Echocardiographic Nomograms for Chamber Diameters and Areas in Caucasian Children

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Background: Although a quantitative evaluation of cardiac chamber dimensions in pediatric echocardiography is often important, nomograms for these structures are limited. The aim of this study was to establish reliable echocardiographic nomograms of cardiac chamber diameters and areas in a wide population of children.

Methods: A total of 1,091 Caucasian Italian healthy children (age range, 0 days to 17 years; 44.8% female) with body surface areas (BSAs) ranging from 0.12 to 1.8 m^2 were prospectively enrolled. Twenty-two two-dimensional and M-mode measurements of atrial and ventricular chamber diameters and areas were performed. Models using linear, logarithmic, exponential, and square-root relationships were tested. Heteroscedasticity was tested by the White test and the Breusch-Pagan test. Age, weight, height, and BSA, calculated by the Haycock formula, were used as the independent variables in different analyses to predict the mean value of each echocardiographic measurement. The influence of various confounders, including gender, type of delivery, prematurity, and interobserver variability, was also evaluated. Structured *Z* scores were then computed.

Results: The Haycock formula provided the best fit and was used when presenting data as predicted values (mean ± 2 SDs) for a given BSA and within equations relating echocardiographic measurements to BSA. Confounders were not included in the final models, because they did not show significant effects for most of the measurements.

Conclusions: Echocardiographic reference values are presented for chamber area and diameters, derived from a large population of healthy children. These data partly cover a gap in actual pediatric echocardiographic nomograms. Further studies are required to reinforce these data, as well as to evaluate other parameters and ethnicities. (J Am Soc Echocardiogr 2014;■:■-■.)

Keywords: Echocardiography, Children, Nomograms

A quantitative assessment of cardiac chambers, valves, and great vessels is often of critical importance in evaluating the severity of any congenital and acquired heart disease and in planning the most appropriate medical, interventional, and/or surgical treatment.[1-5]

Methodologic and numeric limitations of current pediatric echocardiographic nomograms have been recently underscored,[1-9] with ongoing efforts to build new and more robust *Z* scores. At present, pediatric echocardiographic nomograms of good quality exist for cardiac valves, pulmonary arteries, the aorta, and the aortic arch.[7-10] Pediatric nomograms for cardiac chamber diameters and areas, however, are still limited or even absent.[2,11-14] For the left ventricle, there are sufficient nomograms for M-mode measurements,[7-10] while normal values for left ventricular diameters and areas evaluated in two- and four-chamber views are almost absent. Furthermore, pediatric echocardiographic nomograms for right ventricular dimensions[12] and atrial dimensions[15] are also extremely limited.

The primary aim of this work was to establish echocardiographic nomograms for ventricular and atrial dimensions in a population of healthy neonates, infants, and children.

Additional aims were to identify the best body size parameter (i.e., weight, age, or body surface area [BSA])[16-22] to normalize measurements and to determine the effects of confounding factors such as gender, prematurity, type of delivery, and intraobserver variability on echocardiographic measurements.

METHODS

Inclusion Criteria

Healthy Caucasian children evaluated in the outpatient department of the Pediatric Cardiology Department for the screening of congenital heart disease at Fondazione G. Monasterio CNR–Regione

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Abbreviation
BSA = Body surface area

Toscana of Massa eligible for inclusion into the study were prospectively enrolled.

The presence of innocent defects such as a patent ductus arteriosus with small or less left-to-right shunting seen in the first 3 days of life or a patent foramen ovale was considered to be normal.[7,9] Premature neonates were included only if they had Apgar scores ≥8, did not require ventilatory support, and had good clinical status.

Exclusion Criteria

All subjects with clinical, electrocardiographic, or echocardiographic evidence of congenital or acquired heart disease were excluded. Children with a inadequate or incomplete echocardiographic examinations were also excluded. Other exclusion criteria included known or suspected neuromuscular disease, genetic syndromes, or chromosomal abnormalities; body mass index ≥95th percentile for children ≥2 years old[23] or weight-for-length Z score ≥2 on the basis of the World Health Organization's Child Growth Standards for children <2 years of age[23,24]; pulmonary hypertension; systemic hypertension (for children >4 years of age); connective tissue disease; and family history of genetic cardiac disease (such as Marfan syndrome or cardiomyopathy).[7,9] All non-Caucasian subjects were also excluded to avoid racial variability bias.

Subject Enrollment

Our department provides an outpatient service reserved to neonatologists and pediatricians of nearby hospitals and the local territory to refer children with suspicion of congenital cardiac defects for full cardiologic examinations. The routine evaluation consists of a physical examination plus electrocardiography and echocardiography. No supplemental examinations were performed for the present study.

All patients underwent a complete two-dimensional, color flow Doppler and spectral Doppler examinations. In addition to routine echocardiography, we digitally stored full-cycle movies of two- and four-chamber views, which were subsequently analyzed. To avoid the collection of ambiguous images or movies, for every subject, at least two movies were recorded for every echocardiographic projection.

Approval for this study was obtained from the local ethics committee. Parents or legal guardians of all the children were informed and agreed to participate in the trial by providing written consent.

Echocardiographic Examination

Echocardiographic studies were performed using a Philips iE33 echocardiograph (Philips Medical Systems, Bothell, WA). Offline measurements with automatic calibration were carried out on a computer workstation (EnConcert; Philips Medical Systems, Andover, MA).The two-dimensional measurements were calculated according to recent guidelines.[4,25,26] The measurements obtained by two-dimensional echocardiography, the views from which they were obtained, and the points in the cardiac cycle are displayed in Table 1. For any given structure, measurements were made only if excellent and unambiguous views were available. Thus, not all structures were measured in all patients (Table 2).

Table 1 Description of two-dimensional echocardiographic measurements

Measurement	View	Description
1. LVED area	Apical four-chamber view	Planimetric measurements with manual tracing of the endocardial border
2. LVED area	Apical two-chamber view	Planimetric measurements with manual tracing of the endocardial border
3. LVES area	Apical four-chamber view	Planimetric measurements with manual tracing of the endocardial border
4. LVES area	Apical two-chamber view	Planimetric measurements with manual tracing of the endocardial border
5. LVED length	Apical four-chamber view	Point-to point measurements
6. LVED length	Apical two-chamber view	Point-to point measurements
7. LVES length	Apical four-chamber view	Point-to point measurements
8. LVES length	Apical two-chamber view	Point-to point measurements
9. LVED diameters	Short-axis M-mode	Point-to point measurements
10. LVES diameters	Short-axis M-mode	Point-to point measurements
11. LA AP length	Apical four-chamber view	Point-to point measurements at end-systole
12. LA LL length	Apical four-chamber view	Point-to point measurements at end-systole
13. LA area	Apical four-chamber view	Planimetric measurements with manual tracing at end-systole
14. RA AP length	Apical four-chamber view	Point-to point measurements at end-systole
15. RA LL length	Apical four-chamber view	Point-to point measurements at end-systole
16. RA area	Apical four-chamber view	Planimetric measurements manual tracing at end-systole
17. RVED area	Apical four-chamber view	Planimetric measurements with manual tracing of the endocardial border
18. RVES area	Apical four-chamber view	Planimetric measurements with manual tracing of the endocardial border
19. RVED length (RV3)	Apical four-chamber view	Point-to point measurements
20. RVES length	Apical four-chamber view	Point-to point measurements
21. RVED basal diameter (RV1)	Apical four-chamber view	Maximum diastolic dimension point-to point measurements
22. RVED midcavity diameter (RV2)	Apical four-chamber view	Maximum diastolic dimension point-to point measurements

AP, Anterior-posterior; *LA*, left atrial; *LL*, lateral-lateral; *LVED*, left ventricular end-diastolic; *LVES*, left ventricular end-systolic; *RA*, right atrial; *RVED*, right ventricular end-diastolic; *RVES*, right ventricular end-systolic.
According to latest recommendations,[4,26] end-diastole was defined as the frame at which the mitral valve (MV) closes and end-systole as the frame preceding MV opening; LA measurements were obtained from apical views at end-systole, just before the MV opens; RA measurements were obtained in an apical four-chamber view at end-systole, just before the tricuspid valve opens; and RVED diameters are indicated as RV1, RV2, and RV3.

Table 2 Number of valid measurements and number of measurements necessary to obtain a statistical study power of 99%

Measurement	No. valid	No. measurements (power 99%)
RVED length (RV3)	741	162
RVES length	733	142
RVED area	740	44
RVES area	733	39
RVED basal diameter (RV1)	824	153
RVED midcavity diameter (RV2)	824	179
LVED length 4c	917	173
LVES length 4c	912	149
LVED area 4c	921	44
LVES area 4c	914	42
LVED length 2c	609	169
LVES length 2c	608	150
LVED M-mode	1,003	176
LVES M-mode	1,003	179
LVED area 2c	608	45
LVES area 2c	607	41
LA AP diameter 4c	728	185
LA LL diameter 4c	729	184
LA area 4c	443	49
RA AP diameter 4c	848	169
RA LL diameter 4c	848	166
RA area 4c	558	48

AP, Anterior-posterior; *4c*, four-chamber; *LA*, left atrial; *LL*, lateral-lateral; *LVED*, left ventricular end-diastolic; *LVES*, left ventricular end-systolic; *RA*, right atrial; *RVED*, right ventricular end-diastolic; *RVES*, right ventricular end-systolic; *2c*, two-chamber.

Statistical Methods

The statistical analysis was very similar to the one already presented in our previous work.[9]

To examine the relationships between parameters of body size and each of the echocardiographic variables, multiple models using linear, logarithmic, exponential, and square-root equations were tested. Among the models that satisfied the assumption of homoscedasticity, the model with the highest R^2 value was considered to provide the best fit. The presence or absence of heteroscedasticity, a statistical term used to describe the behavior of variance and normality of the residuals, was also tested by the White test and the Breusch-Pagan test, as described in our previous work.[9,27-30] Age, weight, height, and BSA[9,16-22] were used as the independent variables in different regression analyses to predict the mean values of each echocardiographic measurement. According to previous observations, the Haycock formula[16] was chosen among those available[16-22] to calculate BSA.

The effects of confounding factors such as gender, prematurity, and type of delivery were also evaluated, as previously described.[9] Finally, we computed *Z* scores by dividing the residual values by the modeled standard error of the residual value.

Interobserver and intraobserver agreement was calculated by overall agreement (percentage of observed exact agreement) and was tested by repeated measures with analysis of variance in 30 subjects. Measurements were performed by two independent experienced pediatric cardiologists.

Table 3 Distribution of BSA calculated with the Haycock formula

BSA (m^2)	*n*	%
[0.1–0.15)	7	0.6
[0.15–0.2)	86	7.9
[0.2–0.25)	126	11.5
[0.25–0.3)	79	7.2
[0.3–0.35)	41	3.8
[0.35–0.4)	57	5.2
[0.4–0.45)	52	4.8
[0.45–0.5)	36	3.3
[0.5–0.6)	62	5.7
[0.6–0.7)	71	6.5
[0.7–0.8)	82	7.5
[0.8–0.9)	72	6.6
[0.9–1.0)	51	4.7
[1.0–1.1)	53	4.9
[1.1–1.2)	51	4.7
[1.2–1.3)	35	3.2
[1.3–1.4)	29	2.7
[1.4–1.5)	35	3.2
[1.5–1.6)	28	2.6
[1.6–1.8)	38	3.5
Total	1,091	100.0

The sample size necessary to obtain nomograms with sufficient statistical power was calculated as follows. First, we divided the population into six major age stages (group 1, neonates, 0 to 27 days; group 2, infancy, 28 days to 12 months; group 3, toddlers, 13 months to 2 years; group 4, early childhood, 2 to 5 years; group 5, middle childhood, 6 to 11 years; and group 6, early adolescence, 12 to 17 years).[31] According to previous results,[9] we decided not to divide our population into gender groups. Second, we calculated how many subjects were necessary for each age stage. Assuming a normal distribution of the variables and estimating the population standard deviation at 0.5,[32,33] ≥100 subjects for every age group were necessary to provide a 95% confidence interval with a margin of error of 0.1. However, assuming that not all the echocardiographic studies would contain all the necessary images to perform each of the study measurements, a higher subject number was required for every age group. Assuming ≥70% of studies in which each particular measurement can be made, each of the six study groups required ≥140 patients to satisfy the requirements for the 95% confidence interval and margin of error for the mean. Thus, the total sample size for the study was ≥840 patients.[32,33]

SPSS version 13.0 (SPSS, Inc, Chicago, IL) and Stata version 10 for Windows (StataCorp LP, College Station, TX) were used for analysis.

RESULTS

Subjects

A total of 1,091 children (age range, 0 days to 17 years) were enrolled. The mean age of the study population was 53.3 months (median, 34.9 months; interquartile range, 2.2–95.1 months; range,

Table 4 Coefficients for regression equations relating echocardiographic measurements and BSA, the standard error of the estimate, and the determination coefficient

Measurement	Intercept	*B*	SEE (√MSE)	R^2	Shapiro-Wilk	Kolmogorov-Smirnov	Breusch-Pagan	White
BSA Haycock: $(\ln[y] = a + b \times \ln[x])$; $Z = \{\ln[\text{measurement}] - [\text{intercept} + B \times \ln(\text{BSA})]\}/\sqrt{\text{MSE}}$								
RVED length (RV3)	3.934	0.484	0.098	0.918	0.081	0.093	0.058	0.298
RVED area	2.443	0.955	0.171	0.934	0.152	0.200	0.001	0.127
RVES area	1.542	1.019	0.241	0.890	0.502	0.200	0.000	0.000
RVED basal diameter (RV1)	3.445	0.499	0.113	0.905	0.477	0.200	0.001	0.001
RVEd midcavity diameter (RV2)	3.048	0.461	0.137	0.846	0.409	0.200	0.016	0.063
LVED M-mode	3.634	0.464	0.091	0.928	0.028	0.073	0.044	0.220
LVES M-mode	3.134	0.459	0.137	0.847	0.000	0.001	0.003	0.057
LVED 4c length	4.099	0.469	0.077	0.948	0.130	0.133	0.057	0.175
LVES 4c length	3.778	0.506	0.106	0.919	0.193	0.096	0.092	0.173
LVED 4c area	2.924	0.946	0.132	0.962	0.034	0.200	0.001	0.221
LVES 4c area	2.220	0.975	0.183	0.934	0.372	0.200	0.011	0.142
LVED 2c length	4.097	0.474	0.077	0.946	0.591	0.200	0.483	0.412
LVES 2c length	3.781	0.504	0.106	0.911	0.001	0.001	0.152	0.292
LVED 2c area	2.923	0.934	0.128	0.960	0.214	0.200	0.110	0.106
LVES 2c area	2.211	0.983	0.179	0.931	0.517	0.200	0.366	0.605
LA AP 4c diameter	3.492	0.453	0.102	0.904	0.113	0.168	0.006	0.151
LA LL 4c diameter	3.402	0.454	0.095	0.916	0.190	0.200	0.002	0.059
LA 4c area	2.191	0.894	0.165	0.927	0.871	0.200	0.168	0.328
RA AP 4c diameter	3.528	0.474	0.101	0.915	0.278	0.018	0.958	0.885
RA LL 4c diameter	3.450	0.478	0.105	0.911	0.132	0.200	0.032	0.290
RA 4c area	2.235	0.911	0.178	0.915	0.869	0.200	0.051	0.003
BSA Haycock: $(\sqrt{y} = a + b \times \sqrt{x})$; $Z = [\sqrt{\text{measurement}} - (\text{intercept} + B \times \sqrt{\text{BSA}})]/\sqrt{\text{MSE}}$								
RVES length	2.374	3.307	0.341	0.864	0.462	0.058	0.301	0.289

AP, Anterior-posterior; *4c*, four-chamber; *LA*, left atrial; *LL*, lateral-lateral; *LVED*, left ventricular end-diastolic; *LVES*, left ventricular end-systolic; *RA*, right atrial; *RVED*, right ventricular end-diastolic; *RVES*, right ventricular end-systolic; *2c*, two-chamber.
Normality test: Shapiro-Wilk and Lilliefors (Kolmogorov-Smirnov). Heteroscedasticity tests: White test and Breusch-Pagan test.

0–17 years). Body weight ranged from 1.3 to 88.0 kg (median, 13.7 kg; interquartile range, 4.9–28.0 kg) (Table 3). Height ranged from 41 to 181 cm (median, 93 cm; interquartile range, 57–127 cm). BSA calculated with the Haycock formula[22] ranged from 0.12 to 1.8 m^2 (median, 0.6 m^2; interquartile range, 0.28–0.99 m^2). The distribution for classes of BSA and measurements performed is shown in Tables 2 and 3. Among neonates, 8.8% were premature, and 11.5% had cesarean delivery.

Our data set included 445 children aged 0 to 3 years already presented in a recent work evaluating different measurements. The only measurements that were repeated in both studies were those of M-mode left ventricular diameters.[9]

Preliminary and Final Models

The measurements were first modeled with weight, height, and BSA calculated with the Haycock formula.[9,16] For all measurements, multiple models (linear, logarithmic, exponential, and square root) were evaluated for best fit, and tests for heteroscedasticity were performed (Table 4).

Models with the exponential $(\ln[y] = a + b \times \ln[x])$ and square-root $(\sqrt{y} = a + b \times \sqrt{x})$ equations resulted in the best fit, as they satisfied the assumption of homoscedasticity and normality of residuals and showed the highest R^2 scores (Table 4). The predicted values and *Z*-score boundaries for all measurements are presented in Tables 5 and 6, Figures 1 to 8, and Supplemental Figures 1 to 4 (available at www.onlinejase.com).

Confounders

The influence on measured parameters of gender and, in neonates, the type of delivery (cesarean section vs natural delivery) was evaluated by the use of multiple linear regression models including gender and the type of delivery as covariates along with BSA. We found a slight but significant effect of gender and type of delivery in the model for various measurements (Table 7). However, because we found no significant effects in most of the measurements, gender and type of delivery were not included in the final models.

Interobserver and intraobserver agreement was tested by repeated-measures analysis of variance, and no significant differences were seen for all measurements (Table 8).

DISCUSSION

The importance of accurate pediatric nomograms has recently been addressed by various authors,[1-8] with recommendations to use *Z* scores for quantification during the performance of pediatric echocardiography. Various numeric and methodologic limitations of actual pediatric nomograms have been underscored by multiple authors.[1-8]

The nomograms we present offer the advantage of a rigorous statistical approach[6] whose importance has been widely explained[1-8] and tested[9,10] in previous works. Furthermore, we cover some very

Table 5 Predicted values (mean ± 2 SDs) of measured echocardiographic variables expressed by BSA (Haycock)

Measurement	0.10	0.15	0.20	0.25	0.30	0.35	0.40	0.50
	13.78	16.77	19.28	21.48	23.46	25.28	26.96	30.04
RVED length (RV3)	**16.77**	**20.41**	**23.45**	**26.13**	**28.54**	**30.75**	**32.80**	**36.54**
	20.40	24.82	28.53	31.79	34.72	37.41	39.91	44.46
	7.50	8.84	10.05	11.19	12.27	13.31	14.32	16.24
RVES length	**11.69**	**13.36**	**14.85**	**16.22**	**17.52**	**18.75**	**19.94**	**22.21**
	16.82	18.81	20.57	22.18	23.69	25.12	26.50	29.10
	0.91	1.34	1.76	2.18	2.59	3.00	3.41	4.22
RVED area	**1.28**	**1.88**	**2.47**	**3.06**	**3.64**	**4.22**	**4.80**	**5.94**
	1.80	2.65	3.48	4.31	5.13	5.94	6.75	8.36
	0.28	0.42	0.56	0.70	0.85	0.99	1.13	1.42
RVES area	**0.45**	**0.68**	**0.91**	**1.14**	**1.37**	**1.60**	**1.84**	**2.31**
	0.72	1.10	1.47	1.84	2.22	2.60	2.98	3.73
	7.92	9.70	11.20	12.52	13.71	14.81	15.83	17.69
RVED basal diameter (RV1)	**9.93**	**12.16**	**14.04**	**15.69**	**17.19**	**18.56**	**19.84**	**22.18**
	12.45	15.25	17.60	19.67	21.55	23.27	24.87	27.80
	5.54	6.68	7.63	8.46	9.20	9.88	10.50	11.64
RVED midcavity diameter (RV2)	**7.29**	**8.79**	**10.03**	**11.12**	**12.10**	**12.99**	**13.81**	**15.31**
	9.59	11.56	13.20	14.63	15.91	17.08	18.17	20.13
	17.55	21.23	24.29	26.97	29.38	31.58	33.62	37.33
LVED 4c length	**20.47**	**24.76**	**28.34**	**31.46**	**34.27**	**36.84**	**39.22**	**43.55**
	23.88	28.88	33.06	36.70	39.98	42.98	45.75	50.80
	11.03	13.55	15.67	17.54	19.24	20.80	22.25	24.91
LVES 4c length	**13.64**	**16.74**	**19.37**	**21.68**	**23.78**	**25.71**	**27.50**	**30.79**
	16.86	20.70	23.94	26.80	29.39	31.78	34.00	38.06
	1.62	2.38	3.12	3.85	4.58	5.30	6.01	7.42
LVED 4c area	**2.11**	**3.09**	**4.06**	**5.02**	**5.96**	**6.90**	**7.82**	**9.66**
	2.74	4.03	5.29	6.53	7.76	8.98	10.19	12.58
	0.68	1.00	1.33	1.65	1.97	2.29	2.61	3.25
LVES 4c area	**0.98**	**1.45**	**1.92**	**2.38**	**2.85**	**3.31**	**3.77**	**4.68**
	1.41	2.09	2.76	3.44	4.10	4.77	5.43	6.75
	17.32	20.98	24.05	26.73	29.15	31.36	33.40	37.13
LVED 2c length	**20.20**	**24.48**	**28.05**	**31.18**	**34.00**	**36.58**	**38.97**	**43.31**
	23.56	28.55	32.72	36.38	39.66	42.67	45.45	50.52
	11.12	13.64	15.77	17.64	19.34	20.90	22.36	25.02
LVES 2c length	**13.74**	**16.86**	**19.49**	**21.81**	**23.91**	**25.84**	**27.64**	**30.93**
	16.99	20.84	24.09	26.96	29.55	31.94	34.16	38.23
	1.68	2.45	3.20	3.94	4.68	5.40	6.12	7.54
LVED 2c area	**2.16**	**3.16**	**4.14**	**5.09**	**6.04**	**6.98**	**7.90**	**9.73**
	2.80	4.08	5.34	6.58	7.80	9.01	10.21	12.57
	0.66	0.99	1.31	1.63	1.95	2.27	2.59	3.23
LVES 2c area	**0.95**	**1.41**	**1.88**	**2.34**	**2.79**	**3.25**	**3.71**	**4.62**
	1.36	2.02	2.68	3.34	4.00	4.65	5.30	6.60
	10.84	13.09	14.96	16.59	18.05	19.39	20.63	22.88
LVED M-mode	**13.01**	**15.70**	**17.94**	**19.90**	**21.66**	**23.26**	**24.75**	**27.45**
	15.61	18.84	21.53	23.87	25.98	27.91	29.69	32.93
	6.07	7.31	8.34	9.24	10.05	10.78	11.47	12.70
LVES M-mode	**7.98**	**9.61**	**10.97**	**12.15**	**13.22**	**14.18**	**15.08**	**16.71**
	10.50	12.64	14.43	15.99	17.38	18.66	19.83	21.97
	9.44	11.34	12.92	14.30	15.53	16.65	17.69	19.57
LA AP 4c diameter	**11.58**	**13.91**	**15.85**	**17.53**	**19.04**	**20.42**	**21.69**	**24.00**
	14.20	17.06	19.43	21.50	23.35	25.04	26.60	29.43
	8.73	10.49	11.96	13.23	14.37	15.42	16.38	18.13
LA LL 4c diameter	**10.56**	**12.69**	**14.46**	**16.00**	**17.38**	**18.64**	**19.81**	**21.92**
	12.76	15.34	17.48	19.35	21.02	22.54	23.95	26.50
	0.82	1.18	1.53	1.86	2.19	2.52	2.83	3.46
LA 4c area	**1.14**	**1.64**	**2.12**	**2.59**	**3.05**	**3.50**	**3.94**	**4.81**
	1.59	2.28	2.95	3.60	4.24	4.87	5.48	6.69

(*Continued*)

Table 5 (*Continued*)

Measurement	0.10	0.15	0.20	0.25	0.30	0.35	0.40	0.50
	9.34	11.32	12.98	14.42	15.73	16.92	18.02	20.03
RA AP 4c diameter	**11.43**	**13.86**	**15.88**	**17.65**	**19.25**	**20.71**	**22.06**	**24.52**
	13.99	16.96	19.44	21.60	23.55	25.34	27.00	30.01
	8.49	10.31	11.83	13.16	14.36	15.46	16.48	18.33
RA LL 4c diameter	**10.48**	**12.72**	**14.60**	**16.24**	**17.72**	**19.07**	**20.33**	**22.62**
	12.93	15.69	18.01	20.03	21.86	23.53	25.08	27.90
	0.80	1.16	1.51	1.85	2.19	2.52	2.84	3.48
RA 4c area	**1.15**	**1.66**	**2.16**	**2.64**	**3.12**	**3.59**	**4.06**	**4.97**
	1.64	2.37	3.08	3.77	4.46	5.13	5.79	7.10

AP, Anterior-posterior; *4c*, four-chamber; *LA*, left atrial; *LL*, lateral-lateral; *LVED*, left ventricular end-diastolic; *LVES*, left ventricular end-systolic; *RA*, right atrial; *RVED*, right ventricular end-diastolic; *RVES*, right ventricular end-systolic; *2c*, two-chamber.
The estimated values are in boldface type, the values above are −2 SDs, and the values below are +2 SDs.

important age groups (i.e., neonates and infants) that have been poorly addressed before.

Notably, the present work provides reference values for right ventricular areas and diameters, which have been poorly studied so far. Echocardiographic measurements of right ventricular areas have gained a lot of attention in recent years, as they seem to correlate well with data from magnetic resonance imaging.[4,34] In particular, in children with pulmonary regurgitation after surgical correction of various congenital heart diseases involving right ventricular outflow (i.e., tetralogy of Fallot, truncus arteriosus, double-outlet right ventricle), end-diastolic area was an accurate marker to predict ventricular volumes calculated by magnetic resonance imaging.[34] The availability of reference values may certainly help in improving the accuracy of right ventricular echocardiographic measurements, with the ultimate goal of limiting the repetition of more expensive magnetic resonance imaging examinations.[34] Atrial dimension evaluation is also of great importance for the evaluation of various congenital and acquired heart diseases characterized by left and/or right volumetric and pressure overload.[35-38] In particular, the availability of nomograms for such measurements may increase the accuracy of the echocardiographic estimation of a defect severity, especially in borderline conditions.[37]

Another innovative aspect of our report is our presentation of left ventricular diameters and areas calculated in various projections. Pediatric nomograms for left ventricular dimensions have been built mainly by using M-mode measurements,[7-10] while data on four- and two-chamber views are very limited. Although M-mode measurements are actually recommended as the method of choice for left ventricular quantification in the pediatric age group, their use may lead to overestimation of ventricular diameters.[4] Furthermore, in children with abnormally shaped ventricles, multiple measurements obtained by different views may be helpful for a more complete estimation of ventricular dimensions.[4] The availability of new data may also be of help in such a case, as well as in challenging conditions such as borderline left ventricles.[39]

Regarding confounders, we confirm preliminary observations[9] showing only a slight effect on the basis of gender and, in neonates, by both prematurity and type of delivery on cardiac dimensions.

Strengths and Limitations

This study has several strengths. First, we evaluated some clinically important ultrasound parameters whose pediatric nomograms were limited or even absent. Second, we prospectively enrolled a homogeneous cohort of healthy children, including a wide population of healthy neonates and infants. Third, by the use of a rigorous prospective cohort design, we addressed some important methodologic issues that are of great importance in building a pediatric nomogram.

All reported measurements in the database represent only those performed with excellent visualization and no ambiguity.

The principal limitation of the study was the lack of data from subjects of different ethnic origins. However, this may paradoxically result in a strength of the study, because different racial compositions in a study group may present a bias when interpreting data.

Moreover, the use of a homogeneous cohort (i.e., 100% Caucasian) makes it possible not only to derive normal values for a specific population (Italian in particular and Caucasian in general) but also to compare these data with those from populations composed of different races and ethnicity.

This crucial point will need to be better elucidated in multiethnic studies. Although race and environment are expected to have influence on some cardiac and physiologic parameters (such as blood pressure, heart rate, and cardiac size), some studies have revealed contrasting results, particularly in terms of blood pressure.[40,41]

This study also presents some additional limitations. A complete set of measurements was not available for all subjects studied. Particularly the evaluation of left atrial area in the four-chamber view at times may be difficult,[4,15] thus many data were ambiguous and were deleted from the final database.

It is important to note that even slight differences in view angle may result in substantial differences in area and diameter quantification.[42] As a consequence, to obtain good reproducibility of chamber dimensions, we recommend storing several images and performing measurements only in unambiguous views.

Some sources of error cannot be easily eliminated when dealing with a population consisting primarily of neonates and infants. For example, there are some rapid changes in physiology with increasing body size during the first few months of life that may significantly affect echocardiographic measurements.[43-46] These variations may introduce an unpredictable bias in echocardiographic measurements, because they may occur at different times for each subject and may be influenced by heterogeneous external conditions,[45,46] including patient compliance and operator skill and experience.[43]

Table 6 Predicted values (mean ± 2 SDs) of measured echocardiographic variables expressed by BSA (Haycock)

Measurement	0.6	0.7	0.8	0.9	1.0	1.1	1.2	1.3	1.4	1.5	1.6	1.7
	32.81	35.35	37.71	39.93	42.01	44.00	45.89	47.70	49.44	51.12	52.75	54.32
RVED length (RV3)	**39.92**	**43.01**	**45.88**	**48.57**	**51.11**	**53.52**	**55.83**	**58.03**	**60.15**	**62.19**	**64.17**	**66.08**
	48.56	52.32	55.81	59.09	62.18	65.11	67.91	70.60	73.17	75.66	78.06	80.38
	18.09	19.88	21.62	23.32	24.99	26.63	28.25	29.84	31.41	32.97	34.52	36.05
RVES length	**24.36**	**26.43**	**28.43**	**30.37**	**32.27**	**34.13**	**35.96**	**37.76**	**39.53**	**41.27**	**43.00**	**44.70**
	31.56	33.91	36.17	38.36	40.49	42.57	44.60	46.60	48.57	50.50	52.40	54.28
	5.02	5.81	6.61	7.39	8.17	8.95	9.73	10.50	11.27	12.04	12.81	13.57
RVED area	**7.07**	**8.19**	**9.30**	**10.41**	**11.51**	**12.60**	**13.70**	**14.78**	**15.87**	**16.95**	**18.03**	**19.10**
	9.95	11.52	13.09	14.65	16.20	17.74	19.28	20.81	22.34	23.86	25.38	26.89
	1.72	2.01	2.30	2.59	2.89	3.18	3.48	3.77	4.07	4.36	4.66	4.96
RVES area	**2.78**	**3.25**	**3.72**	**4.20**	**4.67**	**5.15**	**5.63**	**6.11**	**6.59**	**7.07**	**7.55**	**8.03**
	4.50	5.26	6.03	6.80	7.57	8.34	9.11	9.89	10.66	11.44	12.22	13.00
	19.38	20.93	22.37	23.72	25.00	26.22	27.38	28.50	29.57	30.61	31.61	32.58
RVED basal diameter (RV1)	**24.29**	**26.23**	**28.04**	**29.74**	**31.34**	**32.87**	**34.33**	**35.73**	**37.07**	**38.37**	**39.63**	**40.84**
	30.45	32.89	35.15	37.28	39.29	41.21	43.03	44.79	46.47	48.10	49.68	51.20
	12.66	13.59	14.46	15.26	16.02	16.74	17.43	18.08	18.71	19.32	19.90	20.46
RVED midcavity diam (RV2)	**16.65**	**17.88**	**19.01**	**20.07**	**21.07**	**22.02**	**22.92**	**23.78**	**24.61**	**25.40**	**26.17**	**26.91**
	21.90	23.51	25.01	26.40	27.72	28.96	30.15	31.28	32.37	33.41	34.42	35.40
	40.67	43.72	46.54	49.18	51.68	54.04	56.29	58.44	60.51	62.50	64.42	66.28
LVED 4c length	**47.44**	**50.99**	**54.29**	**57.37**	**60.28**	**63.04**	**65.66**	**68.17**	**70.58**	**72.91**	**75.15**	**77.31**
	55.34	59.48	63.33	66.93	70.32	73.53	76.59	79.52	82.34	85.04	87.66	90.19
	27.32	29.53	31.60	33.54	35.37	37.12	38.79	40.40	41.94	43.43	44.87	46.27
LVES 4c length	**33.77**	**36.51**	**39.06**	**41.46**	**43.73**	**45.89**	**47.95**	**49.94**	**51.84**	**53.69**	**55.47**	**57.20**
	41.74	45.13	48.28	51.25	54.05	56.73	59.28	61.73	64.09	66.36	68.57	70.70
	8.82	10.20	11.58	12.94	14.30	15.65	16.99	18.32	19.65	20.98	22.30	23.62
LVED 4c area	**11.48**	**13.28**	**15.07**	**16.85**	**18.62**	**20.37**	**22.12**	**23.86**	**25.59**	**27.32**	**29.04**	**30.75**
	14.95	17.30	19.63	21.94	24.24	26.53	28.80	31.07	33.32	35.57	37.81	40.04
	3.88	4.51	5.14	5.76	6.39	7.01	7.63	8.25	8.86	9.48	10.10	10.71
LVES 4c area	**5.60**	**6.50**	**7.41**	**8.31**	**9.21**	**10.10**	**11.00**	**11.89**	**12.78**	**13.67**	**14.56**	**15.45**
	8.07	9.38	10.68	11.98	13.28	14.57	15.86	17.15	18.43	19.71	20.99	22.27
	40.48	43.55	46.40	49.06	51.57	53.96	56.23	58.40	60.49	62.50	64.44	66.32
LVED 2c length	**47.22**	**50.80**	**54.12**	**57.23**	**60.16**	**62.94**	**65.59**	**68.13**	**70.56**	**72.91**	**75.17**	**77.36**
	55.08	59.26	63.13	66.76	70.18	73.42	76.51	79.47	82.31	85.05	87.69	90.24
	27.43	29.64	31.71	33.65	35.48	37.23	38.90	40.50	42.04	43.53	44.96	46.36
LVES 2c length	**33.90**	**36.64**	**39.19**	**41.59**	**43.86**	**46.02**	**48.08**	**50.06**	**51.97**	**53.80**	**55.58**	**57.31**
	41.91	45.30	48.45	51.41	54.22	56.89	59.44	61.88	64.24	66.51	68.71	70.84
	8.93	10.32	11.69	13.05	14.40	15.74	17.07	18.39	19.71	21.02	22.33	23.63
LVED 2c area	**11.54**	**13.33**	**15.10**	**16.85**	**18.60**	**20.33**	**22.05**	**23.76**	**25.46**	**27.16**	**28.85**	**30.53**
	14.91	17.22	19.50	21.77	24.02	26.26	28.48	30.69	32.89	35.08	37.26	39.43
	3.86	4.49	5.12	5.75	6.38	7.01	7.63	8.26	8.88	9.50	10.13	10.75
LVES 2c area	**5.52**	**6.43**	**7.33**	**8.23**	**9.12**	**10.02**	**10.92**	**11.81**	**12.70**	**13.59**	**14.48**	**15.37**
	7.90	9.19	10.48	11.77	13.05	14.33	15.61	16.89	18.17	19.44	20.72	21.99
	24.90	26.75	28.46	30.06	31.56	32.99	34.35	35.65	36.90	38.10	39.26	40.38
LVED M-mode	**29.87**	**32.09**	**34.14**	**36.06**	**37.86**	**39.58**	**41.21**	**42.77**	**44.26**	**45.70**	**47.09**	**48.43**
	35.84	38.49	40.95	43.25	45.42	47.48	49.43	51.30	53.10	54.82	56.49	58.10
	13.81	14.82	15.76	16.64	17.46	18.24	18.99	19.70	20.38	21.03	21.67	22.28
LVES M-mode	**18.17**	**19.50**	**20.73**	**21.88**	**22.97**	**23.99**	**24.97**	**25.90**	**26.80**	**27.66**	**28.50**	**29.30**
	23.89	25.64	27.26	28.78	30.20	31.56	32.84	34.07	35.25	36.38	37.48	38.53
	21.26	22.79	24.21	25.54	26.79	27.97	29.10	30.17	31.20	32.19	33.15	34.07
LA AP 4c diameter	**26.07**	**27.95**	**29.69**	**31.32**	**32.85**	**34.30**	**35.68**	**37.00**	**38.26**	**39.48**	**40.65**	**41.78**
	31.96	34.28	36.41	38.41	40.29	42.06	43.75	45.37	46.92	48.41	49.84	51.23
	19.69	21.12	22.44	23.67	24.83	25.93	26.97	27.97	28.93	29.85	30.73	31.59
LA LL 4c diameter	**23.81**	**25.54**	**27.13**	**28.62**	**30.02**	**31.35**	**32.62**	**33.82**	**34.98**	**36.09**	**37.17**	**38.20**
	28.79	30.88	32.81	34.61	36.31	37.91	39.44	40.90	42.30	43.64	44.94	46.20
	4.07	4.67	5.27	5.85	6.43	7.00	7.57	8.13	8.69	9.24	9.79	10.33
LA 4c area	**5.67**	**6.50**	**7.33**	**8.14**	**8.94**	**9.74**	**10.53**	**11.31**	**12.08**	**12.85**	**13.62**	**14.37**
	7.88	9.04	10.19	11.32	12.44	13.55	14.64	15.73	16.81	17.88	18.94	19.99

(*Continued*)

Table 6 (*Continued*)

Measurement	0.6	0.7	0.8	0.9	1.0	1.1	1.2	1.3	1.4	1.5	1.6	1.7
	21.84	23.50	25.03	26.47	27.83	29.11	30.34	31.51	32.64	33.72	34.77	35.78
RA AP 4c diameter	**26.73**	**28.76**	**30.64**	**32.40**	**34.06**	**35.63**	**37.13**	**38.57**	**39.94**	**41.27**	**42.55**	**43.79**
	32.72	35.20	37.50	39.65	41.68	43.61	45.44	47.20	48.89	50.51	52.08	53.60
	20.00	21.53	22.95	24.28	25.53	26.72	27.86	28.95	29.99	30.99	31.97	32.91
RA LL 4c diameter	**24.68**	**26.56**	**28.31**	**29.95**	**31.50**	**32.97**	**34.37**	**35.71**	**37.00**	**38.24**	**39.44**	**40.59**
	30.44	32.77	34.93	36.95	38.86	40.67	42.40	44.05	45.64	47.17	48.65	50.08
	4.11	4.73	5.34	5.95	6.55	7.14	7.73	8.31	8.90	9.47	10.05	10.62
RA 4c area	**5.87**	**6.75**	**7.63**	**8.49**	**9.35**	**10.19**	**11.04**	**11.87**	**12.70**	**13.52**	**14.34**	**15.16**
	8.38	9.64	10.89	12.12	13.34	14.55	15.75	16.95	18.13	19.31	20.47	21.64

AP, Anterior-posterior; *4c*, four-chamber; *LA*, left atrial; *LL*, lateral-lateral; *LVED*, left ventricular end-diastolic; *LVES*, left ventricular end-systolic; *RA*, right atrial; *RVED*, right ventricular end-diastolic; *RVES*, right ventricular end-systolic; *2c*, two-chamber.
The estimated values are in boldface type, the values above are −2 SDs, and the values below are +2 SDs.

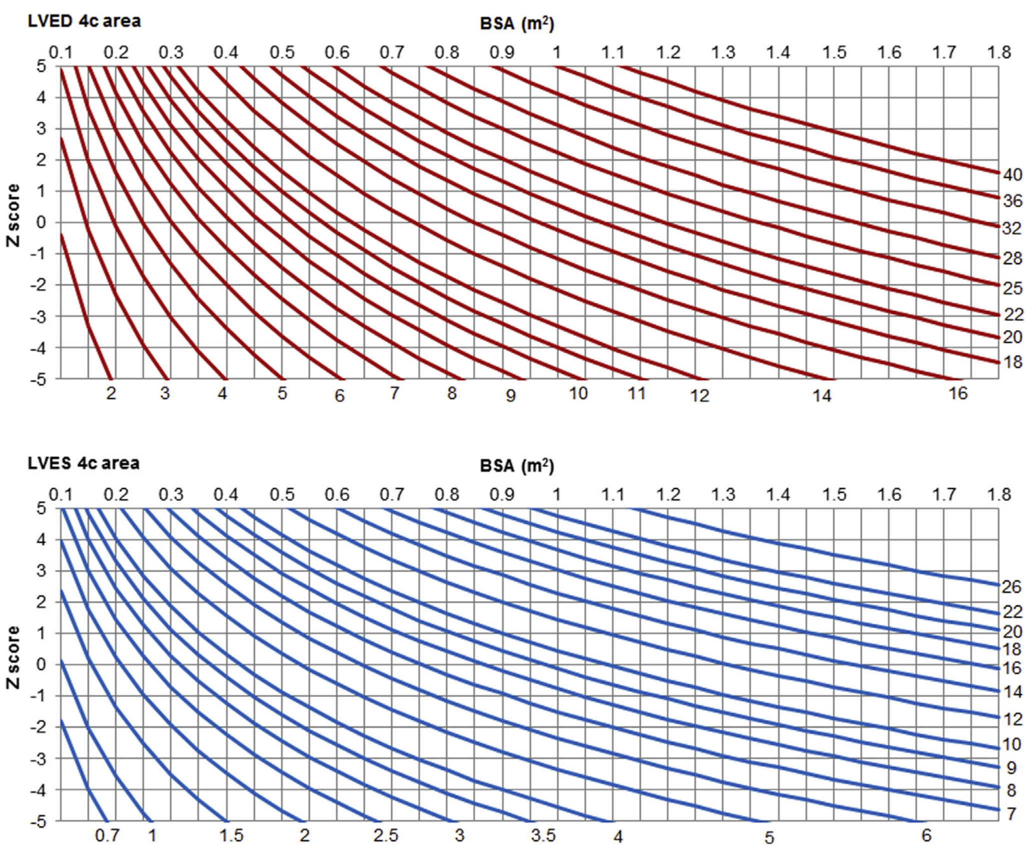

Figure 1 Percentile charts for left ventricular end-diastolic (LVED) and left ventricular end-systolic (LVES) area in the four-chamber (4c) view according to BSA calculated by Haycock.

CONCLUSIONS

The nomograms provided in the present report may be considered helpful tools for clinicians to perform quantitative measurements of cardiac chamber areas and diameters in children with various acquired and congenital heart defects.

In particular, this work substantially covers the gap of knowledge on chamber dimensions in children with the advantage of a rigorous statistical design.

Further studies, however, are required to reinforce these data, as well as to evaluate other parameters of clinical interest and the role of different ethnicities.

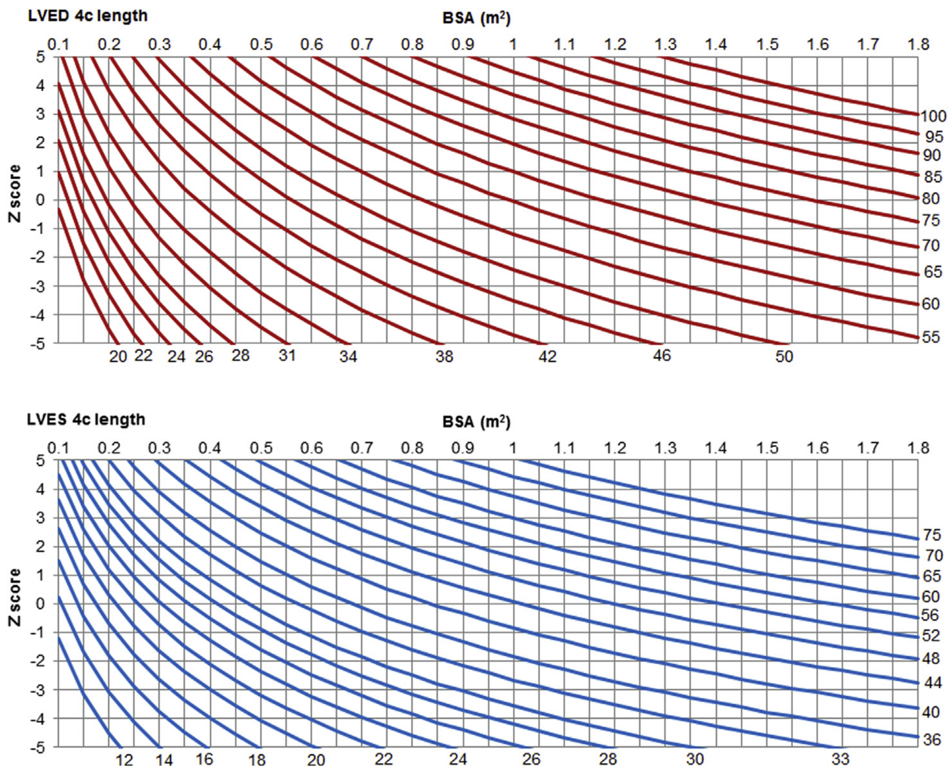

Figure 2 Percentile charts for left ventricular end-diastolic (LVED) and left ventricular end-systolic (LVES) length in the four-chamber (4c) view according to BSA calculated by Haycock.

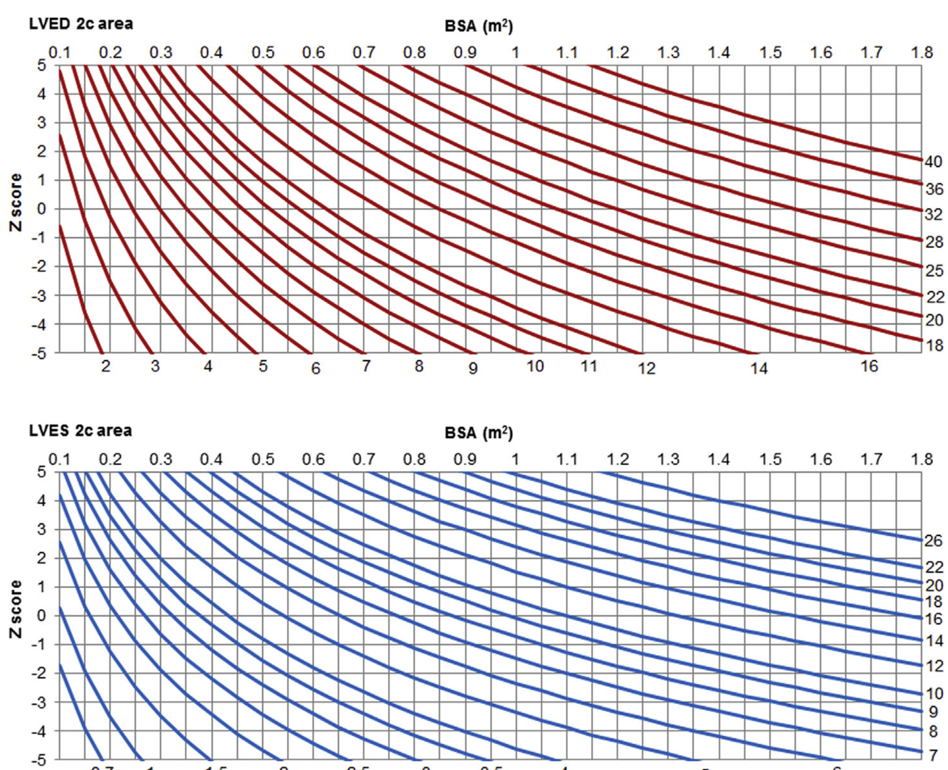

Figure 3 Percentile charts for left ventricular end-diastolic (LVED) and left ventricular end-systolic (LVES) area in the two-chamber (2c) view according to BSA calculated by Haycock.

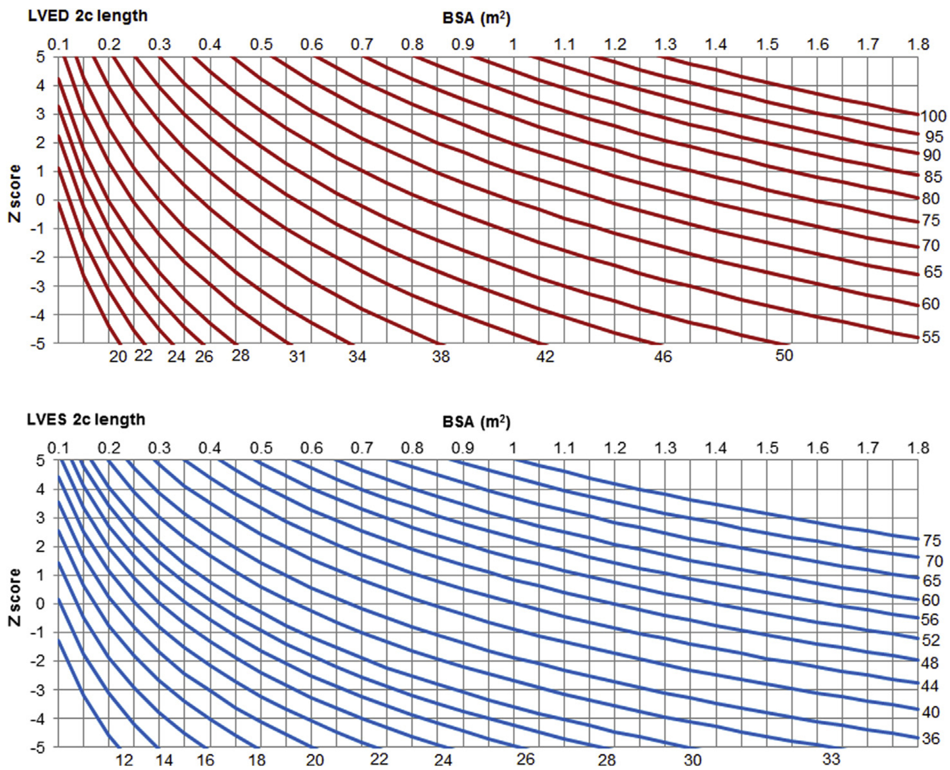

Figure 4 Percentile charts for left ventricular end-diastolic (LVED) and left ventricular end-systolic (LVES) length in the two-chamber (2c) view according to BSA calculated by Haycock.

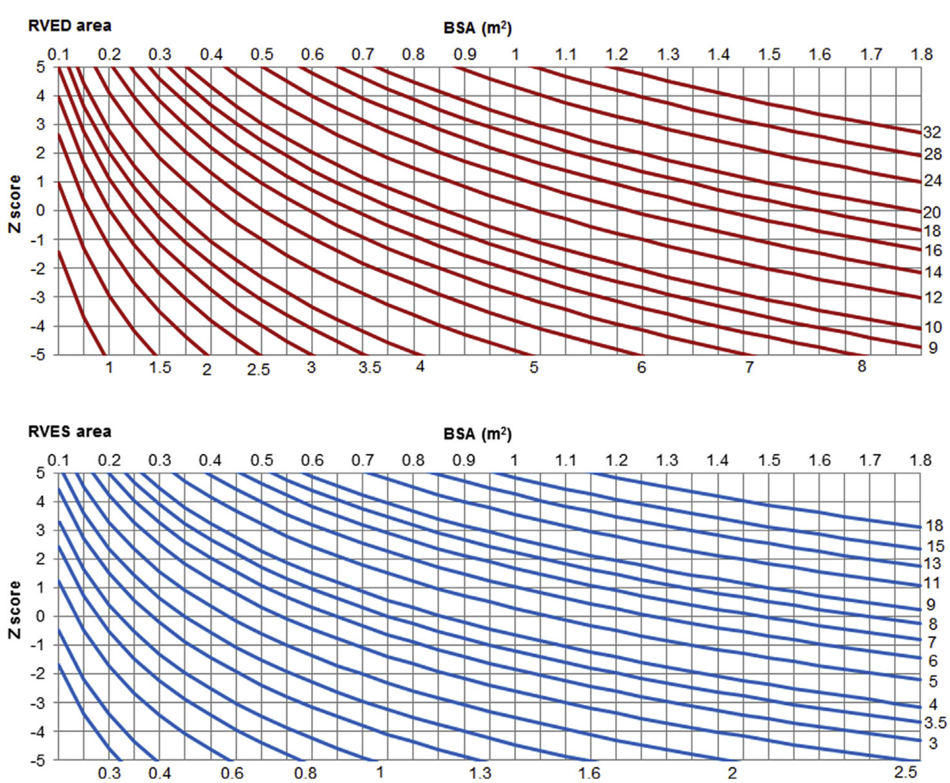

Figure 5 Percentile charts for right ventricular end-diastolic (RVED) and right ventricular end-systolic (RVES) area according to BSA calculated by Haycock.

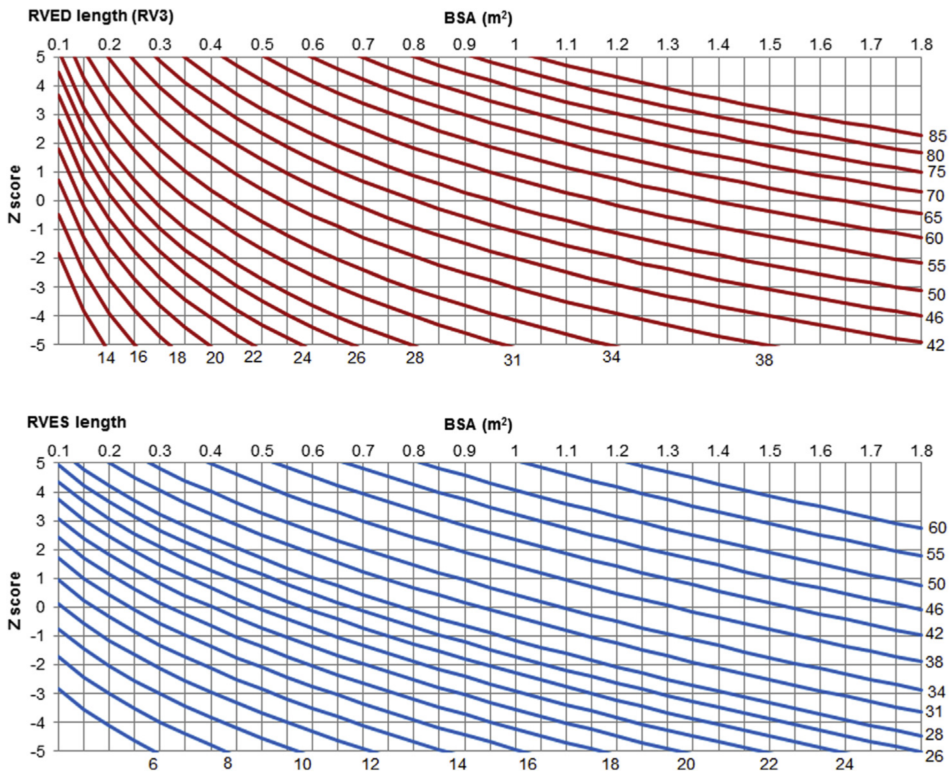

Figure 6 Percentile charts for right ventricular end-diastolic (RVED) and right ventricular end-systolic length according to BSA calculated by Haycock. *RV3*, RVED length.

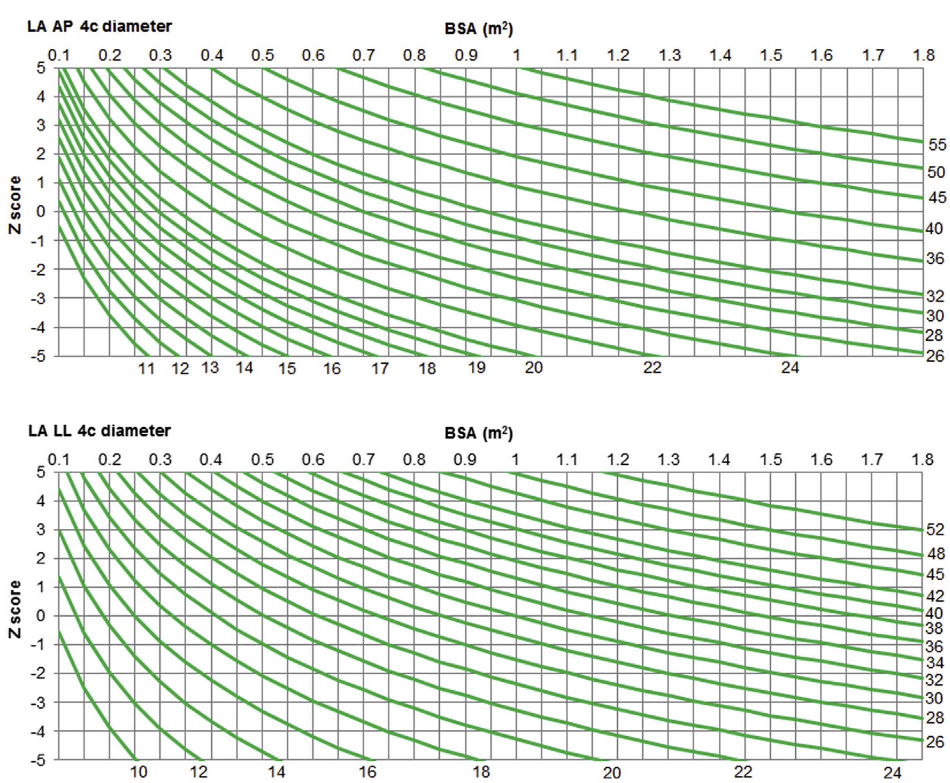

Figure 7 Percentile charts for left atrial diameters in the four-chamber (4c) view according to BSA calculated by Haycock.

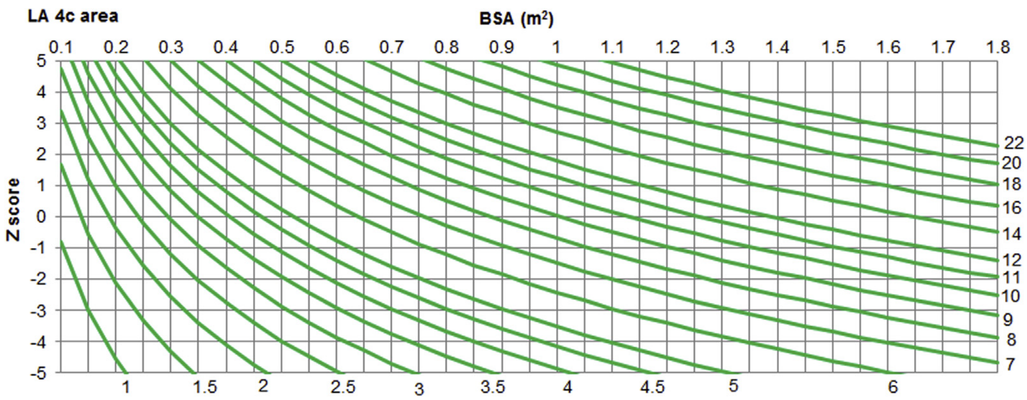

Figure 8 Percentile charts for left atrial (LA) anterior-posterior and lateral-lateral diameters in the four-chamber (4c) view according to BSA calculated by Haycock.

Table 7 Coefficients for regression equations relating echocardiographic measurements to BSA (Haycock) and gender

Measurement	B_2		P
Measurement = intercept + B_1 × BSA + B_2 × gender (male)			
LVED M-mode	0.952		<.001
LVES M-mode	0.572		.001
RVED length (RV3)	0.948		.006
RVES length	1.015		<.001
RVED area	0.672		<.001
RVES area	0.375		<.001
RVED basal diameter (RV1)	0.715		.001
RVED midcavity diam (RV2)	0.542		.002
LVED 4c length	0.668		.026
LVED 4c area	0.595		<.001
LVES 4c area	0.295		<.001
LVED 2c area	0.692		.002
LVES 2c area	0.294		.013
LA LL 4c diameter	0.433		.018
RA AP 4c diameter	0.819		<.001
RA LL 4c diameter	1.037		<.001
RA 4c area	0.544		<.001
	B_3	B_4	
Measurement = intercept + B_1 × BSA + B_2 × gender + B_3 × caesarean + B_4 × premature			
LVED M-mode	—	−1.580	.001
LVES M-mode	—	−0.866	.023
RVED length (RV3)	−1.664	—	.022
RVES length	−1.777	—	.003
RVED basal diameter (RV1)	−1.201	—	.002
LVED 4c length	—	−1.990	.001
LVES 4c length	—	−1.594	.005
LVES 2c length	−1.829	—	.029
LA AP 4c diameter	—	−0.986	.020
RA AP 4c diameter	—	−1.399	.001
RA LL 4c diameter	—	−1.067	.008

AP, Anterior-posterior; *4c*, four-chamber; *LA*, left atrial; *LL*, lateral-lateral; *LVED*, left ventricular end-diastolic; *LVES*, left ventricular end-systolic; *RA*, right atrial; *RVED*, right ventricular end-diastolic; *RVES*, right ventricular end-systolic; *2c*, two-chamber.

Table 8 Inter- and intraobserver analysis calculated on 30 subjects

Measurement	*P* value, interobserver	*P* value intraobserver
LVED M-mode	.313	.827
LVES M-mode	.175	.882
RVED length (RV3)	.741	.933
RVES length	.158	.866
RVED area	.563	.885
RVES area	.412	.810
RVED basal diameter (RV1)	.205	.820
RVED midcavity diam (RV2)	.191	.827
LVED length 4c	.492	.829
LVES length 4c	.773	.936
LVED area 4c	.601	.976
LVES area 4c	.910	.910
LVED length 2c	.994	.997
LVES length 2c	.751	.819
LVED area 2c	.513	.939
LVES area 2c	.145	.843
LA AP diameter 4c	.088	.842
LA LL diameter 4c	.082	.816
LA area 4c	.096	.831
RA AP diameter 4c	.075	.845
RA LL diameter 4c	.322	.864
RA area 4c	.603	.810

AP, Anterior-posterior; *4c*, four-chamber; *LA*, left atrial; *LL*, lateral-lateral; *LVED*, left ventricular end-diastolic; *LVES*, left ventricular end-systolic; *RA*, right atrial; *RVED*, right ventricular end-diastolic; *RVES*, right ventricular end-systolic; *2c*, two-chamber.

The recent advances in three-dimensional echocardiography seem to indicate how this technique could become the gold standard for the estimation of chamber dimension,[47] and robust nomograms for three-dimensional echocardiography are also advised.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.echo.2014.08.005.

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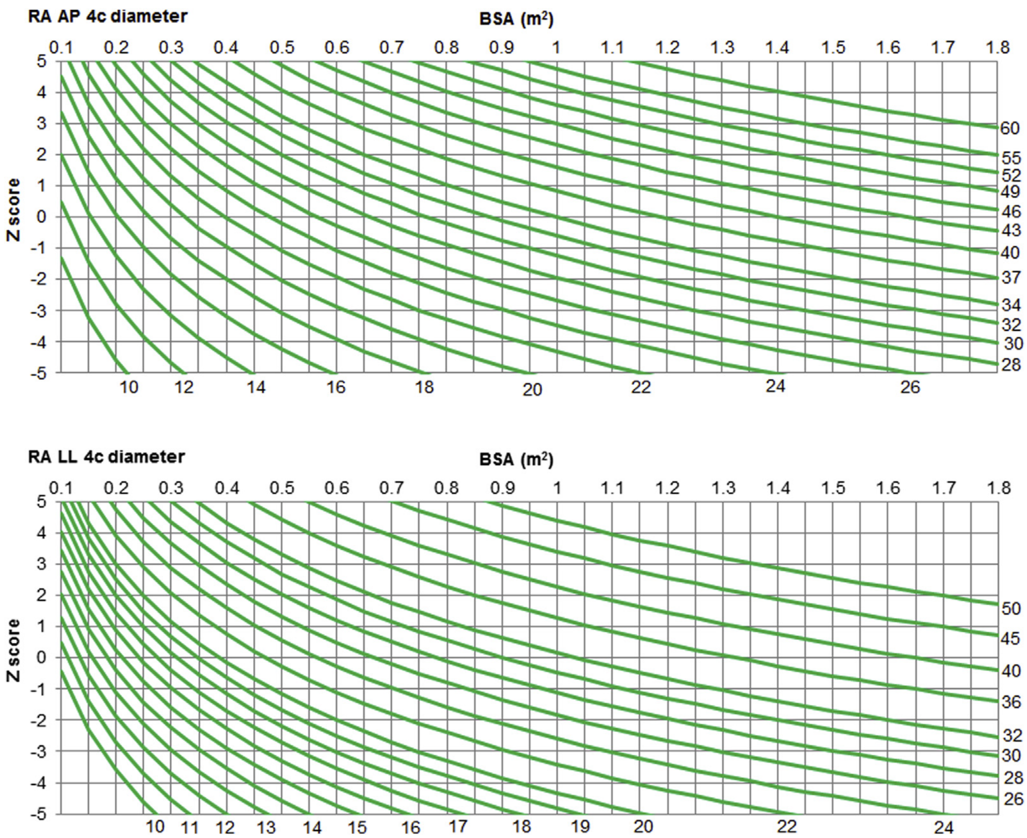
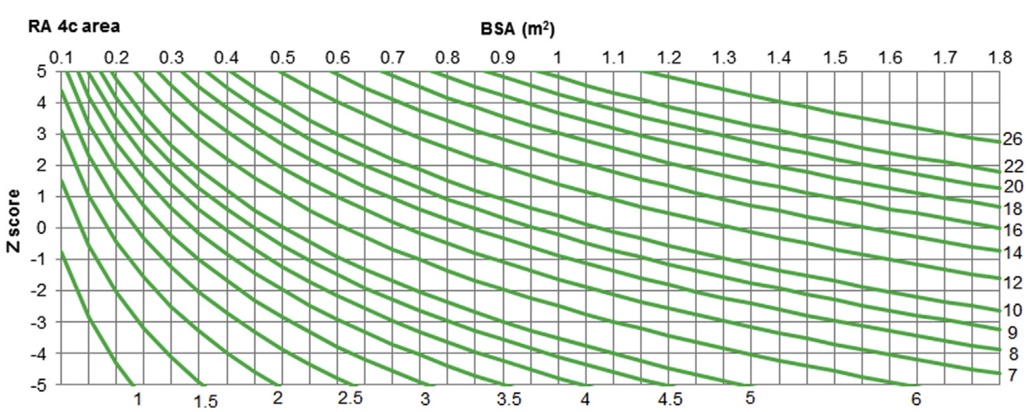
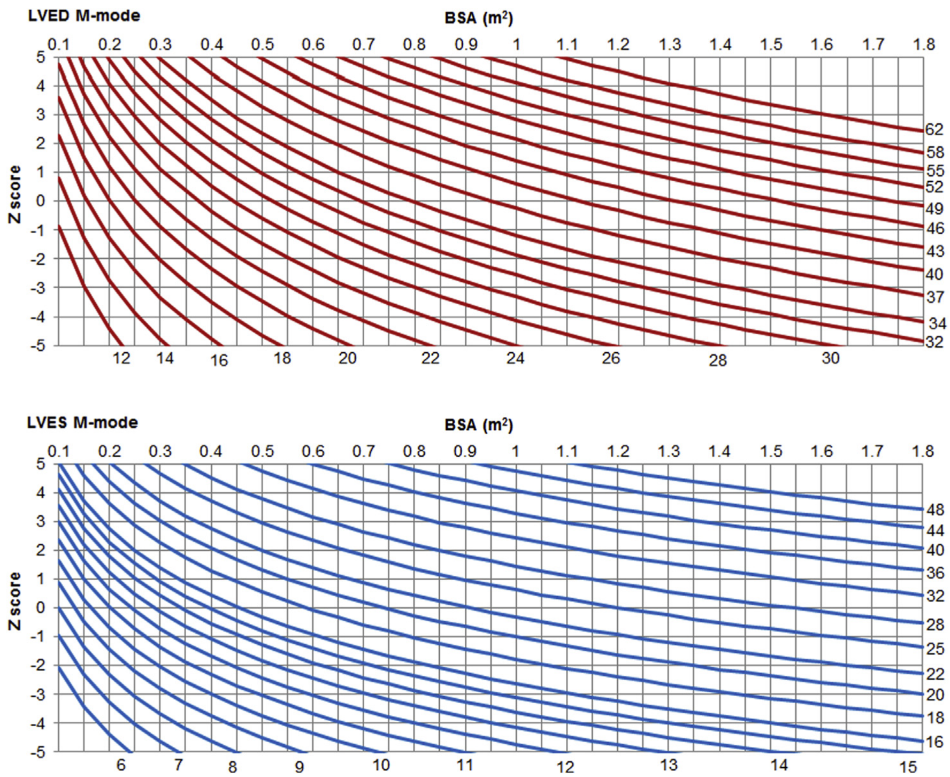


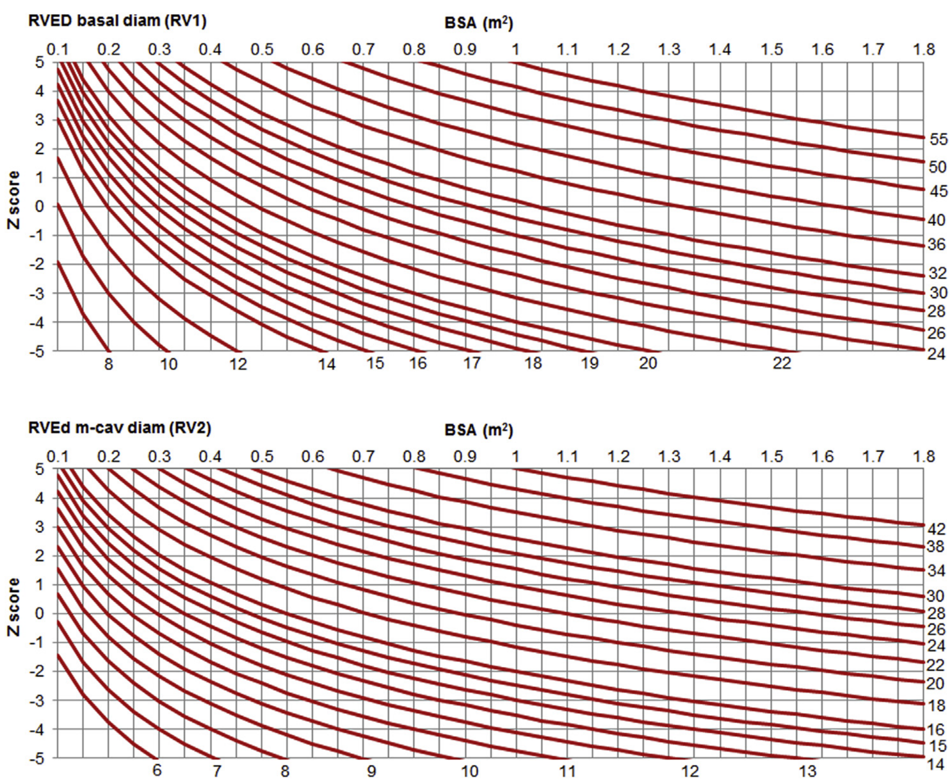
Supplemental Figure 1 Percentile charts for right atrial (RA) anterior-posterior (AP) and lateral-lateral (LL) diameters in the four-chamber (4c) view according to BSA calculated by Haycock.



Supplemental Figure 2 Percentile charts for right atrial (RA) area in the four-chamber (4c) view according to BSA calculated by Haycock.



Supplemental Figure 3 Percentile charts for left ventricular diameters on M-mode echocardiography according to BSA calculated by Haycock. *LVED*, Left ventricular end-diastolic; *LVES*, left ventricular end-systolic.



Supplemental Figure 4 Percentile charts for right ventricular basal and midcavity (m-cav) diameters (diam) according to BSA calculated by Haycock. *RVED*, Right ventricular end-diastolic; *RV1*, RVED basal diameter; *RV2*, RVED midcavity diameter.