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LV Mass as a Predictor of CVD Events in Older Adults With and Without Metabolic Syndrome and Diabetes

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ABSTRACT

OBJECTIVES The purpose of this study was to examine the prognostic significance of left ventricular (LV) mass for cardiovascular disease (CVD) events in older adults with and without metabolic syndrome (MetS) and diabetes mellitus (DM).

BACKGROUND MetS and DM are associated with increased CVD risk, but it is unclear in these groups whether subclinical CVD as shown by increased LV mass improves risk prediction compared to standard risk factors in older individuals.

METHODS We studied 3,724 adults (mean 72.4 ± 5.4 years of age, 61.0% female, 4.4% African-American) from the Cardiovascular Health Study who had MetS but not DM or had DM alone or had neither condition. Cox regression was used to examine the association of LV mass, (alone and indexed by height and body surface area [BSA]) as determined by echocardiography, with CVD events, including coronary heart disease (CHD), stroke, heart failure (HF), and CVD death, as well as total mortality. We also assessed the added prediction, discriminative value, and net reclassification improvement (NRI) for clinical utility of LV mass compared to standard risk factors.

RESULTS Over a mean follow-up of 14.2 ± 6.3 years, 2,180 subjects experienced CVD events, including 986 CVD deaths. After adjustment for age, sex and standard risk factors, LV mass was positively associated with CVD events in those with MetS (hazard ratio [HR]: 1.4, $p < 0.001$) and without MetS (HR: 1.4, $p < 0.001$), but not DM (HR: 1.0, $p = 0.62$), with similar findings for LV mass indexed for height or BSA. Adding LV mass to standard risk factors moderately improved the prediction accuracy in the overall sample and MetS group from changes in C-statistics ($p < 0.05$). Categorical-free net reclassification improvement increased significantly by 17% to 19% in those with MetS. Findings were comparable for CHD, CVD mortality, and total mortality.

CONCLUSIONS LV mass is associated with increased CVD risk and provides modest added prediction and clinical utility compared to standard risk factors in older persons with and without MetS but not with DM. (J Am Coll Cardiol Img 2015;8:1007–15) © 2015 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

BMI = body mass index
BSA = body surface area
CHD = coronary heart disease
CVD = cardiovascular disease
DM = diabetes mellitus
LDL-C = low-density lipoprotein cholesterol
LV = left ventricular
MetS = metabolic syndrome
NRI = net reclassification index

Older persons with metabolic syndrome (MetS) and diabetes mellitus (DM) are more likely to have subclinical atherosclerosis and are at greater risk of cardiovascular disease (CVD) events (1–3) and mortality (4). Previous studies have identified left ventricular (LV) mass independently predicts CVD events (5–7). Although the association of MetS (5) and the number of MetS risk factors (7) with LV mass has been demonstrated, and DM adversely impacts hypertrophic remodeling through increased LV mass and larger cavity dimensions (8), there are limited data examining the value of LV mass for predicting CVD events in persons with MetS or DM. Although a smaller previous study compared the prognosis of increased LV mass in diabetic and nondiabetic hypertensive individuals (9), to our knowledge, no population-based study has compared the prognostic significance of LV mass in persons with and without MetS and DM. Although

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DM is a well-known risk factor for coronary heart disease (CHD), it has been shown by some studies to confer a lower risk of subsequent cardiac complications than CHD (10). There is a need to better identify what other screening methods for subclinical CVD can further improve risk prediction in persons with MetS and DM (11). For instance, it is known such persons demonstrate a greater extent of myocardial ischemia (12) and coronary calcium (13,14), with the latter providing prognostic value for CVD events (15). Whether subclinical CVD as shown by higher LV mass provides significant incremental prognostic value in predicting CVD events compared to standard risk factors under these conditions is unclear, especially in those with MetS and DM and in older persons who have a longer exposure to these conditions. Such information would be useful to judge the utility of LV mass assessment in these groups.

This study examined whether readily available echocardiographic measurements of LV mass added to standard CVD risk factors in the prediction of CVD events in older persons with and without MetS or DM. Our analysis addressed the question of whether there is a role for these readily available measurements in risk stratification for these populations.

METHODS

STUDY SAMPLE AND RECRUITMENT. Our analyses included 3,724 adults 65 to 95 years of age from the Cardiovascular Health Study (CHS), a prospective U.S. National Institutes of Health-sponsored study of older adults, which studied risk factors and subclinical measurements of CVD and their outcomes. Initial enrollment from 1989 to 1990 recruited 5,201 participants, whereas a second cohort of 687 African-American participants was recruited from 1992 to 1993. Specifically, of the initial cohort of 5,201 subjects, the current analysis included CHS participants who had baseline measurements of LV mass from 2-dimensionally directed M-mode echocardiography as well as information for incidence of CVD events; patients with prior CVD events were excluded. Participants were initially recruited from Heath Care Financing Administration Medicare eligibility lists and other household members from 4 U.S. geographic regions: Forsyth County, North Carolina; Sacramento County, California; Washington County, Maryland; and Pittsburgh, Pennsylvania. Participant consent was obtained during baseline examination. Baseline examination data consisted of medical history, physical examination, and fasting blood analyses. The methodology and design of CHS have been previously reported (15). Up to 22 years of follow-up data were available through June 30, 2004, with vital status known for all 3,724 subjects included in the study, with complete risk factor data (no persons lost to follow-up). This project was exempt from Institutional Review Board review due to the use of de-identified data.

MEASUREMENTS. Risk factors were measured by standardized methodology, as previously described, and included systolic and diastolic blood pressure (BP), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein-cholesterol (HDL-C), triglycerides, glucose, waist circumference, and body mass index (BMI) (15). Subjects were classified as having MetS without DM (according to American Heart Association/National Heart, Lung, and Blood Institute [AHA/NHLBI] criteria], or DM, or neither condition. MetS (n = 1,178) without DM was defined, according to the AHA/NHLBI definition (16), as having any 3 of the following 5 criteria: elevated BP (≥130 systolic or ≥85 mm Hg) or treatment for hypertension; low HDL-C (<40 mg/dl in males or <50 mg/dl in females); elevated triglycerides (≥150 mg/dl); increased waist circumference (>88 cm [35 inches] in females or >102 cm [40 inches] in males); or impaired fasting glucose (100 to 125 mg/dl). DM (n = 485 subjects) was defined as having a fasting glucose concentration of ≥6.9 mmol/l (126 mg/dl), taking oral hypoglycemic medication, or self-reported use of insulin. Subjects with neither condition (n = 2,061) were also included in our analyses.