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EDITORIAL COMMENT

Left Ventricular Size, Mass, and Shape

Is the Sum Greater Than the Parts?*

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Alterations in cardiac structure and function have long been recognized as markers of heightened risk for cardiovascular events. Indeed, even before the advent of noninvasive imaging, electrocardiographic left ventricular hypertrophy (LVH) was identified as one of the earliest "factors of risk" for cardiovascular morbidity and mortality by the Framingham Heart Study investigators, alongside hypertension, hyperlipidemia, smoking, and obesity (1,2). Concurrently, Linzbach (3) used pathology samples to describe 2 distinct patterns of LVH, reflecting the impact of volume and pressure loading on LV muscle mass and chamber size: eccentric (volume) hypertrophy, characterized by increased chamber size and residual volume; and concentric (pressure) hypertrophy, with preserved chamber size and residual volume. Hammermeister et al. used left ventriculography to demonstrate the prognostic importance of LV volumes (4) and ejection fraction (5) for survival in patients with valvular and coronary diseases, respectively.

The invasive nature of these assessments necessitated investigations in only a highly select patient population. The development of echocardiography and, subsequently, other imaging techniques provided a noninvasive and accurate method with which to assess cardiac size and function and made broader population screening feasible. Unlike electrocardiographic LVH, echocardiography also allowed for quantification of LV mass, which proved far more sensitive than the electrocardiogram and still highly prognostic (6,7). The subsequent efficacy of angiotensin-converting enzyme inhibitors in persons with chronic or post-myocardial infarction LV systolic dysfunction without overt heart failure (HF) in the SOLVD (Studies of Left Ventricular Dysfunction) Prevention (8) and SAVE (Survival and Ventricular Enlargement) (9) trials provided impetus to screen asymptomatic persons for systolic dysfunction (10–12). These studies also reinforced the prognostic importance of both LV enlargement (13) and hypertrophy (14). Importantly, subsequent investigations demonstrated that both regression of LVH (15) and prevention or reversal of LV enlargement (16–18) is associated with improved clinical outcomes.

While Linzbach (3) described patterns of hypertrophy on the basis of LV mass and volume, the relationship between LV wall thickness and cavity dimension, assessed noninvasively and termed the relative wall thickness (RWT), has been used to further refine risk stratification among patients without hypertrophy. Ganau et al. (19) identified different patterns of ventricular shape within the hypertensive population by incorporating RWT with LV mass (19), while Koren et al. (20) demonstrated the prognostic implications of elevated RWT but normal LV mass for hypertensive patients. The American Society of Echocardiography adapted these patterns on the basis of LV mass and RWT to define LV geometry (21), which have been used to assess a variety of patient populations. Although these geometric patterns have been described in patients with cardiovascular risk factors, prevalent coronary disease,

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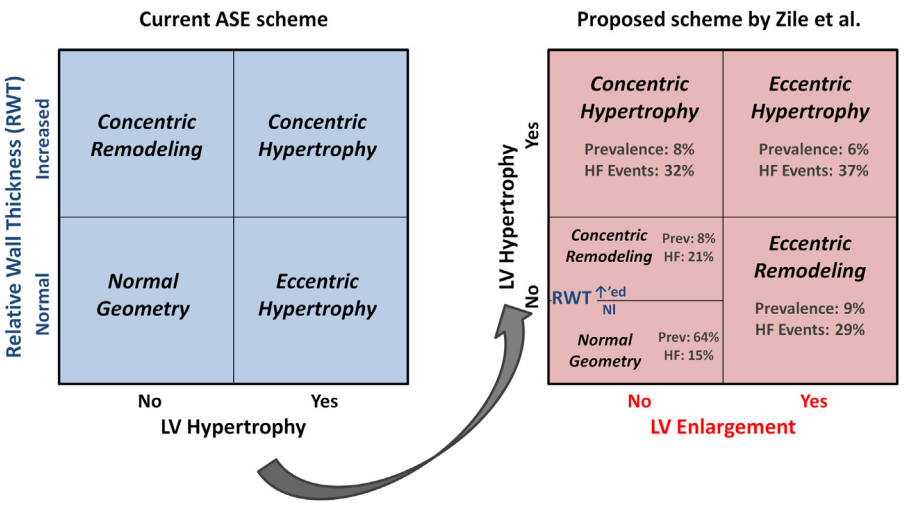

FIGURE 1 Comparison of LV Geometry Classification Schemes

Left ventricular (LV) geometry classification scheme outlined in the American Society of Echocardiography's (ASE) chamber quantification guidelines (12) is compared with that proposed by Zile et al. (27). Prevalence (Prev) denotes the approximate population prevalence in the Cardiovascular Health Study. Heart failure events (HF Events) denotes the approximate percentage of participants in that category who experienced incident HF during study follow-up (adapted from Zile et al. [27]). ASE criteria classifies on the basis of the presence or absence of LV hypertrophy (LVH) and elevated relative wall thickness (RWT). In contrast, the proposed classification by Zile et al. (27) is based on the presence or absence of LV enlargement and LV H, and RWT is valuable primarily for subclassifying persons with normal LV size and mass. Compared with the ASE criteria, the proposed scheme requires normal LV chamber dimension for concentric remodeling and concentric hypertrophy and an enlarged LV chamber dimension for eccentric hypertrophy.

and HF with preserved ejection fraction, the prognostic relevance of increased RWT in the absence of LVH (concentric remodeling) has been inconsistent (22–26).

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In this issue of *JACC: Heart Failure*, Zile et al. (27) report their prospective analysis of 3,181 elderly participants with predominantly preserved left ventricular ejection fraction (LVEF) and without prevalent HF from the CHS (Cardiovascular Health Study) to assess the prognostic implications of a novel LV geometry grading scheme that combines LV enlargement, hypertrophy, and concentric remodeling in a hierarchical fashion. All echocardiograms were centrally analyzed, and cardiovascular endpoints were adjudicated. With 13 years' of follow-up during which a sizeable number of participants experienced incident HF or died, the analysis represents an important contribution. As expected, LV enlargement and LV hypertrophy were each individually associated with greater risk of incident HF and death. The risk associated with each of these 2 measures was additive, with the worst prognosis in those who had both LVH and enlargement. This study is robust and emphatically reaffirms the prognostic importance of LV enlargement and hypertrophy for incident HF and mortality. Despite preserved LVEF in most of the participants, these alterations in LV structure were powerfully prognostic for both incident HF and death beyond standard clinical risk factors and renal function.

This analysis also challenges the widespread scheme that classifies LV geometry on the basis of the presence or absence of LV hypertrophy and increased RWT (**Figure 1**). High RWT was informative only for subsequent cardiovascular risk among participants with normal LV size and mass, although this finding was of borderline significance after multivariate adjustment with a wide 95% confidence interval of 0.95 to 1.80 (see Table 3 in Zile et al. [27]), despite being the largest participant subgroup. The authors provide some indication of the reclassification of participants by using this novel classification scheme compared with the LV geometry classified on the basis of LV mass and RWT. Although provocative, a comprehensive assessment of the incremental value of this new classification scheme, including quantitative reclassification metrics, is not provided. Understanding this incremental benefit is necessary before clinicians can be asked to alter their established practice.

Importantly, this well-designed analysis confirms the prognostic importance of easily assessable noninvasive measures of LV structure and function, with any departure from normal LV structure associated with heightened cardiovascular risk beyond standard clinical risk factors. The patterns of hypertrophy described by Linzbach (3) stand the test of time, as does the further refinement of risk by RWT among those without LV hypertrophy or LV enlargement, shown by Koren et al. (20). Whether the hierarchical scheme to integrate these measures presented by Zile et al. (27) will provide the clinician with information beyond what we already have will require additional studies assessing the incremental value of the proposed scheme in patient populations across the spectrum of cardiovascular disease.

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