Reframing Patterns of Left Ventricular Hypertrophy Using Cardiac MRI

“Brother, Can You Spare a Paradigm?”

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Left ventricular hypertrophy (LVH) is generally considered to be an adaptive response that allows for normal ejection fraction despite abnormal pressure and/or volume load. However, this adaptation is associated with increased cardiac morbidity and mortality, including acute myocardial infarction, heart failure, arrhythmia, and stroke. Insight into the prevalence and consequences of LVH and response to treatment was made possible by the advent of echocardiography, which has been used to measure left ventricular mass for the past 3 decades in cross-sectional and epidemiological studies and serially in clinical trials. Cardiac MRI is accepted as a more precise means to measure LV mass and is being used in large-scale clinical and epidemiological studies. The article by Khouri et al in this issue of Circulation: Cardiovascular Imaging reflects this maturation of cardiac MRI; these authors used MRI-derived mass and volume to refine the paradigm of LV hypertrophic response in a large (2803 subjects) cross-sectional study of participants in theDallas Heart Study.

To understand the importance of this work, some context should be provided. Hypertrophy, defined as an increase in LV mass in relation to body size (ie, high LV mass index), is produced by an increase in chamber size, an increase in wall thickness, or both. For decades, concentric hypertrophy was considered the appropriate, even universal, response to a pressure load, as the heart adapted to maintain normal stroke volume despite high systolic pressure.

In 1992, Ganau et al proposed a simple quantitative classification paradigm based on their study of 165 untreated hypertensive patients and 125 matched control subjects, and, importantly, established partition values for these geometric categories (Figure). Categorization was based on the presence of increased LV mass index (LVH: yes/no) and the ratio of LV wall thickness to LV chamber size—the relative wall thickness (RWT). If RWT was high, the term concentric was applied; if not, the term eccentric was used. Despite the conventional wisdom that pressure overload results in an abnormally high absolute or RWT, the majority of the hypertensive patients had neither hypertrophy nor concentric geometry. Another surprising finding was that eccentric LVH was 3 times more common than concentric LVH. Finally, an intriguing new phenotype was described—concentric remodeling—comprising high RWT without an absolute increase in mass index.

The paradigm developed by Ganau has proven to be robust and conceptually appealing as evidenced by its wide use in hypertensive heart disease and applications to other adult and pediatric conditions, including obesity, metabolic abnormalities, storage disorders, valvular disease, renal insufficiency, respiratory disease, and infectious diseases. There has been investigation into the relationship between geometry and outcome and studies of the physiology of concentric remodeling, which has been shown to be associated with low-to-normal cardiac output and reduced midwall shortening, markers of subtly impaired systolic function. Similar considerations of geometry have provided insight into LV structure and function in heart failure.

The major limitations of the Ganau paradigm have been the accuracy and reproducibility of echocardiographic measurements, the geometric assumptions on LV geometry needed to calculate volume from linear dimensions, and the lack of a specific category identifying patients with concurrent LV hypertrophy and dilated LV chamber. These limitations provide the rationale for the present study of Khouri et al, whose MRI-based volumetric analysis overcomes the limitation of the use of linear parameters to calculate volume. Their major findings are that (1) concentric or eccentric LVH can each be subclassified into 2 subgroups, yielding 4 distinct geometric patterns; (2) most of the subjects classified as having eccentric hypertrophy have a magnification of the normal heart (which the authors term “indeterminate” LVH), a condition associated with normal functional indices and seemingly low cardiovascular risk. The authors also confirm the strong association between obesity and concentric LVH, helping to dispel the notion that LVH in this condition is exclusively eccentric. Finally, the authors suggest classifying LVH based not on the RWT but rather on the independent changes occurring to the 2 parameters.

This work suggests the hypothesis that the adaptation of the LV is the result of the independent increase in wall thickness and/or chamber dimension rather than the effect of their interaction (eg, the RWT) to compensate for increased wall stress. The implication that LV remodeling may be influenced by the neurohumoral axis is supported by the
observation that in patients with diabetes and/or the metabolic syndrome, significant LVH can be observed also in the absence of clear-cut hypertension, that is to say that it is not completely related to normalizing load. Besides relying on the more accurate structural data afforded by MR, the proposed classification emphasizes that subjects with dilation probably are individuals at extremely high risk, as evidenced by their higher troponin and BNP levels and lower mean ejection fraction.

Does the article by Khouri et al warrant revising our current geometric paradigm? Limitations are that the 2 dilated LVH subcategories are relatively uncommon, comprising only 2.3% of the population, and that these were derived not from a rigorously defined normal population. Accordingly, it is likely that dilated LVH might not represent a true adaptation to increased load but is a sign that these individuals have remodeled to a point where hypertrophy is no longer adequate to maintain ejection performance, because of coronary disease or cardiomyopathy. Work by Vasan et al showed that patients with evidence of LV dilation are at high risk of developing future heart failure, and preliminary work on hypertensive subjects enrolled in the LIFE study suggests that progressive dilation of LVH precedes overt heart failure, even in the absence of incident myocardial infarction.

It should also be noted that the occurrence of LVH in the population described by Khouri et al is markedly higher (32%) compared with previous reports, especially considering the relatively low prevalence of arterial hypertension (33%). This probably is the result of the study design’s intentional oversampling of African-Americans and the overall high prevalence of obesity; both factors have been shown to strongly affect cardiac geometry, as reported by Gottdiener et al. Thus, whether the partition values applied in this study are suited to answer. It is hoped that further study will leverage the ability of MRI to characterize the composition of the ventricular wall, especially given the work suggesting that at similar levels of cardiac hypertrophy, neurohumoral tone might cause myocardial alterations at the sarcomeric and extracellular scaffold levels and alter the ratio of muscle to interstitial fibrosis. In chronic renal disease, for example, at similar levels of LV mass, the amount of cardiac fibrosis is significantly higher than in hypertensive patients without chronic renal disease, which may help explain impairment in systolic function and higher cardiovascular risk. A more refined model of LV adaptation might also permit better understanding of which hypertensive patients are at high enough risk for adverse outcomes to warrant early targeted therapy, long before dilation and or even subclinical dysfunction occur.

Disclosures

None.

References

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