CLINICAL INVESTIGATIONS IN CHILDREN NORMALIZING ECHOCARDIOGRAPHIC MEASUREMENTS IN CHILDREN AND NEONATES

Echocardiographic Nomograms for Chamber Diameters and Areas in Caucasian Children

Massimiliano Cantinotti, MD, Marco Scalese, MS, Bruno Murzi, MD, Nadia Assanta, MD, Isabella Spadoni, MD, Vittoria De Lucia, MD, Maura Crocetti, MD, Alberto Cresti, MD, Milena Gallotta, MD, Marco Marotta, MD, Karin Tyack, PhD, Sabrina Molinaro, PhD, and Giorgio Iervasi, MD, *Massa and Pisa, Pisa, Grosseto, and Siena, Italy*

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 m² 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 \pm 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;27:1279-92.)

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,

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Copyright 2014 by the American Society of Echocardiography. http://dx.doi.org/10.1016/j.echo.2014.08.005 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 dimensions¹² and atrial dimensions¹⁵ 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

From Fondazione G. Monasterio CNR–Regione Toscana, Massa and Pisa, Italy (M. Cantinotti, B.M., N.A., I.S., V.D., M. Crocetti, M.M., K.T., G.I.); the Institute of Clinical Physiology, Pisa, Italy (M.S., S.M., G.I.); the Department of Cardiology, USL 9, Grosseto, Italy (A.C.); and the Department of Cardiology, Siena University, Siena, Italy (M.G.).

Reprint requests: Massimiliano Cantinotti, MD, Fondazione Toscana G. Monasterio, Ospedale del Cuore, via Aurelia Sud, 54100 Massa, Italy (E-mail: *cantinotti@ftgm.it*).

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 \geq 95th percentile for children \geq 2 years old²³ or weight-for-length *Z* score \geq 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 twodimensional 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-dimensiona | l echocardiographic | measurements |
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| 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.

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