Method Errors or Unexplained Biological Information?

To the Editor:

Left ventricular mass (LVM) is an indicator of cardiovascular status, integrating multiple adverse pathophysiologic influences and a potent, independent predictor of prognosis, making definition of optimal methods to distinguish abnormal from normal LVM a matter of high clinical priority. Different methods have been used to account for body size in the definition of “normal” LVM, and there is agreement that the ratiometric approach is not sufficient to capture the extent of abnormalities, especially in obese populations. In the July issue of Hypertension, Chirinos et al studied apparently normal members of 2 adult populations aged 35 to 55 and 45 to 84 years old and proposed a new exponent of body height (height1.7) to normalize LVM. This exponent is substantially lower than the allometric signal (height2.7) that we initially proposed, from a normal-weight population including infants, children, adolescents, adults, and elderly. It is also lower than other allometric powers (2.5 to 3.0) identified in other young populations and even lower than the exponent of 2 proposed by the Framingham Heart Study in an adult population.

The allometric approach to identify left ventricular hypertrophy (LVH) increases the prevalence of LVH, without decreasing the LVH-associated relative risk, thus increasing the population risk attributable (PAR) to LVH. PAR is the proportion of cardiovascular events, compared with all other methods, both in the Heart Study cohort used for our previous report. Characteristics of normalization of LVM in the identification of LVH. The normal average value of LVM/height1.7 was 56.4±11.4 g/m1.7 (ie, 59.2±2.6 g/m1.7 in men and 54.3±9.9 g/m1.7 in women). When using the single partition value of 77.5 g/m1.7, the sex-specific prevalence of LVH in the whole population was 17.5% in men and 18.4% in women (exact 2-tail P=0.614), whereas when using sex-specific partition value (83.2 and 73.6 g/m1.7 in men and women, respectively), LVH was found in 10.1% of men and 25.6% of women (P<0.0001).

The age- and sex-adjusted hazard ratios in the whole Strong Heart Study population were 1.76 (1.21 to 2.55; P=0.003) for the single partition value and 1.53 (1.04 to 2.25; P=0.03) for the sex-specific partition value. Thus, the PAR was 12.03% (9.55 to 15.05) and 9.58% (6.98 to 12.18), respectively, both lower than the 15.54% found using LVM/height2.7 in our original report. In the hypertensive subpopulation (354 men and 672 women), prevalence of LVH based on LVM/height1.7 was 25.9% with a single partition value and 27.9% with a sex-specific cut point. The age- and sex-adjusted hazard ratios were 1.59 (1.01 to 2.47; P=0.04) with a single partition value and 1.47 (0.92 to 2.34; P=0.10) with a sex-specific partition value. Respective PAR percentages were 13.30% and 11.63%, both lower than the 16.58% found with LVM/height2.7.

We also tested the new allometric signal (height1.7) in the Massa Ventricolare Sinistra nell’Ipertensione population, using the same criteria as in the original article. The mean normal value of LVM/height1.7 from our reference adult population (n=228) was 57.0±13.2 g/m1.7, and the 95th percentile was 80.2 g/m1.7. The sex-specific average values were 60.7±12.6 g/m1.7 in adult men and 51.3±12.2 g/m1.7 in adult women, and their 95th percentiles were 81.5 and 74.6 g/m1.7, respectively. The prevalence of height1.7-based LVH in the Massa Ventricolare Sinistra nell’Ipertensione population was 51.9% (57.4% in men and 48.5% in women; P=0.006), using the same partition value for men and women, and 58.3% (55.9% in men and 59.8% in women; P=0.214) with sex-specific partition values. The age- and sex-adjusted hazard ratio was 1.53 (0.87 to 2.68; P=0.141) with a single cut point and 1.61 (0.89 to 2.88; P=0.114) with sex-specific cut points. The PAR percentages were 21.6% and 26.1%, respectively, indistinguishable from the PARs obtained with the other indices. This finding confirms that, in the presence of a low prevalence of obesity, there is no appreciable prognostic difference among the different methods of normalization of LVM in the identification of LVH.

Thus, the new allometric signal proposed by Chirinos et al works but is less efficient than the allometric signal obtained using the entire life age span. In agreement with the findings of Chirinos et al, we find a significant negative relation between LVM/height2.7 and height (r=−0.30 in the Strong Heart Study; P<0.0001), but we do not have good reasons to affirm that this is attributed to error rather than to unexplained biological phenomena. The substantial method difference between our original reference populations and the populations studied by Chirinos et al is the age span, and we speculate that the allometric signal obtained from a wide range of age might include biological information that otherwise is lost with a more limited age span. This might well explain the discrepancy between mathematic evidence (residual relation) and prognostic relevance.
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