Pediatr Cardiol (2014) 35:622–626
DOI 10.1007/s00246-013-0829-7

ORIGINAL ARTICLE

Concordance of Measures of Left-Ventricular Hypertrophy in Pediatric Hypertension

D. Mirchandani · J. Bhatia · D. Leisman · E. N. Kwon · R. Cooper · N. Chorny · R. Frank · L. Infante · C. Sethna

Received: 18 July 2013 / Accepted: 24 October 2013 / Published online: 20 November 2013

Abstract The American Academy of Pediatrics (AAP) recommends that any child diagnosed with hypertension have an echocardiogram to evaluate for the presence of left-ventricular (LV) hypertrophy (LVH) and advocates that LVH is an indication to initiate or intensify antihypertensive therapy. However, there is no consensus on the ideal method of defining LVH in the pediatric population. Many pediatric cardiologists rely on wall-thickness *z*-score of the LV posterior wall and/or interventricular septum to determine LVH. Yet, the AAP advocates using LV mass indexed to 2.7 ($LVMI^{2.7}$) $\geq$ 51 $g/m^{2.7}$ to diagnose LVH. Recently, age-specific reference values for LVMI $\geq$ 95 % were developed. The objective of the study was to determine the concordance between diagnosis of LVH by wall-thickness *z*-score and diagnosis by $LVMI^{2.7}$ criteria. A retrospective chart review was performed for subjects diagnosed with hypertension at a single tertiary care center (2009–2012). Echocardiogram reports were reviewed, and assessment of LVH was recorded. Diagnosis of LVH was assigned to each report reviewed according to three criteria: (1) LV wall-thickness *z*-score $>$ 2.00; (2) age-specific reference values for $LVMI^{2.7}$ $>$ 95th percentile; and (3) $LVMI^{2.7} > 51$ $g/m^{2.7}$. Cohen's kappa statistic was used as a measurement of agreement between diagnosis by wall-thickness *z*-score and diagnosis using $LVMI^{2.7}$. A total of 159 echocardiograms in 109 subjects were reviewed. Subjects included 31 females and 77 males, age 13.2 $\pm$ 4.4 years, and 39 (42 %) with a diagnosis of secondary hypertension. LVH was diagnosed in 31 cases (20 %) based on increased wall-thickness *z*-score. Using $LVMI^{2.7} > 95$ %, LVH was found in 75 (47 %) cases (mean $LVMI^{2.7}$42.3 $\pm$ 17.2 $g/m^{2.7}$ [range 11.0–111 $g/m^{2.7}$]). The wall-thickness *z*-score method agreed with $LVMI^{2.7} > 95$ % diagnosis 71 % of the time (kappa 0.4). Using LVH criteria of $LVMI^{2.7} \geq 51$ $g/m^{2.7}$, 33 (21 %) subjects were diagnosed with LVH. There was 79 % agreement in the diagnosis of LVH between the wall-thickness *z*-score method and $LVMI^{2.7} > 51$ $g/m^{2.7}$ (kappa 0.37). There is poor concordance between the diagnosis of LVH on echocardiogram reports using wall-thickness *z*-score and diagnosis of LVH using $LVMI^{2.7}$ criteria. It is important to establish a consensus method for diagnosing LVH because of the high frequency of cardiovascular complications in children with hypertension.

Keywords Left-ventricular hypertrophy · Hypertension · Pediatrics

D. Mirchandani · J. Bhatia
Department of Pediatrics, Cohen Children's Medical Center of New York, North Shore-LIJ Health System, New Hyde Park, NY, USA

D. Leisman · N. Chorny · R. Frank · L. Infante · C. Sethna (✉)
Division of Pediatric Nephrology, Cohen Children's Medical Center of New York, North Shore-LIJ Health System, 269-01 76th Avenue, New Hyde Park, NY 11040, USA
e-mail: csethna@nshs.edu

E. N. Kwon · R. Cooper
Division of Pediatric Cardiology, Cohen Children's Medical Center of New York, North Shore-LIJ Health System, New Hyde Park, NY, USA

Introduction

In adult literature, it is widely recognized that left-ventricular hypertrophy (LVH) resulting from hypertension is associated with an increased risk of myocardial infarction, stroke, and mortality independent of traditional cardiovascular risk factors [15]. Although the degree of blood

pressure elevation that results in end organ damage in children has not yet been established, LVH is the most clinically evident form of target organ damage associated with childhood hypertension. LVH is present in 34–38 % of children with mild, untreated hypertension [4, 26].

The American Academy of Pediatrics (AAP) Fourth Report on the Diagnosis, Evaluation and Treatment of High Blood Pressure in Children and Adolescents recommends that any child diagnosed with hypertension have an echocardiogram to evaluate for the presence of LVH. The report advocates that LVH is an indication to initiate or intensify antihypertensive therapy [19]. However, there is controversy surrounding the measurement of LV mass and no consensus on the ideal method of defining LVH in the pediatric population.

The American Society of Echocardiography (ASE) guidelines for pediatric echocardiogram include the following: recommendations for the measurement of LV size using two-dimensional (2D) linear measurement of short-axis diameters and wall thickness as well as 2D and M-mode volumetric assessment of LV mass [17]. However, there is little guidance regarding the ideal method for diagnosing LVH and indexing of LV mass for body size in the pediatric population. In clinical practice, many pediatric cardiologists rely on z-scores of the thickness of the LV posterior wall (LVPW) and/or interventricular septum (IVS) alone to determine LVH [21]. Alternatively, the AAP Fourth Report recommends the use of the LV mass indexed to height to the 2.7th power ($LVMI^{2.7}$) in grams/meter$^{2.7}$ to diagnose LVH. The report recommends the use of $LVMI^{2.7} > 51$ g/m$^{2.7}$ (>99th % for adults and children) as a conservative cut-off point for the diagnosis of LVH [19]. Since then, age-specific reference values for $LVMI^{2.7}$ have been developed [11]. However, this is not as reliable in infants and patients with a smaller body surface area (BSA) [8].

Clinicians often rely on the results of the echocardiogram to base their decision to treat mild to moderate hypertension in children. Anecdotally, we have noticed that there is often a discrepancy in the diagnosis of LVH between the two metrics of $LVMI^{2.7}$ and LV thickness z-score. The purpose of this study was to analyze the concordance of $LVMI^{2.7}$ and LV mass z-score in the diagnosis of LVH in children with hypertension in a single center.

Methods

Medical records at a single tertiary care pediatric center were retrospectively reviewed for children and adolescents <21 years of age diagnosed with hypertension during a 4-year period (2009–2012). Hypertension was defined as mean blood pressure >95 % for height and sex on 24-h ambulatory blood pressure monitoring [25]. Echocardiograms were performed per institutional protocol according to ASE pediatric guidelines by a pediatric cardiology ultrasound technician [17]. Height and weight were recorded at the time of the study, and BSA was calculated. M-mode measurements were made by the ultrasound technician performing the study, and the final interpretation of the study was performed by 1 of 11 pediatric cardiologists at our center. The primary method of diagnosing LVH was by evaluation of the z-score of the LVPW or IVS thickness. Echocardiograms performed outside of the institution were excluded.

Repeat measurements in a random sample showed excellent reproducibility with intraclass correlations of 0.97 for left-ventricular inner dimension (LVID) and 0.73 for LVPW, but they were suboptimal at 0.42 for IVS. In the same sample, 2D and M-mode measurements showed intraclass correlation coefficients between 0.90 and 0.96 for the three variables. Relative wall thickness (RWT) was calculated to assess LV geometry using the following formula: (IVS + LVPW)/LVID. RWT was considered abnormal if it was $\geq$0.42 [6]. LV geometry was defined as follows: (1) concentric hypertrophy (LVMI > 95 % and RWT > 0.42), (2) concentric remodeling (LVMI < 95 % and RWT > 0.42), (4) eccentric hypertrophy (LVMI > 95 % and RWT < 0.42), and (4) normal. The study was approved by the North Shore-LIJ Health System Institutional Review Board.

Echocardiogram reports were assigned a diagnosis of LVH by three methods: (1) LV wall-thickness (LVPW and IVS) z-score > 2.00; (2) age-specific reference values for $LVMI^{2.7}$ > 95th percentile [11]; and (3) AAP Fourth Report guidelines of $LVMI^{2.7} > 51$ g/m$^{2.7}$ [19]. Wall thickness z-scores of LVPW and IVS were generated from regression equations of LV measurements and obtained directly from the echocardiogram report [22]. $LVMI^{2.7}$ was calculated from each echocardiogram from M-mode measurements of the IVS, LVID, and LVPW. The Devereux formula for LV mass was used ($LV\ mass = 0.8(1.04[(IVS + LVID + LVPW)^3 - LVID^3] + 0.6)$) [8] and indexed to height$^{2.7}$ [7]. Cohen's kappa statistic was performed to measure agreement in the diagnosis of LVH between the LV mass wall-thickness z-score method and the two cut-off points for $LVMI^{2.7}$. Concordance was graded using 0 to indicate no concordance at all and 1 to represent complete concordance. Sensitivity and specificity rates for the wall-thickness method were calculated for the wall-thickness z-score method compared with the $LVMI^{2.7}$ method. To determine whether minor changes in measurement of wall thickness could account for any discrepancy in LVH diagnosis using the two criteria, the number of echocardiograms assigned a diagnosis of LVH using $LVMI^{2.7}$ criteria with wall-thickness z-scores close to 2 (1.75–1.99) were recorded. All statistical calculations and analyses were performed using commercially available software (SPSS version 18.0).

Table 1 Demographics

Subjects (*N*)	109
Male (%)	77 (71)
Female (%)	31 (29)
Mean age (years)	13.2 ± 4.4 (range 1–21)
Secondary hypertension (%)	42 (39)
No. of echocardiogram reports	159
Mean $LVMI^{2.7}$ ($g/m^{2.7}$)	42.3 ± 17.2
$LVMI^{2.7}$ range ($g/m^{2.7}$)	11–111
No. of echocardiograms with LVH reported on echocardiogram by wall-thickness *z*-score criteria (%)	31 (20)
Concentric remodeling (%)	5 (3)
Concentric hypertrophy (%)	18 (15)
Eccentric hypertrophy (%)	47 (30)

Table 2 LVH diagnosed by age-specific $LVMI^{2.7}$ reference values >95 %

No. of echocardiograms with LVH diagnosed by age-specific reference values (%)	75 (47)
Percent agreement with wall-thickness *z*-score diagnosis of LVH (%)	71
Cohen's kappa statistic	0.4

Table 3 LVH diagnosed by AAP Guidelines of $LVMI > 51\ g/m^{2.7}$

No. of echocardiograms with LVH diagnosed by $LVMI^{2.7} > 51\ g/m^{2.7}$ (%)	33 (21)
Percent agreement with wall-thickness *z*-score diagnosis of LVH (%)	79
Cohen's kappa statistic	0.37

Results

One hundred nine children were identified with a diagnosis of hypertension at a mean age of 13.2 ± 4.4 years (median 14 [range 0.67–21]). Of these, 31 (29 %) were female, and 77 (71 %) were male. A total of 159 echocardiogram reports of these patients were reviewed. Forty-two (39 %) patients showed secondary hypertension. Causes for secondary hypertension included systemic lupus erythematosus, polycystic kidney disease, focal segmental glomerulosclerosis, renal scarring, renal transplant, and obstructive uropathy. The mean $LVMI^{2.7}$ for all children was 42.3 ± 17.2 $g/m^{2.7}$ (range 11.0–111). Eccentric hypertrophy was found in 30 % of children, of whom the majority were transplant recipients. Concentric hypertrophy was found in 15 % and concentric remodeling in 3 % of children. Descriptive characteristics for the patient population are listed in Table 1.

Using wall-thickness IVS and LVPW *z*-score criteria, LVH was diagnosed in 31 (20 %) echocardiograms. In contrast, using age-specific $LVMI^{2.7}$ reference values >95 %, LVH was diagnosed in 75 (47 %) echocardiogram reports. This methodology showed a 71 % agreement and a Cohen's kappa coefficient of 0.4 using the wall-thickness *z*-score criteria diagnosis of LVH. Comparisons are listed in Table 2. Age did not appear to impact the concordance rate (<9 years = kappa 0.4, <9 years = kappa 0.46). Sensitivity analysis that considered an $LVMI^{2.7} \geq 95$ % to have LVH indicated a sensitivity of 41 % and a false-negative rate of 1.5 using the wall-thickness *z*-score method. There were no diagnoses of LVH according to the wall-thickness criteria that did not also meet age-specific reference criteria. Of children with abnormal $LVMI^{2.7}$ but no LVH by *z*-score, the *z*-score for LVPW and/or IVS was borderline elevated (1.75–1.99) in 8 echocardiograms. Excluding those cases, the kappa coefficient between the *z*-score and the $LVMI^{2.7}$ method increased slightly to 0.47.

Based on the conservative cut-off point proposed by the AAP guidelines of $LVMI^{2.7} > 51\ g/m^{2.7}$, a diagnosis of LVH was made in 33 (21 %) echocardiograms. There was 79 % agreement in the diagnosis of LVH between the wall-thickness *z*-score method and the $LVMI^{2.7} > 51\ g/m^{2.7}$ method. Cohen's kappa coefficient showed a concordance value of 0.37. Comparisons are listed in Table 3. Age did not appear to impact the concordance rate (<9 years = kappa 0.38, <9 years = kappa 0.34). When patients with $LVMI^{2.7} \geq 51\ g/m^{2.7}$ were considered to have LVH, sensitivity analysis returned a positive *z*-score sensitivity of 94 % and a false-negative rate of 1.01. There were no false-positive results.

Discussion

The results of this study demonstrate that there is poor concordance between the diagnosis of LVH on echocardiogram reports using the wall-thickness *z*-score compared with that using $LVMI^{2.7}$ criteria in children. There was only 71–79 % agreement between the two methods, and kappa scores were highly discordant. When using wall-thickness criteria compared with $LVMI^{2.7}$ age-specific reference criteria, sensitivity analysis suggested that fewer than half of the patients with LVH were actually diagnosed and that a negative diagnosis was more than half as likely to be a misdiagnosis in this cohort. LVH may be underdiagnosed if the classification is based on ventricular wall *z*-score rather than $LVMI^{2.7}$. The study also shows that age-specific reference criteria for $LVMI^{2.7}$ are more sensitive than the AAP Guidelines of $LVMI^{2.7} > 51\ g/m^{2.7}$ in the diagnosis of LVH.

Hypertension is a known risk factor for coronary artery disease and mortality in adults. Numerous studies in the adult literature have found significant correlations between LVH and cardiovascular morbidity and mortality [7, 15, 16]. Studies of long-term cardiovascular outcomes in children with hypertension are lacking; however, there is evidence that childhood hypertension can lead to adult hypertension [12, 23]. In the Bogalusa Heart Study, children with increased blood pressure were 2–3 times more likely to develop essential hypertension as young adults [2]. Therefore, LVH is often used as a surrogate outcome for cardiovascular risk in children and adolescents.

It is widely accepted that accurate measurements of LV wall thickness and LV mass are important to identify LVH in children with hypertension; however, a standardized definition of LVH has not been established by consensus. In terms of volumetric assessment, cardiac magnetic resonance imaging (MRI) has increasingly become accepted as the "gold standard" for quantification of ventricular mass and volumes of both the right and left ventricle in both adult and pediatric patients [18, 20]. However, it is difficult and expensive to perform, and 2D and three-dimensional (3D) echocardiography are considered feasible alternatives for the evaluation of LV mass [14].

As a pediatric imaging modality, 2D echocardiography has long had the advantage of being widely available, inexpensive, and without risk of radiation exposure. 2D echo LV mass measurements are derived from a mathematical formula that assumes an ellipsoid shape for the left ventricle. In adult studies, these assumptions have been shown to be somewhat inaccurate in deformed hearts, including those with hypertension [24]. 3D echocardiography calculates volumes from summing areas of multiple parallel "discs" without relying on geometric assumptions and thus has been deemed more reliable in the assessment of deformed hearts, including those with congenital heart disease and hypertension [1]. In a group of adolescents, Pacileo et al. [20] showed that LV mass obtained by 3D echocardiography had the strongest correlation to MRI compared with 2D and M-mode echocardiography.

A number of controversies surround the measurement of LV mass. There are significant problems in standardizing echocardiographic measurement of LV mass across echocardiography laboratories. Historically, one method for overcoming this variability in adults is to index the LV mass to body size, most commonly BSA, height in meters squared, or to the 2.7th power [10]. Dividing LV mass by height to the power of 2.7 accounts for LV mass and scaling myocardial mass to body size. This useful application has been adapted in children to compensate for normal growth [11]. However, this indexing method is also limited in the pediatric population because $LVMI^{2.7}$ increases with decreasing height [7]. Numerous studies have shown that $LVMI^{2.7}$ overestimates LV mass in adults [5]. Foster et al. [9] showed that expressing LV mass relative to BSA or height has limitations in the pediatric population because LV mass varies in proportion to lean body mass; however scaling LV mass to BSA in children appears to be better than scaling to height.

Most of the literature on LVH and cardiovascular disease outcome is based on various scaling methods of $LVMI^{2.7}$ and not wall thickness. Yet, in clinical practice, LVH is often times diagnosed based on wall thickness alone [13]. Some argue that the most imperative parameter to evaluate on the echocardiogram report is $LVMI^{2.7}$ because LV wall thickness itself is not an accurate measure of LVH [3]. Similar to our results, Leibowitz et al. found that in adult hypertensive subjects, there was poor concordance (60 % agreement) between the wall-thickness and $LVMI^{2.7}$ methods. There was a tendency to underestimate LVH in females and overestimate LVH in males using wall thickness compared with $LVMI^{2.7}$ [13]. One can speculate that a possible reason for the discrepancy between the two methods may be due to small measurement differences. Any small increment in measurement of any wall thickness, even if still within normal limits, will be amplified because LV mass is based on these measurements elevated to the third power. We showed that a few wall-thickness measurements in children with abnormal $LVMI^{2.7}$ were close to a *z*-score of 2. However, even after taking those into consideration, there still was poor concordance between the two methods.

The limitations of this study include the following: the small sample size, the retrospective nature of the design, and the lack of the true gold standard, *i.e.*, cardiac MRI, to assess LV mass. There were also multiple sonographers performing the echocardiograms and measurements and multiple physicians interpreting them. However, the findings of this study bring to light the dilemma that clinicians often face regarding treatment decisions of children with hypertension when they receive conflicting data.

Conclusion

We conclude that there is poor concordance of diagnosis of LVH on echocardiogram reports using wall-thickness *z*-score and that using $LVMI^{2.7}$ criteria. Therefore, it is important to establish a consensus method for diagnosing LVH, as well as the optimal standardization of LV mass for body size, because of the high risk of cardiovascular complications in children with long-standing hypertension. Extrapolation of adult data to children may indicate that long-term LVH may have significant cardiovascular risks in children as they age. The diagnosis of LVH and early implementation of antihypertensive agents may help limit

the degree of progressive cardiovascular morbidity and mortality in children.

References

1. Alfakih K, Reid S, Jones T, Sivananthan M (2004) Assessment of ventricular function and mass by cardiac magnetic resonance imaging. Eur Radiol 10:1813–1822
2. Bao W, Threefoot SA, Srinivasan SR et al (1995) Essential hypertension predicted by tracking of elevated blood pressure from childhood to adulthood: the Bogalusa Heart Study. Am J Hypertens 8:657–665
3. Bauml MA, Underwood DA (2010) Left ventricular hypertrophy: an overlooked cardiovascular risk factor. Cleve Clin J Med 77:381–387
4. Belsha CW, Wells TG, McNiece KL et al (1998) Influence of diurnal blood pressure variations on target organ abnormalities in adolescents with mild essential hypertension. Am J Hypertens 11:410–417
5. Chirinos JA, Segers P, Buyzere ML, Kronmal RA, Raja MW, De Bacquer S et al (2010) Left ventricular mass allometric scaling, normative values, effect of obesity, and prognostic performance. Hypertension 56:91–98
6. Daniels SR, Meyer RA, Liang YC, Bove KE (1988) Echocardiographically determined left ventricular mass index in normal children, adolescents, and young adults. J Am Coll Cardiol 12: 703–708
7. de Simone G, Daniels SR, Devereux RB et al (1992) Left ventricular mass and body size in normotensive children and adults: assessment of allometric relations and impact of overweight. J Am Coll Cardiol 20:1251–1260
8. Devereux RB, Reichek N (1977) Echocardiographic determination of the left ventricular mass in man. Anatomic validation of the method. Circulation 55:613–618
9. Foster BJ, Mackie AS, Mitsnefes M, Ali H, Mamber S, Colan SD (2008) A novel method of expressing left ventricular mass relative to body size in children. Pediatr Cardiol 117:2769–2775
10. Gidding SS (2010) Controversies in the assessment of left ventricular mass. Hypertension 56:26–28
11. Khoury PR, Mitsnefes M, Daniels SR, Kimball TR (2009) Age-specific reference intervals for indexed left ventricular mass in children. J Am Soc Echocardiogr 22:709–714
12. Lauer RM, Clarke WR (1989) Childhood risk factors for high blood pressure: the Muscatine Study. Pediatrics 84:633–641
13. Leibowitz D, Planer D, Ben-Ibgi F et al (2007) Measurement of wall thickness alone does not accurately assess the presence of left ventricular hypertrophy. Clin Exp Hypertens 29:125–199
14. Lenstrup M, Kjaergaard J, Petersen CL et al (2006) Evaluation of left ventricular mass measured by 3D echocardiography using magnetic resonance imaging as gold standard. Scand J Clin Lab Invest 66:647–658
15. Levy D, Garrison RJ, Savage DD, Kannel WB, Kastelli WP (1990) Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. N Engl J Med 322:1561–1566
16. Liao Y, Cooper RS, Durazo-Arvizu R et al (1997) Prediction of mortality risk by different methods of indexation for left ventricular mass. J Am Coll Cardiol 29:641–647
17. Lopez L, Colan SD, Frommelt PC et al (2010) 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 23:465–495
18. Mertens L, Ganame J, Eyskens B (2007) What is new in pediatric cardiac imaging. Eur J Pediatr 16:71–88
19. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents (2004) The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics 114:555–576
20. Pacileo G, Castaldi B, Di Salvo G et al (2013) Assessment of left-ventricular mass and remodeling in obese adolescents: m-mode, 2D, or 3D echocardiography? J Cardiovasc Med 14:144–149
21. Pettersen MD, Du W, Skeens ME, Humes RA (2008) Regression equations for calculation of *z* scores of cardiac structures in a large cohort of healthy infants, children, and adolescents: an echocardiographic study. J Am Soc Echocardiogr 21:922–934
22. Pettersen MD, Du W, Skeens ME, Humes RA (2008) Regression equations for calculation of *z* scores of cardiac structures in a large cohort of healthy infants, children, and adolescents: an echocardiographic study. J Am Soc Echocardiogr 21(8):922–934
23. Redwine KM, Falkner B (2012) Progression of prehypertension to hypertension in adolescents. Curr Hypertens Rep 14:619–625
24. Salcedo EE, Gockowski K, Tarazi RC (1973) Left ventricular mass and wall thickness in hypertension. Am J Cardiol 44:936–940
25. Soergel M, Kirschstein M, Busch C et al (1997) Oscillometric twenty-four hour ambulatory blood pressure values in healthy children and adolescents: a multicenter trial including 1141 subjects. J Pediatr 130:178–184
26. Sorof JM, Alexandrov AV, Cardwell G, Portman RJ (2003) Pediatrics 11:61–66