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Normative Left Ventricular M-mode Echocardiographic Values in Preterm Infants Up To Two Kilograms

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Abstract

Background—There is a paucity of normative echocardiographic data in preterm infants. The objectives of this study were: (1) derive left ventricular (LV) M-mode reference values, and (2) compare the performance of alternative methods of indexing LV dimensions and mass (LVM) in preterm infants. We propose that indexing LV measures to weight in preterm infants is a practical approach given the variability associated with tape-measure length measurement in infants.

Methods—In this retrospective study LV M-mode echocardiographic measurements of end diastolic interventricular septal thickness (IVSd), end diastolic LV posterior wall thickness (LVPWd), LV end diastolic and systolic dimensions (LVEDD, LVESD), LVM, and relative wall thickness (RWT) were remeasured in 503 hospitalized preterm infants ≤ 2 Kg (372 from a retrospective sample and 131 prospectively enrolled). Measures for all variables did not differ between retrospective and prospective samples so results were pooled. LV dimensions and LVM indexed for weight, length, and body surface area (BSA) sex-specific centile curves and corresponding Z scores were generated using Cole's lambda-mu-sigma method. Threshold limits (10^{th}, and 80^{th} percentile; P10, P80) were used to generate RWT normative range.

Results—Sex-specific centile curves using LVM, IVSd, LVPWd, LVEDD, and LVESD indexed to weight were similar to the curves generated using length and BSA. The mean [P10, P80] normal range for RWT was 0.33 (0.26, 0.38).

Conclusions—From this large cohort of preterm infants, we developed LV M-mode dimension and LVM centile curves indexed to weight as a practical method to assess LV morphology in preterm infants.

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Keywords

Echocardiography; Reference values; M-mode; Preterm; Left Ventricle

INTRODUCTION

Two dimensionally guided M-mode echocardiography is commonly used to obtain measures of left ventricular (LV) chamber size and wall thickness as well as derived values of left ventricular mass (LVM) and relative wall thickness (RWT) in children and adults. Because left ventricular hypertrophy (LVH) is known to be associated with adverse cardiac events in adults, increased attention is being paid to the identification of early stages of LVH during childhood.[1–5] Elevated LVM, derived from M-mode echocardiography, is of particular interest because it is often used to define LVH.[6] M-mode echocardiography offers the advantage of quick acquisition in irritable preterm infants with sedation risks. Appropriate normalization of LV measures is especially critical in young infants because of the enormous variability in body size and altered body proportions with variable gestational age and growth.[7] Numerous methods have been proposed to normalize cardiac dimensions to body size, including simple division by height, weight, or body surface area (BSA) or more complex allometric relationships of these body measures.[7–13] LVM indexed to height ($g/m^{2.7}$ or $g/m^{2.16}$) has gained wide acceptance, but may not be an ideal method for standardizing LVM for body size in infants.[4–7, 14] Furthermore indexing to length or body surface may not be optimal in preterm infants because of the inaccuracy of the commonly used tape-measure technique for length measurement in neonates.[15, 16] More recently centile curves used for pediatric growth charts by the National Center for Health Statistics, have been demonstrated to be useful for evaluating LVM in children.[7, 17–20]

Improved survival of extremely premature babies has further led to the recognition of LVH in preterm infants.[21] Studies of former preterm infants at 5 and 7 years of age found decreased LV chamber size and increased ventricular septal thickness but did not track cardiac abnormalities from the nursery.[22, 23] The paucity of normative echocardiographic data in preterm infants limits the identification of patients that might be at risk for persistent cardiac abnormalities. Biased or imprecise cardiac growth curves can lead to inappropriate clinical or management decisions.[8, 24–30] In this study we sought to derive LV M-mode reference values with centile curves as well as compare the performance of alternative methods of indexing LV measures in preterm infants (length, weight, and BSA).

METHODS

Study Design

For the purpose of this retrospective study, LV M-mode echocardiographic remeasurements were made in two cohorts of preterm infants: (1) a prospective cohort of 131 preterm infants (born less than 29 weeks gestational age) was recruited between August 2011 and November 2013, and (2) a retrospective database generated cohort of 372 preterm infants from January 1, 2005 through December 31, 2014. The institutional review board of Washington

University School of Medicine approved the study. All subject guardians in the prospective sample provided written informed consent.

Retrospective study population—Last ten year echocardiographic and clinical databases for St. Louis Children's Hospital were retrospectively reviewed. All preterm infants ≤ 2 Kg born from 2005 to 2014, with a technically adequate echocardiographic evaluation (defined as an echocardiogram with measurable M mode) performed at St. Louis Children's Hospital were eligible for inclusion. Exclusion criteria were: 1) congenital heart disease including moderate or large atrial level shunt; 2) moderate or large patent ductus arteriosus; 3) known genetic cardiomyopathy including hypertrophic cardiomyopathy, genetic syndromes (such as Noonan, Pompe's disease), neuromuscular disease, chromosomal abnormalities, diagnosis of pulmonary hypertension (diagnosed based on clinical chart review or echocardiographic interpretation), connective tissue disease, and clinical or radiologic diagnosis of kidney disease 4) patients with incomplete medical records; 5) enrollment in the prospective sample (described below). Patients with moderate or large shunts on a prior echocardiogram were eligible if at least one month elapsed until the time of the study echocardiogram.

Prospective study population—Additionally, 131 preterm infants were prospectively enrolled from among infants participating in the Prematurity and Respiratory Outcomes Program (PROP), a 7-center initiative sponsored by the National Heart, Lung and Blood Institute (Clinical Trials number: NCT01435187).[31] All infants in the prospective sample were enrolled at St. Louis Children's Hospital neonatal intensive care unit between August 2011 and November 2013. All prospective subjects had structurally normal hearts; none had a family history of genetic cardiomyopathy, genetic syndromes or known chromosomal abnormality. All prospectively enrolled subjects were reevaluated 1 year later to validate that they remained free of any recognizable systemic disorder, including hypertension. All patients enrolled in the prospective study routinely had echocardiograms performed per the Prematurity and Respiratory Outcomes Program study protocol.[31] All subjects with initial echocardiographic readings of moderate or large shunts were excluded without review. If the initial reading of shunt size was small to moderate, a senior echocardiographer (MCJ) reviewed the studies to exclude any with moderate or larger shunts. PDA was graded as small if the ratio of the smallest ductal diameter to ostium of the left pulmonary artery was < 0.5.[32] Atrial shunts were qualitatively graded as small if there was no right ventricular or right atrial enlargement and the color flow Doppler diameter of the shunt was less than 20% of the length of the atrial septum.

Body Size Parameters

Measurements for weight and length were based on neonatal intensive care clinical records with daily weight and weekly tape measured length while the infant was supine with stretched legs. The most recent length, and weight measurement on the day echocardiogram performed was collected. We used the Haycock formula for calculation of body surface area: $\text{weight}^{0.5378} \times \text{height}^{0.3964} \times 0.024265$.[33]

Echocardiography

All echocardiographic studies were performed on commercially available cardiac ultrasound scanners according to the guidelines of the American Society of Echocardiography.[28] All of the 503 echocardiograms were re-measured offline for the purposes of the present study by SC. MCJ remeasured 100 studies in a blinded fashion and was allowed to choose the M-mode image for measurement for interobserver variability determination. Measurements were made by 2-dimensional guided M-mode echocardiography using the parasternal short-axis view at the level of the papillary muscles. End diastole was defined as the time of maximum LV dimension. Electronic calipers were used to measure end diastole interventricular septal thickness (IVSd), left ventricular (LV) posterior wall thickness (LVPWd), and LV dimension at end diastole (LVEDD) and end systole (LVESD). Measurements were repeated over 3 consecutive cardiac cycles and averaged. LVM was estimated by the Devereux equation, LVM (grams) = 0.8{1.04 [(LVEDD + LVPWd + IVSd)^3 − (LVEDD)^3 + 0.6.[34] Relative wall-thickness (RWT) was calculated using 2 formulas: (1) RWT P equals twice the posterior wall thickness (LVPWd) over LVEDD; (2) RWT SP equals the ratio of the sum of LVPWd and IVSd over LVEDD.[35, 36]

Statistical analysis

Descriptive statistics were used to summarize demographic and echocardiographic measures. Continuous variables were summarized as mean ± SD, or mean (10th, and 80thpercentile [P10, P80]), as appropriate. Categorical variables were presented by the absolute and relative frequencies or as numbers and percentages. Comparisons between the retrospective and prospective samples were performed using independent-samples t test or Mann-Whitney U test for continuous variables and chi square or Fisher's exact test for categorical variables. Intraobserver and interobserver variability of IVSd, LVPWd, LVEDD, LVESD and LVM measurements were determined in 100 randomly selected patients using intraclass correlation coefficient (ICC). A 2-sided p value < 0.05 was considered statistically significant and performed by using SAS 9.3 version (SAS Institute, Inc, Cary, NC).

Centile curves—The lambda-mu-sigma (LMS) method was used to construct smoothed reference centile curves for LV dimensions (IVSd, LVPWd, LVEDD, and LVESD) and LVM indexed for three body size parameters (weight, length and body surface area).[37] The LMS method fits 3 curves, lambda (L), mu (M) and sigma (S) which represent the Box-Cox power transformation of skewness, the mean and the coefficient of variation, respectively. The data was assessed for influential outliers using LOESS regression, a robust regression technique, in SAS. Observations with residuals outside of the 2nd and 98th percentiles were removed. Separate sex-specific curves were constructed for each of the above 5 M-mode echocardiographic measures and the 3 body size parameters. Using the LMS function in the Generalized Additive Models for Location, Scale and Shape (GAMLSS) R package, the effective degrees of freedom parameters (for lambda, mu, and sigma) with the lowest generalized Akaike information criterion (gAIC) was identified by an automated algorithm. The reference centile curves were generated to reflect the 5th, 10th, 25th, 50th, 75th, 80th, 90th, and 95th centiles. Z scores were computed using the following formula: $Z\ score$ = [(LVM/M(weight))$^{L(weight)}$ — 1]/(L(weight)xS(weight)). Comparison of Z scores derived

from weight were compared to the indexes of length and Haycock BSA using Bland-Altman plots and the ICC.[38]

Confounding effects—The effect of the following potential confounding factors on LVM indexed to weight were evaluated using quantile regression: 1) postmenstrual age (defined as the time elapsed between the first day of the last menstrual period and birth [gestational age] plus the time elapsed after birth [chronological age],[39] 2) chronological age, 3) sex, and 4) PDA(yes/no). Quantile regression is a robust regression model which does not make any assumption regarding normality and allows for estimation of the quantiles of the distribution of the outcome variable. While it cannot be used to compute Z scores, it can estimate the effect of covariates for different quantiles of LVM. Weight was modeled using a spline effect and covariates considered were postmenstrual age, sex, and PDA(yes/no). An additional model was constructed to consider the effect of chronological age instead of postmenstrual age. Covariate effects were tested using a likelihood ratio test and a significance level of 0.05 was used.

RESULTS

Demographics

We reviewed 692 preterm infant (who were 2 Kilogram or less) charts and their echocardiograms. Of those, 503 patients met inclusion/exclusion criteria and were included in the final analysis. Of the 189 excluded patients 107 had moderate/large PDA and/or atrial level shunt and 82 patients had congenital heart disease. About a third of the patients (n = 39) that were excluded due to moderate/large PDA and or atrial level shunt had underlying pulmonary hypertension. The baseline characteristics of all 503 preterm infants who participated in the study are presented in Table 1. The study population had equal sex distribution (249/503, 49.5% males). A small atrial level shunt was seen in the majority of the patients (90%). Small ductal shunts were noted in about 40% of patients. Of note, 189 patients (37.5%) were extremely low birth weight (weight < 1 Kg on day of scan).

Echocardiographic values—Results were pooled because there were no differences in echocardiographic (mean ± SD) measures when comparing retrospective versus (vs.) prospective groups, respectively: IVSd (2.7 ± 0.6 vs. 2.7 ± 0.4 mm, P = 0.8), LVPWd (2.4 ± 0.5 vs. 2.5 ± 0.4 mm, P = 0.1), LVEDD (13.8 ± 2.9 vs. 14.1 ± 2.2 mm, P = 0.2), LVESD (8.9 ± 2.2 vs. 9.1 ± 1.8 mm, P = 0.3), and LVM (4.27 ± 2.04 vs. 4.38 ± 1.49 g, P = 0.5). LV dimensions (IVSd, LVPWd, LVEDD, and LVESD) and LVM indexed for weight sex-specific centile curves were generated (Figure 1, 2). The L, M and S measures to compute Z scores for weight is provided in Tables 2, and 3 (for males and females respectively). Bland-Altman plots with corresponding ICCs comparing weight versus length or weight versus BSA for all measured indexed LV dimensions including LVM are shown in Supplementary appendix, figure S1–S10. The ICCs demonstrate the strong agreement of weight with both length and BSA. The mean [P10, P80] normal range for RWT was 0.33 (0.26, 0.38).

Confounders—The quantile regression model with postmenstrual age found that weight was independently associated with LVM between the 5^{th} and 95^{th} percentiles (P < 0.0001 for

all percentiles). Sex was independently associated with LVM between the 5th and 75th percentiles where females had lower LVM compared to males in these percentiles (5th, P = 0.04; 10th, P < 0.0001; 25th, P = 0.0002, 50th, P = 0.02, 75th P = 0.04). PDA and postmenstrual age were not found to be independently associated with LVM. The quantile regression model using chronological age as a covariate found that weight, sex, and PDA had associations with LVM similar to the model using postmenstrual age. However, chronological age was independently associated with LVM for the 10th (P = 0.03), 25th (P = 0.006), 75th (P = 0.01) and 80th (P = 0.03) percentiles. For every one-day increase in days of life, the LVM increases by 0.008 (95% confidence interval: 0.0015, 0.0141) to 0.011 grams (95% confidence interval: 0.0023, 0.0190) for the significant quantiles. The impact of chronological age on the model for LVM indexed to weight in males is shown with a graph of the smoothed fitted parameter in Figure 3.

Interobserver and Intraobserver variability—The reproducibility analysis is summarized in Table 3. No significant differences were observed within observers (P > 0.05). For all interobserver measurements, there was an interclass correlation coefficient ≥ 0.96 with $P < 0.01$.

DISCUSSION

This study provides normative M-mode reference values with sex-speific centile curves from a large population of preterm infants up to 2 kilograms. Allometric analysis with LMS centile curves affirmed that indexing these measures to weight is appropriate. Because preterm infants are a heterogeneous group of hospitalized patients, and it is difficult to define a ‘healthy preterm’ population it may be appropriate to use tighter normal ranges than the standard P5 and P95. The smoothed centiles curves along with LMS parameters generated allow for the calculation of the percentiles and Z scores facilitating the interpretation of LV M-mode measures in preterm infants. Additionally, these data allow for graphical or calculated Z score threshold limits to vary depending on the clinical question. We included determination of normal values for RWT because this measure does not require indexing to body size and has been widely used in adults to classify patterns of remodeling.[40] Upper limits of RWT in this preterm population are increased compared to pediatric values possibly in part secondary to morbidity inherent in hospitalized preterm infants or normal age related changes.[41, 42]

Because our retrospective cohort was a 10-year echocardiographic database generated group and did not represent a consecutive birth cohort we validated these results with a smaller prospectively enrolled cohort. The absence of differences between these groups offers some evidence against a bias based on test indication. Our large dataset allowed for a robust comparison of body size indexing methods in preterm infants ≤ 2 Kg. Our results demonstrated that LV dimensions indexed to weight were similar to the curves generated using BSA, and length. Smaller studies of preterm infants by Skelton et al (n = 79), Zecaca et al (n = 35), and Abushaban et al (n = 268) did not explore allometric relationships and did not calculate LVM.[43–45] A study of 40 preterm infants comparing small versus appropriate for gestational age groups included LVM and found that indexing to length as compared with weight removed differences between groups at the same time acknowledging the

practical difficulties of length measurement.[16] Nagasawa et al. concluded length was an appropriate index for LVEDD in patients under age 1 year with only 32 patients less than 32 weeks gestation.[46] These prior studies did not utilize centile curves for LV dimensions.

LVH is recognized as an independent predictor of cardiovascular morbidity and mortality in adults.[1, 2] Accurate diagnosis of LVH depends on normalization of LVM for body size. There has been debate regarding the best method of standardizing LVM.[7, 17, 47] Numerous authors have described both lean body mass (LBM) and fat free mass (FFM) as ideal methods for indexing LVM, however; these measures have practical barriers.[17, 47] Therefore, surrogates of LBM such as weight, height, and BSA, have been used to index LVM in various studies.[7, 14, 48, 49] Although LVM/height$^{2.7}$ is a widely accepted method of normalizing LVM, it has limitations in young children.[7, 17] LVM index is known to increase with decreasing height, particularly for height < 140 cm.[7, 14] Furthermore indexing to length or body surface may not be optimal in preterm infants because of the inaccuracy of the commonly used tape-measure technique.[15, 16] In addition, length is more prone to error because it is obtained less frequently than weight in neonatal intensive care units. In small studies of term and preterm neonates body weight had the best correlation with fat free mass measured with dual energy x-ray absorptiometry (DEXA).[50, 51]

Based on these considerations for LVM we tested weight as a method of indexing for all LV measures and generated sex-specific weight centile curves for these preterm infants ≤ 2Kg. Because weight is a practical measurement in preterm infants and our analysis found that length or BSA were not superior indexes, we propose weight should be used as the index for LV dimensions in small premature infants. Foster et al recently published LBM predictive equations for children and adolescents that have not been validated for young infants.[17] Future work could include deriving similar predictive equation for young infants and validating it with LBM or FFM.

Limitations

This study has some notable limitations. First, the retrospective study population is likely biased because patients underwent echocardiography for clinical reasons and did not represent a consecutive birth cohort. Moreover, all of these infants were cared for at a tertiary care referral center suggesting bias towards worse disease. Next, our cohort comprised heterogeneous ethnic preterm infants. We could not evaluate the effect of ethnicity on LV dimensions. We limited the analysis of confounding factors to LVM secondary to the complex nature of quantile regression and to reduce the potential for multiple comparison errors. The high incidence of PDA in the preterm population makes it difficult to eliminate PDA as a confounding factor. These infants may have had persistent altered LV dimensions from a moderate to large PDA present at some time prior to the study echocardiogram. We did not measure LBM, which is considered the optimal method for standardizing LVM. Although 2-dimensional measurements have been recommended in the pediatric population[28] we found that M-mode had practical advantages in these preterm infants. Methods that use 2 dimensional echocardiography such as the area length algorithm[52] are difficult to utilize in agitated preterm infants with risk factors that prevent sedation. MRI imaging would be an ideal validation tool but also has practical challenges in

this population. Lastly, our analysis of confounding factors for LVM suggests that at ages far from the mean chronological age (80 days and beyond), these centile curves are less accurate. Clinical outcome studies are needed to validate the use of LV dimensions indexed to weight with LMS centile curves.

Conclusions

Data from this large study in preterm infants provide reference values for LV dimensions and LVM with sex-specific weight centile curves as a practical method to assess LV morphology in preterm infants up to 2 kilograms. These findings may influence risk assessment and impact decision making of clinicians caring for these high risk infants. Further long term clinical follow-up of these subjects will enable validation of these reference values and uncover additional links between preterm morbidities and cardiac abnormalities.

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Abbreviations

BSA	Body surface area
DEXA	Dual energy x-ray absorptiometry
EDF	effective degrees of freedom
FFM	Fat free mass
GAMLSS	Generalized Additive Models for Location, Scale and Shape
ICC	intraclass correlation coefficient
gAIC	generalized Akaike information criterion (gAIC)
IVSd	Interventricular septal thickness diastole
LBM	Lean body mass
LV	Left ventricular
LVEDD	Left ventricular end diastolic dimension
LVESD	Left ventricular end systolic dimensions
LVH	Left ventricular hypertrophy
LVM	Left ventricular mass
LVPWd	Left ventricular posterior wall thickness diastole
L	Lamda

M	Mu
PDA	Patent ductus arteriosus
PROP	Prematurity and Respiratory Outcomes Program (PROP)
RWT	relative wall thickness
S	Sigma

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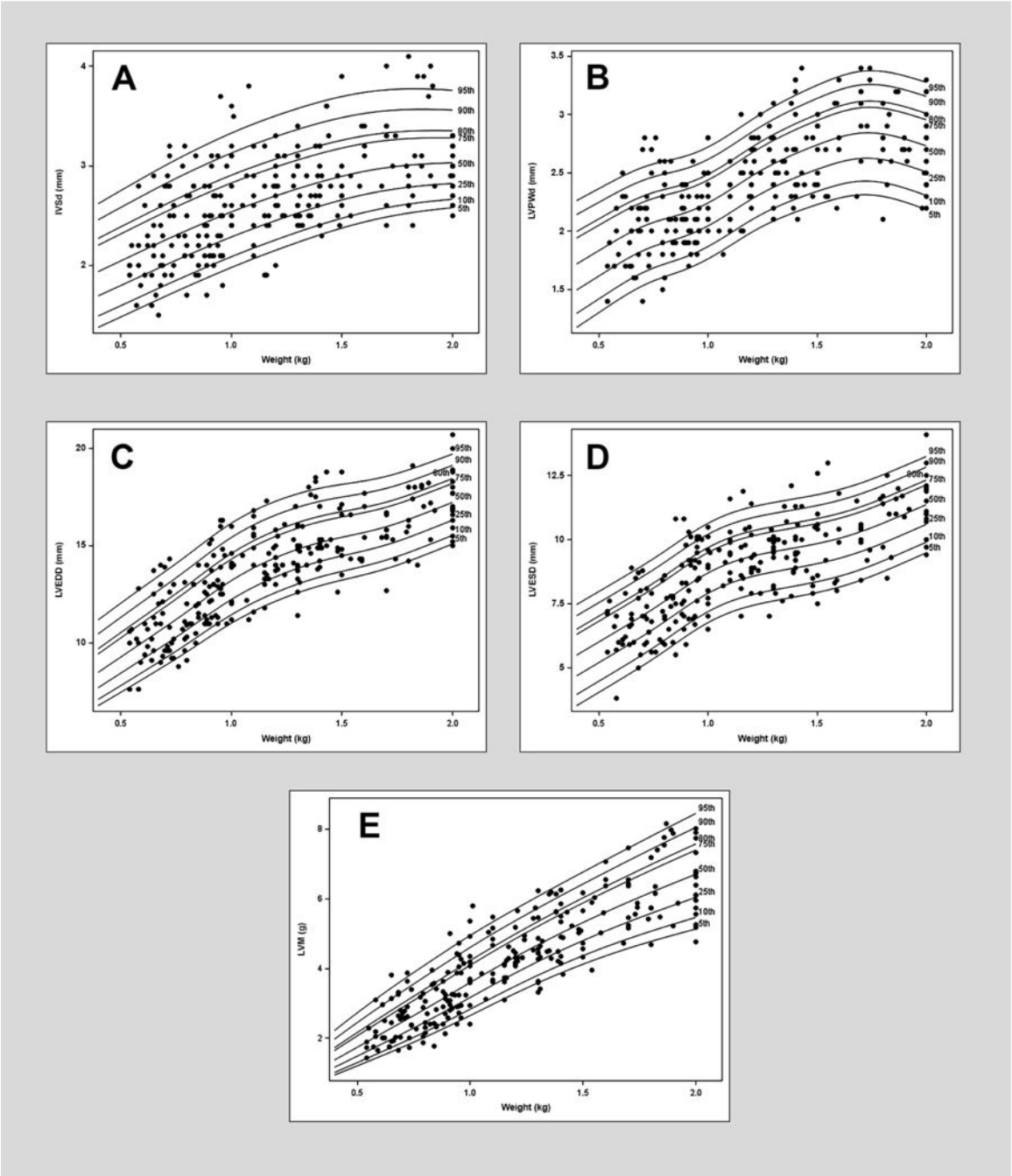

Figure 1.

Reference centile curve for males generated using lambda-mu-sigma (LMS) method for A) end diastole interventricular septal thickness (IVSd) normalized by weight on the day of scan B) left ventricular posterior wall thickness (LVPWd) normalized by weight on the day of scan C) left ventricular dimension end diastole (LVEDD) normalized by weight on the day of scan D) left ventricular dimension end systole (LVESD) normalized by weight on the day of scan E) left ventricular mass (LVM) normalized by weight on the day of scan.

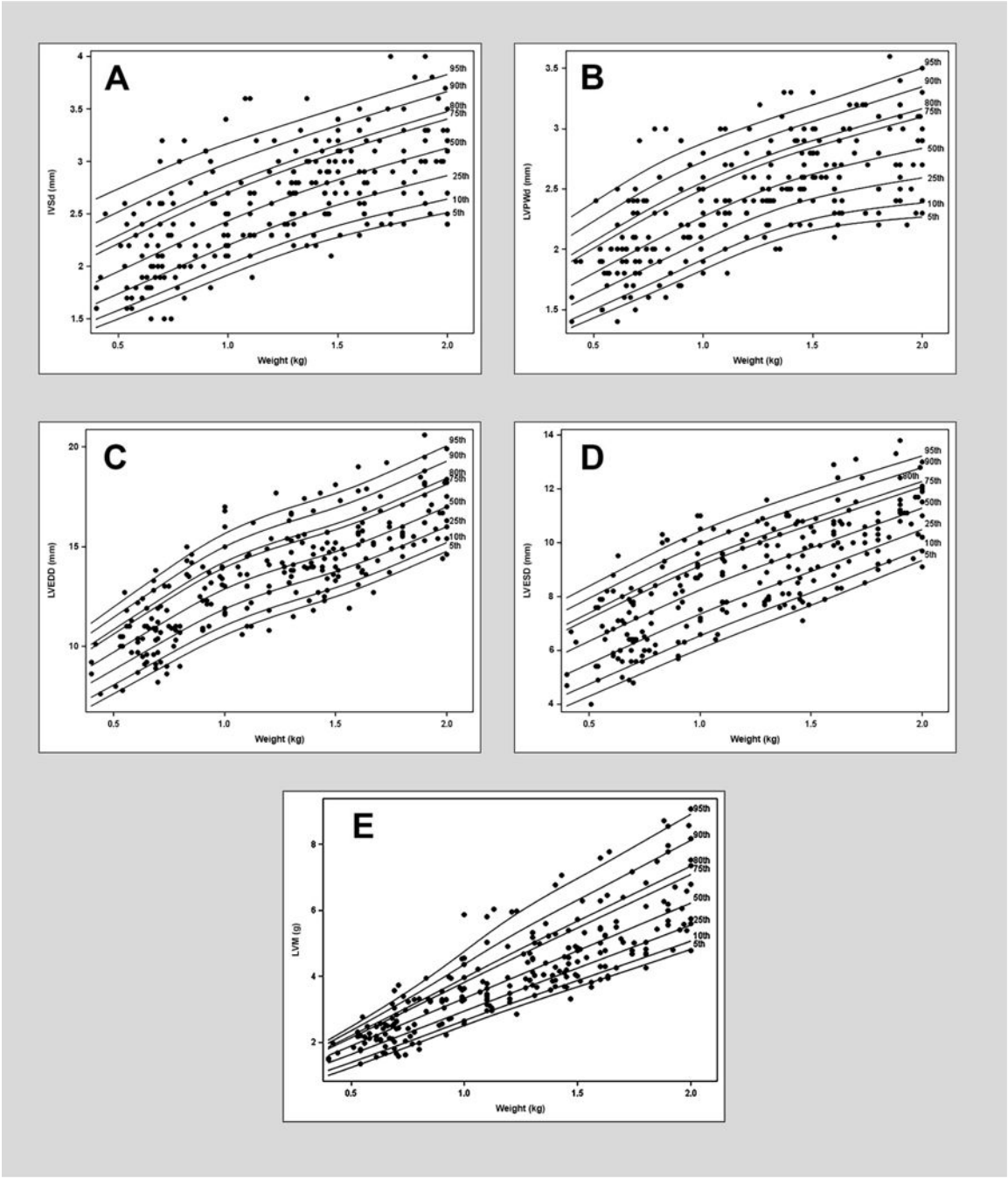

Figure 2.

Reference centile curve for females generated using lambda-mu-sigma (LMS) method for A) end diastole interventricular septal thickness (IVSd) normalized by weight on the day of scan B) left ventricular posterior wall thickness (LVPWd) normalized by weight on the day of scan C) left ventricular dimension end diastole (LVEDD) normalized by weight on the day of scan D) left ventricular dimension end systole (LVESD) normalized by weight on the day of scan E) left ventricular mass (LVM) normalized by weight on the day of scan.

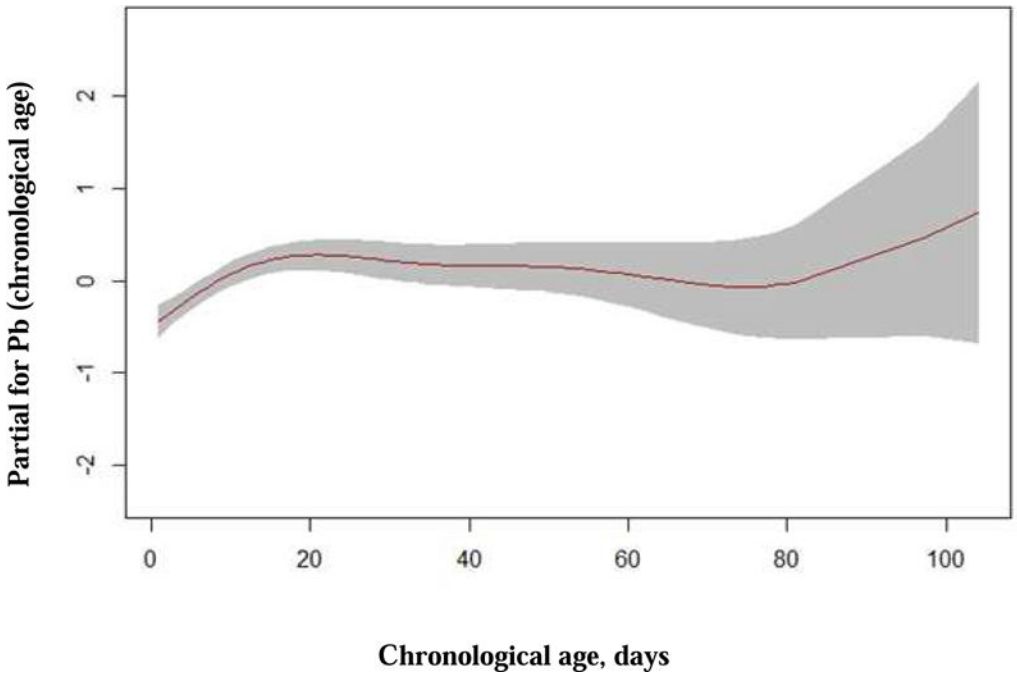

Figure 3.
Fitted smoothing parameter (spline) for the additive predictor chronological age for the model of LVM indexed to weight in males.

Table 1

Baseline patient characteristics.

	Retrospective (n = 372)	Prospective (n = 131)	P value
Males	186 (50%)	63 (48%)	0.7
Weight (kilograms)	1.2 ± 0.47	1.3 ± 0.35	0.01
Gestational age	27.05 ± 3.24	26.27 ± 1.46	0.6
PMA, weeks	30.09 ± 4.29	30.89 ± 2.59	0.004
Chronological age	21.29 ± 22.56	32.4 ± 19.1	<0.0001
Length, cm	36.58 ± 4.95	37.04 ± 2.94	0.2
BSA, Kg/m^2	0.11 ± 0.03	0.12 ± 0.02	0.01
PDA	177 (47.6%)	52 (40%)	0.3
Atrial shunt	332 (89%)	121 (92%)	0.7

Note: Values expressed as mean ± SD or number (percentage). Postmenstrual age (PMA, weeks); Weight, in kilograms on the day of scan; Body surface area (BSA, Kg/m^2); Patent ductus arteriosus (PDA).

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Table 2

L, M and S values for males for each left ventricular M mode echocardiographic measurement indexed using weight.

Weight (Kg)	LVM			IVSd			LVPWd			LVEDD			LVESD		
	M	S	L	M	S	L	M	S	L	M	S	L	M	S	L
0.4	1.366	0.257	−0.563	0.194	0.195	0.389	0.173	0.207	−0.737	0.847	0.151	−0.807	0.548	0.120	1.000
0.5	1.729	0.246	−0.492	0.204	0.188	0.268	0.182	0.190	−0.608	0.924	0.144	−0.764	0.599	0.120	1.000
0.6	2.092	0.236	−0.420	0.214	0.182	0.146	0.190	0.173	−0.479	1.001	0.138	−0.721	0.649	0.119	1.000
0.7	2.456	0.225	−0.348	0.225	0.175	0.025	0.199	0.157	−0.350	1.078	0.132	−0.677	0.701	0.119	1.000
0.8	2.823	0.214	−0.277	0.235	0.169	−0.097	0.207	0.143	−0.221	1.157	0.127	−0.634	0.757	0.119	1.000
0.9	3.200	0.202	−0.205	0.244	0.164	−0.218	0.215	0.131	−0.092	1.240	0.121	−0.591	0.816	0.118	1.000
1	3.583	0.190	−0.134	0.253	0.158	−0.340	0.224	0.122	0.037	1.317	0.116	−0.548	0.868	0.118	1.000
1.1	3.958	0.178	−0.062	0.262	0.153	−0.461	0.235	0.118	0.167	1.382	0.112	−0.504	0.907	0.118	1.000
1.2	4.318	0.168	0.009	0.269	0.147	−0.582	0.246	0.116	0.296	1.435	0.107	−0.461	0.933	0.117	1.000
1.3	4.663	0.160	0.081	0.277	0.142	−0.704	0.258	0.118	0.425	1.479	0.103	−0.418	0.951	0.117	1.000
1.4	4.992	0.155	0.152	0.283	0.137	−0.825	0.268	0.121	0.554	1.514	0.100	−0.374	0.967	0.116	1.000
1.5	5.305	0.151	0.224	0.289	0.133	−0.947	0.274	0.124	0.683	1.541	0.096	−0.331	0.983	0.116	1.000
1.6	5.603	0.149	0.295	0.294	0.128	−1.068	0.278	0.126	0.812	1.566	0.093	−0.288	1.003	0.116	1.000
1.7	5.889	0.148	0.367	0.298	0.124	−1.190	0.279	0.127	0.941	1.595	0.090	−0.244	1.030	0.115	1.000
1.8	6.164	0.148	0.438	0.300	0.120	−1.311	0.278	0.125	1.070	1.632	0.087	−0.201	1.062	0.115	1.000
1.9	6.430	0.149	0.510	0.302	0.115	−1.432	0.277	0.122	1.199	1.675	0.084	−0.158	1.098	0.115	1.000
2	6.690	0.151	0.581	0.303	0.111	−1.554	0.275	0.118	1.328	1.720	0.081	−0.115	1.135	0.114	1.000
gAIC	548.110			−908.968			−1018.491			−228.268			−346.066		

Note: Left ventricular mass (LVM), interventricular septum thickness at end diastole (IVSd), thickness of posterior wall of the left ventricle at end diastole (LVPWd), left ventricular dimension at end diastole (LVEDD) and end systole (LVESD). For calculation of the Z score please use the formula, Weight, $Z\ score = [(LVM/M(weight))^{L(weight)} - 1]/(L(weight)xS(weight))$. LMS corresponds to lambda (L), mu (M), and sigma (S) values respectively.

Table 3

L, M and S values for females for each left ventricular M mode echocardiographic measurement indexed using weight.

Weight (Kg)	LVM			IVSd			LVPWd			LVEDD			LVESD		
	M	S	L	M	S	L	M	S	L	M	S	L	M	S	L
0.4	1.586	0.200	1.741	0.185	0.184	−0.924	0.170	0.155	−0.850	0.900	0.140	0.752	0.577	0.206	0.720
0.5	1.875	0.199	1.349	0.195	0.179	−0.842	0.180	0.154	−0.779	0.968	0.137	0.639	0.618	0.197	0.649
0.6	2.164	0.197	0.954	0.205	0.175	−0.760	0.190	0.153	−0.708	1.035	0.133	0.525	0.661	0.189	0.577
0.7	2.453	0.196	0.554	0.214	0.170	−0.677	0.199	0.151	−0.637	1.101	0.130	0.412	0.706	0.181	0.506
0.8	2.742	0.195	0.140	0.224	0.164	−0.595	0.209	0.148	−0.566	1.167	0.126	0.299	0.751	0.174	0.435
0.9	3.031	0.194	−0.289	0.234	0.158	−0.513	0.218	0.143	−0.495	1.230	0.123	0.185	0.794	0.167	0.363
1	3.319	0.192	−0.687	0.243	0.152	−0.430	0.227	0.138	−0.424	1.285	0.120	0.072	0.830	0.160	0.292
1.1	3.608	0.191	−0.989	0.252	0.147	−0.348	0.235	0.132	−0.353	1.331	0.117	−0.042	0.859	0.153	0.220
1.2	3.897	0.190	−1.157	0.260	0.141	−0.266	0.243	0.127	−0.282	1.371	0.114	−0.155	0.884	0.147	0.149
1.3	4.186	0.189	−1.215	0.268	0.137	−0.184	0.250	0.123	−0.211	1.406	0.111	−0.268	0.905	0.141	0.078
1.4	4.475	0.187	−1.206	0.275	0.134	−0.101	0.256	0.121	−0.140	1.439	0.108	−0.382	0.927	0.135	0.006
1.5	4.764	0.186	−1.167	0.282	0.131	−0.019	0.262	0.120	−0.068	1.473	0.105	−0.495	0.955	0.130	−0.065
1.6	5.053	0.185	−1.132	0.289	0.130	0.063	0.267	0.121	0.003	1.511	0.103	−0.609	0.989	0.125	−0.136
1.7	5.341	0.184	−1.118	0.295	0.129	0.146	0.271	0.123	0.074	1.555	0.100	−0.722	1.025	0.119	−0.208
1.8	5.630	0.183	−1.117	0.301	0.129	0.228	0.275	0.126	0.145	1.601	0.097	−0.835	1.059	0.115	−0.279
1.9	5.919	0.181	−1.121	0.307	0.128	0.310	0.279	0.129	0.216	1.649	0.095	−0.949	1.091	0.110	−0.351
2	6.208	0.180	−1.122	0.312	0.128	0.393	0.283	0.132	0.287	1.697	0.092	−1.062	1.121	0.105	−0.422
gAIC	546.185			−914.746			−1003.141			−218.723			−324.249		

Note: Left ventricular mass (LVM), interventricular septum thickness at end diastole (IVSd), thickness of posterior wall of the left ventricle at end diastole (LVPWd), left ventricular dimension at end diastole (LVEDD) and end systole (LVESD). For calculation of the Z score please use the formula, Weight, $Z\ score = [(LVM/M(weight))^{L(weight)} - 1]/(L(weight) \times S(weight))$. LMS corresponds to lambda (L), mu (M), and sigma (S) values respectively.

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Table 4

Comparison of the interobserver variability of the two observers for measuring the left ventricular dimensions.

Variable	N	ICC (95% CI)	P value
LVM (g)	100	0.99 (0.985, 0.993)	< 0.01
IVSd (mm)	100	0.96 (0.941, 0.973)	< 0.01
LVPWd (mm)	100	0.96 (0.941, 0.973)	< 0.01
LVEDD (mm)	100	0.99 (0.985, 0.993)	< 0.01
LVESD (mm)	100	0.99 (0.985, 0.993)	< 0.01

Note: Interclass Correlation Coefficient (ICC), Left ventricular mass (LVM), interventricular septum thickness at end diastole (IVSd), thickness of posterior wall of the left ventricle at end diastole (LVPWd), left ventricular dimension at end diastole (LVEDD) and end systole (LVESD).