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LV Mass Independently Predicts Mortality and Need for Future Revascularization in Patients Undergoing Diagnostic Coronary Angiography

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ABSTRACT

OBJECTIVES The goal of this study was to assess associations between left ventricular (LV) mass, all-cause mortality, and need for revascularization in patients undergoing coronary angiography.

BACKGROUND LV hypertrophy is associated with adverse cardiovascular outcomes in healthy subjects. However, its influence in those with known or suspected coronary artery disease is poorly understood.

METHODS A total of 3,754 patients (mean age 59.3 ± 13.1 years) undergoing invasive coronary angiography and cardiac magnetic resonance (CMR) (mean interval 1.0 ± 1.5 months) were studied. LV mass and volumes were determined from cine images and indexed to body surface area. Analyses were adjusted for CMR variables, medical comorbidities, and severity of coronary artery disease (Duke Jeopardy Score) and were stratified to LV function.

RESULTS At a median of 44.9 months, 315 patients (8.4%) died and 168 patients (4.5%) underwent revascularization. Multivariable analysis showed that each 10 g/m^2 increase in LV mass index was associated with a 6% greater risk of mortality (hazard ratio: 1.06; 95% confidence interval [CI]: 1.01 to 1.11; $p = 0.02$) and a 10% greater need for revascularization (hazard ratio: 1.10; 95% CI: 1.04 to 1.17; $p < 0.01$). According to pre-defined thresholds, moderate to severe hypertrophy was associated with a 1.7-fold risk of mortality (95% CI: 1.2 to 2.3) and 1.8-fold need for revascularization (95% CI: 1.18 to 2.67). These findings were predominantly observed in those with a left ventricular ejection fraction >35% with respective hazard ratios of 2.93 (95% CI: 1.92 to 4.47) and 2.20 (95% CI: 1.21 to 3.98).

CONCLUSIONS LV mass index is an independent predictor of all-cause mortality and need for revascularization. This finding establishes relevance for LV mass measurements in clinical decision-making surrounding both the need and timing of revascularization in this population. (J Am Coll Cardiol Img 2017;■:■–■) © 2017 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

2D = 2-dimensional

CAD = coronary artery disease

CI = confidence interval

CMR = cardiac magnetic resonance

GRE = gradient echo

HR = hazard ratio

IQR = interquartile range

LGE = late gadolinium enhancement

LV = left ventricular

LVEDV = left ventricular end-diastolic volume

LVEF = left ventricular ejection fraction

LVH = left ventricular hypertrophy

LVMI = left ventricular mass index

SSFP = steady-state free precession

Left ventricular (LV) mass is a recognized marker of cardiovascular risk (1–4). In the Framingham Heart Study, left ventricular hypertrophy (LVH) was an independent predictor of cardiovascular mortality and morbidity in subjects without coronary artery disease (CAD) after adjustment for hypertension (5,6). Among patients with established CAD, limited data have emerged. Although the Heart and Soul Study showed that LVH was associated with sudden cardiac death in this population, this study used 2-dimensional (2D) echocardiographic estimates of LV mass (7). Such estimates are recognized to be less reproducible than those by cardiac magnetic resonance (CMR) (8,9) due to a reliance on geometrical assumptions that may not be valid in some patients (10). Three-dimensional echocardiographic techniques have overcome this limitation and provide estimates very similar to those available from CMR (11); however, prognostic studies have yet to be reported using this technique.

The role for CMR in patients with CAD is increasing due to expanding evidence for robust risk stratification of ischemic and arrhythmic events (12,13). Despite important insights provided by MESA (Multi-Ethnic Study of Atherosclerosis), which performed CMR in healthy subjects, very little is known regarding the prognostic role of LV mass in those with cardiovascular disease (14). A single study, reported by Krittayaphong et al. (15), calculated the left ventricular mass index (LVMI) from gradient echo (GRE) cine images in patients referred for CMR and found associations with major cardiovascular events. However, only 26% of this referral population underwent coronary angiography, limiting any exploration of interactions between CAD burden, cardiovascular events, and LV mass. Accordingly, the relevance of LV mass in the clinical decision-making of patients with CAD remains poorly understood.

To address this knowledge gap, we used a large, well-defined cohort of patients undergoing diagnostic coronary angiography for known or suspected CAD and studied associations between LVMI, as measured by contemporary (steady-state free precession [SSFP]) cine CMR, and the primary outcome of all-cause mortality. The secondary outcome measure of need for revascularization was incrementally studied. Adjustments were performed for both CAD burden (using the Duke Jeopardy Score) and severity of LV dysfunction (using categories of left ventricular ejection fraction [LVEF]).

METHODS

STUDY POPULATION. The patient population was identified from the APPROACH (Alberta Provincial Project for Outcomes Assessment in Coronary Heart Disease) registry, a prospective registry of patients undergoing diagnostic coronary angiography. Database and data collection methods have been previously described in detail (16). In brief, the data collected include demographic characteristics, cardiac risk factors, major clinical comorbidities, previous cardiac events, indication for angiography, coronary anatomy (segmental coding), cardiac medications at the time of angiography, and future clinical outcomes. For the present analysis, we included patients enrolled in the registry between April 1, 2005, and March 30, 2013, with a minimum of 24 months of clinical follow-up and having a CMR examination performed within 3 months of their index angiogram.

All patients provide informed consent at the time of enrollment into the APPROACH registry for their health information to be used for research purposes. Medical comorbidities, including hypertension, are determined at the time of enrollment into the APPROACH registry and represent the attending physician's interpretation of medical comorbidities, as described in the medical record. This study was approved by the Conjoint Health Region Ethics Board at the University of Calgary.

CMR IMAGING AND ANALYSIS. All CMR examinations were performed by using a 1.5-T system (MAGNETOM Avanto, Siemens Healthcare, Erlangen, Germany). Standard cine SSFP imaging was performed for the evaluation of LV volume, function, and mass. Quantitative image analysis was performed by experienced readers using commercially available software (cvi^{42}, Circle Cardiovascular Imaging Inc., Calgary, Alberta, Canada). Cine images underwent semi-automated contour tracing to obtain the left ventricular end-diastolic volume (LVEDV), LV end-systolic volume, LVEF, and LV mass. The latter was determined at end-diastole without the inclusion of papillary muscles. All volume and mass measures were indexed to body surface area.

Using previously published CMR reference values, categories of LVH were defined a priori relative to age and sex-matched control subjects; mild LVH was defined as >2 SDs and moderate to severe LVH as >4 SDs above respective mean reference values, as shown in Online Table 1 (17). Although several SSFP-based studies exist describing similar normal reference values for LV mass (18), for maximal

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