Prognosis of Individuals With Asymptomatic Left Ventricular Systolic Dysfunction in the Multi-Ethnic Study of Atherosclerosis (MESA)

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Background—Limited data exist on the prevalence, associations, and prognosis of individuals with asymptomatic left ventricular systolic dysfunction (ALVSD), especially in populations without previous clinical cardiovascular disease (CVD).

Methods and Results—Kaplan-Meier and Cox proportional hazard analyses were used to assess the association between ALVSD, defined as left ventricular ejection fraction \( \leq 50\% \), and adjudicated incident congestive heart failure (CHF), all-cause mortality, and CVD events. Of 5004 participants, 112 participants had CHF, 321 had a CVD event, and 278 died after 9 years of follow-up. The overall prevalence of ALVSD was 1.7%, with a higher prevalence in blacks (2.6%). ALVSD had a worse cardiovascular risk profile and was also associated with increased risk in unadjusted and adjusted models for incident CHF (HR [hazard ratio] [95% CI {confidence interval}]: 12.0 [7.04–20.3], \( P < 0.0001 \) and 8.69 [4.89–15.45], \( P < 0.001 \) respectively), CVD (HR [95% CI]: 3.32 [1.98–5.58], \( P < 0.001 \) and 2.21 [1.30–3.73], \( P = 0.003 \) respectively), and all-cause mortality (HR [95% CI]: 3.47 [2.03–5.94], \( P < 0.0001 \) and 2.00 [1.13–3.54], \( P = 0.017 \), respectively). A 10% decrement in left ventricular ejection fraction at baseline was associated with an increase in risk in unadjusted and adjusted models for clinical CHF (HR [95% CI]: 2.17 [1.82–2.63], \( P < 0.0001 \) and 2.13 [1.73–2.51], \( P < 0.001 \) respectively) and all-cause mortality (HR [95% CI]: 1.22 [1.05–1.41], \( P = 0.009 \) and 1.17 [1.00–1.36], \( P = 0.047 \), respectively). Among the subset of participants with ALVSD, the left ventricular mass index was particularly informative about risk for incident CHF (c-index = 0.74).

Conclusions—ALVSD is uncommon in individuals without previous clinical CVD, but it is associated with high risk for CHF, CVD, and all-cause mortality. The left ventricular mass index had good discrimination for incident CHF in Multi-Ethnic Study of Atherosclerosis (MESA) participants with ALVSD.

Key Words: heart failure ■ death ■ cardiovascular events ■ cardiovascular imaging ■ asymptomatic left ventricular systolic dysfunction

Despite recent advances in heart failure management, individuals with congestive heart failure still endure high morbidity and mortality. With the exception of congestive heart failure (CHF) precipitated by an extensive myocardial infarction, most patients with heart failure appear to progress from an asymptomatic phase (American Heart Association stage B) to symptomatic phases (American Heart Association stages C and D). The poor prognosis in subjects with symptomatic heart failure is already well established. Current evidence suggests that treatments targeting the asymptomatic phase may slow the progression to the symptomatic phase and reduce subsequent morbidity and mortality. However, current data on the prevalence and prognosis of asymptomatic left ventricular systolic dysfunction (ALVSD) are limited. Most data were obtained from the noninterventional arm of clinical trials and generally include subjects with previous cardiovascular disease (CVD). Similar to the clinical trial data, in the few published epidemiological studies to date, most subjects had a history of myocardial infarction (MI), and, even though previous CVD/MI is accounted for in their models, it limits the generalizability of their findings. Moreover, most ALVSD subjects with previous MI have had contact with healthcare professionals and are likely to have been prescribed the recommended therapy, questioning the impact of public health screening for them in our communities. Finally, almost
all previously published data on this subject are based on echocardiographic measures of left ventricular structure and function rather than MRI-based measures, which have superior accuracy and reproducibility, especially for measures of left ventricular (LV) mass.16

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To address some of these limitations and better characterize the prevalence, associations, and prognosis of individuals with ALVSD assessed by using cardiac MRI from the Multi-Ethnic Study of Atherosclerosis (MESA).

Methods

Study Population and Data Collection

A detailed study design for MESA has been published elsewhere.17 In brief, MESA is a prospective cohort study begun in July 2000 to investigate the prevalence, correlates, and progression of subclinical CVD in individuals without known CVD at baseline. The cohort includes 6814 women and men aged 45 to 84 years recruited from 6 US communities (Baltimore, MD; Chicago, IL; Forsyth County, NC; Los Angeles County, CA; northern Manhattan, NY; and St. Paul, MN). MESA participants were 38% white (n = 2624), 28% black (n = 1895), 22% Hispanic (n = 1492), and 12% Chinese (n = 803). Individuals with a history of physician-diagnosed MI, angina, heart failure, stroke, or transient ischemic attack, or who had undergone an invasive procedure for CVD (coronary artery bypass graft, angio-plasty, valve replacement, pacemaker placement, or other vascular surgeries) were excluded. This study was approved by the institutional review boards of each study site, and written informed consent was obtained from all participants.

Demographics, medical history, and anthropometric and laboratory data for this study were obtained at the first MESA examination (July 2000 to August 2002). Current smoking was defined as having smoked a cigarette in the past 30 days. Diabetes mellitus was defined as fasting glucose ≥126 mg 100 mL−1 or the use of hypoglycemic medications. Use of antihypertensive and other medications was based on the review of prescribed medication containers. Resting blood pressure was measured 3 times in the seated position, and the average of the second and third readings was recorded. Hypertension was defined as a systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg or use of medication prescribed for hypertension. Body mass index was calculated as weight (kg)/height2 (m2). Total and high-density lipoprotein cholesterol were measured from blood samples obtained after a 12-hour fast. Low-density lipoprotein cholesterol was estimated by the Friedewald equation.18

Cardiac MRI

Consenting participants underwent a cardiac MRI scan a median of 16 days after the baseline evaluation; 95% were completed by 11 weeks after the baseline examination. Participation in the MRI examination was voluntary. All imaging was done with a 4-element phased-array surface coil positioned anteriorly and posteriorly, electrocardiographic gating, and brachial artery blood pressure monitoring.19 Imaging consisted of fast gradient echo cine images of the left ventricle with time resolution <50 ms. Functional parameters and mass were determined by volumetric imaging. Imaging data were read by using MASS software (version 4.2, Medis, Leiden, the Netherlands) at a single reading center by trained readers blinded to risk factor information. Papillary muscles were included in the LV volumes and excluded from LV mass. LV end-diastolic volume and LV end-systolic volume were calculated by using the Simpson rule (the summation of areas on each separate slice multiplied by the sum of slice thickness and image gap). LV mass was determined by the sum of the myocardial area (the difference between endocardial and epicardial contour) times slice thickness plus image gap in the end-diastolic phase multiplied by the specific gravity of myocardium (1.05 g/mL). The left ventricular ejection fraction (LVEF) was calculated as LV stroke volume/LV end-diastolic volume × 100. The interobserver variability in estimating LV parameters was: LV mass (6.0 g, 95% confidence interval [CI] 4.6, 7.4); LVEF (5.1%, 95% CI 3.6, 6.7) and intraobserver variability in estimating LV parameters was LV mass (6.3 g, 95% CI 5.17, 7.38); LVEF (3.9%, 95% CI 3.06, 4.72).

Ascertainment of Outcomes

Outcomes in MESA are adjudicated by a committee that includes a cardiologist, a cardiovascular physician-epidemiologist, and a neurologist. Reviewers/adjudicators classified incident CHF as definite, probable, or absent. Definite or probable CHF required heart failure symptoms, such as shortness of breath or edema; probable CHF required CHF diagnosed by a physician and the patient receiving medical treatment for CHF. Definite CHF required other criteria, such as pulmonary edema/congestion by chest x-ray; dilated ventricle or poor LV function by echocardiography or ventriculography; or echocardiography evidence of LV diastolic dysfunction. Participants who had only a physician diagnosis of CHF without any other evidence were classified as “no CHF.” Individuals with adjudicated definite or probable CHF were used in our analysis.

An incident cardiovascular event is a composite of adjudicated MI, stroke, resuscitated cardiac arrest, angina if followed by percutaneous coronary intervention or coronary bypass grafting, and CVD death. To make our results comparable to previously published data,6,14 ALVSD was defined as participants with LVEF <50%. Left ventricular mass index (LVMI) was calculated by using the formula LVMI = LV mass/body surface area (g/m2).

Statistical Analysis

Demographic characteristics of participants with ALVSD are reported as mean±standard deviation for continuous variables and as frequency or percentages for categorical variables in comparison with those without ALVSD during the MESA baseline examination. Kaplan-Meier analysis and log rank test were used to explore the association between ALVSD and incident CHF, CVD, and all-cause mortality. Cox proportional hazards analysis was also used to assess the association between ALVSD and outcomes (incident CHF, CVD, and all-cause mortality) in unadjusted and adjusted models adjusting for covariates including age, sex, race/ethnicity, diabetes mellitus, body mass index, systolic blood pressure, total cholesterol, high-density lipoprotein, triglycerides, cigarette smoking status, blood pressure medication use (angiotensin-converting enzyme inhibitors or β-blockers) and statin use. Interim MI was adjusted for in the adjusted Cox models for incident CHF and all-cause mortality. These covariates were chosen based on their associations in the present study and also in previous publications. The extended Cox model, which used the time-dependent variable approach, was used to test for the proportionality assumption. The discriminative ability of LVMI for incident CHF in the subset with ALVSD was evaluated in a Cox model by using the approach proposed by Pencina et al.20 and a time-dependent receiver-operating characteristic curve was constructed (at 4 years of follow-up) by using the approach by Heagerty et al21 (TDROC macro in SAS authored by Mithat Gonen).

Subsequently, the association between LVEF as a continuous variable and outcomes (incident CHF, CVD, and all-cause mortality) was explored by using Cox proportional hazards analysis in unadjusted and adjusted analyses adjusting for the covariates listed above. We estimated the discriminative ability of a Cox model with LVEF and LVEF+LVMI for incident CHF with the use of the approach by Pencina et al.20 Time-dependent receiver-operating characteristic (ROC) curves were constructed (at 4 years of follow-up) with LVEF/LVEF+LVMI in the model and the area under the ROC curves compared. A 2-tailed value of P<0.05 was considered significant. All statistical analyses were performed using SAS version 9.2 (SAS Institute, NC).
Results

From 6814 overall participants, 5004 participants with no clinical CVD, including valvular heart disease and CHF, underwent cardiac MRI for assessment of LVEF; 1.7% of the cohort had ALVSD. This was highest in blacks (2.6%) followed by whites (1.7%), Hispanic Americans (1.6%), and Chinese Americans (0.15%). After an average of 7.5 years of follow-up (maximum of 9 years), 112 participants had adjudicated incident CHF, 321 had an incident cardiovascular event, and 278 died of various causes.

MESA participants with ALVSD were more likely to be male and black, to have a high LVMI, and, in general, to have poor cardiovascular risk profiles in comparison with participants without ALVSD (Table 1). Use of statins, angiotensin-converting enzyme inhibitors, β-blockers, diuretics, and blood pressure medications did not differ between participants with and without ALVSD. Participants with ALVSD were not significantly obese (based on body mass index) in comparison with those without ALVSD (Table 1). In addition, participants with ALVSD who developed CHF during the follow-up period were not significantly obese in comparison with those who did not develop CHF.

### Table 1. Demographic Characteristics of Study Participants

<table>
<thead>
<tr>
<th>Variable</th>
<th>No ALVSD (n=4918)</th>
<th>ALVSD (n=86)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>61.5±10.1</td>
<td>62.4±10.7</td>
<td>0.432</td>
</tr>
<tr>
<td>Female</td>
<td>2607 (53.1)</td>
<td>15 (17.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>1923 (39.1)</td>
<td>34 (39.5)</td>
<td></td>
</tr>
<tr>
<td>Chinese</td>
<td>652 (13.3)</td>
<td>1 (1.2)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>1252 (25.4)</td>
<td>33 (38.4)</td>
<td></td>
</tr>
<tr>
<td>Hispanics</td>
<td>1091 (22.2)</td>
<td>18 (20.9)</td>
<td></td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27.7±4.9</td>
<td>28.2±4.9</td>
<td>0.353</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>125.4±21.3</td>
<td>129.7±22.3</td>
<td>0.06</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>71.7±10.3</td>
<td>76.9±11.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>503 (10.2)</td>
<td>15 (17.4)</td>
<td>0.07</td>
</tr>
<tr>
<td>Cholesterol, mg/dL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>194.4±35.3</td>
<td>191.2±39.6</td>
<td>0.414</td>
</tr>
<tr>
<td>LDL</td>
<td>117.2±31.3</td>
<td>115.8±32.5</td>
<td>0.685</td>
</tr>
<tr>
<td>HDL</td>
<td>51.2±15.0</td>
<td>46.8±13.1</td>
<td>0.006</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>131.1±85.1</td>
<td>140.6±88.9</td>
<td>0.306</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Never</td>
<td>2546 (51.9)</td>
<td>23 (27.7)</td>
<td></td>
</tr>
<tr>
<td>Former</td>
<td>1749 (35.6)</td>
<td>37 (44.6)</td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>612 (12.5)</td>
<td>23 (27.7)</td>
<td></td>
</tr>
<tr>
<td>LVMI, g/m²</td>
<td>77.5±15.6</td>
<td>103.1±29.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ln(CAC+1)</td>
<td>2.1±2.5</td>
<td>3.1±2.6</td>
<td>0.003</td>
</tr>
<tr>
<td>Framingham Risk Score</td>
<td>8.4±8.0</td>
<td>13.3±8.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Any diuretic</td>
<td>602 (12.3)</td>
<td>8 (9.3)</td>
<td>0.408</td>
</tr>
<tr>
<td>β-blocker use</td>
<td>421 (8.6)</td>
<td>5 (5.8)</td>
<td>0.364</td>
</tr>
<tr>
<td>Statin use</td>
<td>716 (14.6)</td>
<td>11 (12.1)</td>
<td>0.640</td>
</tr>
<tr>
<td>ACE inhibitor use</td>
<td>531 (10.8)</td>
<td>14 (16.3)</td>
<td>0.110</td>
</tr>
<tr>
<td>BP medication use</td>
<td>1541 (31.3)</td>
<td>24 (27.9)</td>
<td>0.496</td>
</tr>
<tr>
<td>LVEF</td>
<td>69.4±6.7</td>
<td>44.4±6.0</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Values displayed are mean±SD or numbers of patients (%). ALVSD indicates asymptomatic left ventricular systolic dysfunction; BMI, body mass index; BP, blood pressure; LDL, low-density lipoprotein; HDL, high-density lipoprotein; LVMI, left ventricular mass index; and ACE, angiotensin-converting enzyme.

Figure 1. A, Kaplan-Meier curves showing the event-free survival of participants with asymptomatic left ventricular systolic dysfunction (ALVSD) and those without ALVSD for incident congestive heart failure after a maximum of 9 years in MESA. B, Kaplan-Meier curves showing the event-free survival of participants with ALVSD and those without ALVSD for incident cardiovascular events after a maximum of 9 years in MESA. C, Kaplan-Meier curves showing the event-free survival of participants with ALVSD and those without ALVSD for all cause mortality after a maximum of 9 years in MESA. MESA indicates Multi-Ethnic Study of Atherosclerosis; CHF, congestive heart failure.
Whites with ALVSD were more likely to be males, but they were not likely to either have diabetes mellitus, be a cigarette smoker, or have hypertension in comparison with those without ALVSD. Blacks with ALVSD were more likely to be males, smoke cigarettes, and have hypertension, but they were not likely to have diabetes mellitus in comparison with those without ALVSD. Hispanics with ALVSD were more likely to be males, smoke cigarettes, and have hypertension, but they were not likely to have diabetes mellitus in comparison with those without ALVSD. The characteristics of Chinese with ALVSD are not provided because of a very small sample size.

**ALVSD and Outcomes**

In Kaplan-Meier analysis, participants with ALVSD had higher incident CHF, CVD, and all-cause mortality in comparison with participants without ALVSD (Figure 1A through 1C). Similarly, ALVSD was associated with higher incident CHF, CVD, and all-cause mortality in our unadjusted and adjusted models (Table 2). Similar estimates were obtained when a measure of socioeconomic status (level of education or income level) was forced into the model (data not shown).

Of participants with ALVSD, 18.6% developed incident CHF during the follow-up period. LVMI had a good discriminative ability for incident CHF in participants with baseline ALVSD (c-index [95% CI] 0.74 [0.56–0.85]). Area under the time-dependent ROC curve at 4 years of follow-up is as shown in Figure 2.

**LVEF and Outcomes**

In the current cohort, a 10% decrement in LVEF at baseline was associated with a significant increase in incident CHF, CVD, and all-cause mortality in unadjusted analysis. In the adjusted analysis, a 10% decrement in LVEF was associated with an increase in incident CHF and all-cause mortality but not CVD events (Table 3). LVEF was predictive of incident CHF. The c-index (95% CI) of LVEF alone was 0.60 (0.41–0.77). Adding LVMI to LVEF improved the discriminative ability for incident CHF (c-index [95% CI] 0.67 [0.51–0.84]). Comparison of the area under the time-dependent ROC curve at 4 years of follow-up for LVEF and LVEF+LVMI is as shown in Figure 3.

**Discussion**

The current study used the MESA cohort, composed of adults free of clinical CVD (including MI), to show that ALVSD is uncommon (prevalence of 1.7%) but nonetheless associated with significant morbidity (CHF and cardiovascular events) and mortality. LVMI improved the accuracy of LVEF for identifying individuals at risk for future incident CHF in the whole cohort and also had a good discrimination among individuals with ALVSD for incident CHF during the follow-up period.

The prevalence of ALVSD has been estimated to occur in 0.9% to 12.9% of the population.14 The wide range is due to differences in study design, setting, characteristics of the study sample, and LVEF threshold used to define ALVSD. The LVEF threshold used in previous studies ranged from 30% to 54%.14 McDonagh et al13 defined ALVSD as LVEF <30% in a cross-sectional survey of a selected urban cohort; in that study, the prevalence of ALVSD was 1.5%. Older men were more likely to have ALVSD, and 83% had evidence of ischemic heart disease as the underlying etiology. In another large practice-based multiethnic cohort, with the use of an LVEF threshold of 40%, the prevalence of ALVSD was 0.89%.15 In a subset of the Strong Heart Study (some of whom had prevalent CHD and clinical CHF), Devereux et

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**Table 2. Association of Asymptomatic Left Ventricular Systolic Dysfunction and Incident Cardiovascular Events, Congestive Heart Failure, and All-Cause Mortality: MESA**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No. of Events</th>
<th>Hazard Ratio (95% CI)</th>
<th>P</th>
<th>Hazard Ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure</td>
<td>112</td>
<td>11.97 (7.94–20.3)</td>
<td>&lt;0.0001</td>
<td>8.69 (4.89–15.45)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cardiovascular event</td>
<td>321</td>
<td>3.32 (1.98–5.58)</td>
<td>&lt;0.0001</td>
<td>2.21 (1.30–3.73)</td>
<td>0.003</td>
</tr>
<tr>
<td>All-cause mortality†</td>
<td>278</td>
<td>3.47 (2.03–5.94)</td>
<td>&lt;0.0001</td>
<td>2.14 (1.21–3.77)</td>
<td>0.009</td>
</tr>
</tbody>
</table>

MESA indicates Multi-Ethnic Study of Atherosclerosis; CI, confidence interval; BMI, body mass index; HDL, high-density lipoprotein; and ACE, angiotensin-converting enzyme.

*Adjusted model adjusted for age, sex, race/ethnicity, diabetes mellitus, BMI, systolic blood pressure, total cholesterol, HDL, triglycerides, cigarette smoking status, blood pressure medication use (β-blocker use, ACE inhibitor use), and statin use.

†For congestive heart failure and all-cause mortality, interim myocardial infarction was adjusted for in the adjusted model.
al\textsuperscript{10} reported that the prevalence of LV dysfunction in Indian Americans, defined as LVEF <54%, was 14%. Gottdiener et al,\textsuperscript{22} in an elderly cohort (mostly white) reported a prevalence of ALVSD of 0.8%. In the Framingham Heart Study, Wang et al\textsuperscript{14} showed that the prevalence of ALVSD (defined as LVEF <50%) in participants with and without previous MI was 3%. These studies are limited by differences in the LVEF threshold, small sample sizes, lack of racial diversity, and the use of echocardiography in estimating LVEF. In addition, almost all included participants with and without previous MI. The present study used a large multiethnic cohort and a more accurate measure of LVEF, cardiac MRI. We found that within population-based adults free of clinical CVD, the prevalence of ALVSD is 1.7% and is mostly in men and blacks.

There is no consensus on how to best identify individuals with ALVSD in the community or on the best, most cost-effective way to do so.\textsuperscript{14} The use of natriuretic peptides to screen for ALVSD in communities has yielded mixed results.\textsuperscript{23–25} Despite the relatively rare prevalence of ALVSD, its presence identified a group of participants at high risk for incident CHF, CVD, and all-cause mortality. Our data also suggest that individuals with ALVSD may not be more likely to have incident MI in comparison with those without ALVSD. Thus, these individuals may evade detection until late in their disease course, increasing the cost of therapy and worsening their prognosis.

Blacks with LV dysfunction appear to be at higher risk for progression of heart failure and death from any cause than similarly treated whites.\textsuperscript{26} In the present cohort, black men had the highest mean blood pressure and LVMI and were more likely to have ALVSD and develop clinical CHF in comparison with other MESA participants. This suggests that community-wide screening for ALVSD and preemptive interventions in hypertensive black men could be explored as an appropriate and cost-effective public health strategy to reduce the heart failure burden in our communities. Current debate should focus on how best to screen for ALVSD in individuals without clinical CVD, because our data suggest that these individuals are at higher risk for CHF, CVD, and all-cause mortality. More research is needed to determine whether preemptive interventions might reduce the risk for CHF, CVD, and death in this high-risk subgroup.

### Table 3. Association of a 10% Decrement in Left Ventricular Ejection Fraction at Baseline and Incident Cardiovascular Events, Congestive Heart Failure, and All-Cause Mortality: MESA

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No. of Events</th>
<th>Hazard Ratio (95% CI)</th>
<th>P</th>
<th>Hazard Ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure†</td>
<td>112</td>
<td>2.17 (1.82–2.63)</td>
<td>&lt;0.0001</td>
<td>2.13 (1.73–2.51)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cardiovascular event</td>
<td>321</td>
<td>1.22 (1.05–1.41)</td>
<td>0.007</td>
<td>1.12 (0.97–1.30)</td>
<td>0.104</td>
</tr>
<tr>
<td>All-cause mortality†</td>
<td>278</td>
<td>1.22 (1.05–1.41)</td>
<td>0.009</td>
<td>1.18 (1.01–1.37)</td>
<td>0.038</td>
</tr>
</tbody>
</table>

MESA indicates Multi-Ethnic Study of Atherosclerosis; CI, confidence interval; BMI, body mass index; HDL, high-density lipoprotein; and ACE, angiotensin-converting enzyme.

*Adjusted model adjusted for age, sex, race/ethnicity, diabetes mellitus, BMI, systolic blood pressure, total cholesterol; HDL, triglycerides, cigarette smoking status, blood pressure medication use (β-blocker use, ACE inhibitor use), and statin use.

†For congestive heart failure and all-cause mortality, interim myocardial infarction was adjusted for in the adjusted model.
Unlike echocardiography, cardiac MRI more accurately measures LV volumes from which LVEF is derived. In addition, other variables, such as LVMI, can be measured during the cardiac MRI scan. The present study shows that adding LVMI as part of a cardiac risk assessment would significantly improve the prognostic accuracy of LVEF in predicting incident CHF. Furthermore, in individuals with ALVSD, LVMI would discriminate accurately among those most likely to progress to clinical CHF. Studies in other cohorts are needed to replicate and extend our findings.

The strengths of this study include the large sample size, long duration of follow-up, adjudicated outcomes, use of cardiac MRI, the multiethnic nature of the cohort, and the fact that, unlike other studies, all participants were free of clinical CVD at baseline. However, given the relatively small prevalence of ALVSD, we did not explore stratified analysis because of limited statistical power. In addition, MESA is an observational study; although we adjusted for most covariates in our adjusted models, our results may still have been influenced by residual confounding. The cardiac MRI results including LVMI was made available to participants and their physicians (if participants consented). MESA does not include other ethnic groups such as American Indians and other Asian groups, with the exception of Chinese. In addition, the proportion of each ethnic group in MESA does not accurately reflect the proportion of each ethnic group of the US population. This limits the generalizability of our findings. At present, other cardiac MRI data, including left atrial size and structure, etc, likely to influence the development of CHF, cardiovascular events, and mortality are not available in MESA. Inclusion of such data and a more comprehensive analysis of the MESA cardiac MRI data may further inform risk prediction of these outcomes in this population. Last, because the present study involved individuals without clinical CVD at baseline, our results may not be applicable to other populations.

Conclusions

In a population-based multiethnic adult population free of clinical CVD, the prevalence of ALVSD was relatively low but carried significant risk for incident CHF, CVD, and all-cause mortality. LVMI may be a good screening tool for identifying individuals with ALVSD who would develop CHF. LVMI may also improve the discriminative ability of LVEF for identifying adults free of clinical CVD who are at risk for CHF.

Acknowledgments

The authors thank the investigators, the staff, and the participants of the MESA study for their valuable contributions. We also thank Karen P. Klein, MS, for editing this article.

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Disclosures

None.

References


**CLINICAL PERSPECTIVE**

Individuals with congestive heart failure still endure high morbidity and mortality despite recent advances in management. Studies have shown that early identification and treatment of individuals with the asymptomatic phase of heart failure could slow the progression to the symptomatic phase and reduce subsequent morbidity and mortality. However, data on the prevalence and prognosis of individuals with asymptomatic left ventricular systolic dysfunction (ALVSD) are limited. The few available data included ALVSD individuals with known myocardial infarction, a subgroup who most likely have had contact with healthcare professionals and have been prescribed the needed therapy. The public health impact of screening for this subgroup of ALVSD is likely to be of limited value. The present study used a large multiethnic cohort, free of clinical cardiovascular disease including myocardial infarction to show that ALVSD is uncommon (prevalence of 1.7%). This low prevalence, however, translates into several hundred thousand, if not millions of community-dwelling Americans. The highest prevalence was in blacks (2.6%) and the least in Chinese Americans (0.15%). Black men with hypertension had the highest prevalence of ALVSD. The risk of developing congestive heart failure was ≈9 times higher in individuals with ALVSD in comparison with those without ALVSD after 9 years of follow-up. Individuals with ALVSD were about twice as likely to die or develop a cardiovascular event as those without ALVSD during the follow-up period. Current debate and more research should focus on how best to screen for ALVSD in individuals without clinical cardiovascular disease, because our data suggest that these individuals are at higher risk for congestive heart failure, cardiovascular disease events, and all-cause mortality.
Prognosis of Individuals With Asymptomatic Left Ventricular Systolic Dysfunction in the Multi-Ethnic Study of Atherosclerosis (MESA)
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