

Determining the normal effective diameter of thoracic aorta in pediatric population of India

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Abstract

Background: It is imperative to establish normative ranges of aortic diameter to diagnose various aortic pathologies. There have been very few studies establishing the normal aortic diameter on cross-sectional imaging, and none pertaining to the Indian pediatric population. The objective of this study was, therefore, to establish the normal effective diameter of thoracic aorta at multiple levels using computed tomographic data, calculate z-scores, and plot reference curves. **Subjects and Methods:** The effective thoracic aorta diameters (average of anteroposterior and lateral diameters) were measured at predefined levels (aortic root, ascending aorta at the level of right pulmonary artery, aortic arch, proximal descending aorta, and aorta at the level of diaphragmatic hiatus) on double-oblique reconstructed computed tomography (CT) images perpendicular to the direction of the vessel. Multiple functional forms relating the effective diameter to subjects' age were evaluated with least square regression methods, and further R^2 was used to ascertain the best model. Age-based formulas to derive normal aorta diameters and mean squared errors (MSEs) were established. **Results:** Two hundred and seven contrast-enhanced CT (CECT) thorax studies of children without known cardiovascular disease were studied. The polynomial regression model relating the effective diameter that included linear, quadratic, and cubic age terms as independent variables were found to be the best statistical model. The z scores were calculated, and normative curves were plotted. **Conclusions:** We have established normative effective diameters of the thoracic aorta at multiple levels in Indian children of different age groups. Measurements outside of the normal ranges are indicators of ectasia, aneurysm, hypoplasia, or stenosis.

Key words: Effective aortic diameter; Indian pediatric population; thoracic aorta

Introduction

The normal standards for the aortic diameter at various levels have been established for the adult population and can be used to determine aneurysm formations or stenosis.^[1] In contrast, similar standards for infants (1 month to 1 year old), children (1–12 years old), and adolescents (13–17 years old) are not as well established,^[2] and such standards pertaining to Indian pediatric population have not yet been published in the literature.

A prerequisite for identifying abnormal is to establish the normal. Effective aortic diameter assumes significance in early detection of diffuse aortic hypoplasia in conditions such as Williams syndrome or aneurysmal dilatation in children with connective tissue disorder.^[3] Anomalies of the aorta in pediatric age group include coarctation, residual findings after catheter-guided interventions or surgery,

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connective tissue diseases such as Marfan syndrome and dilatation of the aortic root associated with aortic valve anomalies, non-specific aorto-arteritis or post-surgical in patients with congenital heart diseases.^[4]

Though echocardiography is the standard method for determining the size of the thoracic aorta in children, a recent review of echocardiographic methods showed a general lack of standardization in technique.^[2] The evaluation of thoracic aorta on echocardiography relies on planar measurements rather than on transverse measurements. Cross-sectional imaging using computed tomography (CT) and magnetic resonance imaging (MRI) with multiplanar reconstructions does overcome these limitations.

Effective aortic diameter is average of the transverse and anteroposterior diameters of the aorta, this method of measurement nullifies errors due to obliquity and has been previously used for similar studies.^[2,5]

Subjects and Methods

This was a single institutional cross-sectional observation study. The study included children and young adults of age group 'zero' to eighteen years who underwent contrast-enhanced CT (CECT) thorax scans at our institute during the 13-month period between January 2016 and January 2017. Exclusion criteria included a) History of congenital heart disease/dysmorphisms. b) History of cardiovascular disease or cardiothoracic surgery. c) Patients who are being evaluated for cardiac diseases. In patients where multiple CT examinations were performed during the study period, only the first of such CT scans were included in the study. The study was approved by our Institutional Ethics Committee.

During the study period of 13 months, a total of 321 CT studies were evaluated, out of which 207 satisfied the above-described inclusion and exclusion criteria. Out of the excluded studies ($n = 114$), prior history of cardiovascular diseases or surgeries and subjects under evaluation for cardiac diseases ($n = 68$) formed the majority followed by repeat examinations in the study window ($n = 27$) and scans excessively degraded by motion artifacts ($n = 19$).

All the CT scans included in the study were performed on a 64-slice CT scanner (Philips Brilliance 64-slice CT, Koninklijke Philips N.V). Non-ionic iodinated contrast agent with an administration rate of 1-2.5 mL and a dose of 1-2 mL/kg [not exceeding 100 mL] along the peripheral venous route, followed by a saline chaser of 10-20 cc was used. CT data were obtained in keeping with the as low as reasonably achievable (ALARA) principle with a weight-based variable dose parameters (80-120 kVp, 20-150 mAs) with scans performed from thoracic inlet to the level L1-L2. Image data were analyzed on a workstation (Tera-recon AQI viewer) after

image reconstruction of 1-mm slice thickness. Multiplanar reformations (MPR) were created using a workstation. All MPR with double-oblique reconstructions were obtained perpendicular to the aorta [Figure 1].

The effective diameter at each level was determined by averaging the anteroposterior and lateral diameter measurements. Measurements were obtained by using an electronic cursor at the outer widest diameter of the vessels. The measurements were obtained at the following five predefined locations: Aortic root, ascending aorta at the level of the right pulmonary artery, aortic arch, proximal descending aorta (distal to the aortic arch where the descending aorta obtains a cranial-caudal orientation), and aorta at the level of diaphragmatic hiatus.

Statistics

The effective diameters at various levels were tabulated against the subject's age. Descriptive statistics were employed to calculate the mean, standard error (SE), and standard deviation (SD) of the aortic diameter at various levels for different age groups separately for both boys and girls.

Regression analysis was used to describe the relationship between the aortic diameter (dependent variable) and the subject's age (independent variable). Multiple regression models as described by previous studies^[2,5,6] were analyzed to determine the best fit model. Linear, logarithmic, exponential, and polynomial regression models with quadratic, cubic, and linear terms were evaluated using the R^2 value to determine the best fit functional form. The intercepts for linear, cubic, and quadratic terms were determined and were tested for significance. Scatter plots were used to determine the equation of independent variables at various levels. The best regression model was used to plot the trend line in the scatter plot. From the slope estimates of the best fit model, formulas were specified for the predicted diameters along with R^2 for each of them. The effect of gender on the aortic diameter was determined by comparing the means of the diameter in male and female subjects. From these regression formulas, estimated mean squared error (MSE) was calculated. Predicted estimates of the aortic diameter were then calculated using the regression models. The z scores were calculated and then used to plot charts that can be used to determine the normal aortic diameter within the confidence interval of 95% ($z = 2$).

These statistical analyses were performed on Excel (Microsoft) and Statistical Package for the Social Sciences (SPSS) (IBM) software.

Results

The age and sex distributions are summarized in Table 1. The youngest patient included in the study was a 10-day-old

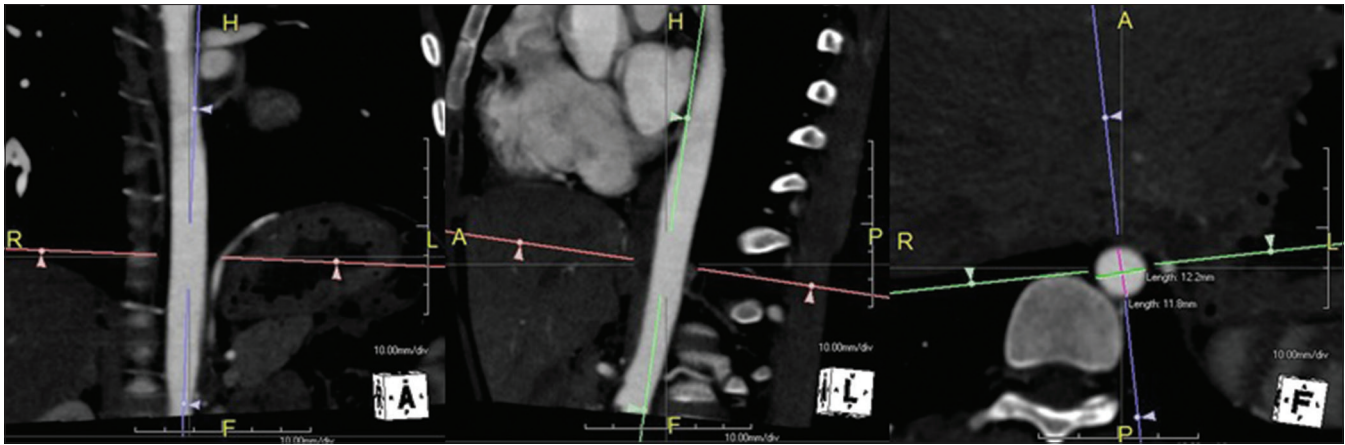


Figure 1: Coronal and sagittal oblique multiplanar reconstructions perpendicular to the aorta created to determine the cross section of the descending aorta

Table 1: Age and sex distribution of the subjects

Age group	Male	Female	Total
≤ 2 years	14	18	32
>2 years to ≤5 years	18	13	31
>5 years to ≤9 years	22	19	41
>9 years to ≤14 years	23	28	51
>14 years to ≤18 years	28	24	52
Total	105	102	207

infant, and the oldest patient was 18 years old. The median age of the study population was nine years.

The descriptive statistics data of the effective diameter of aorta and multiple locations has been summarized in Table 2, and further subgroup analyses have been made and specified. Table 3 summarizes the mean, SD, and the SE of the effective aortic diameter at different levels in gender subgroups.

On regression analysis, the best model was the polynomial regression model of an effective diameter that included linear, quadratic, and cubic terms as independent variables. An example of regression models employed for selection of the best fit model is provided in Table 4 along with respective R^2 scores.

For all levels, the intercept and linear, quadratic, and cubic terms were significant (all $P < 0.05$). The formulae for calculating the predicted diameters along with R^2 for the model used (polynomial regression model of order three) are tabulated in Table 5.

Predicted diameters were calculated for each level and age group using the polynomial regression models with cubic terms determined previously. MSE was also calculated for each of the models. z scores were then calculated using the following formula, $z = (\text{observed diameter} - \text{predicted diameter}) / \sqrt{\text{MSE}}$. The z scores

calculated are of approximate normal distribution, they have a mean of zero and SD of one. They represent how many SDs above or below the observation is in relation to the mean (predicted regression line). A z value of 1 signifies that the observed value is 1 SD above the estimated mean of that level at that age-group, whereas a z of -1 signifies that the value is 1 SD below the mean. Assuming a normal distribution, approximately 68.3% of the population will fall within the mean ± 1 SD interval. Whereas 95.4% of the population is within the mean ± 2 SDs.

This data has been plotted in the form of graphs [Figures 2-6] that do not require any complex calculations to determine the normal. These graphs contain the mean for age group and ± 2 z score barricade lines.

Discussion

It is imperative to acquire a complete and thorough knowledge of normality and its variants to study and diagnose abnormalities and pathologies with certainty. Although the normal standards for the diameter of thoracic aorta have been established for adults, such standards are not well established in pediatric population. Though echocardiography is the standard method for determining the size of the thoracic aorta in children. A recent review of echocardiographic methods showed a general lack of standardization in technique.^[1]

Table 2: Summary of descriptive statistics

Effective diameter	Group	Mean	Standard Deviation (SD)	Standard error of Mean (SEM)	P
Aortic Root	0-2	12.09	2.45	0.45	<0.01
	3-5	18.02	1.28	0.23	
	6-9	21.32	1.74	0.27	
	10-14	24.58	1.90	0.27	
	15-18	27.27	1.37	0.19	
Ascending Aorta	0-2	9.82	1.90	0.35	<0.01
	3-5	15.06	1.46	0.27	
	6-9	17.69	1.78	0.28	
	10-14	21.00	1.84	0.26	
	15-18	23.68	1.38	0.19	
Arch of aorta	0-2	8.97	1.83	0.33	<0.01
	3-5	12.70	1.65	0.30	
	6-9	15.22	1.53	0.24	
	10-14	18.28	1.91	0.27	
	15-18	20.13	1.38	0.20	
Proximal descending Aorta	0-2	7.08	1.18	0.22	<0.01
	3-5	10.18	1.08	0.20	
	6-9	11.95	1.28	0.20	
	10-14	14.37	1.54	0.22	
	15-18	16.41	1.32	0.19	
Diaphragmatic hiatus	0-2	6.71	1.15	0.21	<0.01
	3-5	9.64	1.03	0.19	
	6-9	11.53	1.25	0.20	
	10-14	13.96	1.51	0.21	
	15-18	15.92	1.30	0.18	

Table 3: Summary of the mean, standard deviation, and the standard error of mean of the effective aortic diameter in gender subgroups

Effective diameter at	Group	Mean	Standard Deviation	Standard Error of Mean
Aortic Root	Female	21.72	5.41	0.54
	Male	21.76	5.38	0.54
Ascending Aorta	Female	18.39	4.86	0.49
	Male	18.49	5.03	0.50
Arch of aorta	Female	15.86	4.15	0.42
	Male	15.93	4.24	0.42
Proximal descending Aorta	Female	12.56	3.38	0.34
	Male	12.79	3.47	0.35
Diaphragmatic hiatus	Female	12.14	3.33	0.33
	Male	12.31	3.48	0.35

Cross-sectional imaging (CT & MRI) standards of the normal aortic diameter in children are not established. Our study aims to establish the normal aortic diameter at various levels of the thoracic aorta on CECT thorax studies. We analyzed CECT studies in 207 children who had no history of cardiovascular disease or cardiothoracic surgery. Effective diameters of the thoracic aorta were measured by double-oblique reconstructions perpendicular to the aorta. Measurements were acquired at the aortic root, ascending

aorta, arch of the aorta, proximal descending aorta, and the descending aorta at diaphragmatic hiatus. The effective diameter is the average of anteroposterior and transverse measurements.

The youngest subject of our study was a 10-day-old infant and the eldest was 18 years of age. Regression analyses of the data were done, multiple regression models like linear, logarithmic, exponential, polynomial with quadratic, and cubic terms were analyzed and the best fit functional form for our data was selected by comparing the R^2 values for each model. The best-fit form was found to be polynomial regression with cubic terms at all the levels studied and had R^2 values of more than 0.9.

Fitzgerald *et al.*^[7] in 1987 studied thoracic aortic diameter in 97 children aged between 2 weeks and 19 years and found a linear relationship with thoracic aortic diameter at various levels with age and with thoracic vertebral body width. Like our study, they did not find a significant distinction between male and female groups. However, they used only axial CT images with 5-10 mm thick axial sections without multiplanar reconstructions perpendicular to the aorta.

Akay *et al.*^[6] reviewed CECT chest scans of 133 pediatric patients to measure descending and ascending thoracic aortic diameter. They found that the ratio of the aortic

diameter to that of the thoracic vertebral diameter is a constant, about 1.1 at the level of ascending aorta.

Wolak *et al.*^[8] determined the aortic diameter at various levels on non-contrast cardiac CT and defined the normal limits in relation to age, sex, and body surface area (BSA). However, pediatric population was not included in the study.

Kaiser *et al.*^[4] assessed the normal values for aortic diameters in 53 children and adolescents by contrast-enhanced cardiovascular magnetic resonance (CMR)-angiography, with double-oblique maximum intensity projections perpendicular to the aorta. Their study found a linear relationship between the cross-sectional aortic diameter with the square root of BSA. However, their study lacked any data on children aged less than 2 years.

Mohiaddin *et al.*^[9] measured the normal dimensions of the thoracic aorta in 70 healthy volunteers on MR imaging. They used end-diastolic spin-echo images in oblique planes through the ascending aorta, transverse aorta, and the descending aorta. They correlated these measurements with the BSA and found a linear correlation. However, the youngest subject of the study was 10 years old, and the study had no information on children aged younger than 10 years. The youngest subject of our study was 10 days old.

Hegde *et al.*^[2] determined the normal effective diameter at various levels of the aorta on CECT studies in children. They included 88 thoracic and 110 abdominal scans in the

study. They measured the average of the antero-posterior and the lateral diameters of the thoracic and abdominal aorta at various levels on 1 mm collimation double oblique reconstructions perpendicular to the course of the vessel. They calculated the z scores at each level for a particular age group. As with our study, they derived a polynomial regression model with cubic terms relating to the aortic diameters and log BSA. They found a significant sex difference in the study population.

Bayindir *et al.*^[10] evaluated thoracic CECT studies, and measured the diameters of ascending aorta, descending aorta, main pulmonary artery, and right and left pulmonary arteries. They concluded that the diameters of the thoracic vascular structures increased with age and found a significant statistical difference among the age groups and genders, with higher dimensions in male children. However, the study measured aortic dimensions at two locations and did not attempt regression analysis of the statistical data.

Limitations of our study

As the scans included in the study were done for non-cardiac indications, electrocardiographic gating was not routinely performed. This resulted in significant cardiac motion

Table 4: Regression analysis of aortic root diameter to patients age

Model	Equation	R ²
Exponential	Ao Rt= 13.552e ^{0.0464 (age)}	0.7897
Linear	Ao Rt=0.8909 (age) + 13.405	0.8876
Logarithmic	Ao Rt=4.2768ln (age) + 13.866	0.8827
Polynomial		
Order 2	Ao Rt= -0.0428 (age) ² +1.6724 (age) + 11.22	0.9334
Order 3	Ao Rt=0.0045 (age) ³ -0.1647 (age) ² +2.5385 (age) + 10.09	0.9443
Order 4	Ao Rt= -0.0006 (age) ⁴ +0.0279 (age) ³ -0.4384 (age) ² +3.609 (age) + 9.2832	0.933

(Ao Rt- Effective diameter of the aortic root, age in years). Polynomial regression model of third order was selected as it had the highest R² value as the best fit model among all the regression models analysed

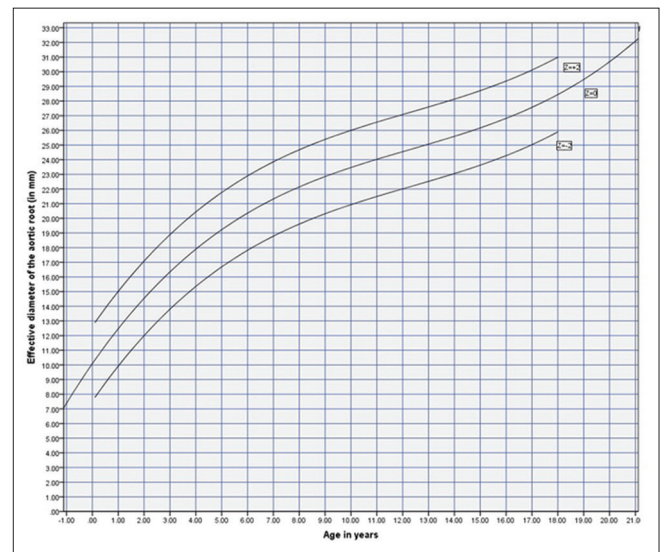


Figure 2: Effective diameter of the aorta at the aortic root (in mm) versus age (in years). Central line represents the mean (predicted normal diameter), above and below are the z = ±2 score lines

Table 5: Formulae to calculate the predicted effective aortic diameter as a function of subjects age

Aortic level	Formulae	R ²
Aortic root	EAD=0.0045 (age) ³ -0.1647 (age) ² +2.5385 (age) + 10.09	0.9443
Ascending aorta	EAD=0.0035 (age) ³ -0.1278 (age) ² +2.0796 (age) + 8.25	0.937
Arch of aorta	EAD=0.0021 (age) ³ -0.0831 (age) ² +1.5785 (age) + 7.579	0.903
Proximal descending Aorta	EAD=0.0024 (age) ³ -0.0796 (age) ² +1.2802 (age) + 6.064	0.9122
Aorta at diaphragmatic hiatus	EAD=0.0023 (age) ³ -0.0743 (age) ² +1.2337 (age) + 5.71	0.9195

EAD: Effective aortic diameter in mm, age in years

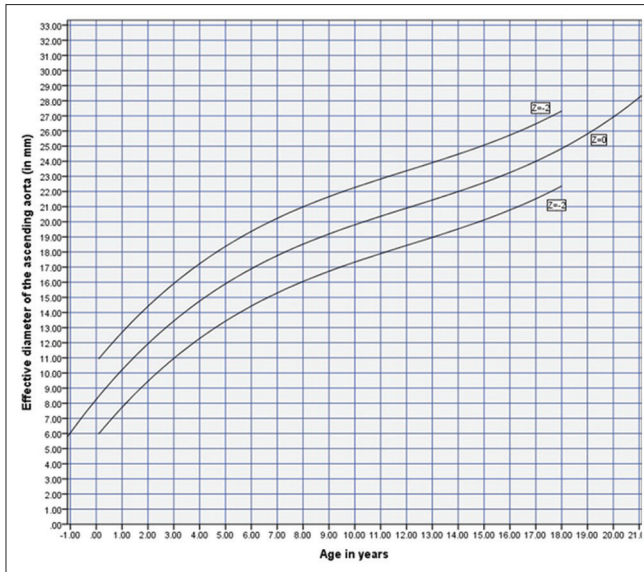


Figure 3: Effective diameter of the ascending aorta (in mm) versus age (in years). Central line represents the mean (predicted normal diameter), above and below are the $z = \pm 2$ score lines

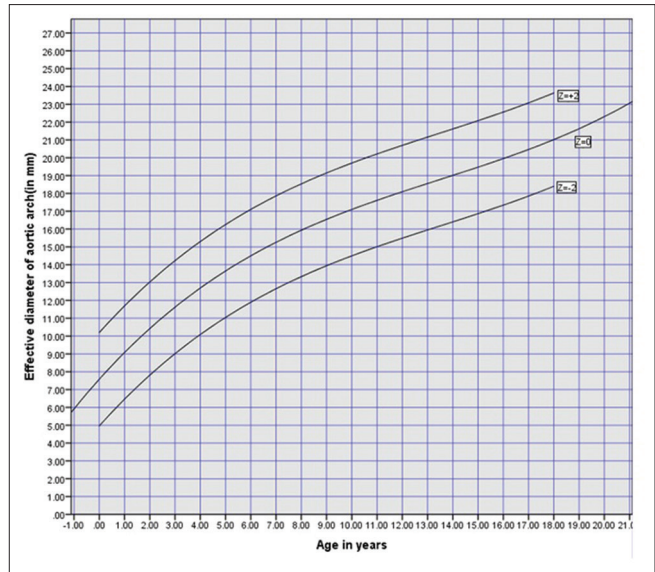


Figure 4: Effective diameter of the aortic arch (in mm) versus age (in years). Central line represents the mean (predicted normal diameter), above and below are the $z = \pm 2$ score lines

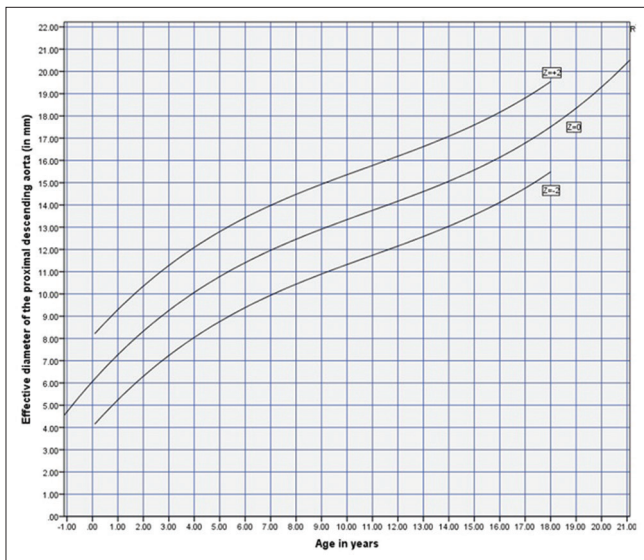


Figure 5: Effective diameter of the proximal descending aorta (in mm) versus age (in years). Central line represents the mean (predicted normal diameter), above and below are the $z = \pm 2$ score lines

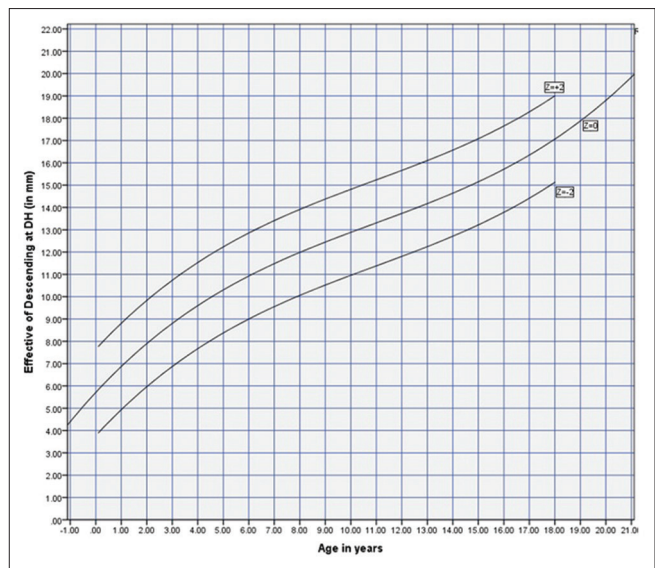


Figure 6: Effective diameter of the aorta at diaphragmatic hiatus (in mm) versus age (in years). Central line represents the mean (predicted normal diameter), above and below are the $z = \pm 2$ score lines

artifacts in some cases, which could have introduced error in measurements, especially at the aortic root.

The measurements acquired are neither end-systolic nor end-diastolic measurements. The measurements were neither the true maximum nor minimum but rather intermediate effective diameters.

A major limitation of the study was the small number of the study population and the fact that it was carried out at a single institution which might not be a true representation of the normal population.

Conclusions

Effective aortic diameter increases with age, however, their relationship with age is not linear. A polynomial regression model with cubic terms is the best fit functional form to describe the relation between aortic diameter and age, at all the levels studied. The R^2 values of the study model were high (>0.9) and significant at all levels.

The range of normal effective diameters of the aorta at multiple levels, the predicted mean and the ± 2 SDs values were determined and plotted on graphs. The knowledge

of these normal ranges and the use of graphs can aid the radiologist in diagnosing abnormalities like ectasia, aneurysm, stenosis, hypoplasia, etc.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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