NOMOGRAMS FROM NEONATES

Echocardiography nomograms in Black South African neonates

Nondumiso M. Hadebe[1], D.R. Prakaschandra[2], Bongiwe J. Beckerling[1], Antoinette M. Cilliers[3] and Hopewell N. Ntsinjana[4]

[1]Nelson Mandela Children's Hospital, Durban University of Technology, Durban, KwaZulu-Natal, South Africa
[2]Department of Biomedical and Clinical Technology, Durban University of Technology, Durban, KwaZulu-Natal, South Africa
[3]Chris Hani Baragwanath Academic Hospital, University of the Witwatersrand, Johannesburg, South Africa
[4]Nelson Mandela Children's Hospital, University of the Witwatersrand, Johannesburg, South Africa

Address for correspondence:
Dr D.R. Prakaschandra
Department of Biomedical and Clinical Technology
Durban University of Technology
Durban
KwaZulu-Natal
4001
South Africa

Email:
rosaleypra@dut.ac.za

ABSTRACT

Background: Quantitative estimation of cardiac chambers, valve annulus and great vessel dimensions in paediatric echocardiography is necessary in clinical management. Various studies have already provided normal values in the paediatric population that represent most populations of the world but there is paucity of data originating from sub-Saharan Africa, particularly in neonates. We sought to establish reliable echocardiography nomograms for cardiac chambers, valve annulus, great vessels, and thymus dimensions in the Black South African neonatal population.

Methods: This was a descriptive, cross-sectional study evaluating cardiac chamber, valve annuli, thymus, and great vessel dimensions in Black South African neonates with normal hearts using echocardiography.

Results: This study recruited 386 neonates (51% females, 49% males; Weight range: 2.50 - 4.43kg [mean, 3.180; SD, 0.38]; BSA range: 0.17 - 0.24m^2 [mean, 0.20; SD, 0.01]). After controlling for the effects of confounders, good correlation for most cardiac dimensions were observed. Inter-observer variability revealed a strong correlation (ICC=0.50-0.82) with most measurements. All cardiac dimensions correlated well with body weight and were within ±2 standard deviation with few exceptions.

Conclusion: This study presents nomograms from data acquired from healthy neonates which contributes to the current body of knowledge on cardiac dimensions in the African neonatal age group. SA Heart® 2024;21:6-16

INTRODUCTION

The quantification of cardiac dimensions derived from echocardiography is necessary in assessing cardiac disease in paediatric practice. Evaluation of size and growth of cardiac chambers, valves, and great vessels plays a key role in the diagnosis and management of cardiac disease in children.[1] However, nomograms for these structures are limited in children. Various studies have already provided normal values in the paediatric population that represent most populations throughout the world but there is paucity of data originating from sub-Saharan Africa.[2,3,4] The lack of representative nomograms points to the need for more extensive studies to create reliable, accurate nomograms and reproducible results.[1] Specifically, these studies needed to include larger populations of healthy children and neonates. Other authors have indicated deficiencies in data normalisation according to BSA, and possible differences in normal values related to ethnicity.[1, 5, 6]

The size of cardiovascular structures in neonates is influenced by many elements including growth, gender, race, body composition, basal metabolic rate, haematocrit, exercise, type of delivery, gestational age, and geographical factors.[6] Furthermore, growth of children may be impacted by other influences such as environmental, social, and economic factors of a region; therefore, the development of regional echocardiography nomograms is essential.[4]

This study was undertaken to establish reliable echocardiography nomograms for cardiac chambers, valve annuli, thymus, and great vessels dimensions in Black South African neonatal population at a Southern African tertiary care centre.

METHODOLOGY

Design and population

This was a descriptive, cross-sectional study conducted at Chris Hani Baragwanath Academic Hospital, which evaluated cardiac chambers, valve annuli, the thymus, and great vessel dimensions in Black South African neonates with normal hearts.

Following approval from the "Human Research Ethics Committee (Medical), Ethics Clearance Certificate no. M150721" from the University of the Witwatersrand, a total of 386 participants met the inclusion criteria (healthy Black South African newborns born by normal vertex delivery and by Caesarian section with structural normal hearts, at an age of 12 - 24 hours after birth) were enrolled after informed consent was acquired from all the mothers of participating neonates.

Data acquisition and image post processing

Demographic data was collected from the clinical notes. Echocardiographic measurements were performed in accordance with the guidelines by the American Society of Echocardiography[7], using the GE Healthcare Vivid e Compact Digital Ultrasound system. Scanning was done using a 7.5MHz transducer (S6). Cardiovascular structures were measured in millimetres.

Aortic (AO) and LA diameters were measured using M-mode in the parasternal long axis (PLAX) or parasternal short axis (PSAX) views depending on which view had the better image. The aortic diameter was measured during peak systole using the outer edge to inner edge technique. The LA diameter was measured during end-ventricular systole at its greatest dimension and measured from the leading edge of the posterior aortic wall to the leading edge of the posterior LA wall, following which the LA to AO ratio was calculated. LV dimensions [left ventricle internal diameter (LVID), left ventricular posterior wall (LVPW) and interventricular septum (IVS)] were measured on M-mode during end-diastole and during end-systole using the PSAX view.

Semilunar valve annulus (aortic and pulmonary valve) diameters were measured in the 2D view during peak systole, from hinge point to hinge point. The aortic valve annulus (AV ANN) was measured in the PLAX view and pulmonary valve annulus (PV ANN) in the PSAX view at the level of the aorta. Atrioventricular valve annulus (MV and TV) diameters were measured in diastole at the point of maximal valve excursion and the dimensions were measured from hinge point to hinge point in the apical 4 chamber view. The abdominal aorta (ABD AO), main pulmonary artery (MPA) and pulmonary branches (left and right pulmonary artery) were measured in 2D during systole. The MPA, left pulmonary artery (LPA) and right pulmonary artery (RPA) were measured in the PSAX view at the level of the aorta. The ABD AO was measured in 2D in the subcostal view at the point of maximal systolic dimension at the level of the diaphragm. The thymus was measured in the PSAX view at level of aorta using 2D and was measured from anterior chest wall to the most anterior great artery.

Statistical analysis

Collected data was cleaned and entered onto an Excel spreadsheet, and then analysed using XLSTAT v2019 to obtain baseline demographics such as mean, standard deviation and Z-scores. Data was then exported into STATISTICA (v13.5.0) statistical package for further analyses.

Height, weight, body length (BL), body surface area (BSA), mode of delivery (MOD), and gender were used as independent variables in a regression model to predict the effects of confounding factors. Weight was used to express measurements according to body size and Z-scores were calculated to predict mean values of each echocardiographic measurement. Z-scores were computed using formula:[8]

$$Zscore = \frac{x - \mu}{\sigma}$$

Where x is the measured dimension, μ is the mean of the sample and σ is the standard deviation of the sample. ±2 or 3 standard deviation (SD) was calculated using formula:[9]

$$SD = \sqrt{\frac{\Sigma(x - \bar{x})^2}{n - 1}}$$

Where x is the measured dimension, $\bar{x}$ is the predicted mean, and n is the sample size. Predicted mean values were calculated using linear regression model (y = bx + c). The SD was then multiplied by 2 or 3 and added or subtracted from the predicted mean to obtain ±2 or ±3 SD. The inter-observer variability was tested using intraclass correlation coefficient to detect bias. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Demographic data

A total of 386 patients were studied. There was a slightly higher percentage of females (195, 51%), than males (191, 49%). The study cohort consisted of neonates born both by normal vaginal delivery (NVD) and by Caesarian section (C/S) with equal distribution. Weight ranged from 2.50 - 4.43kg (mean, 3.180; SD, 0.38), BL ranged from 39 - 62cm (mean, 5.6; SD, 3.8), BSA

TABLE I: Effects of confounding factors.

Variable	Weight		MOD		Gender		BSA	
	b	p-value	b	p-value	b	p-value	b	p-value
LA	*1.06	*0.000	0.11	0.499	-0.04	0.807	-7.38	0.257
AO DIA	*1.11	*0.000	0.07	0.512	-0.14	0.219	-4.42	0.331
LVIDd	*1.94	*0.000	-0.37	0.143	-0.19	0.444	-6.97	0.507
LVIDs	*1.19	*0.001	-0.32	0.152	-0.19	0.393	-8.70	0.344
MPA	*1.00	*0.000	*-0.48	*0.000	*-0.30	*0.027	1.16	0.836
RPA	*0.31	*0.002	*-0.17	*0.008	*-0.18	*0.005	2.42	0.360
LPA	*0.37	*0.001	*-0.31	*0.000	-0.04	0.572	-1.15	0.708
MV ANN	*0.74	*0.001	*-0.44	*0.002	-0.11	0.455	*12.84	*0.028
TV ANN	*1.28	*0.000	*-0.50	*0.004	0.10	0.578	-5.65	0.434
AV ANN	*0.50	*0.000	-0.10	0.178	-0.01	0.901	-4.35	0.149
PV ANN	*0.95	*0.000	-0.12	0.372	0.13	0.335	4.92	0.391

*LA: left atrium, AO DIA: aortic diameter, LVIDd: left ventricular internal diameter in diastole, LVIDs: left ventricular internal diameter in diastole, MV ANN: mitral valve annulus, TV ANN: tricuspid valve annulus, AV ANN: aortic valve annulus, PV ANN: pulmonary valve annulus, MPA: main pulmonary artery, RPA: right pulmonary artery, LPA: left pulmonary artery. *: significant values.*

TABLE II: LA and AO diameter M-mode measurements in millimetres.

Cardiac dimensions measurements	Standard deviation	Group 1: 2.50 - 2.99	Group 2: 3.00 - 3.49	Group 3: 3.50 - 4.50
LA	3+	15.42	15.88	16.34
	2+	13.91	14.37	14.83
	MEAN	**10.89**	**11.35**	**11.81**
	2-	7.87	8.33	8.79
	3-	6.37	6.82	7.28
AO diameter	3+	12.04	12.52	13.01
	2+	10.98	11.47	11.95
	MEAN	**8.87**	**9.36**	**9.84**
	2-	6.76	7.25	7.73
	3-	5.71	6.19	6.68
LA/AO ratio	3+	1.96	1.97	1.99
	2+	1.76	1.77	1.78
	MEAN	**1.36**	**1.37**	**1.38**
	2-	0.95	0.96	0.97
	3-	0.75	0.76	0.77

LA: left atrium, AO: aorta.

ranged from 0.17 - 0.24me2 (mean, 0.20; SD, 0.01) and gestational age (GA) ranged from 37 - 42 weeks (mean, 39.0; SD, 1.4).

Effects of confounding factors

Multiple linear regression analysis was used to test the effects of confounding factors (weight, MOD, BSA, BL and GA) on all cardiovascular measurements (Table I). Body weight showed a significant relationship with all cardiovascular dimension

TABLE III: LV M-mode measurements in millimetres.

Cardiac dimensions measurements	Standard deviation	Group 1: 2.50 - 2.99	Group 2: 3.00 - 3.49	Group 3: 3.50 - 4.50
IVSd	3+	7.64	7.80	7.97
	2+	6.59	6.76	6.92
	MEAN	**4.50**	**4.66**	**4.83**
	2-	2.41	2.57	2.73
	3-	1.36	1.52	1.68
IVSs	3+	8.61	8.82	9.02
	2+	7.42	7.62	7.82
	MEAN	**5.02**	**5.22**	**5.43**
	2-	2.63	2.83	3.03
	3-	1.43	1.63	1.83
LVIDd	3+	22.79	23.66	24.53
	2+	20.43	21.30	22.17
	MEAN	**15.73**	**16.59**	**17.46**
	2-	11.02	11.88	12.75
	3-	8.66	9.53	10.40
LVIDs	3+	15.88	16.43	16.98
	2+	13.75	14.30	14.86
	MEAN	**9.50**	**10.05**	**10.60**
	2-	5.24	5.79	6.34
	3-	3.11	3.66	4.21
LVPWDd	3+	5.74	5.93	6.11
	2+	4.88	5.06	5.24
	MEAN	**3.14**	**3.33**	**3.51**
	2-	1.41	1.59	1.78
	3-	0.54	0.73	0.91
LVPWDs	3+	7.52	7.62	7.73
	2+	6.53	6.63	6.74
	MEAN	**4.55**	**4.65**	**4.76**
	2-	2.56	2.67	2.77
	3-	1.57	1.68	1.78

IVSd: interventricular septum in diastole, IVSs: interventricular septum in systole, LVIDd: left ventricle internal diameter in diastole, LVIDs: left ventricle internal diameter, LVPWDd: left ventricle posterior wall diameter in diastole, LVPWDs: left ventricle posterior wall diameter in systole.

TABLE IV: Valve 2D measurements in millimetres.

Cardiac dimensions measurements	Standard deviation	Group 1: 2.50 - 2.99	Group 2: 3.00 - 3.49	Group 3: 3.50 - 4.50
MV ANN	3+	12.38	12.80	13.21
	2+	11.03	11.45	11.87
	MEAN	**8.34**	**8.75**	**9.17**
	2-	5.64	6.06	6.47
	3-	4.29	4.71	5.12
TV ANN	3+	14.06	14.64	15.23
	2+	12.39	12.97	13.55
	MEAN	**9.04**	**9.62**	**10.20**
	2-	5.69	6.27	6.86
	3-	4.02	4.60	5.18
PV ANN	3+	10.78	11.19	11.61
	2+	9.47	9.88	10.30
	MEAN	**6.85**	**7.26**	**7.68**
	2-	4.22	4.64	5.05
	3-	2.91	3.33	3.74
AV ANN	3+	7.69	7.91	8.14
	2+	6.99	7.22	7.44
	MEAN	**5.60**	**5.82**	**6.05**
	2-	4.21	4.43	4.66
	3-	3.51	3.73	3.96

MV ANN: mitral valve annulus, TV ANN: tricuspid valve annulus, PV ANN: pulmonary valve annulus, AV ANN: aortic valve annulus.

measurements (p<0.005). Mode of delivery (MOD) had significant associations with atrioventricular valves (p<0.005), main pulmonary artery, and branch pulmonary artery measurements. There were no significant relationships between all cardiac dimension measurements and body length (BL) or gestational age (GA), (p=0.122 - 0.969), nor for gender and BSA (p=0.149 - 0.836).

Inter-observer variability

The inter-observer variability showed a strong correlation in most measurements, (ICC=0.50 - 0.82). The exceptions included PV and TV annulus, with moderate correlation observed (ICC=0.44 - 0.49) and the LVPWD with weak correlation (ICC=0.30 - 0.35).

Echocardiography measurements

All cardiac dimensions correlated well with body weight. All echocardiographic measurements are presented as mean (shown as bold number) and ±3 standard deviations (SD) (Tables II - V). All cardiac dimensions were within ±2 standard deviations, with a few exceptions-score boundaries which are presented as straight lines with actual values as dots in between the boundary lines. Z-scores for each cardiac dimension are

TABLE V: Arterial and thymus 2D echocardiography measurements in millimetres.

Cardiac dimensions measurements	Standard deviation	Group 1: 2.50 - 2.99	Group 2: 3.00 - 3.49	Group 3: 3.50 - 4.50
MPA	3+	10.76	11.25	11.75
	2+	9.45	9.94	10.44
	MEAN	**6.83**	**7.32**	**7.82**
	2-	4.21	4.71	5.21
	3-	2.90	3.40	3.90
RPA	3+	4.81	4.99	5.17
	2+	4.22	4.39	4.57
	MEAN	**3.03**	**3.21**	**3.38**
	2-	1.84	2.02	2.20
	3-	1.25	1.42	1.60
LPA	3+	5.53	5.70	5.88
	2+	4.84	5.01	5.18
	MEAN	**3.45**	**3.62**	**3.79**
	2-	2.06	2.23	2.40
	3-	1.36	1.54	1.71
THYMUS	3+	24.90	25.63	26.36
	2+	22.11	22.84	23.57
	MEAN	**16.53**	**17.25**	**17.98**
	2-	10.94	11.67	12.40
	3-	8.15	8.88	9.61
ABD AO	3+	7.93	8.21	8.50
	2+	7.13	7.42	7.70
	MEAN	**5.53**	**5.82**	**6.11**
	2-	3.94	4.22	4.51
	3-	3.14	3.42	3.71

MPA: main pulmonary artery, RPA: right pulmonary artery, LPA: left pulmonary artery. ABD AO: abdominal aorta.

shown as dots against weight. Z-scores and Z-score boundaries for all measurements are presented graphically in Figures 1 - 9.

DISCUSSION

Quantitative assessment of the heart is critical for assessments of deviation from the normal but can only be done if there are normative values available against which to make comparisons and to identify abnormalities. Paediatric 2D and M-mode echocardiography nomograms of good quality which are available for chamber size, cardiac valve annulus, and great vessel dimensions have been derived mainly from European and American populations.[6,10,11,12,13,14,15]

This study aimed to establish reliable echocardiography nomograms of Black South African neonates. There were only 2 other studies[4,16] from sub-Saharan Africa found in the literature namely, Majonga, et al.[4] who focused on children and

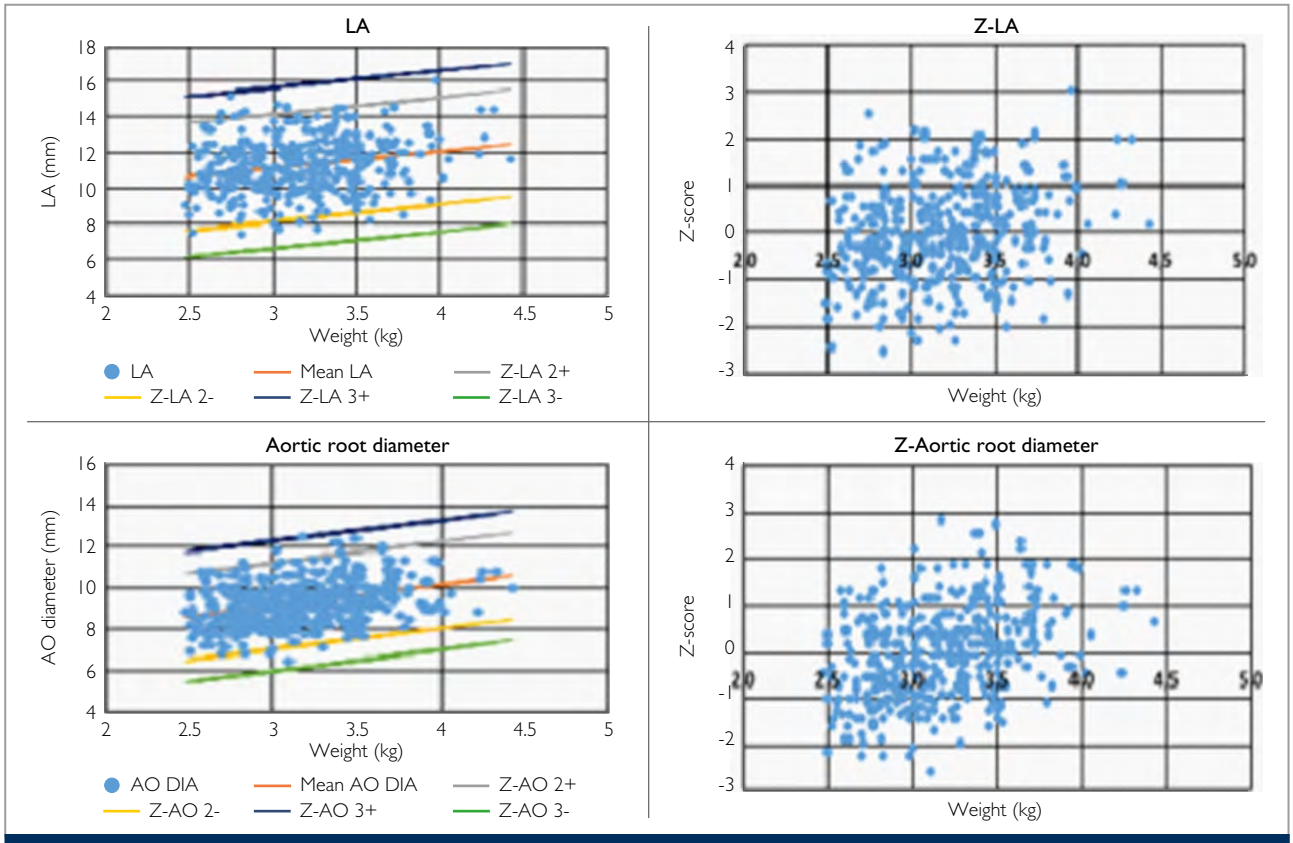

FIGURE 1: Left atrium and aortic root diameter dimension Z-scores and Z-score boundaries by body weight.

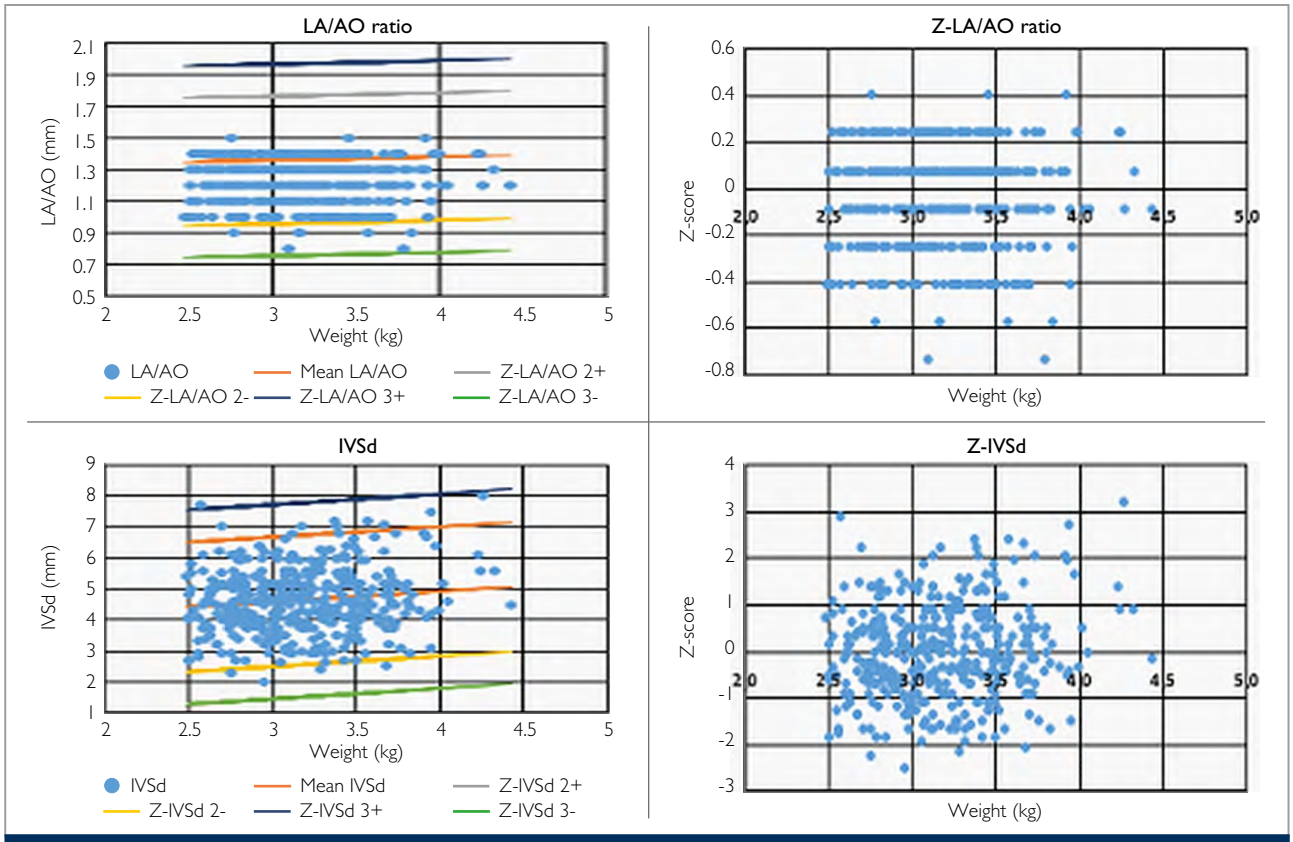

FIGURE 2: LA / AO ratio and IVSd dimension Z-scores and Z-score boundaries by body weight.

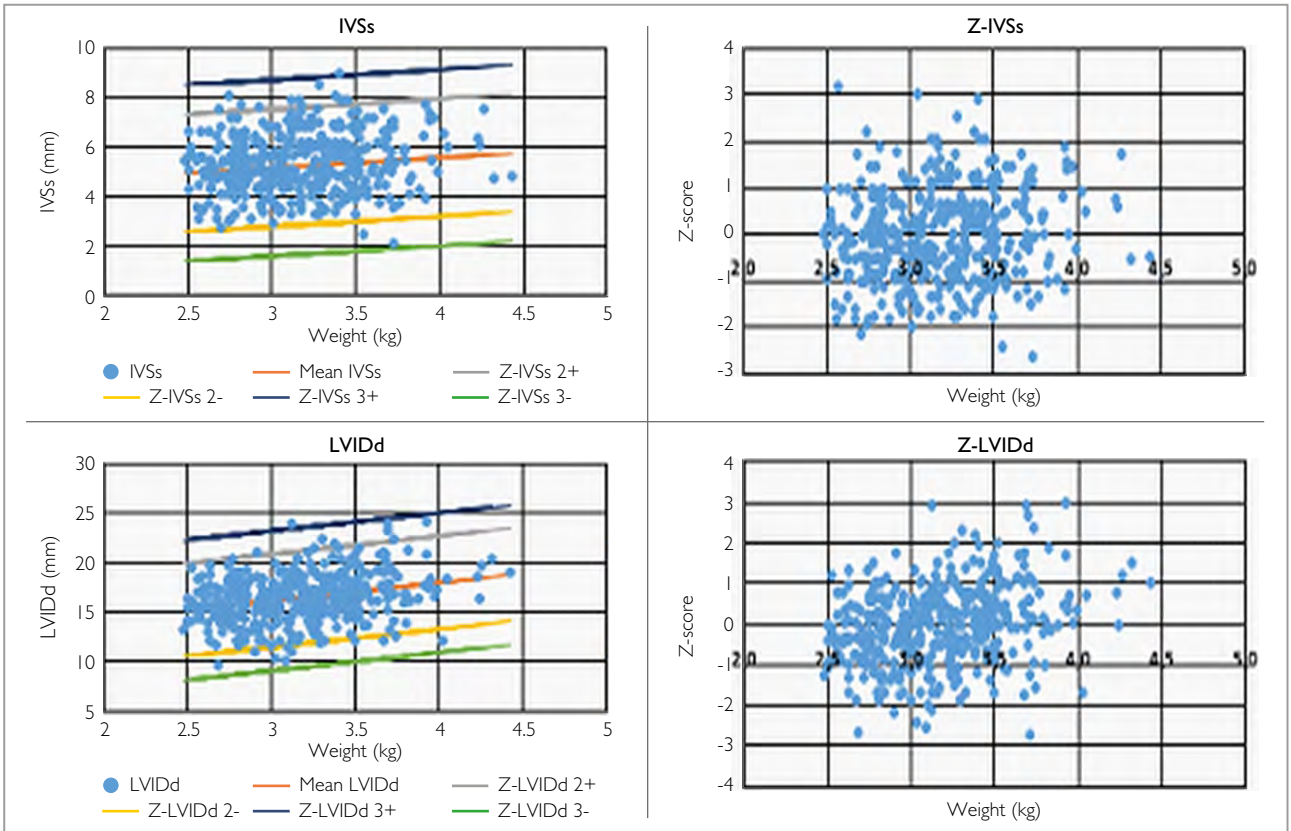

FIGURE 3: IVSs and LVIDd dimension Z-scores and Z-score boundaries by body weight.

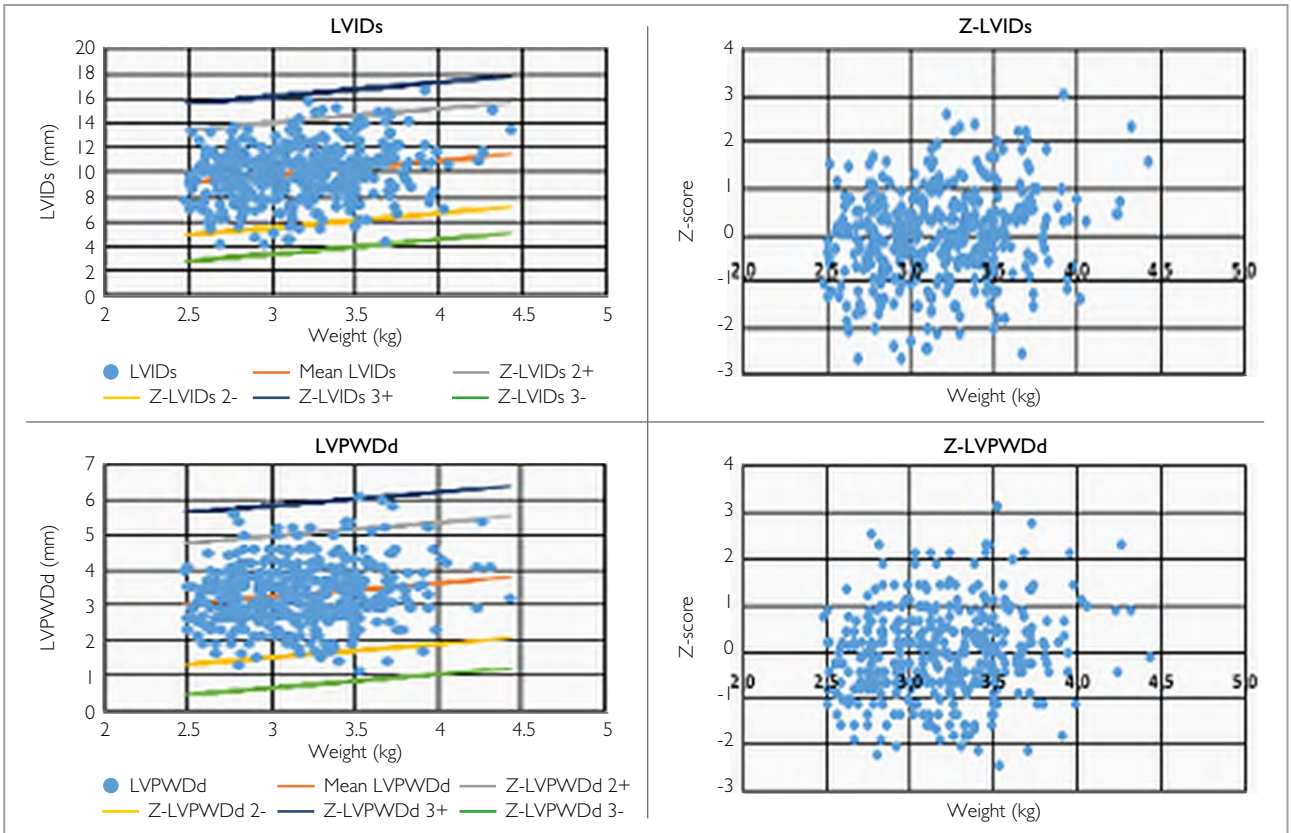

FIGURE 4: LVIDs and LVPWDd dimension Z-scores and Z-score boundaries by body weight.

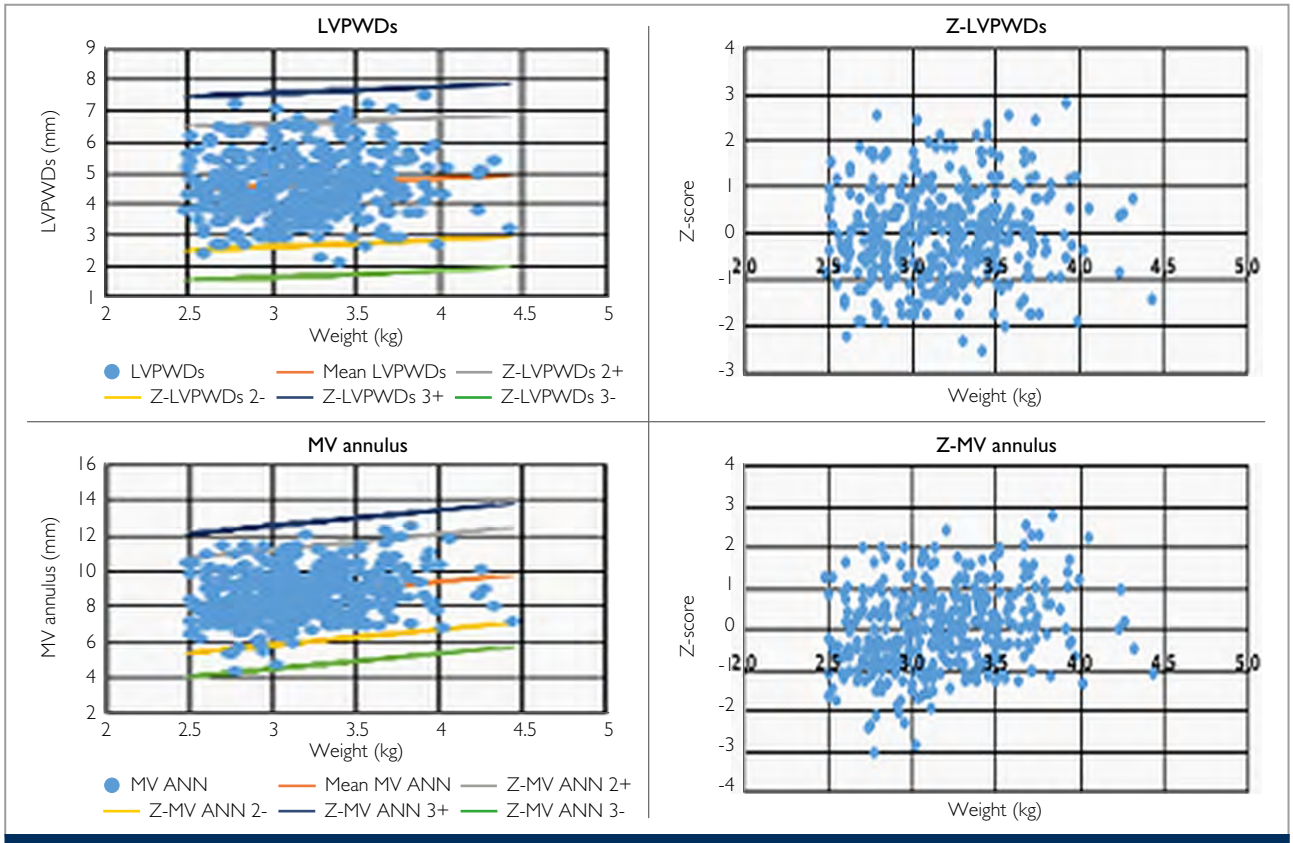

FIGURE 5: LVPWs and MV annulus dimension Z-scores and Z-score boundaries by body weight.

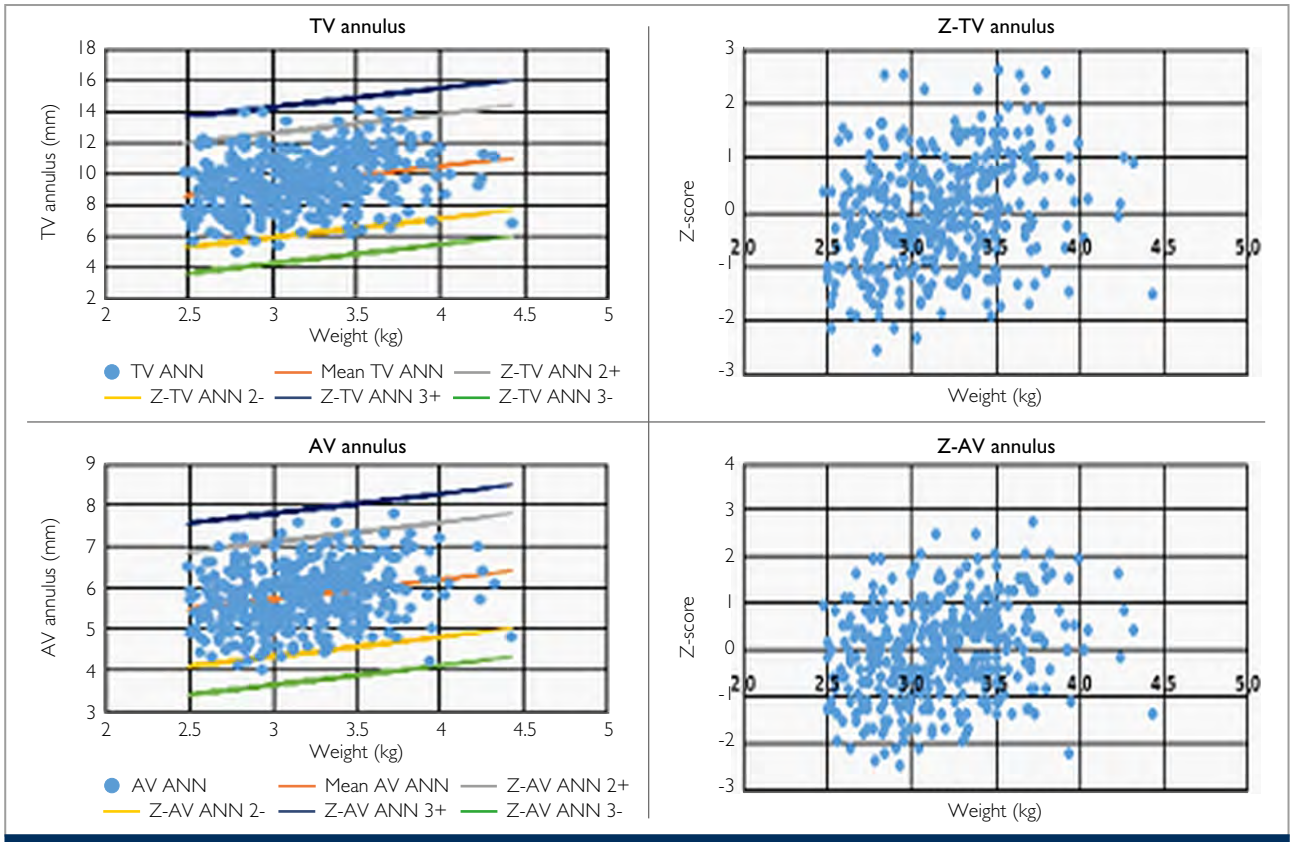

FIGURE 6: TV and AV annulus dimension Z-scores and Z-score boundaries by body weight.

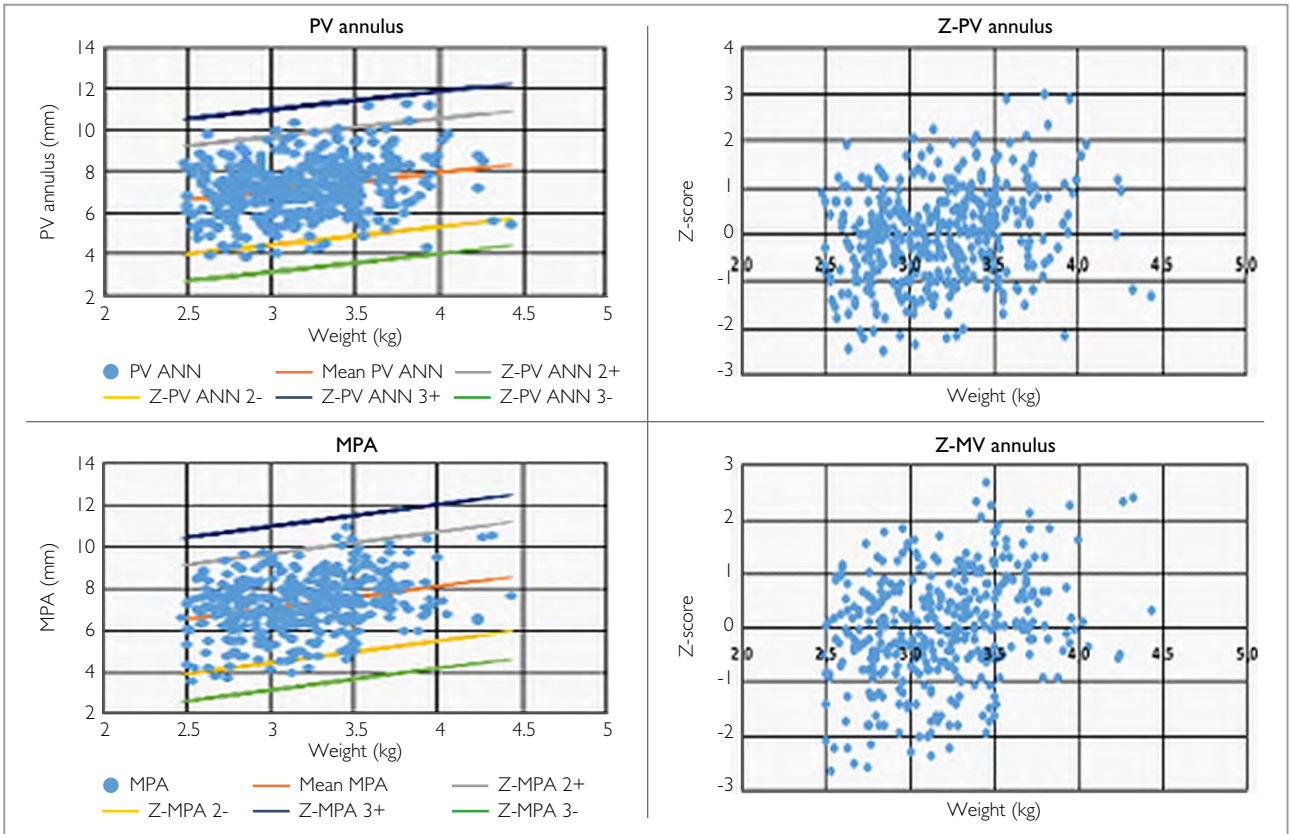

FIGURE 7: PV annulus and MPA dimension Z-scores and Z-score boundaries by body weight.

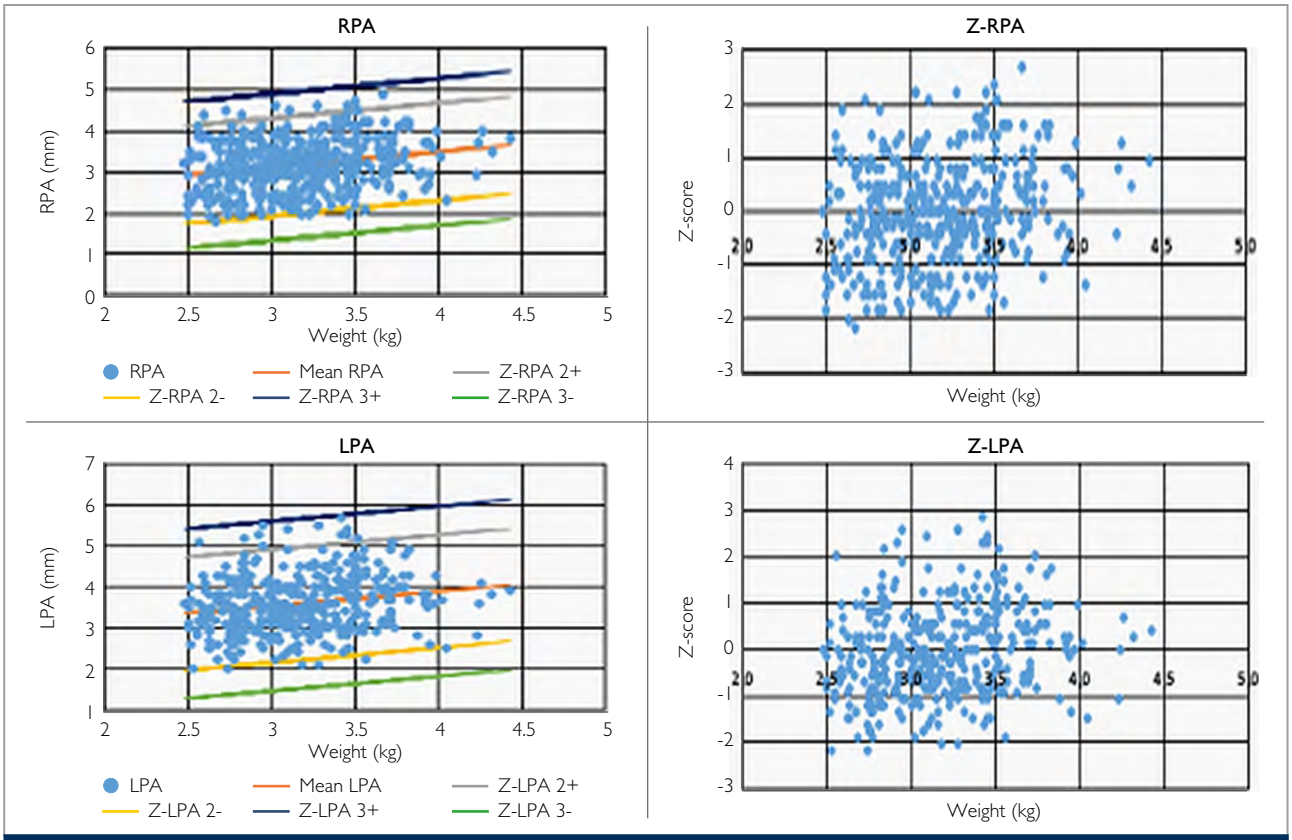

FIGURE 8: RPA and LPA dimension Z-scores and Z-score boundaries by body weight.

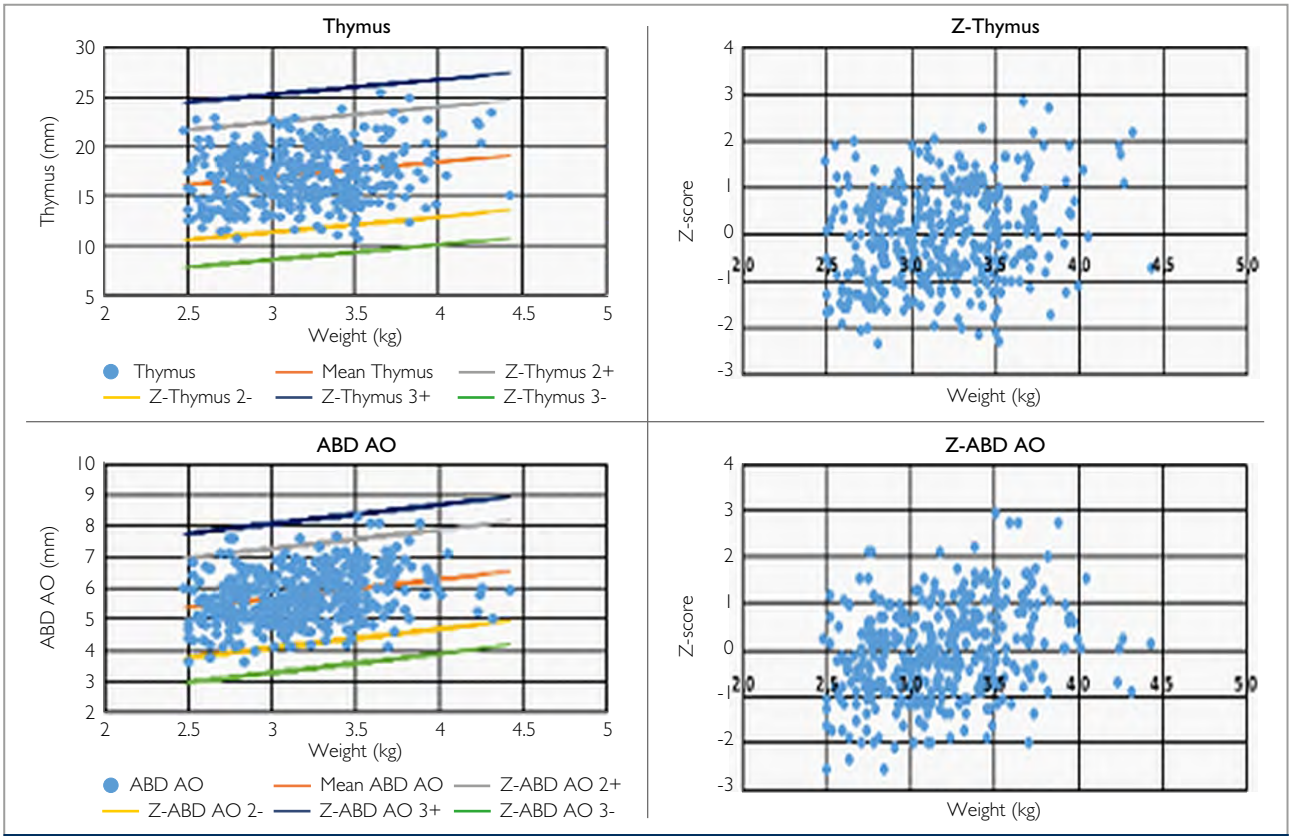

FIGURE 9: Thymus and ABD AO dimension Z-scores and Z-score boundaries by body weight.

adolescents without any neonates with a sample size of 282, and Jacobs[16] who concentrated on preterm neonates with a sample size of 290. Therefore, our study represents the first full-term neonatal echocardiography nomograms from sub-Saharan Africa to date, consisting of the largest sample size compared to previous studies.[4,16]

In this study we showed that body weight had a significant linear relationship with studied cardiovascular structures suggesting a linear relationship between foetal somatic growth and size of cardiovascular structures. Interestingly about 45% of cardiac dimensions showed linear relationship to mode of delivery similarly to a previous study.[6] Smaller dimensions were found in neonates born by C/S. Despite an intensive literature search, there is no known reason to explain this relationship between mode of delivery and cardiovascular dimensions. Gender had a minimal influence on cardiovascular structures, since we found no significant differences between boys and girls with regards to cardiovascular dimensions in accordance with findings from Kammann[10] and Guizeltas and Eroglu.[13] However, 2 studies[5,17] found significant differences between the 2 genders with boys having larger dimensions than girls.

Using interobserver variability we found a strong correlation between measurements done by a senior echocardiographer and junior echocardiographer suggesting that the methods used to measure are reproducible regardless of experience. Of note LVPW dimensions which are M-mode based and PV annulus which is 2D based both failed the interobserver variability testing. Our findings agree with other studies[6,7] which highlighted the issue of overestimation in the leading edge to leading edge measurements, particularly when performed by less the experienced echocardiographer. Furthermore, LV dimension and wall thickness echocardiography measurements are widely used in clinical practice and for research purposes. M-mode ventricular diameter measurements in the paediatric age group is the preferred method for LV quantification but can lead to overestimation of measurements.[6] This lack of accuracy in measurements may explain the poor inter-observer variability calculated for the LVPWd and LVPWDs measurements in our study. Similarly, the reason for the PV annulus measurements having a moderate inter-observer variability correlation may be due to measurements being acquired in the PSAX, which has a relatively low resolution and an oblique orientation resulting in a possible suboptimal measurement accuracy.[7]

We have presented normal cardiovascular dimension reference values that are expressed as Z-scores recommended by the American Society of Echocardiography and other authors.[6,14,18] Our study cohort showed higher dimensional measurements of M-mode cardiac structures compared to those of published literature.[10,13] Majonga, et al.[4] also showed that interventricular septum and left posterior wall dimensions acquired using M-mode were similar to published non-African references. These findings suggest that other factors such as environmental, social, economic, racial, and ethnic factors of the population may influence growth or development and thus account for these minor differences. In generating Z-scores as recommended by the American Society of Echocardiography, our study cohort shows that M-mode based measurements were higher than those of similar studies done in neonates.[10,13,14] Some of the study measurements exceeded Z-scores above +2 and below -2. To accommodate these extremes, Z-scores of +3 and -3 Z-scores were added.

STUDY STRENGTHS AND LIMITATIONS

This study is unique as it represents a homogenous South African population and focuses on an understudied neonatal age group in an African cohort. In addition, structures that have been poorly studied in both African and non-African neonatal subjects, such as the left atrium to aortic root ratio, thymus and abdominal aorta have been included. Interobserver variability was comparable for all measurements.

Limitations of the study include the omission of right ventricle, right atrium, and inferior vena cava dimensions which has been generally understudied.

CONCLUSION

This study has provided echocardiographic nomograms of normal Black South African neonates. Using the same methodology as other studies in the same area, our findings agreed with other published literature. The interobserver variability showed differences between experienced and less experienced echocardiographers for two measurements that used leading edge to leading edge approach. This study therefore contributes valuable data which can be adopted by clinicians for clinical decision making when it comes to interventions for patients with abnormal cardiovascular structures.

ACKNOWLEDGEMENTS

The authors acknowledge Chris Hani Baragwanath Academic Hospital for permission for data collection and equipment in conducting this study, as well as the participants for making this research possible.

AUTHORS' CONTRIBUTION

Ms Hadebe is the principal author of the study. She collected and entered all study data, interpreted data analysis, complied data and is the primary author of the manuscript.

Dr Prakaschandra was the supervisor from the Durban University of Technology. She assisted with guidance, advice, reviewing, and revision of the protocol and manuscript.

Ms Beckerling assisted with data collection, analysis, and interpretation process.

Prof Cilliers was the unit co-supervisor. She conceptualised the study, co-ordinated and assisted with data collection, reviewing and revision of protocol and manuscript.

Prof Ntsinjana was the main unit supervisor. He assisted with development of protocol, supervised data collection and analysis, reviewing and revision of protocol and manuscript.

Conflict of interest: none declared.

REFERENCES

1. Kaski JP, Daubeney PE. Normalisation echocardiographically derived paediatric cardiac dimensions to body surface area: Time for a standardised approach. Eur J. Echocardiogr [internet]. 2008 [cited 2015 Sep 10];1-2. Available from: http://ehjcimaging.oxfordjournals.org/content/ejechocard/early/2008/01/01/ejechocard.jen242.full.pdf. DOI:10.1093/ejechocard/jen242.
2. Lemmer CE, Engel ME, Stanfliet JC, Mayosi BM. Reference Intervals for the echocardiographic measurements of right heart in children and adolescent: A systemic review. Cardiovascular ultrasound [internet]. 2014 [cited 2015 Sep 27];12(3):1-7. Available from: http://www.cardiovascularultrasound.com/content/12/1/3.
3. Roge CL, Silverman NH, Hart PA, Ray RM. Cardiac structure growth patterns by echocardiography. J Am Heart Assoc [internet]. 1978 [cited 2015 Sep 10]; 57(2):285-290. Available from: http://circ.ahajournals.org/content/57/2/285.
4. Majonga ED, Rehman AM, McHugh G, Mujuru HA, Nathoo K, Patel M, et al. Echocardiographic reference ranges in older children and adolescents in sub-Saharan Africa. Int J Cardiol [internet] 2017 Jun [cited 2019 Jan 21];248: 409-413. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28711335.
5. Cantinotti M, Scalese M, Molinaro S, Murzi B, Passino C. Limitations of current echocardiographic nomograms for left ventricular, valvular and arterial dimensions in children: A critical review. J Am Soc Echocardiogr [internet]. 2012 [cited 2015 Sep 10];25:142-152. Available: from: http://www.onlinejase.com/article/S0894-7317(11)00790-5/pdf DOI:10.1016/j.echo.2011.10.016.
6. Cantinotti M, Scalese M, Murzi B, Assanta N, Spadoni I, Festa P, et al. Echocardiographic nomograms for chamber diameters and areas in Caucasian children. J Am Soc Echocardiogr [internet] 2014 [cited 2015 Sep 10];27(12): 1279-1292. Available from: http://www.onlinejase.com/article/S08947317(14)00586-0/pdf DOI:10.1016/j.echo.2014.08.005.
7. Lopez L, Colan SD, Frommelt PC, Ensig G J, Kendall K, Younoszai A K, et al. Recommendations for quantification methods during the performance of a paediatric echocardiogram: A report from the Paediatric Measurements Writing Group of the American Society of Echocardiography Paediatric and Congenital Heart Disease Council. J Am Soc Echocardiogr [internet] 2010 [cited 2015 Sep 27];23:465-495. Available from: http://www.onlinejase.com/article/S0894-7317(10)00266-X/pdf DOI:10.1016/j.echo.2010.03.019.
8. McLeod SA. Z-score: Definition, calculation, and interpretation [internet]. United Kingdom. Creative commons attribution - non-commercial - no derivative works; 2019 [updated 2019 May 17; cited 2019 June 03]. Available from: https://www.simplepsychology.org/z-score.html.
9. Glen S. Standard deviation: Simple definition, step-by-step video [internet]. Florida: Statistics How To. Com; 2019 [cited 2019 June 03]. Available from https://www.statisticshowto.com/probability-and-statistics/standard-deviation/.
10. Kapmann C, Wiethoff CM, Wenzel A, Stolz G, Betancor M, Wippermann CF, et al. Normal values of m-mode echocardiographic measurements of more than 2 000 healthy infants and children in central Europe. Heart [internet] 2000 [cited 2016 Apr 09];83:667-672. Available from: https://www.ncbi.nlm.nih.gov/pubmed/10814626.
11. Overbeek LIH, Kapusta L, Peer PGM, de Korte CL, Thijssen JM, Daniels O. New reference values for echocardiographic dimensions of healthy Dutch children. Eur J Echocardiogr [internet] 2005 [cited 2016 Apr 09];7:113-121. Available from: https://www.ncbi.nlm.gov/m/pubmed/ DOI:10.1016/j.euje.2005.03.012.
12. Neilan TG, Pradhan AD, King ME, Weyman AE. Derivation of a size-independent variable for scaling of cardiac dimensions in a normal paediatric population. Eur J Echocardiogr [internet] 2009 [cited 2016 Apr 09];10:50-55. Available from: https://academic.oup.com/ehjimaging/article/ DOI:10.1093/ejechocard/jen110.
13. Guzeltas A, Eroglu AG. References values for echocardiographic measurements of healthy newborns. Cardiol Young [internet] 2012 [cited 2015 Sep 10];22:152-157. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21933471 DOI: 10.1017/S1047951111001259.
14. Cantinotti M, Scalese M, Murzi B, Assanta N, Spadoni I, Festa P, et al. Echocardiographic nomograms for ventricular, valvular and arterial dimensions in Caucasian children with a special focus on neonates, infants and toddlers. J Am Soc Echocardiogr [internet] 2014 [cited 2015 Sep 10];27: 179-191. Available from: http://www.onlinejase.com/article/S0894-7317(13)00770-0/pdf DOI:10.1016/j.echo.2013.10.001.
15. Cantinotti M, Giordano R, Scalese M, Murzi B, Assanta N, Spadoni I, et al. Nomograms for 2D echocardiography derived valvular and arterial dimensions in Caucasian children. J Cardiol [internet] 2016 [cited 2016 Jun]; 69:208-215. Available at https://www.ncbi.nlm.nih.gov/pubmed/27118699 DOI: 10.1016/j.jjcc.2016.03.010.
16. Jacobs S. Referencing echocardiographic measurements for premature and low-birth weight infants. M. Tech. Central University of Technology [internet] 2016 [cited 2017 May 22]. Available at ir.cut.ac.za> handle.
17. Zilberman MV, Khoury PR, Kimball RT. Two Dimensional echocardiography valve measurements in healthy children: Gender-specific differences. Paediatr Cardiol [internet] 2005 [cited 2016 Apr 09];26(4):356-60. Available at https://pubmed.ncbi.nlm.nih.gov/16374684/ DOI: 10.1007/s00246-004-0736.
18. Mawad W, Drolet C, Dahdah N, and Dallaire F. A review and critique of the statistical methods used to generate reference values in paediatric echocardiography. J Am Soc Echocardiogr [internet] 2013 [cited 2016 Jan 14]; 26:29-37. Available at https://www.ncbi.nlm.nih.gov>pubmed DOI: 10.1016/j.echo.2012.09.021.