Segmental variation in left ventricular (LV) wall thickness is important in characterizing hypertrophic cardiomyopathy, post-infarction remodeling, and myocardial noncompaction. In each of these disorders, cardiac magnetic resonance (CMR) has greatly extended our understanding due to its ability to comprehensively assess LV structure, function, and myocardial composition over the entire LV chamber and myocardial volumes. In this issue of *JACC*, de Marvao et al. (1) combine CMR with computational anatomy techniques to demonstrate that segmental wall thickness variation of lesser degree is also prevalent in normotensives, pre-hypertensives, and hypertensives. Though the patterns are similar in each category, the degree of variation and the relationship of wall thickness to systolic blood pressure (BP) vary. However, the general theme is that wall thickness and relative wall thickness tend to increase in parallel with BP in each subset with the greatest effects seen in the septum and anterior wall. The effect on relative wall thickness is greatest in mid-LV in normotensives and pre-hypertensives but shifts to basal segments of the septum and anterior wall in overt hypertensives.

The data supporting these fundamental observations, obtained using novel methods including an approach to automated image segmentation and a normalized 3-dimensional atlas approach, are convincing and the concept may have important implications. Atlas-based approaches have been successful in characterizing neurological disease (2) and are becoming more widespread in the evaluation of subtle changes in cardiac morphology due to subclinical and clinical disease (3–5). In the current paper, the methods are important because the findings have been overlooked in earlier studies, likely due to the increased robustness of determination of local LV wall thickness and curvature.

However, the pathophysiologic basis and clinical implications of the findings are not clear. The investigators imply, beginning with their title ("Precursors of the Hypertensive Heart Phenotype Develop in Normotensive Adults") that the results reflect a process of evolution from normal to pre-hypertensive to hypertensive LV structure and function, but this is just a cross-sectional study and does not depict the serial evolution of normal ventricles in response to rising BP. They also use the LaPlace analysis of segmental wall stress to relate wall thickness to myocardial afterload and show, as expected, that thicker segments in the septum and anterior wall have normal wall stress values, whereas thinner segments elsewhere have elevated wall stress because both types of segment are exposed to the same BP. They suggest that this reflects intrinsic differences in adaptive remodeling responses of the myocytes in these regions. However, this wall stress approach simply captures geometric determinants of myocardial afterload and requires the assumption that the myocardium is a thin-walled, linearly elastic, physically uniform material. This is not the case, due to the helical orientation of myocytes and their systematic differences in orientation from endocardium to epicardium, as well as the presence of a complex myocardial interstitium, constituting up to over 25% of myocardial volume in normotension, and more in many disease states. Ideally, to estimate actual wall stress, or tension per unit cross-sectional area of...
myocardium, one would need to determine the physical stiffness, active tension, and deformability of myocardium at each locus in the LV. Finite element models of cardiac mechanics are becoming available for this purpose (6), and it is conceivable that CMR elastography may provide complementary information (7). However, for now, the link between segmental wall stress and regional hypertrophy is unclear. Other limitations include the fact that the BP values used were obtained outside the CMR magnet, whereas actual LV pressure at the time of imaging is unknown. Anyone who has monitored patient BP before and during CMR knows all too well how variable and labile it can be.

That said, this study makes an important, novel point. We clearly need to better understand the phenomenon of segmental thickness variation in normotension, pre-hypertension, and overt hypertension and its response to the development of hypertrophy. We also need to understand the relationship of this phenomenon to regulation of overall LV mass, mass index, and mass/volume ratio. Another important question is whether there is a relationship between segmental thickness findings in normotensives and the likelihood of future hypertension in those patients. In addition, attention needs to be paid to sex differences in wall thickness variability, because, as illustrated in data from the Framingham Heart Study and MESA (Multi-Ethnic Study of Atherosclerosis), younger normal women have lower BP, lower LV mass index, and mass/volume ratios than age-matched normal men do, whereas normal BP values converge between the sexes in their 60s and 70s and LV mass index and mass/volume ratios also converge. Thus the need for further large-scale prospective studies and, perhaps, retrospective analyses of existing serial population databases are clearly needed.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Nathaniel Reichek, St. Francis Hospital—The Heart Center, 100 Port Washington Boulevard, Roslyn, New York 11576. E-mail: Nathaniel.Reichek@chsli.org.

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