Heart of Ethnicity

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It has long been appreciated\(^1\) that left ventricular (LV) chamber size, thickness, and weight (commonly referred to as mass) are subject to a large number of physiologic (eg, sex, familial/genetic factors, body weight and height, blood pressure, physical activity, and age) and pathophysiologic (eg, obesity, hypertension, and diabetes mellitus) influences. Nonetheless, in statistical models studying a large number of risk factors, at most only \(\approx 60\%\) of the variance in LV mass can be explained by known correlates of LV mass, even when using cardiac magnetic resonance imaging—a more precise way to measure LV mass than echocardiography as is used in most research studies.\(^2\)

Research has shown associations of self-identified race and ethnicity with LV mass in normotensives and LV hypertrophy and concentric remodeling in hypertensives.\(^3,4\) However, findings have not always been consistent,\(^5,6\) and it is difficult to separate the contribution of genetic composition from environmental factors. In part, this may be because of difficulties in how to define race and ethnicity. Also, many environmental factors, including diet, socioeconomic status, biobehavioral stress, and comorbidities, variably attach to race and ethnicity; however, they are defined. Although genome-wide association studies of genetic contribution to LV mass have in fact shown several gene loci associated with LV size,\(^7,8\) only a small proportion of the variance of LV mass can be explained by genetic factors, and structural components of LV mass calculation may differ from LV mass in their genetic associations.

Given the above, it comes as no surprise that establishing normal reference values for measures of heart size and function can be problematic particularly when applied to large numbers of individuals spanning differences in culture, race, ethnicity, and lifestyle factors. Moreover, what is normal? It can be defined in various ways based on the purpose of the designation and available phenotypic information on the population of interest. Commonly normal is used to designate absence of clinically evident disease. However, it would perhaps be better to use the term that denote the absence of subclinical disease as well, or to identify truly healthy normal individuals who are known to have long and healthy life. However fine-tuning reference values in that way can be complex and highly skewed by differences between population studies in data collection.

Compounding the difficulty of establishing partition values for LV mass and other cardiac measurements has been the substantial variability of measurement with echocardiography, the most convenient way to assess cardiac structure and function in hypertension, which can occur in clinical practice and in large research studies.\(^9\)

In this issue of *Circulation: Cardiovascular Imaging*,\(^10\) investigators in The Echocardiographic Study of Latinos (ECHO-SOL) evaluated a moderately large \((n=524)\) healthy subset of the Hispanic Community Health Study/SOL study of Hispanic subgroups living in the United States, and clearly showed that reference values for LV and left atrial measurements differed substantially from those published in the American Society of Echocardiography (ASE) 2005,\(^11\) as well as the updated 2014, guidelines for chamber quantification.\(^12\)

As pointed out by the authors, the differences in reference values are of clinical importance in that the use of the ASE guidelines in Hispanics would result in overestimation of LV hypertrophy and potential overtreatment to minimize end-organ damage. In contrast, the lower cutoff values for LV diastolic dimension could result in underestimation of LV dilation and influence decision making for aortic valve replacement in patients with aortic regurgitation.

Of interest, was the finding of different cutoff values for LV and left atrial measurements even between subgroups of Hispanic ethnicity, with highest values in Cuban and other Caribbean groups in comparison with Mexican Hispanics who have lower proportions of African ancestry in comparison with Caribbean Hispanics. Hence, determination of healthy reference values is further complicated even within Hispanic ethnicity.

A possible and important implication of these findings is that these differences are because of true population differences, whether genetic or acquired, between Hispanics and the largely white, Hispanic-free groups evaluated in the individual studies (eg, Asklepios, Coronary Artery Risk Development in Young Adults Study \([\text{CARDIA5, CARDIA25}]\), and Normal Reference Ranges for Echocardiography Study \([\text{NORRE}]\)\) that form the basis of the ASE partition values.

However, they could also be because of a large number of technical differences including machine selection, machine settings, temporal variability, and differences in reading styles between those of investigators in the present study from the multiple readers in the individual population studies that were used in formulating the ASE 2005 and 2014 guidelines.

Hence, there are some caveats in understanding some of the limitations of this and some other population studies using echocardiography. The presence of a non-Hispanic reference group of healthy non-Hispanic whites and non-Hispanic blacks would have been of benefit. This would have reduced the reliance on

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guidelines based on population studies other than ECHO-SOL where subtle differences in methodology and interpretation from that in the present study could affect findings.

Moreover, defining health is problematic. Because 41% of the healthy reference group in the present study were smokers, 34% had dyslipidemia, and self-report was the only measure of absence of coronary heart disease, it can be questioned whether this group might have differed in important characteristics from those used to derive healthy reference values reported in the ASE guidelines. This being said, a study in Multi-ethnic Study of Atherosclerosis reported by a coauthor of the present article did in fact compare Mexican, Caribbean, and Central/South American Hispanics to non-Hispanic whites. In participants in whom prevalent cardiovascular disease was excluded, all Hispanic subgroups had greater LV mass and LV hypertrophy (both concentric and eccentric) than non-Hispanic whites even after adjustment for hypertension and other covariates.

Because normal LV mass is related to several factors, rather than use of simple partition values, its deviation from a reference value is probably best expressed as the percent variation of the measured value from that predicted based on appropriate statistical models, taking into account contributing factors such as sex, body size, and perhaps ethnicity. This approach, rarely used in clinical practice or research, may be a simpler way to account for racial, ethnic, body size, sex, and other physiologic influences on cardiac size and function than generation of multiple tables of normal values for each population subgroup.

The present study by Qureshi et al. adds to the body of literature supporting the importance of ethnicity, for whatever reasons, to cardiac structural adaptations in health and disease. Whether this represents nature, nurture, or combination reasons, to cardiac structural adaptations in health and disease: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. J Am Heart Assoc. 2015;4:e001264. doi: 10.1161/JAHA.114.001264.


Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pelikka PA, Picard MH, Roman MJ, Seward J, Shapenwe JS, Solomon SM, Spencer KT, Sutton MS, Stewart WJ; Chamber Quantification Writing Group; American Society of Echocardiography’s Guidelines and Standards Committee; European Association of Echocardiography. Recommendations for chamber quantification: a report from the American Society of Echocardiography’s Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr. 2005;18:1440–1463. doi: 10.1016/j.echo.2005.10.005.


