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EXAMINING ECHOCARDIOGRAPHIC PERCENTILE VALUES AND CURVES: A COMPARATIVE ANALYSIS BETWEEN LMS AND QR TECHNIQUES IN FEMALE RESIDENTS OF MULTAN, PAKISTAN

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Abstract

There is scanty literature on percentile curves for echocardiographic measures in Pakistan particularly for women. This study adds to the existing literature by examining echocardiographic percentile values and curves corresponding to body surface area through LMS and QR techniques in female residents of Multan, Pakistan. To achieve this goal, a survey was conducted through a questionnaire among 685 female patients at the Chaudhry Pervaiz Elahi (CPE) Institute of Cardiology Multan to get the data. We have applied Lambda-Mu-Sigma (LMS) and Quantile Regression (QR) methods to compute percentile values of echocardiographic measures. The study suggests that when estimating certain measurements, like AR (mm), the LMS method might give more varied results than quantile regression, especially for people with larger body sizes. The trends for LA (mm) measurements at the 50th percentile are different. EF (mm) measurements are mostly alike though there are some exceptions. LVIDD measurements do not vary much with LMS, but these are more consistent with quantile regression. With LVIDS, quantile regression tends to give slightly higher results as compared to LMS for most body sizes. LMS provides more detailed information for LVISD (mm) while quantile regression offers a broader view. Lastly, LVPWD (mm) percentiles between LMS and quantile regression for each body size are similar.

Keywords: Quantile Regression, Lambda-Mu-Sigma Method, Percentile Curves, Female Patients.

1. INTRODUCTION

Echocardiography is a pain-free diagnostic tool that gives the images of heart as well as its adjacent structures. It is used extensively for assessing cardiovascular diseases including ischemic heart disease, valvular heart disease, and heart failure (Yao et al. 2022; Lang & Badano, 2011). It is also considered a useful instrument for the providers of healthcare in the management and diagnosis of different conditions related to cardiac situations. However, the understanding of the measurement of echocardiography is rigorous, and needs to understand the values of normal reference (Liu et al.2022; Devereux & Reichek, 1977).

The values of reference as well as the percentile curves are fundamental components for the echocardiographic interpretation and need a starting point for the echocardiographic results of patients. The percentile curves and the reference values are naturally derived from the studies of population-based and are usually utilized to evaluate the normal range of the measurement of echography for a given population. The utilization of the graph curves and the reference values help the providers of healthcare to recognize patients who possess abnormal measurements of echography, that may show the existence of the cardiovascular disease (Zhou et al., 2022; Lang & Badano, 2011).

In current years, there has been a rising interest in the advancement of percentile curves and reference values for the measurement of echocardiographics (Bonatto et al, 2006; Lang & Badano, 2011). Many studies have been done to create the percentile curves and reference values for the measurement of echocardiography by using various methods of statistics i.e. quantile regression (QR) and Lambda-Mu-Sigma (LMS) method. The method of LMS has generally been used method for deriving the percentile curves and reference values, but the QR is a recent method that is used in current years to evaluate the data of echocardiography. Both methods have their strengths and limitations, and the choice of method depends on the specific research question and the type of data being analyzed (Wang et al., 2018).

Despite the availability of reference values and percentile curves for echocardiographic measurements in many countries, there is a lack of data for the population in the province of Punjab, Pakistan. This is a significant gap in the literature, as reference values and percentile curves specific to the population in Punjab would provide valuable information for healthcare providers in the diagnosis and management of various cardiac conditions. This study aims to fill this gap by establishing percentile curves of some echocardiographic measures using different statistical methods for the population in the province of Punjab, Pakistan.

This study is the first of its kind to develop percentile charts for echocardiographic measures, filling a significant gap in the existing literature. Moreover, no such study has been conducted in Multan, Pakistan, making the findings particularly valuable for the local population and healthcare providers. The data collection process was thorough, and several echocardiographic measures were assessed providing a comprehensive understanding of cardiovascular health in the study population. By utilizing both the Lambda-Mu-Sigma (LMS) method and Quantile Regression (QR) to compare different percentiles of echocardiographic measures, the study provides a robust analysis and allows for a more accurate assessment of the results. This dual-method approach enhances the validity of the study and offers valuable data on the evolution of percentile curves for echocardiographic measures. This paper aims to describe the development of echocardiographic percentile reference values and percentile curves of women along with body surface area (BSA) using quantile regression and LMS methods.

2. MATERIALS AND METHODS

2.1 Lambda-Mu-Sigma (LMS) Method

Numerous percentile charts and numerous data kinds that fluctuate with BSA have been smoothed using the LMS technique. After the 1977 NCHS percentile charts were released, Cole (1990) developed the LMS method, a complete smoothing approach for percentile curves that made it possible to construct smoothed curves and quickly determine z scores. Based on the selection of a skewness parameter and Box-Cox transformations to normalcy, the LMS technique is used. The generalized coefficient of variation (S), the median (M), and the power of the Box-Cox transformation (L) are the LMS parameters. With these parameters and the assumption that the residuals follow a normal distribution, any desired percentile can be calculated.

The following LMS values are calculated using the Cole's LMS technique (Cole, 1990):

This provides a detailed explanation of the steps involved in calculating L, M, and S for each age group, along with formulas for standard errors.

1. Determine the average & Standard Deviation (SD) of the measurements' natural logarithms. The geometric mean of the quantity known as Mg is this antilog of the mean. Similar to how the SD is referred to, the Sg is the "geometric" CV.
2. Find the mean and standard deviation of the initial measurements. This is the measurement's AM. The 'arithmetic' CV, Sa, is obtained by dividing the SD by the geometric mean, Mg.
3. Calculate the measurements' reciprocals' mean and standard deviation. The harmonic mean Mh of the measurement is the mean's reciprocal. To obtain the 'harmonic' CV, Sh, multiply the SD by the geometric mean, Mg.
4. Sa, Sg, and Sh values ought to be quite close. Put them in the equations now as follows:

$A = \ln (S_a / S_h)$ **(1)**

$B = \ln (S_a S_h / S_g{}^2)$

Where A and B ought to be tiny. The Box-Cox power L estimate is then provided by

$L = -A / (2B)$ **(2)**

and its SE is

$$\frac{1}{\sqrt{(nB)}} \quad \textbf{(3)}$$

Where n denotes how many measurements were taken for the age group.

5. Next, at this value of L, calculate the generalized coefficient of variation S.,

$S = S_g \exp (AL/4)$ **(4)**

In order to get the least value, this interpolates between the three CVs, making S somewhat smaller than Sa, Sg, and Sh. Then, the approximation of S's standard error is

$$S\sqrt{(\left[S^2+0.5\right]/n)}$$

6. Finally, by interpolating between the generalized mean M and the power L, S_a, S_g and S_h to give

$M = M_g + (M_a - M_h)L / 2 + (M_a – 2M_g + M_h)L^2 /2$, **(5)** With standard error is:

$$\frac{MS}{\sqrt{n}}$$

Keep in mind that the standard errors of L, M, and S are all inversely correlated with n's square root. The desired percentiles are then built using these factors. The formulas below can be used to determine the value of X at the desired percentile, where X stands for the value of the echocardiographic variable and Z stands for the desired percentile in SD units.:

$$X = M(1 + LSZ)^{1/L} \quad ; \qquad L \neq 0 \qquad \textbf{(6)}$$

Or

$$X = M\exp(ZS)^{1/L} \quad ; \qquad L = 0 \qquad \textbf{(7)}$$

On the other hand, the following formula can be used to get the corresponding z score (Z) for any value of X:

$$Z = \frac{\left[\left(X/M\right)^{L-1}\right]}{LS} \quad ; \qquad L \neq 0 \qquad \textbf{(8)}$$

Or

$$Z = \frac{\log\left(X/M\right)}{S} \qquad L = 0 \qquad \textbf{(9)}$$

The primary presumption underpinning the LMS approach is that the data at each age are normally distributed after the Box-Cox power transformation.

Cole (1990) has presented a seminal study on the LMS method. This method is established on three aspects i) Lambda (L) ii) Mu (M) and iii) Sigma (S). The quantity of lambda (L) is based on the Box-Cox power transformation while Mu is the Median and Sigma is the generalized coefficient of variation. We have performed the cubic spline functions' polynomial regressions after computing the parameters for L, M, and S (Kato et al., 2011) for smoothing the values of L, M, and S as:

$$EM(L, M, S) = \phi_0 + \phi_1 BSA + \phi_2 BSA^2 + \phi_3 BSA^3 + \varepsilon \qquad \textbf{(10)}$$

EM shows echocardiographic factors i.e., Aortic Root (AR), Left Atrium (LA), Ejection fraction (EF), Left ventricular dimension in end-diastole (LVIDD), Left ventricular internal dimension in end-systole, Left ventricular internal septum in end-systole (LVISD), Left ventricular posterior wall dimension in end-diastole (LVPWD).

The estimated values of L, M, and S have been found from these regressions. Afterward, we computed percentile values against BSA using the equation:

$$C = M(1+LSZ)^{1/L} \ \ where\ L \neq 0 \qquad \textbf{(11)}$$

Where Z denotes the normal distribution of Z-Score or standard deviation scores (SDS) because it has zero mean and unit standard deviation.

Cole (1990) gives SD Scores for given centile values. We may compute the percentile values using equation (12) for example, in the case of the 3rd percentile and the BSA range is 1.60-1.70, if L=1.45, M=32.47, S=0.057 and Z= -1.881

$$C_3 = 32.47[1+(1.45)(0.057)(-1.881)]^{1/1.45} = 28.90 \qquad \textbf{(12)}$$

2.2 Quantile Regression Method

The quantile regression Koenker and Bassett (1978) is a tool to give quantiles of a dependent variable, depending on different covariates, without any distributional assumptions. The general functional form of echocardiographic measures can be explained below:

$$Y \Box g(X)+\varepsilon \qquad \textbf{(13)}$$

Where *Y* represents the response to echocardiographic measures, *X* represents the regressor and *ε* represents the usual random error. While regression models (using the conventional least square method) minimize the sum of the squared residuals, quantile regression minimizes the weighted sum of the absolute deviations of the error term.

Following Koenker and Bassett (1978), a model for QR is;

$$Q^{(\tau)}(y \mid X = x) = \delta_0^{(\tau)} + \sum_{j=1}^{k} \delta_j^{(\tau)} x_j = \delta^{(\tau)} X \qquad \textbf{(14)}$$

Where $\delta^{(\tau)}$ is the vector of coefficient for specific τ^{th} quantile for τ = 0.01, …,0.99.

When $\tau = 0.5$ it is considered a special case of quantile regression i.e. the median regression. The median regression line crosses through the pair (Y_i, X_i) while dividing half of data falling the above and the rest half falling below this line. Chen (2022), the median regression of echo measures was estimated for different BSA. For the usual linear regression, the following polynomial regression model is used for the echocardiographic measurements:

$$E(Y) = \beta_0 + \beta_1 BSA + \beta_2 BSA^2 + \beta_3 BSA^3 \qquad \textbf{(15)}$$

The original estimates are then derived by using

$$e^{\hat{y}} = \exp(\beta_0 + \beta_1 BSA + \beta_2 BSA^2 + \beta_3 BSA^3) \qquad \textbf{(16)}$$

For the establishment of echocardiographic percentile curves using quantile regression, we may take the natural logarithm of each echocardiographic measurement by in equation (14) i.e. *Y* = *ln* (echocardiographic measurement) as a dependent variable and it will be established to take three powers of BSA, *BSA*, BSA^2 (*BSA*.*BSA*) and BSA^3

(*BSA*.*BSA*.*BSA*) as covariates for the quantile regression. See Pettersen et al. (2008) for more details.

$$Q_{EM_i}(\tau \,|\, \phi, \delta, BSA) = \phi_i + \delta_i + \beta_1^{\tau} BSA + \beta_2^{\tau} BSA^2 + \beta_3^{\tau} BSA^3 + \varepsilon_{\tau} \qquad \textbf{(17)}$$

For the computation of the 3rd, 5th, 10th, 25th, 50th, 75th, 90th, 95th, and 97th percentiles of any specific echocardiographic measurement using the quantile regression, we choose = 0.03, 0.05, 0.10, 0.25, 0.50, 0.75, 0.90, 0.95, and 0.97.

3. RESULTS AND DISCUSSIONS

In this section, we compare the LMS and QR-based echocardiographic percentile values and curves for female patients of Multan. Based on Table 1 and Figure 1, we can compare the 50th LMS percentile of AR (mm) versus the 50th QR percentile of AR (mm) for body surface area for female adults. For female adults with a BSA of 1.14, the 50th LMS percentile of AR (mm) is 29.12, and the 50th QR percentile of AR (mm) is 30.21. As we move down the table, we can observe that the values of the 50th LMS percentile of AR (mm) increase steadily from 29.12 to 32.49, while the values of the 50th QR percentile of AR (mm) remain relatively stable, ranging from 29.71 to 32.25. This suggests that the LMS method may provide more variation in the estimates of AR (mm) than the quantile regression method, especially at higher levels of BSA.

Table 1: Comparison of LMS and QR-based 50th Percentiles of AR versus Body Surface Area for Female Adults (aged 14 years or more)

BSA	P50	
	LMS	QR
1.14	29.12	30.21
1.24	29.14	29.77
1.34	29.40	29.71
1.44	29.84	29.94
1.54	30.38	30.37
1.64	30.98	30.90
1.74	31.56	31.44
1.84	32.06	31.91
1.94	32.43	32.21
2.04	32.59	32.25
2.14	32.49	31.95

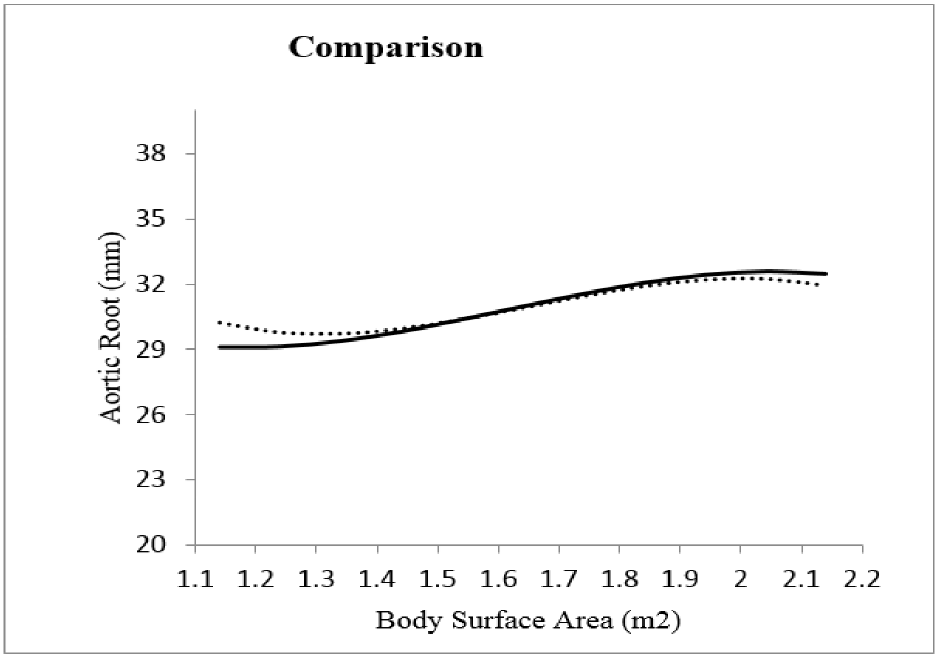

Figure 1: Comparison of LMS and QR-based 50th Percentiles of AR Versus Body Surface Area for Female Adults (aged 14 years or more)

Based on Table 2 and Figure 2 the 50th LMS percentiles of LA (mm) and the 50th QR percentiles of LA (mm) for body surface area for female adults show slightly different trends. The 50th LMS percentiles of LA (mm) generally decrease as body surface area increases until 1.64 BSA, where it begins to level off and then slightly increase at 1.94 BSA. On the other hand, the 50th QR percentiles of LA (mm) increase continuously as body surface area increases, with a steeper slope at 1.74 BSA and above. Therefore, the two percentiles present different trends, and their comparison cannot be conclusive.

Table 2: Comparison of LMS and QR-based 50th Percentiles of LA Versus Body Surface Area for Female Adults (aged 14 years or more)

BSA	P50	
	LMS	QR
1.14	31.25	30.60
1.24	33.82	34.11
1.34	34.98	35.61
1.44	35.13	35.69
1.54	34.68	34.91
1.64	34.05	33.85
1.74	33.65	33.07
1.84	33.89	33.17
1.94	35.18	34.70
2.04	37.93	38.25
2.14	42.56	44.38

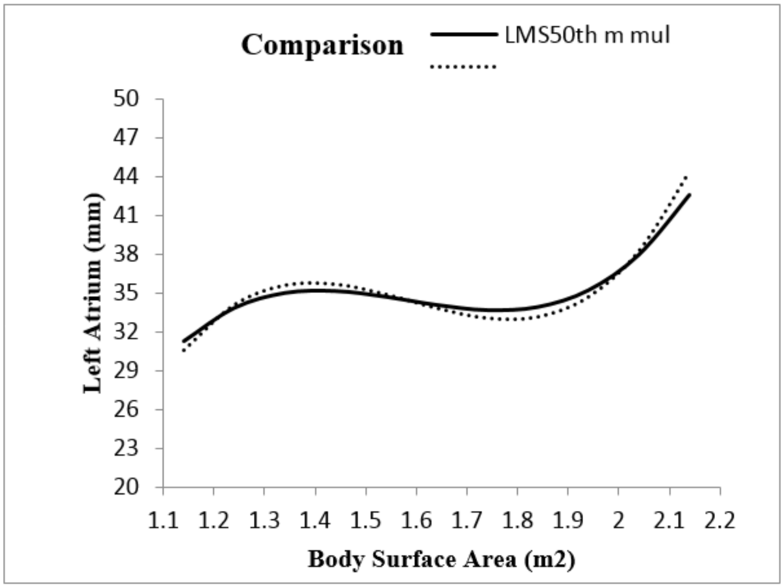

Figure 2: Comparison of LMS and QR-based 50th Percentiles of LA versus Body Surface Area for Female Adults (aged 14 years or more)

In Table 3 and Figure 3, the 50th LMS percentile of EF (mm) represents the median value of the EF distribution for female adults with a particular body surface area, whereas the 50th QR percentile of EF (mm) represents the median value of the EF distribution for the same group of female adults based on the quartile range. Comparing the two percentiles for EF (mm) reveals that, for the most part, the values are quite close, with only small differences between them. However, there are some notable discrepancies in the data. For example, at a BSA of 1.14, the 50th LMS percentile of EF is 51.50 mm, while the 50th QR percentile is 48.18 mm. Similarly, at a BSA of 1.94, the 50th LMS percentile of EF is 60.53 mm, while the 50th QR percentile is 60.24 mm. It appears that the 50th LMS percentile and the 50th QR percentile of EF (mm) for female adults are generally similar, with a few exceptions where the values diverge.

Table 3: Comparison of LMS and QR-based 50th Percentiles of EF Versus Body Surface Area for Female Adults (aged 14 years or more)

BSA	**P50**	
	LMS	**QR**
1.14	51.50	48.18
1.24	52.59	51.13
1.34	53.91	53.65
1.44	55.33	55.76
1.54	56.77	57.46
1.64	58.11	58.75
1.74	59.25	59.64
1.84	60.09	60.13
1.94	60.53	60.24
2.04	60.45	59.98
2.14	59.76	59.33

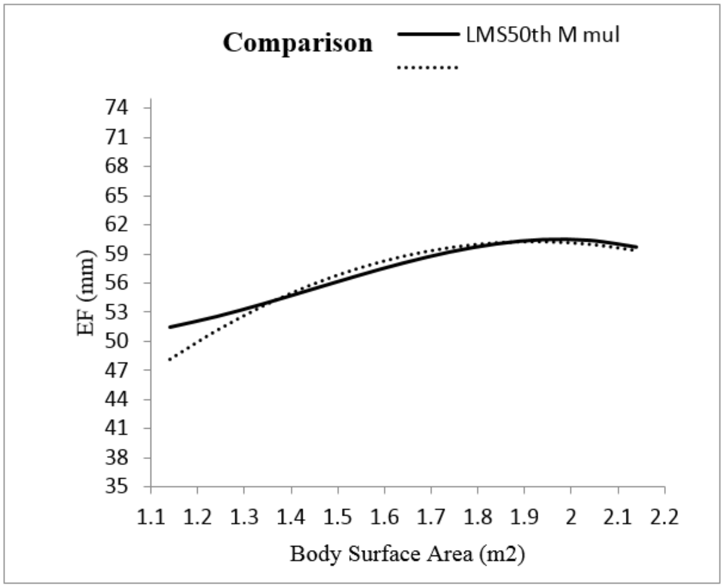

Figure 3: Comparison of LMS and QR-based 50th Percentiles of EF Versus Body Surface Area for Female Adults (aged 14 years or more)

Table 4 and Figure 4 compare the 50th percentile values of LMS and QR for left ventricular internal diastolic dimension (LVIDD) in millimeters, about body surface area (BSA) for female adults. The LMS percentiles of LVIDD increase gradually from 37.35 mm to 52.43 mm as the BSA increases from 1.14 to 2.14. On the other hand, the QR percentiles of LVIDD show a more consistent increase from 38.10 mm to 53.20 mm across the range of BSA. While there is some variability in the LMS percentiles, the QR percentiles appear to be more stable across the BSA range. The QR percentiles provide a more consistent representation of the relationship between LVIDD and BSA for female adults than the LMS percentiles.

Table 4: Comparison of LMS and QR-based 50th Percentiles of LVIDD versus Body Surface Area for Female Adults (aged 14 years or more)

BSA	P50	
	LMS	QR
1.14	37.35	38.10
1.24	40.41	40.50
1.34	41.97	41.68
1.44	42.48	42.04
1.54	42.36	41.95
1.64	42.03	41.78
1.74	41.94	41.93
1.84	42.50	42.77
1.94	44.15	44.67
2.04	47.32	48.02
2.14	52.43	53.20

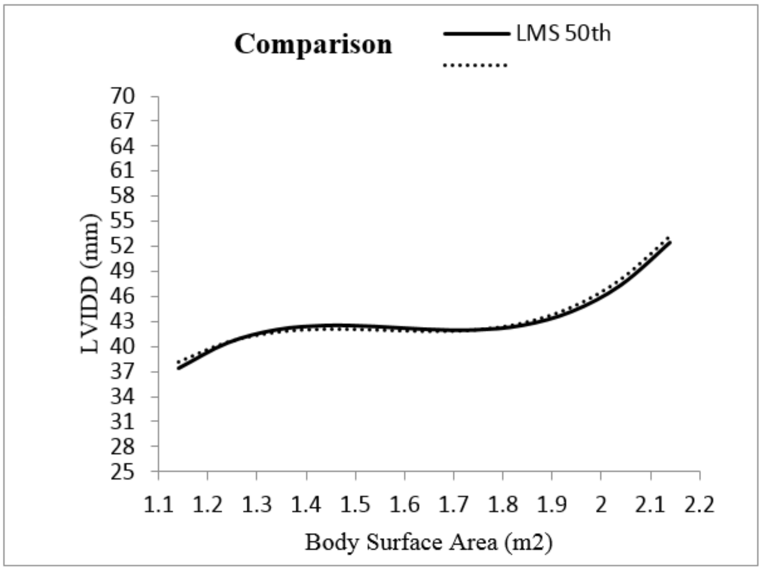

Figure 4: Comparison of LMS and QR-based 50th Percentiles of LVIDD Versus Body Surface Area for Female Adults (aged 14 years or more)

Table 5 and Figure 5 shows the 50th LMS percentiles and 50th QR percentiles of left ventricular internal diameter at end-systole (LVIDS) in millimeters for female adults of varying body surface areas (BSA). Comparing the 50th LMS percentiles to the 50th QR percentiles for LVIDS, it can be observed that the values generally increase with increasing BSA for both methods. However, the 50th QR percentiles tend to be slightly higher than the 50th LMS percentiles for most BSAs, indicating that the quantile regression method yields slightly higher median values for LVIDS compared to the LMS method. This difference is most noticeable for the higher BSAs, where the 50th QR percentiles are consistently higher than the 50th LMS percentiles by around 0.5 to 1 millimeter.

Table 5: Comparison of LMS and QR-based 50th Percentiles of LVIDS Versus Body Surface Area for Female Adults (aged 14 years or more)

BSA	P50	
	LMS	QR
1.14	28.80	30.12
1.24	29.10	29.72
1.34	29.24	29.38
1.44	29.26	29.12
1.54	29.25	28.97
1.64	29.26	28.97
1.74	29.36	29.15
1.84	29.62	29.53
1.94	30.11	30.16
2.04	30.88	31.07
2.14	32.00	32.28

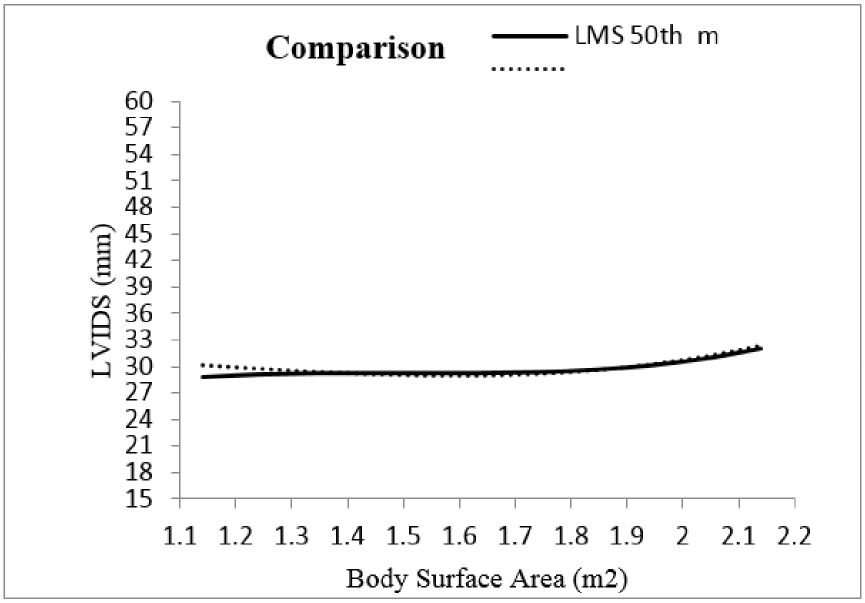

Figure 5: Comparison of LMS and QR-based 50th Percentiles of LVIDS Versus Body Surface Area for Female Adults (aged 14 years or more)

Based on Table 6 and Figure 6, it can be observed that the 50th LMS percentiles of LVISD (mm) for BSA of female adults range from 9.72 mm to 10.34 mm, whereas the 50th QR percentiles of LVISD (mm) for BSA of female adults are consistently at 10.00 mm for all BSA values. This indicates that the 50th LMS percentiles of LVISD (mm) vary slightly for different BSA values, while the 50th QR percentiles of LVISD (mm) remain constant for all BSA values. Therefore, it can be concluded that the 50th LMS percentiles provide more detailed information about the variation in LVISD (mm) for different BSA values, while the 50th QR percentiles provide a more generalized view of the distribution of LVISD (mm) across all BSA values for female adults.

Table 6: Comparison of LMS and QR-based 50th Percentiles of LVISD versus Body Surface Area for Female Adults (aged 14 years or more)

BSA	**P50**	
	LMS	**QR**
1.14	9.72	10.00
1.24	9.72	10.00
1.34	9.81	10.00
1.44	9.97	10.00
1.54	10.14	10.00
1.64	10.28	10.00
1.74	10.36	10.00
1.84	10.34	10.00
1.94	10.17	10.00
2.04	9.81	10.00
2.14	9.22	10.00

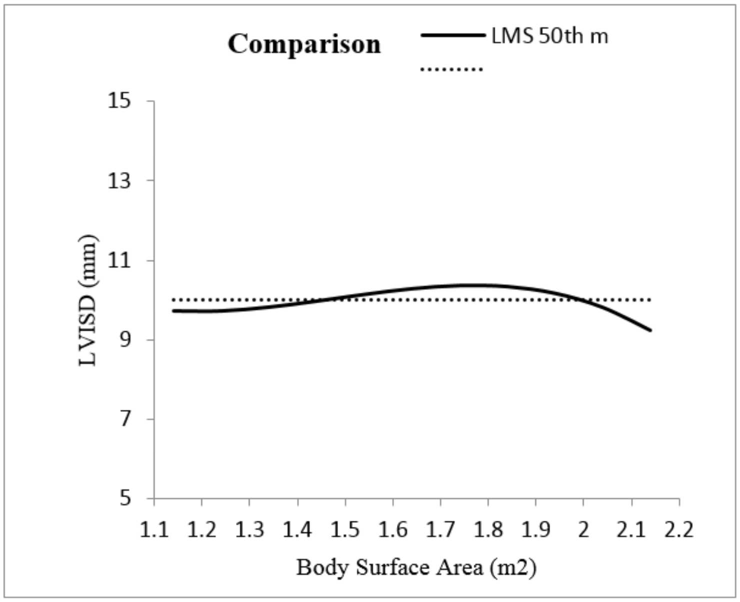

Figure 6: Comparison of LMS and QR-based 50th Percentiles of LVISD Versus Body Surface Area for Female Adults (aged 14 years or more)

Table 7 and Figure 7 present the 50th LMS percentiles and the 50th QR percentiles of LVPWD (mm) for female adults of different body surface areas (BSA). The 50th LMS percentile is a measure of central tendency that combines information about the median, skewness, and variability of the data, while the 50th QR percentile is a measure of the median that is resistant to outliers. Comparing the 50th LMS percentiles to the 50th QR percentiles of LVPWD (mm) for each BSA shows that the values are generally similar, but there are some differences. For BSA values of 1.14 to 1.64, the 50th LMS percentiles are higher than the 50th QR percentiles, while for BSA values of 1.74 to 2.14, the 50th QR percentiles are slightly higher or equal to the 50th LMS percentiles.

Table 7: Comparison of LMS and QR-based 50th Percentiles of LVPWD Versus Body Surface Area for Female Adults (aged 14 years or more)

BSA	P50	
	LMS	QR
1.14	8.87	8.65
1.24	8.98	9.14
1.34	9.16	9.50
1.44	9.38	9.74
1.54	9.60	9.90
1.64	9.80	9.98
1.74	9.95	10.01
1.84	10.01	10.01
1.94	9.96	9.99
2.04	9.76	9.99
2.14	9.39	10.01

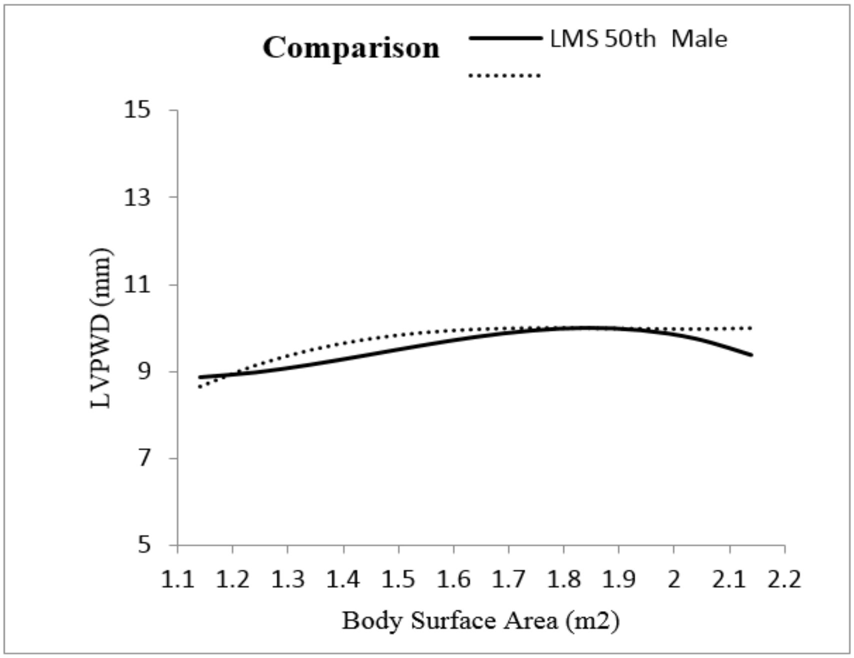

Figure 7: Comparison of LMS and QR-based 50th Percentiles of LVPWD Versus Body Surface Area for Female Adults (aged 14 years or more)

4. CONCLUSION

The main objective of this study is to estimate various percentile values of different echocardiographic measures against a given BSA, establish median percentile curves of echocardiographic measures against BSA for females, compare the echocardiographic measures for females, and make comparisons of different percentiles of echocardiographic measures derived by LMS and QR methods. We have collected data from a public cardiac institution, Chaudhry Pervaiz Elahi (CPE) Institute of Cardiology, Multan. We have compared the 50th LMS percentile versus the 50th QR percentile.

The study suggests that the LMS method may provide more variation in the estimates of AR (mm) than the quantile regression method, especially at higher levels of BSA. The two percentiles for LA (mm) present different trends, and their comparison cannot be conclusive. EF (mm) for female adults are generally similar, with a few exceptions where the values diverge. For LVIDD, there is a little variability in the LMS percentiles, the QR percentiles appear to be more stable. In the case of LVIDS, QR percentiles tend to be slightly higher than LMS percentiles for most BSAs. For LVISD (mm), LMS percentiles provide more detailed information, while QR percentiles provide a more generalized view of the distribution of LVISD. Finally, LMS percentiles to the QR percentiles of LVPWD (mm) for each BSA show that the values are generally similar.

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