Evaluation of Concentric Left Ventricular Geometry in Humans
Evidence for Age-Related Systematic Underestimation

Giovanni de Simone, Stephen R. Daniels, Thomas R. Kimball, Mary J. Roman, Carmela Romano, Marcello Chinali, Maurizio Galderisi, Richard B. Devereux

Abstract—There might be limitations in identifying concentric left ventricular (LV) geometry by ratio of diastolic posterior wall thickness (WTp) to cavity radius, defined as relative wall thickness (RWTp). This study has been designed to evaluate age effects on RWTp, WTp mean of septal thickness and WTp (WTm), and cavity radius were cross-sectionally evaluated in 766 1- to 85-year-old, normotensive, nonobese subjects and 331 hypertensive Italians (used as a test series). RWTp ≥0.43 defined “traditional” concentric LV geometry. The ratios WTm/radius (RWTm) and RWTp increased by 0.005 and 0.006 per year of age in the age stratum up to 17 years and by 0.002 in the older age stratum (18 years or older; all P<0.0001). Thus, RWTm and RWTp were normalized to average age in both age strata (10 and 46 years) by age-specific regression coefficients. The 90th and 95th percentiles of age-normalized RWTm or RWTp were 0.40 and 0.42 or 0.41 and 0.43, respectively, in adults and 0.36 and 0.39 or 0.36 and 0.38, respectively in young subjects. In hypertensive subjects, traditional RWTp cutoff identified 74 subjects (22%) with concentric LV geometry; by 95th or 0.42 or 0.41 and 0.43, respectively, in adults and 0.36 and 0.39 or 0.36 and 0.38, respectively in young subjects. In hypertensive subjects, traditional RWTp cutoff identified 74 subjects (22%) with concentric LV geometry; by 95th or concentration of LV geometry increases with age-normalized RWT. Accordingly, we suggest that concentric LV hypertrophy be defined by coexistence of high LV mass with age-normalized RWTm >0.41 or RWTp >0.40. Further studies are required to establish prognostic implications of our findings. (Hypertension. 2005;45:64-68.)

Key Words: hypertension, arterial □ hypertrophy □ aging

Evaluation of concentricity of left ventricular (LV) geometry is usually performed using echocardiographic relative wall thickness (RWT), ie, the ratio of wall thickness to LV radius, which was originally shown to be closely related with the severity of aortic stenosis.1 Combining RWT with the value of LV mass allows determination of the presence of LV hypertrophy and type of geometric pattern.2 From a number of studies using these 2 measures, the most common LV geometric abnormality in arterial hypertension is eccentric LV hypertrophy,3^-5 although a pressure-overload component is of course present by definition in hypertension-related LV hypertrophy. An accepted explanation for this evidence is that LV geometry reflects the impact of volume as well as pressure overload.6 Arterial hypertension is in fact a composite condition in which volume and pressure overloads can be differently combined, and volume load plays an important role in sustaining high blood pressure values.7 8

However, other reasons for the evidence of the substantial predominance of eccentric LV hypertrophy might be in the limitations of the method used to identify concentric LV geometry. Potential pitfalls in the calculation of RWT might include a nonlinear relation between wall thickness and LV internal radius and the effect of aging or body growth. This study has been performed in a large normotensive, nonobese population, encompassing a wide range of age, to test the hypotheses that relation between wall thickness and LV chamber dimension is linear and that RWT is positively correlated to age. We also evaluated new indicators of concentric LV geometry in a test population of hypertensive patients.

Methods

Participants
Two-dimensional echocardiograms were performed in 766 normotensive, nonobese individuals,5 10 aged 1 to 85 years, 373 of whom were children or adolescents (1 to 17 years, 166 females) and 393 were adults (164 women). This reference population was studied in 3 University Hospitals: from New York, NY, from Cincinnati, Ohio, and from Naples, Italy. Detailed characteristics of this population are available at http://www.hypertensionaha.org

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and method of merging from different settings have been previously reported repeatedly.11–14

A clinical population of 331 untreated hypertensive Italians was used as a test series to verify distribution of LV geometric pattern according to traditional or new criteria. Details about recruitment and characteristics of this test series have also been previously reported.15

### Echocardiography

Two-dimensionally targeted M-mode echocardiograms were performed and read by expert sonographers as previously described in detail.16–18 Measurements were taken according to the American Society of Echocardiography recommendations.19 LV mass was calculated by the adjusted American Society of Echocardiography method20 and divided for body height raised to the power of 2.7, an allometric signal able to linearize the LV mass/height relations and to generate indexed values, which can be compared independently of the presence of obesity and during body growth.11 After evaluating best-fitting models between wall thickness and LV internal dimension (LVIDd) in diastole (see Results), RWT was calculated with 2 simple methods:

\[
RWT_m = \frac{WT_p}{LVID_d}
\]

\[
RWT_p = 2\frac{WT}{LVID_d}
\]

where WTp is posterior wall thickness, WTm is WTp plus interventricular septal thickness (IVST), and LVIDd is diastolic LV internal diameter.

Concentric LV geometry was traditionally defined for RWTm > 0.43.21 Alternative definitions were generated by “normalized” partition values of both RWTm and RWTp, as explained in next paragraph and detailed in the Results section.

### Statistical Analysis

As previously reported in detail,13 primary echocardiographic variables were adjusted for a “center effect” using the linear coefficient of regression of the relation of each variable with a dichotomous independent variable representing the center, in age, gender, and body size-matched groups of subjects (20 in each group).13,14

The study population was divided into groups of children and adolescents up to 17 years old and adults 18 years or older, a stratification that takes into account the estimated period of body growth already used in previous analyses.12–14 Kolmorov–Smirnov test was used to assess deviations from normal distribution.

Data are expressed as mean±1 SD. Proportion of concentric LV geometry and distribution of categories were studied by \( \chi^2 \) and, when needed, exact tests were performed using Monte Carlo method. To test the hypothesis that change in the binary outcome defining concentric LV geometry occurred in relation to the type of method of definition, the McNemar test for 2 related samples was used, based on \( \chi^2 \) distribution. Least squares linear and nonlinear regression analyses were used to describe relations between study variables. Differences between regression lines were tested by computing F-statistics of the between-slopes sum of squares. RWT was adjusted to the average value of age in each age stratum using the age-specific coefficient of regression. For convenience, this adjusted value was called “normalized” RWT.

The null hypothesis was rejected at 2-tailed \( \alpha=0.05 \).

### Results

In the whole population, WTm and WTp were best related to LVIDd by power regressions, which did not significantly deviate from linearity \( r=0.69 \) and 0.67, respectively. Thus, for simplicity, linear models were assumed \( r=0.67, WT_p=0.38\times LVID_d-0.25; \) and \( r=0.65, WT_p=0.18\times LVID_d-0.09 \); respectively; both \( P<0.0001 \).

When the 2 age strata were separately examined, in children and adolescents \( (n=373) \) both WTm and WTp were best related to LVIDd by power regressions, which did not significantly deviate from linearity \( r=0.67 \) and 0.67, respectively. Thus, for simplicity, linear models were assumed \( r=0.67, WT_p=0.38\times LVID_d-0.25; \) and \( r=0.65, WT_p=0.18\times LVID_d-0.09 \); respectively; both \( P<0.0001 \).

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### Reclassification of Hypertensive Subjects With Concentric LV Geometry

Based on distribution reported in the Figure, partition values of normalized RWTm and RWTp were compared with the best related to LVIDd by linear regressions, but the relations were less close \( r=0.55, WT_m=0.28\times LVID_d+0.04; \) and \( r=0.53, WT_p=0.15\times LVID_d-0.02, \) respectively. Similarly, in adults \( (n=393) \) both WTm and WTp were related to LVIDd by linear regressions \( r=0.26, WT_m=0.13\times LVID_d+1.02; \) and \( r=0.29, WT_p=0.07\times LVID_d+0.45, \) respectively; all \( P<0.0001 \) more weakly than in the whole population sample. The appreciable linearity of relations between WT and LVIDd demonstrated the legitimacy of calculating RWT by a simple (linear) ratio.

### Age Effect

Figure I, available online at http://www.hypertensionaha.org shows that the relations between wall thickness and LV internal diameter were also influenced by age. Thus, relations of RWT to age were examined. In the whole population, both RWTm and RWTp were linearly related to age (Table I). In children and adolescents, RWTm increased by 0.005 for each year of age, whereas in adults the increase was slightly less \( (0.002/year; \) Table I). Similarly, RWTp increased by 0.006/year in children and adolescents, whereas this increase was significantly lower in adults \( (0.0015/year; P<0.01 \) between slopes). Residuals of these regressions were plotted against body height in each age stratum to exclude any heteroscedasticity of distribution referred to increasing height (not shown). Residual influence of body size could therefore be excluded.

Thus, RWT was normalized to the average age of each age stratum \( (9.91 \pm 3.15 \) and 45.64±12.19 years, respectively) by using the age-specific regression coefficient, obtained in both methods of computation (ie, WTm or WTp), as shown in Table I. No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)). No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)). No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)). No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)). No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)). No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)). No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)). No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)). No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)). No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)). No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)). No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)). No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)). No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)). No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)). No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)). No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)). No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)). No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)). No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)). No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)). No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)). No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)). No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)). No residual regression with age could be found in either age stratum for normalized RWTm values (all \( r<0.001 \)).
traditional cutoff point of 0.43 for unadjusted RWTₚ. Using 0.43 for unadjusted RWTₚ, identified 74 of 331 hypertensive patients with concentric LV geometry (22.4%). The 95th percentile of normalized RWTₘ identified 33.8% of patients with concentric LV geometry (n=112; Figure II) and, perhaps even more important, could reclassify 47 of them, otherwise classified as with normal LV geometry, whereas 9 individuals classified as concentric with the traditional method could be reclassified as normal. These differences were statistically significant by the McNemar test. When examining the 90th percentile of the normalized RWTₘ, these differences were even more evident: 149 subjects (45%) could be classified as concentric LV geometry (Figure II) and reclassification involved 78 individuals with normal and 3 individuals with concentric LV geometry by the traditional method. Similar results were found with normalized RWTₚ (Figure II).

We examined the main hemodynamic characteristics of hypertensive individuals classified using traditional 0.43 and the 90th percentile of RWTₘ. As expected, subjects classified as having concentric LV geometry with the traditional method were significantly older and exhibited higher blood pressure values and LV mass index and LV functional pattern consistent with concentric LV geometry (ie, normal ejection fraction and reduced mid-wall shortening; Table 2). In contrast, classifying by the 90th percentile of normalized RWTₘ, the difference in average age and LV mass index disappeared, whereas significant differences in blood pressure and mid-wall shortening remained (Table 2). Similar results were obtained using normalized RWTₚ (not shown).

### Discussion

Arterial hypertension is clinically appreciable, mainly as pressure overload condition, although its pathogenesis is in

| TABLE 2. Comparison Between Normal and Concentric LV Geometry Based on Classification Using Traditional Methods or Using Normalized RWT (by WTₘ/LVIDₐ) |
|-------------------------|----------------------------------|--|-------------------------|----------------------------------|--|
|                        | Normal LV Geometry (n=256) | | Concentric LV Geometry (n=74) | | Normal LV Geometry (n=181) | | Concentric LV Geometry (n=149) |
| Age, y                  | 45.65±11.25 | | 50.99±8.89€§ | | 47.22±10.89 | | 46.39±11.12 |
| BMI, kg/m²              | 27.69±4.65 | | 27.61±3.70 | | 27.73±4.76 | | 27.60±4.06 |
| Systolic BP, mm Hg      | 149.72±18.01 | | 156.70±17.98€§ | | 149.46±18.02 | | 153.54±18.26* |
| Diastolic BP, mm Hg     | 94.79±8.78 | | 98.04±9.64€¶ | | 94.57±9.00 | | 96.70±9.05* |
| Heart rate, bpm         | 72.80±11.12 | | 72.76±12.12 | | 72.65±10.74 | | 72.97±12.02 |
| LV mass index, g/m²²    | 46.50±12.98 | | 51.24±10.63€¶ | | 46.70±12.94 | | 48.62±12.20 |
| Unadjusted RWTₚ         | 0.36±0.04 | | 0.48±0.07€§ | | 0.35±0.04 | | 0.44±0.07€§ |
| Adjusted RWTₘ           | 0.39±0.05 | | 0.49±0.06€§ | | 0.37±0.03 | | 0.46±0.05€§ |
| Ejection fraction, %     | 66.02±5.43 | | 66.18±6.11 | | 65.84±5.57 | | 66.33±5.60 |
| Mid-wall fraction, %     | 17.26±2.09 | | 14.74±1.99€§ | | 17.70±2.13 | | 15.47±1.92€§ |

BP indicates blood pressure; BMI, body mass index.
*P<0.05; †P<0.01; ‡P<0.005; §P<0.0001.
the alteration of the flow resistance relation; therefore, it can be also associated with volume overload. In contrast with this common pressure overload-oriented view, however, most epidemiological studies\(^2\)–\(^5\) have shown that the predominant LV geometric abnormality is characterized by the increase in LV mass, without significant alteration of wall thickness/LV radius ratio, a pattern defined eccentric LV hypertrophy,\(^2\) although a predominant concentric LV geometry could be expected.

In this study, we found that although the relation between wall thickness and LV chamber radius can be legitimately assumed to be linear, aging has a potent influence both during body growth and during adulthood. If the definition of concentric LV geometry does not take into account this aspect, concentric LV geometry might be severely underestimated, especially during younger age, because the partition values normally used are derived from populations with a large prevalence of elderly subjects. The consequence of this underestimation is significant no matter what percentile of normal distribution of normalized RWT is taken as the cutoff point. In a cross-sectional analysis performed in a “test series” of hypertensive subjects, there are 2 relevant differences emerging using traditional or normalized RWT. In contrast with the traditional partition of 0.43 of RWT, definition of concentric LV geometry by age-normalized RWT did not highlight significant differences in age, LV mass, and LV chamber dimension, although blood pressure remained higher in the concentric pattern. Thus, with this classification, the alteration of LV geometry was in fact isolated from other anatomic abnormalities. LV chamber and mid-wall function distribution did not change between the methods of classification. According to our results, concentric LV hypertrophy should be better-defined by coexistence of cutoff values for LV mass/height\(^2\)\(^7\) (ie, \(\geq 51 \text{ g/m}^2\) in adults) and age-normalized RWT (ie, \(>0.41\) or \(>0.40\) for adults with \(\text{RWT}_m\) or \(\text{RWT}_p\), respectively). Use of mean wall thickness might be preferable to the sole posterior wall thickness, because it is more consistent with the calculation of LV mass obtained including both posterior wall and septal thickness.

Differentiating concentric from normal LV geometry might be important for refining risk stratification and, possibly, for addressing treatment. Eccentric LV hypertrophy is characteristic of volume overload and has been thought to be associated with less severe degrees of LV mass increase\(^2\)\(^2\) and with more benign myocardial structural modifications.\(^2\)\(^3\)–\(^2\)\(^5\) Recently, Muijesan et al\(^2\) demonstrated that for similar degrees of LV mass index, concentric LV geometry was associated with significantly greater cardiovascular risk, an observation already proposed by others.\(^2\)\(^7\)\(^2\)\(^8\) Taking into account age increases the proportion of subjects with concentric LV geometry and redistribute them. Thus, because of this redistribution, the prognostic independent impact of concentric LV geometry might also change, especially considering that LV mass does not differ, as shown in Table 2.

One explanation for the increase in RWT observed with aging in adults\(^2\)\(^1\) is that concentricity of the LV follows the increased pressure overload associated with the age-related stiffening of conduit arteries,\(^2\)\(^9\) a condition not necessarily normal. There is evidence that blood pressure does not increase with age in nonindustrialized populations,\(^3\)\(^0\)\(^3\)\(^1\) and also in Western countries when particular environmental conditions occur.\(^3\)\(^0\)\(^3\)\(^2\) Thus, age-related increase in blood pressure might not be “normal” in absolute terms. However, even when brachial blood pressure is maintained stable during aging, this stability is unlikely to occur in central blood pressure.\(^3\)\(^3\) Accordingly, the apparent stability of brachial blood pressure with aging is associated with age-related increase in central blood pressure, accounting for the “physiological” increase in RWT.

**Perspectives**

The substantial finding emerging from this study is that consideration of age as a physiological confounder of RWT yields a reclassification of hypertensive patients, substantially based on the pure difference in LV geometry, given the similarity in age, LV mass, and chamber dimension between LV geometric patterns. Thus, this method appears to better-discriminate the underlying fundamental type of overload abnormality associated with arterial hypertension. Detailed analysis on flow/resistance relations, especially in younger hypertensive individuals, should be performed to better-discriminate between volume and pressure overload components of arterial hypertension. Possible evolution from an initial state of concentric LV remodeling to concentric LV hypertrophy should also be examined and, eventually, outcome analyses should be designed to explore this reclassification.

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Table I: Best fitting relations between relative wall thickness and age, encompassing the whole life span or in separate age strata.

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