Comparison of Left Ventricular Mass Calculation Methods via Two-Dimensional Echocardiogram in Children, Adolescents, and Young Adults With Systemic Hypertension

Sean M. Lang, MD[a,b,*], Benjamin R. Ittleman, MD[c], Eunice Hahn, MD[a,b], Ryan A. Moore, MD[a,b], Philip R. Khoury, PhD[a,b], Nicholas J. Ollberding, PhD[a,b], Thomas R. Kimball, MD[a,b], and Christopher J. Statile, MD[a,b]

Left ventricular (LV) mass is a major determining tool for myocardial injury in hypertensive patients. Issues with LV mass calculations exist given that there are multiple methods to assess mass, including from the parasternal long axis (PLA), parasternal short axis (PSA), and 2-dimensional (2D) volumetric methods. The aim of this study was to compare the agreement of LV mass calculations using the PLA, PSA, and 2D volumetric methods. This study retrospectively reviewed 200 consecutive, initial echocardiograms for the indication of hypertension. A single reader calculated the LV mass in each patient via the PLA, PSA, and 2D volumetric methods. Percent differences for each study were calculated. LV mass threshold cutoffs of 51 g/m$^{2.7}$ (cardiac organ injury) and 38.6 g/m$^{2.7}$ (elevated LV mass) were used to compare categorical differences between the different measurement methods. Paired comparisons demonstrated an absolute mean percent difference of 8.46% to 9.41% among the different methods. LV mass calculated by the 2D volumetric method was less compared with PLA and PSA methods (31.64 vs 33.90 vs 35.51 g/m$^{2.7}$; $p < 0.0001$). Fewer patients were classified as having cardiac target organ injury or elevated LV mass via 2D volumetric calculation, compared with PLA and PSA methods ($p = 0.02$ and $p = 0.03$, respectively). In conclusion, there is a small but important difference in LV mass calculations for patients with hypertension. These results emphasize the need for consistency within echocardiography laboratories as surveillance studies are common in this patient population. **(Am J Cardiol 2019;124:239−244)**

Left ventricular (LV) mass assessment via echocardiography is a major determining tool for myocardial target organ injury in patients with hypertension.[1] In adults, there is a strong relation of LV mass to blood pressure, as well as a strong and independent relation of LV hypertrophy to adverse cardiovascular outcomes.[1−3] Pediatric guidelines recommend assessment via echocardiography for LV mass, ventricular geometry, and ventricular function, at the time of consideration for pharmacologic treatment of hypertension. Echocardiography measures of LV mass, as well as systolic function represent the best-studied measures of LV organ injury.[4,5] In addition, follow-up assessment is recommended to monitor for improvement or progression of target organ damage.[1] Issues with LV mass calculations exist given that there are multiple methods to assess mass, including linear dimensions from either the parasternal short axis (PSA) or parasternal long axis (PLA), as well as 2-dimensional (2D) volumetric methods.[4,6] Whereas adult guidelines recommend the linear PLA method, pediatric guidelines recommend PSA for linear LV calculations.[4,6] Given the variation of techniques and the need for longitudinal follow-up in hypertensive patients, comparing the LV mass methods for differences and reliability is extremely important. The aim of our study was to compare the agreement of LV mass calculations using the linear PLA and PSA methods, as well as the 2D volumetric method.

Methods

This study was approved by Cincinnati Children's Hospital Medical Center Institutional Review Board. We retrospectively reviewed 200 consecutive, initial echocardiograms for the indication of hypertension in patients 7 years of age and older, performed at Cincinnati Children's Hospital Medical Center. Cincinnati Children's Hospital Medical Center Echocardiography laboratory is an accredited Facility of the Intersocietal Accreditation Commission and performs approximately 18,000 total studies a year. As protocol at our institution, all initial echocardiograms are complete studies. Care is taken to obtain 2D imaging in the PLA, aligning to the true long axis of the heart. Dedicated PSA 2D imaging is obtained

[a]Heart Institute, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio; [b]Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, Ohio; and [c]University of Vermont Medical Center, Burlington, Vermont. Manuscript received January 24, 2019; revised manuscript received and accepted April 9, 2019.

Grants: The authors report no financial disclosures, or funding sources.

See page 243 for disclosure information.

*Corresponding author: Tel: (513) 536-9806, fax: (513) 803-0564.

E-mail address: sean.lang@cchmc.org (S.M. Lang).

0002-9149/
https://doi.org/10.1016/j.amjcard.2019.04.023

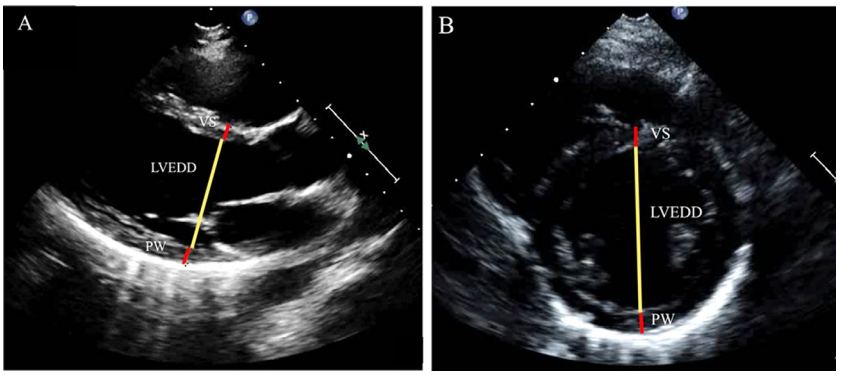

Figure 1. Linear measurements for LV mass calculation via parasternal long axis (A) and parasternal short axis (B). VS = interventricular septum; LVEDD = left ventricular end-diastolic dimension; PW = posterior wall.

at the maximum dimension, usually between the level of the mitral valve leaflet tips and papillary muscles, as recommended by the American Society of Echocardiography Pediatric and Congenital Heart Disease Council.[6] Dedicated 2D imaging from the apex is obtained with care to acquire the maximum volume and avoid ventricular foreshortening as recommended by the American Society of Echocardiography.[4,6]

Echocardiograms were reviewed by an attending cardiologist (SML) with advanced training in cardiac imaging. Echocardiograms were excluded for congenital heart disease, known or diagnosed cardiomyopathy, poor acoustic windows, segmental wall motion abnormalities, or septal flattening. Linear dimensions were measured in the dedicated PLA and PSA views. Linear dimensions were obtained at end-diastole, defined as the frame with the maximum LV intraluminal area. Linear measurements were taken at the interface between the blood and endocardium for LV end-diastolic dimension (LVEDD) and ventricular septum (VS), as well as the interface between the endocardium and pericardium for the posterior wall (PW) (Figure 1). In addition, 2D LV mass volumetric assessment was measured using images from the apical window for LV length (l), and PSA for cross-sectional areas of the epicardium (A_1) and endocardium (A_2) (Figure 2). Measurements were obtained offline using a Syngo Dynamics Echocardiography workstation (Siemens Medical Solutions, Munich, Germany). LV mass was calculated by 2D linear measurements using the cube formula ($LVM = 0.8 \times 1.04 \times [(VS + LVEDD + PW)^3 - LVEDD^3] + 0.6g$). Volumetric assessment was calculated using the area-length method ($LVM = 1.05\ [(5/6\ A_1\ (l + t)) - (5/6\ A_2\ (l))]$). Mean thickness (t) was calculated as $(\sqrt{A_1/\pi}) - (\sqrt{A_2/\pi})$.[4] Area measurements excluded papillary muscles and trabeculations. Indexed LV mass was derived by dividing LV mass in grams by the subject's height in meters to the 2.7 power, as previously reported.[7]

All data analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, North Carolina). Summary statistics were expressed as means (standard deviation) for continuous variables and counts (percentage) for categorical variables. Linear dimensions were compared between the PLA and PSA methods using 2-tailed paired *t* tests. The percent difference of LV mass for each method was calculated as the absolute difference between the measurement and the mean, divided by the mean. Classification of cardiac organ injury and elevated LV mass was assessed using the cutoffs of 51 $g/m^{2.7}$and 38.6 $g/m^{2.7}$; respectively. The threshold of 51 $g/m^{2.7}$ was chosen based on American Academy of Pediatrics clinical practice guidelines.[1] The threshold of elevated LV mass at 38.6 $g/m^{2.7}$ was selected based on previous normative pediatric data corresponding to the 95th percentile, and our institutional experience.[7–11] Differences in categorical classification of target organ injury and elevated LV mass among the measurement methods was assessed by chi-square tests. Multivariate models for LV mass percent difference were performed taking into account patient's age and body mass index. Bland-Altman plots were generated to assess

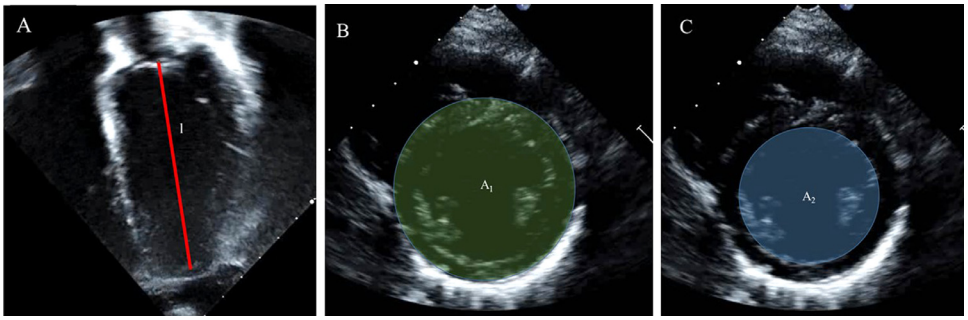

Figure 2. 2D volumetric method for LV mass calculation using apical 4 chamber (A) to measure length (l) and parasternal short axis (B and C) to measure the epicardial (A_1) and endocardial (A_2) cross-sectional area.

method agreement. Intraclass correlations were calculated for 20 randomly selected echocardiograms read by a second attending reader (CJS) with training in advanced imaging. The readers made measurements on the same clip number and frame number to eliminate intra-acquisition variability. Among this smaller sample, interobserver percent differences of LV mass were calculated for each method. For all statistical analyses p values <0.05 were deemed statistically significant.

Results

A total of 200 consecutive echocardiograms were reviewed. There were 22 patients excluded; 1 patient was excluded for the previous diagnosis of dilated cardiomyopathy, 2 patients were excluded secondary to previously diagnosed congenital heart disease, and 19 patients were removed secondary to poor acoustic windows. Final analysis consisted of 178 patients (89%). Patient characteristics are provided on Table 1. Patient age ranged from 7 to 24 years of age. There was a moderate positive association with body mass index and indexed PLA LV mass (Pearson correlation 0.49; $p < 0.0001$). Apical images were suboptimal in 8 patients leaving 170 studies available for comparison of all 3 methods of LV mass calculation.

Paired comparisons of the linear dimensions are displayed in Table 2. Among the study measures, there were differences in both the LVEDD and VS. LVEDD was measured larger from the PSA (4.97 vs 4.78 mm; $p < 0.0001$), whereas VS thickness was larger measured from PLA (0.88 vs 0.84 mm; $p = 0.0002$). There was no statistical difference in LV mass calculated by PLA and PSA among the group (33.96 vs 35.00 g/m$^{2.7}$; $p = 0.051$).

Comparisons of the 170 studies with all 3 calculation methods are displayed in Table 3. The absolute maximum percent difference was 34% in 1 patient example. Mean percent difference ranged from 8.46% to 9.41% among the different methods. Overall the 2D volumetric indexed LV mass was less compared with the PLA and PSA methods (31.64 vs 33.90 vs 35.15 g/m$^{2.7}$; $p < 0.0001$).

Cardiac target organ damage, classified by LV mass ≥ 51 g/ m$^{2.7}$, was seen in 5 patients (3%) via PLA, 10 patients (6%) via PSA, and 1 patient (1%) by the 2D volumetric method. Using the LV mass threshold of 38.6 g/m$^{2.7}$ as criterion for elevated LV mass, 45 patients (26%) met criterion via PLA, 52 patients via PSA (31%), and 31 patients (18%) via the 2D volumetric assessment. For the 2D volumetric method, fewer patients were classified as having target organ injury (LV mass > 51 g/m$^{2.7}$) and elevated LV mass (>38.6 g/m$^{2.7}$) compared to PLA and PSA methods ($p = 0.02$, $p = 0.03$; respectively). Comparing PLA and PSA, there was no difference in the number of patients classified as target organ injury or elevated LV mass ($p = 0.187$, $p = 0.4$; respectively).

Bland-Altman plots comparing the absolute LV mass differences compared to the means are provided in Figure 3. The absolute difference between PSA LV mass and PLA LV mass (Figure 3) showed a small positive association with increasing mean (Pearson correlation, $p = 0.025$). This associated was no longer significant when repeating the analyses using a natural log transformation of the variables. The absolute difference between 2D Volumetric LV mass and PLA LV mass (Figure 3) showed PLA LV mass tending to be larger than volumetric LV mass, but there was little association between the difference and the mean. The absolute difference between 2D Volumetric LV mass and PSA LV mass (Figure 3) showed PSA LV mass tending to be larger than volumetric LV mass (mean difference of 14 g), and positive association between the difference and the mean ($p < 0.0001$). When repeating the analyses using a natural log transformation of the variables, the association was no longer statistically significant. LV mass percent difference was not associated with patient's age, sex, or BSA.

Intraclass correlation analysis demonstrated good reliability for all 3 measurements.[12] PLA LV mass intraclass

Table 1
Patient characteristics (n = 178)

Variable	
Male	113 (63%)
Age (years)	15.68 ± 3.21
Weight (kg)	85.4 ± 31.1
Height (cm)	167.5 ± 13.7
Body surface area (m^2)	1.99 ± 0.44
Body mass index (kg/m^2)	29.8 ± 8.6
Systolic blood pressure (mm Hg)	132 ± 13.5
Diastolic blood pressure (mm Hg)	73 ± 11.6
White	120 (67%)
Black	54 (30%)
Hispanic	3 (2%)
Asian	1 (0.6%)

Data presented as mean (standard deviation) unless otherwise stated.

Table 2
Linear measurement comparisons

Variable	PLA	PSA	p
Left ventricular end-diastolic dimension (cm)	4.78 (±0.60)	4.97 (±0.62)	<0.0001
Ventricular septum (cm)	0.88 (±0.17)	0.84 (±0.17)	0.0002
Posterior wall (cm)	0.81 (±0.14)	0.80 (±0.16)	0.583
Left ventricular mass (g/m$^{2.7}$)	33.96 (±7.96)	35.00 (±9.49)	0.051

Data presented as mean (standard deviation) unless otherwise stated.
p Values based on 2-tailed, paired *t* test.

Table 3
Left ventricular mass comparisons

Variable	Left ventricular mass (g/m$^{2.7}$)	Absolute % difference
Parasternal long axis method	33.90 (±8.07)	9.41 (±8.10)
Parasternal short axis method	35.15 (±9.65)	8.46 (±6.77)
Volumetric method	31.64 (±7.70)*	8.71 (±6.32)

Data presented as mean (standard deviation) unless otherwise stated. Absolute % difference represents the mass difference for specific method and mean of all methods, divided by the mean for each patient.
p Values based on 2-tailed, paired *t* test.
* $p < 0.0001$, 2-tailed paired *t* test comparing volumetric to both PLA and PSA groups.

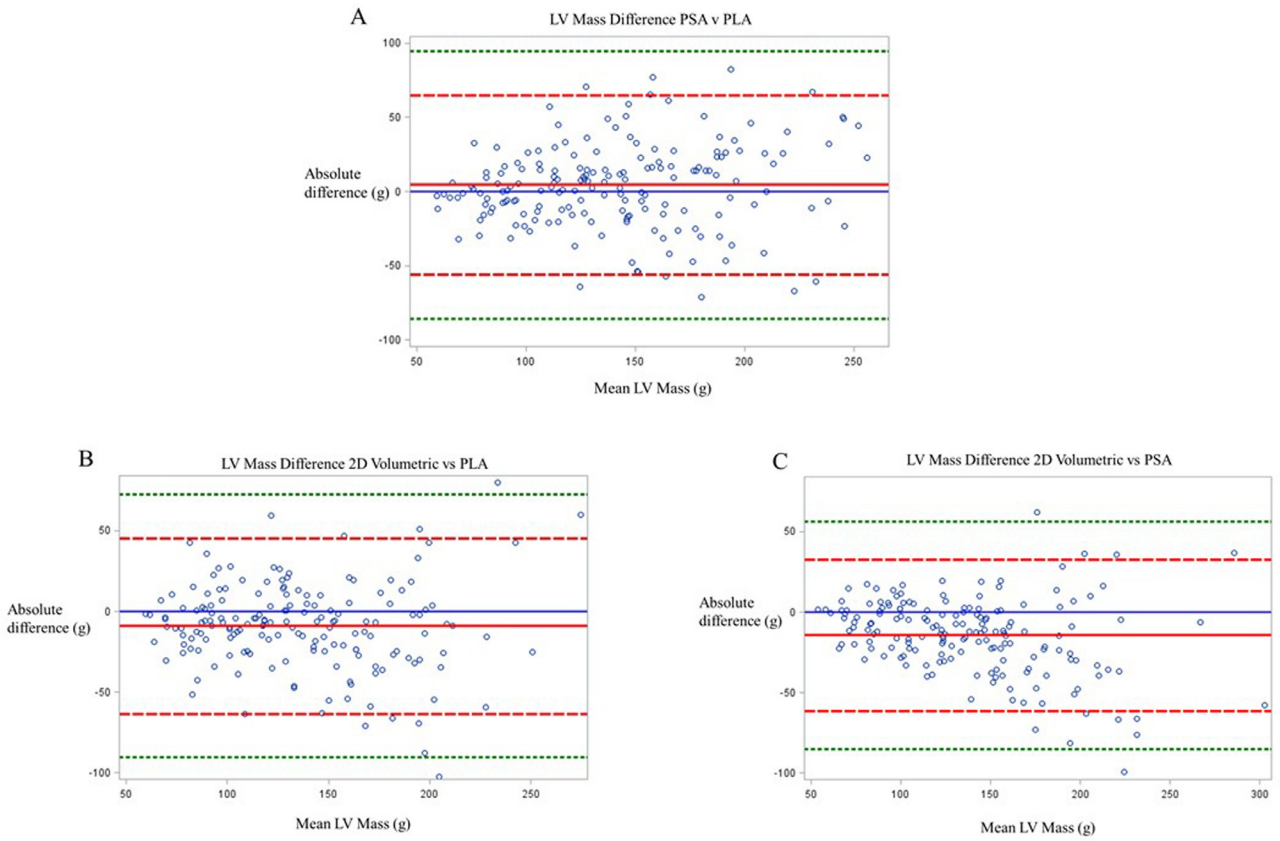

Figure 3. Bland-Altman Plots comparing LV mass differences between PSA and PLA (A), 2D volumetric and PLA (B), and 2D volumetric and PSA (C). Red solid line indicates the mean, dashed red lines indicate ±2 standard deviations, dashed green lines indicate ±3 standard deviations from mean. (Color version of figure is available online.)

correlation with 95% confidence interval was 0.90 (0.78, 0.96), PSA 0.89 (0.77, 0.95), and 2D volumetric 0.88 (0.75, 0.95). Among the 20 patient subset for intraclass correlation, interobserver percent differences were not different among the PLA (12.64 ± 11.80), PSA (13.04 ± 11.57), and 2D volumetric (12.92 ± 8.59) methods.

Discussion

This study is the first to our knowledge to assess the difference in LV mass calculated with various 2D methods used in different pediatric echocardiography laboratories. Our results suggest an important variation within the different methods. Although overall paired comparison did not reveal a difference between PLA and PSA, 2D volumetric assessment demonstrated lower overall values, with fewer patients categorized with LV target organ damage and elevated LV mass.

Echocardiography is the primary tool for assessing LV target organ damage, given its relative ease and accessibility compared with other noninvasive measurements like cardiac MRI.[1,2] In adults, LV mass correlates with adverse cardiovascular outcomes in hypertension patients.[3] However, adult studies have previously brought up concern of the variability and reproducibility of LV mass calculations.[13,14] Our study demonstrates a similar problem in pediatric patients, especially considering the difference in methods. This study is not designed to assess accuracy of the different measurements but to reinforce the need for consistency within individual echocardiography laboratories, especially in this population where surveillance echocardiograms may be performed at 6 to 12 month intervals.[1] In addition, for laboratories which prefer 2D volumetric assessment, providers need to recognize that fewer patients may be classified as having LV target organ damage, compared with labs which assess via linear dimensions. Our Bland-Altman analysis suggests that these differences are relatively stable with regard to mean LV mass, and do not widen as LV mass increases. Percent differences also were not associated with patient's age, sex, or BSA.

There exists strengths and limitations of each of the different measurement techniques. The PLA method often ensures perpendicular orientation between the measurement and the LV long axis. However there is only opportunity for a single measurement for the minor dimension or LVEDD. A single dimension can be challenging with trabeculations along the LV free wall, or right ventricular bundles at the VS.[6] In contrast, the PSA method offers possible alternative diameters or linear measurements across the circular cross-sectional LV image. This method may avoid trabeculations while measuring VS, PW, and LVEDD. However the LVEDD may be overestimated if the PSA image is inadvertently obliquely oriented toward the apex.[6] These particular strengths and weaknesses of the 2 methods correlate with our findings of larger VS measurements in the PLA method and larger LVEDD measurements in the PSA method. An

additional limitation of both methods involves making 3D assumptions using linear measurements. In such scenarios, small errors are cubed.[4,6] For volumetric LV mass assessment, underestimation has been hypothesized by adult studies. A possible reason is that the septal and free wall dimensions at the mid ventricular level may not represent the maximal thickness.[4] In addition, the calculation requires multiple measurements, and may be subject to endocardial dropout or foreshortening of the LV apex.[4] Lastly, this method required images obtained both from the PSA and apex for the LV major dimension. In our study, additional patients were removed from analysis for inadequate measures of LV length or cross-sectional areas.

The variability within different measurement techniques is consistent with other echocardiography studies. In patients with aortic valve disease or dilation, different aortic measurement conventions were shown to have a difference of 3 to 6 mm, resulting in statistically significant changes in the classification of aortic dilation and severity.[15] The variability in our study is similar to intra-acquisition variability (single reader, interpreting different sonographer images of the same patient) seen in a reproducibility study in dilated cardiomyopathy patients by Selamet Tierney et al. That particular study showed a mean % difference of 7.3% ± 7.3% for LV mass looking at a single reader interpreting different sonographer image acquisitions via 2D volumetric calculations, and 12.9 ± 12.9 via M-mode calculations.[16] Similar to the Selamet Tierney et al study, our results show no difference regarding inter-observer percent difference between the linear or 2D volumetric methods.

This study is not without limitations. The study was a retrospective study and susceptible to those inherent limitations. In addition it looked at clinical studies performed by various sonographers. As mentioned previously this study did not have CMR for correlation, therefore the 2D echocardiography methods could not be assessed for accuracy, and only the variability was evaluated. However given that most clinical decisions are made based on these different 2D echocardiogram methods, we believe the variability is an important finding. Previous studies have shown increased reliability of measures by averaging over 3 consecutive cardiac cycles.[17] Given the retrospective nature of this clinical study we did not reliably have 2D images for 3 consecutive heart beats for that analysis. In addition, the comparison between 2D and M-mode linear measurements was not performed as M-mode per our protocol is not performed on both the PSA and PLA images routinely. Historically M-mode measurements were favored, however given improvements in temporal and spatial resolution 2D imaging has become the recommended measuring approach.[6] Lastly we evaluated LV mass cutoffs indexed to height to the 2.7 th power as recommended by the American Academy of Pediatrics clinical practice guidelines.[1] This indexing convention is secondary to adult data suggesting this method most closely approximates lean body mass, however this may not be as applicable in children.[7–11]

In conclusion, our study suggests small but important differences in LV mass calculations using the different conventional 2D echocardiography methods. The results demonstrate that these methods of calculation are not interchangeable and consistency within echocardiography laboratories is important. In addition, recognition from the providers of the unique echocardiography measurements and their laboratory's preference is important for the management of individual patients.

Disclosures

The authors declare that they have no conflicts of interest.

1. Flynn JT, Kaelber DC, Baker-Smith CM, Blowey D, Carroll AE, Daniels SR, de Ferranti SD, Dionne JM, Falkner B, Flinn SK, Gidding SS, Goodwin C, Leu MG, Rea C, Samuels J, Simasek M, Thaker VV, Urbina EM. Clinical practice guideline for screening and management of high blood pressure in children and adolescents. *Pediatrics* 2017;140:2018–2096.
2. Armstrong AC, Gidding S, Gjesdal O, Wu C, Bluemke DA, Lima JA. LV mass assessed by echocardiography and CMR, cardiovascular outcomes, and medical practice. *JACC Cardiovasc Imaging* 2012;5:837–848.
3. Armstrong AC, Jacobs DR Jr., Gidding SS, Colangelo LA, Gjesdal O, Lewis CE, Bibbins-Domingo K, Sidney S, Schreiner PJ, Williams OD, Goff DC, Liu K, Lima JA. Framingham score and LV mass predict events in young adults: CARDIA study. *Int J Cardiol* 2014;172:350–355.
4. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Emande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P, Muraru D, Picard MH, Rietzschel ER, Rudski L, Spencer KT, Tsang W, Voigt JU. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2015;28:1–39.
5. Daniels SR, Kimball TR, Morrison JA, Khoury P, Witt S, Meyer RA. Effect of lean body mass, fat mass, blood pressure, and sexual maturation on left ventricular mass in children and adolescents. Statistical, biological, and clinical significance. *Circulation* 1995;92:3249–3254.
6. Lopez L, Colan SD, Frommelt PC, Ensing GJ, Kendall K, Younoszai AK, Younoszai AK, Lai WW, Geva T. Recommendations for quantification methods during the performance of a pediatric echocardiogram: a report from the Pediatric Measurements Writing Group of the American Society of Echocardiography Pediatric and Congenital Heart Disease Council. *J Am Soc Echocardiogr* 2010;23:465–495.
7. Khoury PR, Mitsnefes M, Daniels SR, Kimball TR. Age-specific reference intervals for indexed left ventricular mass in children. *J Am Soc Echocardiogr* 2009;22:709–714.
8. Daniels SR, Kimball TR, Morrison JA, Khoury P, Meyer RA. Indexing left ventricular mass to account for differences in body size in children and adolescents without cardiovascular disease. *Am J Cardiol* 1995;76:699–701.
9. Khoury M, Khoury PR, Dolan LM, Kimball TR, Urbina EM. Clinical Implications of the Revised AAP Pediatric Hypertension Guidelines. *Pediatrics* 2018;142:e20180245.
10. de Simone G, Daniels SR, Devereux RB, Meyer RA, Roman MJ, de Divitiis O, Alderman MH. Left ventricular mass and body size in normotensive children and adults: assessment of allometric relations and impact of overweight. *J Am Coll Cardiol* 1992;20:1251–1260.
11. de Simone G, Devereux RB, Daniels SR, Koren MJ, Meyer RA, Laragh JH. Effect of growth on variability of left ventricular mass: assessment of allometric signals in adults and children and their capacity to predict cardiovascular risk. *J Am Coll Cardiol* 1995;25:1056–1062.
12. Koo TK, Li MY. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. *J Chiropr Med* 2016;15:155–163.
13. Lipshultz SE, Easley KA, Orav EJ, Kaplan S, Starc TJ, Bricker JT, Lai WW, Moodie DS, Sopko G, Schluchter MD, Colan SD. Reliability of multicenter pediatric echocardiographic measurements of left ventricular structure and function: the prospective P(2)C(2) HIV study. *Circulation* 2001;104:310–316.

14. Muiesan ML, de Simone G, Ganau A, Longhini C, Verdecchia P, Mancia G, Agabiti-Rosei E. Inappropriate left ventricular mass: reliability and limitations of echocardiographic measurement for risk stratification and follow-up in single patients. *J Hypertens* 2006;24:2293–2298.
15. Rodriguez-Palomares JF, Teixido-Tura G, Galuppo V, Cuellar H, Laynez A, Gutierrez L, Gonzalez-Alujas MT, Garcia-Dorado D, Evangelista A. Multimodality assessment of ascending aortic diameters: comparison of different measurement methods. *J Am Soc Echocardiogr* 2016;29:819–826.
16. Selamet Tierney ES, Hollenbeck-Pringle D, Lee CK, Altmann K, Dunbar-Masterson C, Golding F, Lu M, Miller SG, Molina K, Natarajan S, Taylor CL, Trachtenberg F, Colan SD. Reproducibility of left ventricular dimension versus area versus volume measurements in pediatric patients with dilated cardiomyopathy. *Circ Cardiovasc Imaging* 2017;10:e006007.
17. Colan SD, Shirali G, Margossian R, Gallagher D, Altmann K, Canter C, Chen S, Golding F, Radojewski E, Camitta M, Carboni M, Rychik J, Stylianou M, Tani LY, Selamet Tierney ES, Wang Y, Sleeper LA. The ventricular volume variability study of the Pediatric Heart Network: study design and impact of beat averaging and variable type on the reproducibility of echocardiographic measurements in children with chronic dilated cardiomyopathy. *J Am Soc Echocardiogr* 2012;25:842–854.