV wall thickness into a summary letter of visit 5 test results, which was sent to participants as a courtesy. Additionally, clinically relevant findings identified by ERC over-readers were also reported in this letter.

Training and Certification

In April 2011, all ARIC field center sonographers underwent an intensive 3-day centralized training at the Brigham and Women’s Hospital consisting of didactic sessions reviewing the examination protocol, machine presets, required views, and image acquisition/optimization tips and hands-on sessions led by an ERC senior sonographer to facilitate image optimization.

In the weeks after training, all sonographers were required to perform and submit 2 complete echocardiographic studies in accordance with the study protocol specifications and using study echocardiographic equipment. Studies were reviewed at the ERC and scrutinized for adherence to protocol, acquisition of all required views, and image quality. After submission of 2 adequate echocardiographic...
Intraobserver Variability and Temporal Drift Metrics for Key Echocardiographic Measures

<table>
<thead>
<tr>
<th>Measure</th>
<th>Mean±SD</th>
<th>CV, %</th>
<th>ICC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cycle 1</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEDV, mL</td>
<td>95.7±4.3±7.8</td>
<td>8.2</td>
<td>0.98</td>
</tr>
<tr>
<td>LVESV, mL</td>
<td>41.4±0.4±5.2</td>
<td>12.5</td>
<td>0.99</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>59.5±-2.3±5.2</td>
<td>8.7</td>
<td>0.93</td>
</tr>
</tbody>
</table>

**Analyst 1**
- LVEDV, cm: 4.74±0.14±0.24, 5.1, 0.95
- LVESV, cm: 3.22±0.09±0.14, 4.3, 0.99
- IVS, cm: 0.9±-0.00±0.10, 11.2, 0.84
- LV mass, g: 156.7±-3.2±20.2, 12.9, 0.97

**Analyst 2**
- E wave, cm/s: 67.0±2.1±2.2, 3.3, 0.98
- A wave, cm/s: 61.3±0.3±1.7, 2.8, 0.99
- e’ lateral, cm/s: 10.3±-0.3±0.6, 5.6, 0.99
- e’ septal, cm/s: 8.5±0.2±0.5, 5.7, 0.98
- E/e’ ratio: 7.2±0.4±0.3, 3.8, 0.99
- TR velocity, cm/s: 215.3±-13.2±4.6, 2.1, 0.95

**Cycle 2**
- LVEDV, mL: 99.9±-12.7±11.1, 11.2, 0.96
- LVESV, mL: 42.5±-1.8±5.2, 12.3, 0.98
- LVEF, %: 59.5±-2.8±6.0, 10.0, 0.88

**Cycle 3**
- LVEDV, cm: 4.72±-0.05±0.20, 4.2, 0.97
- LVESV, cm: 3.12±0.11±0.26, 8.4, 0.96
- IVS, cm: 0.93±-0.02±0.09, 9.8, 0.89
- LV mass, g: 157±-2.1±10.2, 6.5, 0.99

**Analyst 3**
- E wave, cm/s: 68.6±-1.1±1.9, 2.7, 0.99
- A wave, cm/s: 62.6±-2.5±1.3, 2.1, 0.99
- e’ lateral, cm/s: 10.2±0.1±0.8, 8.1, 0.97
- e’ septal, cm/s: 8.3±0.7±0.4, 4.5, 0.99
- E/e’ ratio: 7.5±-0.2±0.6, 7.5, 0.98
- TR velocity, cm/s: 217.2±-17.0±8.5, 4.0, 0.87

A wave indicates peak late diastolic transmitral flow velocity; CV, coefficient of variation; E wave, peak early diastolic transmitral flow velocity; e’ lateral, peak early diastolic mitral annular tissue velocity at lateral mitral annulus; e’ septal, peak early diastolic mitral annular tissue velocity at septal mitral annulus; ICC, intraclass correlation coefficient; IVS, interventricular septal wall thickness; LVEDD, left ventricular end-diastolic dimension; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic dimension; LVESV, left ventricular end-systolic volume; and TR, tricuspid regurgitation.

Standard descriptive statistics were used to define the population distribution of echocardiographic measures. The association of these measures with demographic, clinical, and physiological variables will be assessed using correlation analysis, in addition to univariable and multivariable regression. The relationships between cardiac structural and functional measures and clinical outcomes will be evaluated using univariable and multivariable Cox proportional hazard regression models. Incurrence events expected to alter cardiac structure and function, including definite or probable myocardial infarction or coronary revascularization, will be introduced into Cox proportional hazard regression models as time-varying covariates. Additional sensitivity analyses will exclude individuals with intercurrent events. Stratified analyses will also be performed by sex and race/ethnicity.

These power estimates model echocardiographic measures as dichotomous variables and assume =726 incident cases of heart failure during the follow-up on the basis of an estimated incidence of heart failure of ~2%/y in a study population of 6000. Power calculations were performed using the stpower function in Stata 11.
Table 6. Summary of Some Major Population Studies That Incorporated Echocardiographic Examination

<table>
<thead>
<tr>
<th>Study</th>
<th>Dates</th>
<th>Sampling Comments</th>
<th>n</th>
<th>Mean Age, y</th>
<th>Women, %</th>
<th>Nonwhite, %</th>
<th>TDI</th>
<th>Pulmonary Vascular/ RV Assessment</th>
<th>Strain</th>
<th>3D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Framingham Heart Study&lt;sup&gt;20&lt;/sup&gt;</td>
<td>1979–1983</td>
<td></td>
<td>4977</td>
<td>≈51±15</td>
<td>55</td>
<td>NR</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Flemish Study on Environment, Genes, and Health Outcomes&lt;sup&gt;21&lt;/sup&gt;</td>
<td>1985–2005</td>
<td></td>
<td>539</td>
<td>52.4±15.3</td>
<td>51</td>
<td>NR</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Cardiovascular Health Study&lt;sup&gt;22,23&lt;/sup&gt;</td>
<td>1987–1993</td>
<td></td>
<td>5201</td>
<td>73±5.6</td>
<td>57</td>
<td>7</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
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<tr>
<td>Coronary Artery Risk Development in Young Adults&lt;sup&gt;24,25&lt;/sup&gt;</td>
<td>1990–1991</td>
<td></td>
<td>4243</td>
<td>25–36</td>
<td>55</td>
<td>48*</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
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<tr>
<td>Coronary Artery Risk Development in Young Adults&lt;sup&gt;24,25&lt;/sup&gt;</td>
<td>1995–1996</td>
<td></td>
<td>1536</td>
<td>=30±3</td>
<td>54</td>
<td>41*</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Rotterdam Study&lt;sup&gt;26&lt;/sup&gt;</td>
<td>1990–1993</td>
<td></td>
<td>7983</td>
<td>70.5±9.6</td>
<td>61</td>
<td>NR</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Strong Heart Study&lt;sup&gt;27&lt;/sup&gt;</td>
<td>1993–1995</td>
<td></td>
<td>3501</td>
<td>=60±8</td>
<td>=64</td>
<td>100†</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>MONICA-KORA&lt;sup&gt;28&lt;/sup&gt;</td>
<td>1984–1985; 1994–1995</td>
<td></td>
<td>2200</td>
<td>51±14</td>
<td>51</td>
<td>NR</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Echocardiographic Heart of England Screening study&lt;sup&gt;29&lt;/sup&gt;</td>
<td>1995–1999</td>
<td>PCP</td>
<td>3960</td>
<td>61±11</td>
<td>50</td>
<td>3%</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Olmsted County Study&lt;sup&gt;30&lt;/sup&gt;</td>
<td>1997–2000</td>
<td></td>
<td>2042</td>
<td>62±10.6</td>
<td>≈53</td>
<td>NR</td>
<td>Yes</td>
<td>Yes§</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>London Life Sciences Prospective Population&lt;sup&gt;31&lt;/sup&gt;</td>
<td>2004–2007</td>
<td>PCP, Healthy</td>
<td>453</td>
<td>51</td>
<td>44</td>
<td>57‡</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Nord-Trøndelag Health study&lt;sup&gt;32&lt;/sup&gt;</td>
<td>2006–2008</td>
<td>Healthy</td>
<td>1266</td>
<td>=49±13.7</td>
<td>52</td>
<td>NR</td>
<td>Yes</td>
<td>Yes§</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Gutenberg Heart Study&lt;sup&gt;33&lt;/sup&gt;</td>
<td>2007–2008</td>
<td></td>
<td>5000</td>
<td>56±11</td>
<td>49</td>
<td>NR</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Atherosclerosis Risk in Communities Study</td>
<td>2011–2013</td>
<td></td>
<td>&gt;6000</td>
<td>=76±5</td>
<td>=59</td>
<td>24*</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

3D indicates 3-dimensional; Healthy, participants selected to be free of cardiovascular disease or traditional cardiovascular risk factors; NR, not reported; PCP, participants sampled from primary care clinics; RV, right ventricular; and TDI, tissue Doppler imaging.
*Nonwhites were predominantly blacks.
†Nonwhites were Native Americans.
‡Nonwhites were predominantly South Asians.
§Peak tricuspid regurgitation jet velocity obtained.

This study is one of the largest and most comprehensive echocardiographic data sets in an elderly cohort, including elderly women and blacks. Multiple analyses are, therefore, expected, including descriptive analyses to establish normative values, cross-sectional association studies to investigate predictors and correlates, and time-to-event analyses to assess the relationship to clinical outcomes. Echocardiographic measures are intercorrelated and, for statistical purposes, did not represent completely independent hypotheses. No unitary approach to adjustment for multiple testing was prespecified for all anticipated analyses. Instead, the most appropriate approach will be selected for each analysis. Similarly, study power varies broadly between analyses, as does power to detect effect modification by sex or race/ethnicity. We anticipate the study power to be most limited for the prospective association of measures of cardiac structure and function with incident cardiovascular events, including incident HF. Power calculations for these time-to-event analyses were performed with log-rank tests with significance defined as a 2-sided value of $P<0.05$ and with echocardiographic measures modeled dichotomously, using the stpower function in Stata 11. ARIC participants will be followed up for incident HF events for >5 years after visit 5 (up to 2017). On the basis of the observed HF incidence in ARIC from 2004 to 2008, we estimated an incidence of HF of ≈2% per year, with ≈726 incident cases of HF during follow-up. This estimate is conservative because events would also accumulate during the 2.5-year period when visit 5 is ongoing. Assuming a study population of ≈6000, our projected power based on effect size, prevalence of abnormal, and projected follow-up time is shown in Table 5. These power estimates are conservative because modeling echocardiographic measures as continuous variables (as opposed to dichotomous) will likely result in greater power. Power estimates for interaction testing by sex and race/ethnicity are provided in the Data Supplement.

Comparison of ARIC to Other Population-Based Echocardiographic Studies

Compared with existing population-based echocardiographic studies, the ARIC echocardiographic study is one of the largest (Table 6).<sup>20–33</sup> ARIC is also studying one of the most elderly cohorts with a sizeable proportion of black participants. The ARIC echocardiographic study is uniquely comprehensive, using 2D, 3D, Doppler, tissue Doppler, and speckle-tracking echocardiographic to quantify LV structure and function, ventricular deformation, pulmonary arterial pressure and vascular resistance, and RV function.

Conclusions

The aim of the ARIC echocardiographic study is to uniformly acquire and measure cardiac structure and function, including novel assessments of myocardial deformation, in ≈6000 elderly cohort participants. Comprehensive echocardiography in this large, well-phenotyped, elderly, biracial cohort will offer the unique opportunity for an integrated characterization of perturbations of cardiac structure and function and of ventricular-arterial interactions in advanced age. This comprehensive cardiovascular assessment is necessary (1) to define age-specific normative values for echocardiographic measures of cardiac structure and function in the elderly; (2) to further elucidate the mechanisms by which HF risk factors such as hypertension, diabetes mellitus, obesity, and renal insufficiency influence cardiac structure and function in older adults; and (3) to determine how these age- and risk factor–related perturbations differ in critically understudied populations, namely women and blacks.

Acknowledgments

We thank the staff and participants of the ARIC study for their important contributions.
Sources of Funding
The ARIC study was supported by National Heart, Lung, and Blood Institute (NHLBI) contracts (HHSN26820110005C, HHSN26820110006C, HHSN26820110007C, HHSN26820110008C, HHSN2682011009C, HHSN26820110010C, HHSN26820110011C, and HHSN26820110012C). This work was also supported by NHLBI cooperative agreement NHLBI-HC-11-08 (Brigham and Women’s Hospital) and grant 1K08HL116792-01A1 (to Dr Shah).

Disclosures
None.

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**CLINICAL PERSPECTIVE**

Heart failure is an important public health concern among elderly persons. However, limited normative and prognostic data exist on measures of cardiac structure, diastolic function, and novel measures of systolic deformation in older adults living in the community. Women and blacks, in particular, represent critically understudied populations. The Atherosclerosis Risk in Communities (ARIC) study is a large, predominantly biracial, National Heart, Lung, and Blood Institute–sponsored epidemiological cohort study. Between 2011 and 2013, ≈6000 surviving participants, now in their seventh to ninth decade of life, underwent comprehensive 2-dimensional, Doppler, tissue Doppler, and speckle-tracking echocardiography to address the following objectives: (1) to characterize cardiac structural and functional abnormalities among the elderly and to determine how they differ by sex and race/ethnicity, (2) to determine the relationship between ventricular and vascular abnormalities, and (3) to prospectively examine the extent to which these noninvasive measures associate with incident heart failure. We describe the design, imaging acquisition and analysis methods, and quality assurance metrics for echocardiography in the ARIC cohort. A better understanding of the differences in cardiac structure and function through the spectrum of heart failure stages in elderly persons generally, and between sexes and racial/ethnic groups specifically, will deepen our understanding of the pathophysiology driving heart failure progression in these at-risk populations and may inform novel prevention or therapeutic strategies.
Rationale and Design of a Multicenter Echocardiographic Study to Assess the Relationship Between Cardiac Structure and Function and Heart Failure Risk in a Biracial Cohort of Community-Dwelling Elderly Persons: The Atherosclerosis Risk in Communities Study


_Circ Cardiovasc Imaging_. 2014;7:173-181; originally published online November 8, 2013; doi: 10.1161/CIRCIMAGING.113.000736

_Circulation: Cardiovascular Imaging_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

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Print ISSN: 1941-9651. Online ISSN: 1942-0080

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SUPPLEMENTAL MATERIAL
Supplemental Methods

The table below demonstrates the estimated power to detect interaction between echocardiographic measures and gender or race/ethnicity for time-to-event analyses using a Cox model. These power estimates model echocardiographic measures as dichotomous variables and assume approximately 726 incident cases of HF during follow-up, based on an estimated incidence of HF of ~2%/year, in a study population of 6,000. This calculation assumes a 30% prevalence of abnormality for the echo measure, and a cohort that is 59% female and 24% African American. Calculations were performed using R powerSurvEpi package.1 We are powered to detect interactions in which the association between echo abnormality and clinical outcomes is 1.5 to 1.7 times stronger in one gender or race/ethnicity subgroup. We expect power to be greater for both cross-sectional analyses and time-to-event analysis modeling echocardiographic measures as continuous variables.

<table>
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<tr>
<th>Interaction</th>
<th>70% Power</th>
<th>80% Power</th>
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<tbody>
<tr>
<td>Hazard Ratios</td>
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<tr>
<td>Interaction by Gender</td>
<td>1.5</td>
<td>1.6</td>
</tr>
<tr>
<td>Interaction by Race</td>
<td>1.6</td>
<td>1.7</td>
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</table>
Supplemental Tables

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Biostatistician
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<table>
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<tr>
<th>Field Center</th>
<th>Echo Director</th>
<th>Sonographers</th>
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<tr>
<td>Forsyth County, NC</td>
<td>Dalane Kitzman MD</td>
<td>Heather Duncan</td>
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Supplemental References