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Original article

Nomograms for two-dimensional echocardiography derived valvular and arterial dimensions in Caucasian children

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ABSTRACT

Background: Despite recent advances, current pediatric echocardiographic nomograms for valvular and arterial dimensions remain limited.
Methods: We prospectively studied healthy Caucasian Italian children by two-dimensional (2D) echocardiography. Echocardiographic measurements for 18 valvular and arterial dimensions were performed and models were generated testing for linear, logarithmic, exponential, and square root relationships. Heteroscedasticity was accounted for by White or Breusch–Pagan test. Age, weight, height, heart rate, and body surface area (BSA) were used as independent variables in different analyses to predict the mean values of each measurement. Structured *Z*-scores were then computed.
Results: In all, 1151 subjects (age 0 days to 17 years; 45% females; BSA 0.12–2.12 m^2) were studied. The Haycock formula was used when presenting data as predicted values (mean ± 2 SDs) for a given BSA and within equations relating echocardiographic measurements to BSA. The predicted values and *Z*-score boundaries for all measurements are presented.
Conclusions: We report echocardiographic nomograms for valvular and arterial dimensions derived from a large population of children. Integration of these data with those of previous reports would allow for a comprehensive coverage of pediatric 2D echocardiographic nomograms for measurement of 2D cardiac structures.

Introduction

Echocardiography is the front-line modality for the diagnosis and management of children with congenital and acquired cardiac disease, and quantification is an essential aspect of this modality [1–3]. In the pediatric age group, echocardiographic measurements need to be normalized according to age and somatic growth [1–5]. The availability of a robust range of normality is essential for accurate evaluation of disease severity [1–5]. Despite this, as we and others have underscored [6–12], most available nomograms have multiple numerical and methodological limitations [2,3,5]. Multiple efforts have been initiated both in Europe and in North America [6,13] for creation of more reliable nomograms. Our group recently reported echocardiographic nomograms for left ventricular, valvular, and arterial dimensions in neonates and infants up to 3 years of age, and bi-ventricular and bi-atrial dimensions for the entire pediatric age (0–18 years) [6]. These reports however lacked data for valvular and major vessels dimensions (i.e. aorta, aortic arch, and pulmonary arteries) in children aged 3–18 years. Although nomograms of vessel dimensions are of great relevance in the evaluation of several forms of heart disease, they are either limited (for example, for the aortic arch and pulmonary artery) [7,10,14] or very limited (for example, for the ascending aorta) [11,12,14]. For valvular

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dimensions, echocardiographic nomograms do exist but present significant limitations, affecting their accuracy and reproducibility [2,6].

The primary aim of this investigation was to establish pediatric nomograms for two-dimensional (2D) echocardiographic valvular and arterial measurements derived from a wide population of healthy neonates, infants and children. The secondary aims were (1) to identify the best body size parameter to normalize cardiac measurements and (2) to determine the effects of confounding factors such as gender and prematurity, and evaluate intra-observer variability of these measurements.

Materials and methods

Inclusion and exclusion criteria

These data are derived from healthy children partly presented in two recent investigations that evaluated other measurements [6,8]. The inclusion and exclusion criteria have been reported elsewhere [6,8]. Briefly, consecutive healthy Caucasian children evaluated from February 2012 to June 2015 in the outpatient pediatric cardiology department at the Fondazione G. Monasterio CNR-Regione Toscana of Massa for congenital heart disease (CHD) screening were prospectively recruited.

Only those with technically adequate echocardiographic examinations were enrolled in the study. The presence of intra-cardiac defects that represent normal circulatory physiology such as a patent ductus arteriosus with small left-to-right shunting in the first 3 days of life, or a patent foramen ovale, was considered normal [6,7]. Premature neonates were included only if they had an APGAR score $\geq$8, did not require ventilatory support, and had good clinical status [6,7].

All subjects with clinical, electrocardiographic, or echocardiographic evidence of congenital or acquired heart disease were excluded. Other exclusion criteria consisted of patients with known or suspected neuro-muscular disease, genetic syndromes, or chromosomal abnormalities; body mass index (BMI) $\geq$95th percentile for children $\geq$2 years old [15,16], or weight-for-length *Z*-score $\geq$2 based on the World Health Organization (WHO) Child Growth Standards for children <2 years old [15,16]; pulmonary hypertension; systemic hypertension (for children >4 years of age), connective tissue disease; or family history of genetic cardiac disease (such as Marfan syndrome or cardiomyopathy) [6,8,15,16]. All non-Caucasian subjects were also excluded to avoid racial variability bias.

All patients underwent a complete 2D, color flow Doppler, and tissue Doppler examination and images were digitally stored for subsequent offline analysis.

Approval for this study was obtained from the Local Ethics Committee. Parents or legal guardians of all the children were informed and accepted to participate in the study by signing a written consent.

Echocardiographic examination

Echocardiograms were performed using Philips iE33 systems (Philips Medical Systems, Bothell, WA, USA). Offline measurements were performed on a commercially available computer workstation (EnConcert, Philips Medical Systems, Andover, MA, USA) according to guidelines [1]. The measurements, the view from which they were obtained, and the point in the cardiac cycle are displayed in Table 1. For any given parameter, measurements were only made if excellent and unambiguous views were available. Thus, not all parameters were measured in all patients (Table 2).

Statistical methods

Statistical methods have been described in previous works [6,8,17–23] and will be briefly summarized. To examine the relationship between parameters of body size, heart rate, age, and each of the echocardiographic variables, multiple models using linear, logarithmic, exponential, and square root equations were tested [17–23]. 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 tested by the White test and the Breusch–Pagan test as described previously [6,8,22,23]. To test the normality of residuals, the Shapiro–Wilk and Lilliefors (Kolmogorov–Smirnov) tests were used. Age, weight, height, heart rate (HR), and body surface area (BSA) [19] were used as independent variables in different regression analyses to predict the mean values of each echocardiographic measurement. The Haycock formula was used to calculate BSA [19]. Outliers to be

Table 1
Two-dimensional echocardiographic anatomical measurements.

Measurement	View	Description
1. Inferior vena cava	Sub-costal long axis	Maximal systolic dimension at the level of the diaphragm
2. Mitral valve annulus	Apical 4 chamber	Distance between the hinge points during diastole
3. Tricuspid valve annulus	Apical 4 chamber	Distance between the hinge points during diastole
4. Aortic valve annulus	Para-sternal long axis	Maximal distance between hinge points during systole
5. Sinuses of Valsalva	Para-sternal long axis	Maximum systolic dimension
6. Sino-tubular junction	Para-sternal long axis	Maximum systolic dimension
7. Transverse arch after the origin of innominate artery	Supra-sternal long axis	Maximum systolic dimension between the innominate and left carotid artery
8. Transverse arch after the origin of left carotid artery	Supra-sternal long axis	Maximum systolic dimension between the left carotid arteries and the left subclavian artery
9. Transverse arch after the origin of left subclavian artery	Supra-sternal long axis	Maximum systolic dimension immediately after the left subclavian artery
10. Aortic isthmus	Supra-sternal long axis	Maximum systolic dimension at the narrowest point beyond left subclavian artery
11. Distal aortic arch	Supra-sternal long axis	Maximum systolic dimension immediately beyond aortic isthmus
12. Aorta at diaphragm	Sub-costal long axis	Maximal systolic dimension at the level of the diaphragm
13. Superior vena cava	Supra-sternal long axis	Maximal systolic dimension
14. Pulmonary valve annulus	Para-sternal long axis	Distance between hinge points during systole
15. Main pulmonary artery	Para-sternal short axis	Maximal systolic dimension
16. Right pulmonary artery	Para-sternal short axis	Maximal systolic dimension immediately beyond the bifurcation
17. Left pulmonary artery	Para-sternal short axis	Maximal systolic dimension immediately beyond the bifurcation

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