Journal of the American College of Cardiology
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Published by Elsevier Inc.

Vol. 57, No. 17, 2011
ISSN 0735-1097/$36.00
doi:10.1016/j.jacc.2010.10.060

Regional Left Ventricular Myocardial Dysfunction as a Predictor of Incident Cardiovascular Events

MESA (Multi-Ethnic Study of Atherosclerosis)

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Objectives We sought to examine the prognostic value of subclinical left ventricular (LV) regional myocardial dysfunction (RMD) measured by magnetic resonance imaging (MRI) among asymptomatic individuals.

Background LV RMD, defined as segmental impairment in systolic wall thickening, predicts adverse events in patients with established cardiovascular disease. MRI is highly accurate for detecting subtle RMD, of which the prognostic significance in a large multiethnic asymptomatic population is not known.

Methods We used MRI to evaluate baseline regional LV myocardial function and prospectively followed a multiethnic (African American, Caucasian, Chinese, and Hispanic) population-based sample of 4,510 men and women without cardiovascular disease for a mean of 4.6 years. Regional myocardial dysfunction was defined as the presence of impaired systolic wall thickening (<10th percentile of segment-specific population distribution) in ≥2 contiguous LV segments within any given coronary artery territory.

Results Baseline prevalence of RMD was 25.6%. Heart failure developed in 34 (1.0%) and 30 (2.6%) participants without and with RMD, respectively ($p < 0.001$). After adjustment for demographics and traditional risk factors, RMD remained independently associated with incident heart failure (hazard ratio [HR]: 2.62; 95% confidence interval [CI]: 1.56 to 4.39; $p < 0.001$). The relationship persisted after further adjustment for biomarkers of reported association with cardiovascular disease and indexes of global LV systolic dysfunction and hypertrophy (HR: 1.80; 95% CI: 1.02 to 3.20; $p = 0.044$). Similarly, RMD independently conferred an increased risk for hard coronary events (myocardial infarction or death from coronary heart disease; HR: 1.75; 95% CI: 1.06 to 2.89; $p = 0.029$), the composite of hard coronary events and stroke (HR: 1.72; 95% CI: 1.16 to 2.56; $p = 0.005$), and all atherosclerotic cardiovascular events (HR: 1.50; 95% CI: 1.09 to 2.07; $p = 0.012$).

Conclusions Among an asymptomatic multiethnic American cohort, RMD is an independent predictor beyond traditional risk factors and global LV assessment for incident heart failure and atherosclerotic cardiovascular events. The clinical utility of early recognition of this subclinical phenotype deserves further investigation. (Multi-Ethnic Study of Atherosclerosis [MESA]; NCT00005487) (J Am Coll Cardiol 2011;57:1735–44) © 2011 by the American College of Cardiology Foundation

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Manuscript received July 2, 2010; revised manuscript received October 5, 2010, accepted October 19, 2010.

Abbreviations and Acronyms

CI = confidence interval
HR = hazard ratio
LAD = left anterior descending artery
LCx = left circumflex artery
LV = left ventricle
MRI = magnetic resonance imaging
RCA = right coronary artery
RMD = regional myocardial dysfunction
SWT = systolic wall thickening

Epidemiologic studies have reported that left ventricular (LV) hypertrophy and depressed ejection fraction predict development of heart failure in asymptomatic individuals (1–4). These global alterations in LV structure and function have since been recognized as important subclinical therapeutic targets in the effort to delay progression to symptomatic heart failure (5,6). However, the unfavorable progressive nature of heart failure underscores the importance of better defining its earlier subclinical manifestations. Because coronary artery disease is the major cause of LV dysfunction (7,8), it is conceivable that as with coronary atherosclerosis, incipient myocardial dysfunction would commence as a regional process antedating global LV dysfunction.

The assessment of systolic wall thickening (SWT) is a validated technique for evaluating regional LV myocardial function (9). Magnetic resonance imaging (MRI) is the reference standard for assessing regional LV structure and function (10,11). In this study, we used the data collected from the MESA (Multi-Ethnic Study of Atherosclerosis) cohort to evaluate the relationship between subclinical regional myocardial dysfunction (RMD), detected by MRI as reduced SWT, and incident cardiovascular events in a large, multiethnic, asymptomatic population without baseline clinical cardiovascular disease.

Methods

Study design and participants. MESA was a multicenter, prospective cohort study designed to examine the prevalence, correlates, and progression of subclinical cardiovascular disease. Details of its rationale and methodology have been published (12). Briefly, the MESA cohort comprised 6,814 men and women and was a population-based sample from 6 communities (Baltimore County, Maryland; Chicago, Illinois; Forsyth County, North Carolina; Los Angeles County, California; Northern Manhattan and the Bronx, New York; and St. Paul, Minnesota) recruited between 2000 and 2002. Eligible participants were between 45 and 84 years of age from 4 self-identified ethnicities (African American, Caucasian, Chinese, and Hispanic) without known clinical cardiovascular disease at enrollment. The study was approved by the institutional review board of each center, and all participants provided written informed consent.

Cardiac MRI. Consenting eligible participants underwent cardiac MRI at enrollment. The complete MRI protocol was detailed elsewhere (13,14). Briefly, MRI was performed using commercially available 1.5-T scanners. After acquisition of scout images, 2- and 4-chamber cine images were obtained. Short-axis cine images covering the entire LV were then acquired from above the mitral valve plane to LV apex using segmented k-space, electrocardiogram (ECG)-triggered flow-compensated fast gradient echo sequence (time to repetition/echo time: 8 to 10 ms/3 to 5 ms, flip angle: 20°, slice thickness/gap: 6 mm/4 mm, in-plane resolution: 1.4 to 1.6 mm × 2.2 to 2.5 mm, temporal resolution: 46 ± 8 ms).

Using Q-MASS software (version 4.2, Medis, the Netherlands), the endocardial and epicardial borders of the LV were traced semiautomatically at end-systole and end-diastole on short-axis cine images. Regional wall thickness was determined by Q-MASS, which uses the validated modified centerline method incorporating a 3-dimensional analytic approach (15). Systolic wall thickening was calculated as the percentage change in wall thickness from end-diastole to end-systole: SWT (in %) = (ESWT − EDWT)/EDWT × 100%, where ESWT indicates end-systolic wall thickness and EDWT indicates end-diastolic wall thickness, and was measured separately for 6 equally partitioned segments on each of the 3 short-axis planes (apex, mid-cavity, and base) of the LV. The 6 apical segments as partitioned and quantified were condensed into 4 segments by combining, respectively, the 2 adjacent septal and lateral wall segments for consistency with published segmentation definition (16). Because there were segmental variations in SWT measured by MRI among MESA participants without traditional risk factors, abnormal values of SWT on MRI were expected to be segment specific. Accordingly, abnormal SWT in a specific segment was defined a priori as below the 10th percentile of its segment-specific distribution among a healthy reference MESA population without obesity, hypertension, or diabetes (n = 1,778; age 59 ± 10 years; female 49.9%; African American 16.3%, Caucasian 45.9%, Chinese 17.0%, Hispanic 20.8%). LV RMD was defined as the presence of abnormal SWT in ≥2 contiguous segments within the same coronary arterial territory. The assignment of LV segments to coronary territories (left anterior descending [LAD], left circumflex [LCx], and right coronary artery [RCA]) followed published recommendations (16). The means ± SD of the segment-specific abnormal segmental SWT threshold of the LAD, RCA, and LCx segments were 22 ± 9%, 24 ± 14%, and 28 ± 10%, respectively. A participant was considered as having RMD if it was present in at least 1 coronary territory. Details on image analysis, data quality control, calculations for LV ejection fraction and mass, and reproducibility of these global LV measurements have been published (14). For regional LV myocardial function in accordance with the 16-segment model (16), reliability for single segmental measurement of SWT (intraobserver and interobserver intraclass correlation coefficients of 0.73, 95% confidence interval [CI]: 0.69 to 0.76; and 0.68, 95% CI: 0.63 to 0.72, respectively) and its overall variability (intraobserver and