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NORMATIVE DATA FOR ECHOCARDIOGRAPHIC CHAMBER DIMENSIONS IN SOUTH-ASIANS

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Date Received: November 30, 2012
Date Revised: December 15, 2012
Date Accepted: December 20 , 2012

Contribution
All the authors contributed significantly to the research that resulted in the submitted manuscript.

All authors declare no conflict of interest.

ABSTRACT

Objectives: The study was carried out in an attempt to establish normograms for chamber sizes in local setting, define the normal reference intervals and formulate prediction equations.

Methodology: The final study group consisted of 1311 subjects. Echocardiographic dimensions were measured with "Powervision 7000" scanner (Model SSA-380A software version 4.0, Toshiba, Nasu, Japan) using a 2.5 MHz sector probe with the subjects in left lateral position.

Results: The study included 713 men and 598 women aged 47.9±18.5 and 46.9±14.8 years respectively. Men generally had greater average height, weight, BSA and BMI than women (p values <0.005). Gender specific aortic root and LA diameters and their BSA and height derived indices are described as mean ± SD and 5th and 95th percentile ranges along with ASE recommended reference intervals for comparison. The centile values for LA diameter showed a wider range than the ASE recommended limits. The values for PWT, RWT, EF and FS carried higher 95th percentiles than ASE recommended upper limits. All chamber parameters showed significant correlations with BSA ($p < 0.005$).

Conclusion: The practice of utilizing normograms in adult echocardiographic examinations is poorly applied and the scientific data for predictive equations in adults is scarce. Large enough studies on ethnically diverse populations, using allometric scaling to FFM and redefining the cutoffs call for future research.

Key Words: Normative data, Echocardiographic chamber dimensions, LV mass.

INTRODUCTION

Stratification of the grey zone areas for cardiac chamber sizes into normality and diseased states requires accurate dimensional and functional quantification. Technological leaps in improved image acquisition and display systems have greatly improved the accuracy of these measurements in recent era; however, overlaps are often encountered between limits of normality and the deranged states. The widely evident effect of body size on cardiac chambers adds greatly to this ambiguity. In contrast to pediatric cardiology where cardiovascular measurements are universally indexed to body size, scaling of cardiac chamber quantification remains poorly applied in adult clinical practice despite ample scientific evidence for relationship between body size and cardiovascular dimensions.[1]

The guidelines from American Society of Echocardiography (ASE) standardized the reference limits for adult echocardiographic chamber quantification along with appropriate methods for recording these measurements.[2] No single methodology could be used for all parameters and the tables of cutoffs represented a consensus of a panel of experts using standard deviation values from previous studies.[2] The normative data represent by those studies was not based on large enough population groups; reference values for LV linear dimensions were based on a population of 510 subjects, LA linear measurements taken from a Framingham Heart Study cohort of 1099 participants and aortic root diameter assessment based on study of 187 subjects back in 1989, which remains the only dimension for which predictive regression equations and normograms were published in these guidelines.[2-4] The guidelines considered these consensus-based values to be more robust for some parameters than others and pointed towards the need for future research that may redefine the cutoffs.[2]

Most of the published normative data is based on Caucasian studies and in some cases African Americans as well. Effect of ethnic variations on cardiac dimensions is evident from published data.[5] Efforts are required to formulate normograms in large enough population groups worldwide that would incorporate data from wide range of ethnic diversities. Concerns exist as weather to follow the ASE recommended intervals or to work towards defining the local norms that could be more representative of the local ethnicity and body built as the South Asian races may differ in this regard. We carried out the study in an attempt to establish normograms for chamber sizes in local setting, define the normal reference intervals and formulate prediction equations.

METHODOLOGY

The study population consisted of 1950 healthy adults without history of heart diseases or hypertension over a period of five years starting from May 2005. All participants had a normal physical examination along with normal baseline ECG and chest x-ray. BSA was calculated according to the DuBois and DuBois formula. Subjects with BMI $>30 Kg/m^2$ ($n=351$) were excluded from the study to avoid the independent effect of obesity on cardiac chamber sizes. Echocardiographic evidence of pericardial effusion, valvular lesions, left ventricular (LV) wall motion abnormalities or diastolic dysfunction was also considered an exclusion criterion for the study ($n=288$). The final study group consisted of 1311 subjects.

ECHOCARDIOGRAPHIC MEASUREMENTS

Echocardiographic dimensions were measured with "Powervision 7000" scanner (Model SSA-380A software version 4.0, Toshiba, Nasu, Japan) using a 2.5 MHz sector probe with the subjects in left lateral position. All echocardiographic examinations were performed and analyzed by a single experienced operator following the guidelines for chamber quantification by ASE. The parameters were recorded by M-mode readings from standard parasternal long axis views, taking mean of three consecutive readings. Two-dimensional imaging was used to guide M-mode reading where appropriate. The left ventricular internal diameters (LVID), left ventricular (LV), septal wall thickness (SWT) and posterior wall thickness (PWT) were recorded in end diastole, defined by the beginning of QRS complex on integrated ECG. LV internal systolic dimensions were recorded at peak systole, defined as the smallest diameter during the time interval of systolic septal thickening and maximum anterior motion of posterior wall. LV ejection fraction (EF) and endocardial fractional shortening (FS) were calculated using the cubed assumption. LV mass was calculated by ASE recommended formula of LV linear dimensions:

$$LV\ mass = 0.8X\{1.04[(LVIDd + PWTd + SWTd)^3 - (LVIDd)^3]\} + 0.6\ g$$

Relative wall thickness (RWT) was calculated by the formula (2XPWTd)/LVIDd. The aortic root diameters were recorded at end diastole in the views displaying its maximum diameter with the imaging plane perpendicular to aortic long axis traversing the widest portion of the root, using the leading edge technique. The linear left atrial (LA) dimensions were measured at ventricular end-systole when LA size was at its maximum taking care that the imaging plane traverses the widest portion of LA. The measurements were taken from the trailing edge of posterior aortic wall to the leading edge of posterior LA wall as per ASE recommendations.

The echocardiographic measurements were computed for analysis into the software "Statistical Package for Social Sciences (SPSS) version 15". Gender specific values for body size variables namely height, weight, BSA and BMI were described as means and standard deviations (SD) and were compared for gender differences. After being stratified for genders, the chamber dimensions were indexed for BSA as well as height. The cardiac dimensions and their indices were tabulated in terms of mean ± SD and 5th and 95th percentiles. Each measurement was fitted into linear regressions models with BSA.

The measurements were tested for correlations with BSA and then related to BSA by the general regression model $y=m(BSA)+c$, where "y" is the predicted value of echocardiographic measurement, "m" is the slope of regression equation and "c" is the value of y-intercept. The y-intercept and slope values for chamber dimensions were tabulated for both genders. The regression coefficient (R) was also calculated for the measurements related to BSA. Normograms were plotted for individual echocardiographic chamber dimensions for both genders, displaying the regression and 95% prediction lines according to BSA.

RESULTS

The study included 713 men and 598 women aged 47.9±18.5 and 46.9±14.8 years respectively. Men generally had greater average height, weight, BSA and BMI than women (p values <0.005) (Table 1). Gender specific aortic root and LA diameters and their BSA and height derived indices are described as mean± SD and 5th and 95th percentile ranges along with ASE recommended reference intervals for comparison (Table 2). The centile values for LA diameter showed a wider range than the ASE recommended limits. Gender specific LV measurements including LVID, PWT, SWT, LV mass, RWT, EF and FS are described similarly including their respective indices (Table 3). The values for PWT, RWT, EF and FS carried higher 95th percentiles than ASE recommended upper limits.

All chamber parameters showed significant correlations with BSA ($p < 0.005$). The values of y-intercepts and slopes are described along with the R values for individual parameters when fitted into regression model with BSA (Table 4). The gender specific normograms for chamber parameters are plotted (Figure 1) using the linear regression model relating the cardiac parameters to BSA. The normograms display mean lines in the middle along with 95% confidence interval lines above and below for estimation of upper and lower limits of a given cardiac parameter according to respective BSA. The regression equations for chamber parameter prediction are displayed as well.

Table 1: Anthropometric Measures for Both Genders

	Men		Women		p-value for gender differences
	n	Mean± SD	n	Mean±SD	
Height (m)	713	1.67±0.08	598	1.54±.07	< 0.005
Weight (KG)	713	62.9±2.6	598	56.8±10.6	< 0.005
BSA (m^2)	713	1.7 ± .18	598	1.54 ± .15	< 0.005
BMI (Kg/m^2)	713	22.2 ± 4.3	598	23.6 ± 4.1	< 0.005

Table 2: Aortic Root and LA Diameter Measurements

	Men				Women			
	n	Mean±SD	5th and 95th percentiles	ASE reference limits	n	Mean±SD	5th and 95th percentiles	ASE reference limits
Aortic root diameter (cm)	712	3.3 ± .40	2.6–3.9	-	597	3.0 ± .33	2.4–3.5	-
Aortic root diameter/BSA (cm/m^2)	712	1.9 ± .26	1.5–2.4	-	597	1.9 ± .27	1.5–2.4	-
Aortic root diameter/Height (cm/m)	712	1.9 ± .25	1.5–2.4	-	597	1.9 ± .22	1.6–2.3	-
LA diameter (cm)	713	3.5 ± .48	2.6–4.2	3.0 – 4.0	597	3.3 ± .47	2.5–4.1	2.7 – 3.8
LA diameter/BSA (cm/m^2)	713	2.1 ± .29	1.6–2.5	1.5 – 2.3	597	2.2 ± .30	1.7–2.7	1.5 – 2.3
LA diameter/Height (cm/m)	713	2.1 ± .30	1.6–2.6	-	597	2.1 ± .31	1.7–2.6	-

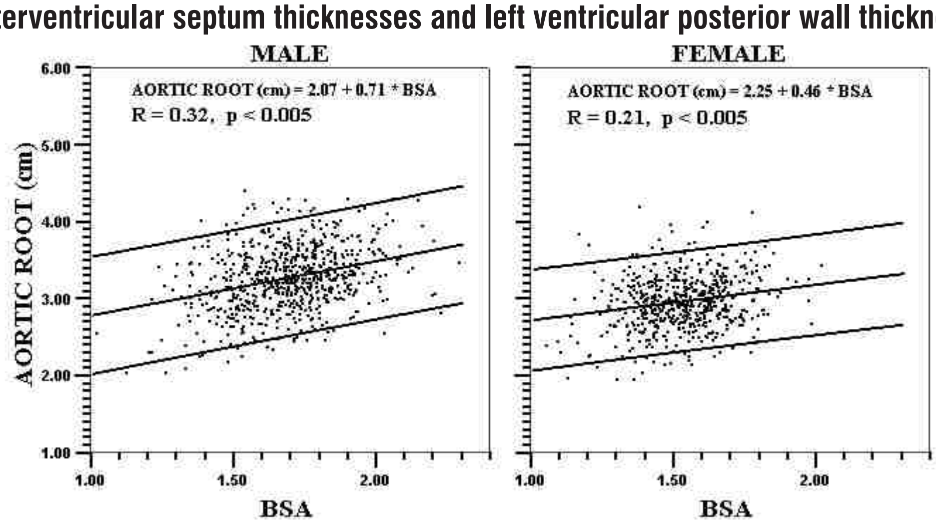
Table 3: Measurements for LVIDd, SWT, PWT, LV mass, RWT, EF and FS

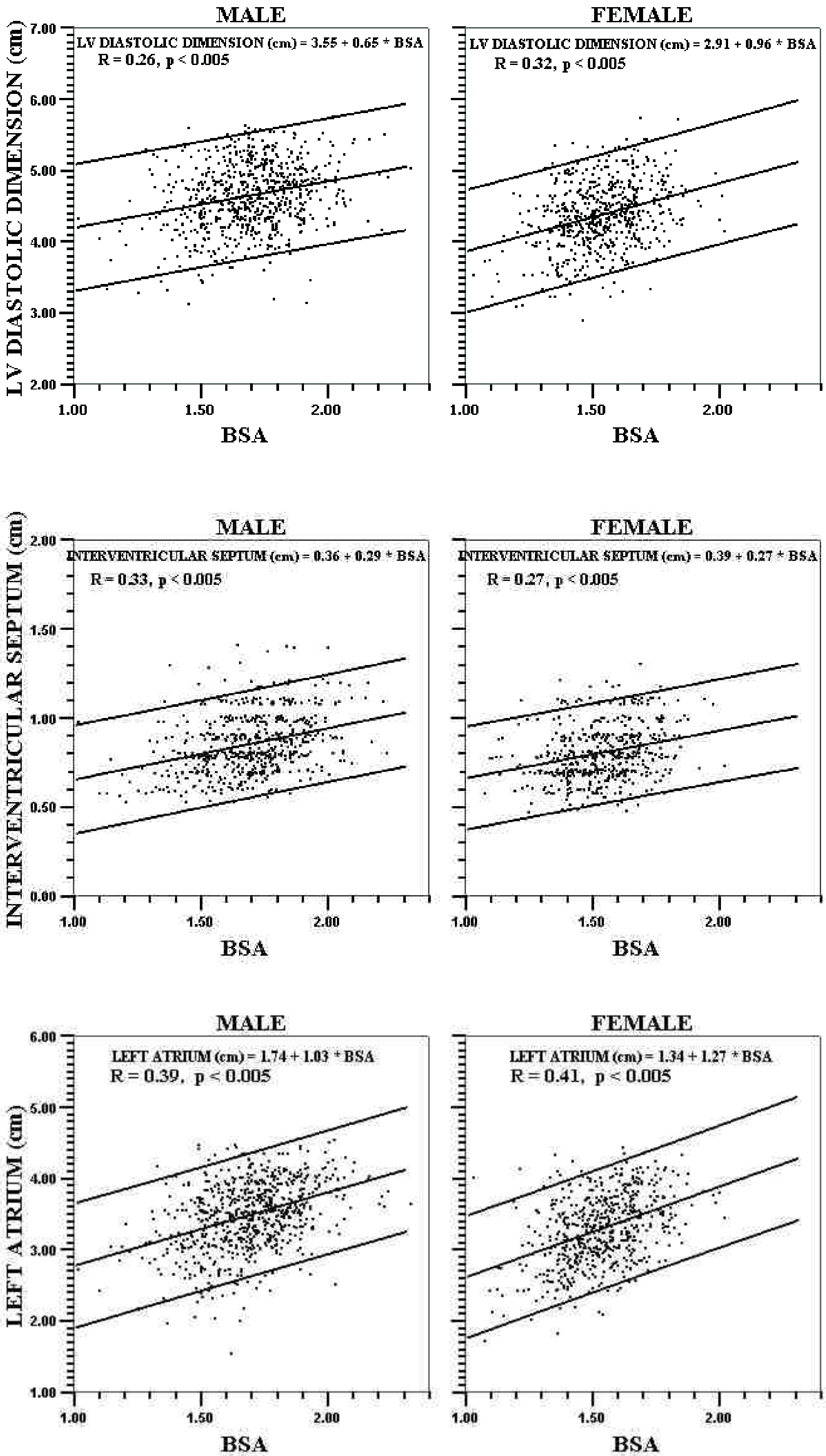
	Men				Women			
	n	Mean ± SD	5th and 95th percentiles	ASE reference limits	n	Mean ± SD	5th and 95th percentiles	ASE reference limits
LVIDd (cm)	713	4.7 ± .46	3.9–5.4	4.2–5.9	598	4.4 ± .46	3.6–5.1	3.9–5.3
LVIDd /BSA (cm/m^2)	713	2.8 ± .36	2.2–3.4	2.2–3.1	598	2.9 ± .34	2.3–3.5	2.4–3.2
LVIDd /Height (cm/m)	713	2.8 ± .29	2.4–3.3	2.4–3.3	598	2.8 ± .30	2.4–3.4	2.5–3.2
SWT (cm)	604	0.9 ± .10	0.6–1.1	0.6–1.0	535	0.8 ± .15	0.6–1.1	0.6–0.9
SWT /BSA (cm/m^2)	604	0.5 ± .10	0.4–0.7	-	535	0.5 ± .10	0.4–0.7	-
SWT /Height (cm/m)	604	0.5 ± .10	0.4–0.7	-	535	0.5 ± .10	0.4–0.7	-
PWT (cm)	611	0.8 ± .15	0.5–1.0	0.6–1.0	537	0.7 ± .14	0.5–1.0	0.6–0.9
PWT /BSA (cm/m^2)	611	0.5 ± .08	0.3–0.6	-	537	0.5 ± .10	0.3–0.6	-
PWT /Height (cm/m)	611	0.5 ± .08	0.3–0.6	-	537	0.5 ±0.10	0.3–0.6	-
LV mass (g)	604	127.4±36.2	74.3–188	88–224	533	104.9±29.1	64.2–159.3	67–162
LV mass/BSA (g/m^2)	604	74.9 ±19.5	47.3–108.8	49–115	533	67.9 ± 16.7	43.7–98.8	43–95
LV mass/Height (g/m)	604	76.3 ± 21.4	44.9–113.8	52–126	533	67.8 ± 18.3	41.2–101.8	41–99
RWT (cm)	611	0.34 ± .07	0.23 – 0.47	0.24 – 0.42	537	0.34 ± .08	0.22 – 0.49	0.24 – 0.42
EF (%)	673	66.2 ± 6.1	57 – 77	= 55	576	67.4 ± 6.3	58.0 – 78.2	= 55
Endocardial FS (%)	577	37.1 ± 5.0	30 – 46.1	25 – 43	518	37.9 ± 7.2	30.0 – 49.0	27 – 45

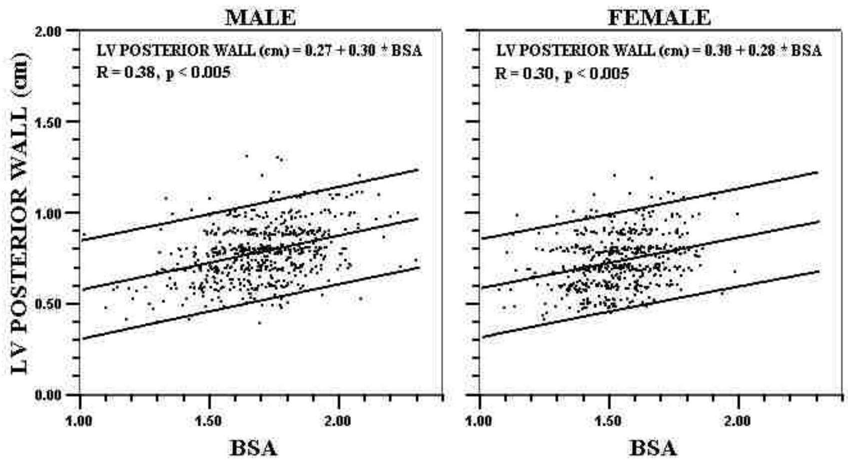
Table 4: Values of Y-intercepts, Slopes and R values from Regression Analysis

	Men				Women			
	y-intercept	Slope	R value	p value	y-intercept	Slope	R value	p value
Aortic root diameter	2.07	0.71	0.32	< 0.005	2.25	0.46	0.21	< 0.005
LA diameter	1.74	1.03	0.39	< 0.005	1.34	1.27	0.41	< 0.005
LVID	3.55	0.65	0.26	< 0.005	2.91	0.96	0.32	< 0.005
SWT	0.36	0.29	0.33	< 0.005	0.39	0.27	0.27	< 0.005
PWT	0.27	0.30	0.38	< 0.005	0.30	0.28	0.30	< 0.005

Figure 1: Normograms with mean and 95% prediction intervals and regressions equations for aortic root diameters, left atrial diameters, left ventricular internal diastolic dimension, interventricular septum thicknesses and left ventricular posterior wall thicknesses




MALE
FEMALE
LV DIASTOLIC DIMENSION (cm) = 3.55 + 0.65 * BSA
R = 0.26, p < 0.005
LV DIASTOLIC DIMENSION (cm) = 2.91 + 0.96 * BSA
R = 0.32, p < 0.005
LV DIASTOLIC DIMENSION (cm)
BSA
MALE
FEMALE
INTERVENTRICULAR SEPTUM (cm) = 0.36 + 0.29 * BSA
R = 0.33, p < 0.005
INTERVENTRICULAR SEPTUM (cm) = 0.39 + 0.27 * BSA
R = 0.27, p < 0.005
INTERVENTRICULAR SEPTUM (cm)
BSA
MALE
FEMALE
LEFT ATRIUM (cm) = 1.74 + 1.03 * BSA
R = 0.39, p < 0.005
LEFT ATRIUM (cm) = 1.34 + 1.27 * BSA
R = 0.41, p < 0.005
LEFT ATRIUM (cm)
BSA



DISCUSSION

We derived gender specific reference intervals in healthy adult subjects for LA, aortic root, and LV linear measurements that can be used in South-Asian epidemiological studies and clinical practice. The physical characteristics of the subjects in current study (Table-1) differ from those reported in healthy sample of men and women from Framingham Heart Study.[6] The later study incorporated predominantly white subjects mainly of European ancestry. The anthropometric measures and indexed limits for cardiac chamber sizes are thus not applicable on non-white subjects.

The choice of statistical techniques for determining the threshold values is an ongoing debate. Most of the existing normative data is based on SD values and thus carries the advantage of universality but it however, has the disadvantage that not all echocardiographic parameters follow a Gaussian pattern of distribution. Percentile based reference limits carry the advantage of accounting for the asymmetric distribution of echocardiographic parameters.[2] Lack of large enough normative data for most cardiac dimensions limits the use of percentile values for defining the reference limits. We were able to collect good enough data for all the studied parameters and described our cutoffs as percentiles.

There is conflicting evidence regarding the most appropriate body size parameter for scaling of cardiovascular variable. Despite the popularity of scaling cardiac dimensions to BSA and height, the most appropriate indicator of body size is yet to be defined and remains controversial.[7-9] Height has been suggested to be superior to BSA for normalization as it is not altered by large volumes of adipose tissue or extravascular fluid and body size has been shown to interact significantly with cardiovascular variables that were scaled to height.[7,10] Anthropomorphic variables like BSA and total body mass quantify the tissues with greater metabolic potentials as well as those with relatively little metabolic potential. Theoretically, scaling of cardiovascular parameters to tissue mass with high metabolic potential (i.e., FFM or lean body mass) seems more appropriate than to scale with whole body mass. Independent effect of waist circumference and BMI on cardiac chamber sizes (p values of 0.05 and 0.001 respectively) were shown in a recent study by Mehta et al.[11] Despite the wide range of normative data available for children, the controversy persists regarding the choice of most appropriate scaling parameter in this age group as well. Nagasawa advocated body height as the best scaling tool in a recent study measuring LV diastolic dimensions in Japanese children and neonates by comparing his regressions equations with those based on BSA and body weight from earlier studies[12] In an earlier study, Devereux et al investigated the association LV dimensions with body size and lean body mass.[13] The dimensions were found to correlate with variables of body size as well as lean body mass. In addition, consideration of lean body mass eliminated the gender differences in LV mass measurements.[13] Recommendations from ASE define cutoffs indices based on BSA and body height; however, BSA remains as the commonly utilized one in adult practice. The comparison for regression equations derived from the two parameters needs further research.

Another issue in defining the reference intervals for indexed parameters is regarding the method of scaling. Most scaling approaches exclusively use simple ratiometric relationships where the cardiac parameter is simply divided by a measure of body size. Such approaches assume a straight forward linear relationship between the cardiac parameter and the body size variable which does not always hold true.[14] Chamber dimensions indexed by this method have been shown to retain their correlations with body size.[14,15] Such observations form the basis for adopting allometric scaling techniques where the cardiac parameter is divided by a body size variable raised to a scalar power. In fact, allometric scaling techniques have been shown eliminate the effect of body size on cardiac dimensions and echocardiographic dimensions have been allometric modeled in a number of cross-sectional studies.[14,16-20] Neilan et all proved allometric scaling a better practice than simple linear isometric scaling using LA diameter as an example. Normalization by the optimal allometric exponent (BW = 0.262; HT = 0.428; BSA = 0.449; body mass index = 0.266) eliminated the association of the indexed variable with body size.[15]

Cardiac dimensions in males are considered to be larger than in females even after scaling for body size. Studies have shown to eliminate the gender differences when cardiac dimensions were scaled allometrically.[21] Statistically significant gender differences in anthropometric measures were observed in our study (Table 1). Cardiac chamber dimensions were generally larger in males, but the gender differences nearly abolished after scaling for BSA and height using the ratiometric scaling model; however, small gender differences for LV mass were seen to persist even after scaling.

CONCLUSION

The practice of utilizing normograms in adult echocardiographic examinations is poorly applied and the scientific data for predictive equations in adults is scarce. Large enough studies on ethnically diverse populations, using allometric scaling to FFM and redefining the cutoffs call for future research.

ACKNOWLEDGMENT

We are grateful to Mr. Faisal Nisar, the data entry operator for this study for his hard work and dedication towards this study.

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