Real-Time Three-Dimensional Echocardiography of the Left Ventricle—Pediatric Percentiles and Head-to-Head Comparison of Different Contour-Finding Algorithms: A Multicenter Study

Kristina Krell, Kai Thorsten Laser, MD, Robert Dalla-Pozza, MD, Christian Winkler, Ursula Hildebrandt, MD, Deniz Kececioglu, MD, Johannes Breuer, MD, and Ulrike Herberg, MD,
Bonn, Bad Oeynhausen, and Munich, Germany

Background: Real-time three-dimensional echocardiography (RT3DE) is a promising method for accurate assessment of left ventricular (LV) volumes and function, however, pediatric reference values are scarce. The aim of the study was to establish pediatric percentiles in a large population and to compare the inherent influence of different evaluation software on the resulting measurements.

Methods: In a multicenter prospective-design study, 497 healthy children (ages 1 day to 219 months) underwent RT3DE imaging of the LV (ie33, Philips, Andover, MA). Volume analysis was performed using QLab 9.0 (Philips) and TomTec 4DLV2.7 (vendor-independent; testing high ($TomTec_{75}$) and low ($TomTec_{30}$) contour-finding activity). Reference percentiles were computed using Cole's LMS method. In 22 subjects, cardiovascular magnetic resonance imaging (CMR) was used as the reference.

Results: A total of 370/497 (74.4%) of the subjects provided adequate data sets. LV volumes had a significant association with age, body size, and gender; therefore, sex-specific percentiles were indexed to body surface area. Intra- and interobserver variability for both workstations was good (relative bias ± SD for end-diastolic volume [EDV] in %: intraobserver: QLab = −0.8 ± 2.4; $TomTec_{30}$ = −0.7 ± 7.2; $TomTec_{75}$ = −1.9 ± 6.7; interobserver: QLab = 2.4 ± 7.5; $TomTec_{30}$ = 1.2 ± 5.1; $TomTec_{75}$ = 1.3 ± 4.5). Intervendor agreement between QLab and $TomTec_{30}$ showed larger bias and wider limits of agreement (bias: QLab vs $TomTec_{30}$: end-systolic volume [ESV] = 0.8% ± 23.6%; EDV = −2.2% ± 17.0%) with notable individual differences in small children. QLab and TomTec underestimated CMR values, with the highest agreement between CMR and QLab.

Conclusions: RT3DE allows reproducible noninvasive assessment of LV volumes and function. However, intertechnique variability is relevant. Therefore, our software-specific percentiles, based on a large pediatric population, serve as a reference for both commonly used quantification programs. (J Am Soc Echocardiogr 2018;■:■-■.)

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Echocardiographic assessment of left ventricular (LV) size and function is one of the most important tools in pediatric cardiology: it is essential for diagnosis, prognosis, and management in various congenital as well as acquired heart diseases.[1-4] Accurate and reproducible LV volume measurements and assessment of the ejection fraction (EF) in particular play an

From the Department of Pediatric Cardiology, Children's Hospital, University of Bonn (K.K., C.W., U.H., J.B., U.H.), Bonn; Department of Congenital Heart Defects, Heart and Diabetes Center, North Rhine Westphalia Ruhr University Bochum (K.T.L., D.K.), Bad Oeynhausen; and Department of Pediatric Cardiology and Pediatric Intensive Care, Ludwig Maximilians University, Medical Hospital of the University of Munich (R.D.-P.), Munich, Germany.

K.K. and K.T.L. contributed equally to this work.

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Reprint requests: Ulrike Herberg, MD, PhD, Department of Pediatric Cardiology, University of Bonn, Adenauerallee 119, 53113 Bonn, Germany (E-mail: ulrike.herberg@ukb.uni-bonn.de).

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Abbreviations

3D = Three-dimensional

BSA = Body surface area

CFA = Contour-finding activity

CMR = Cardiovascular magnetic resonance imaging

EDV = End-diastolic volume

EF = Ejection fraction

ESV = End-systolic volume

LOA = Limits of agreement

LV = Left ventricular

RT3DE = Real-time three-dimensional echocardiography

SV = Stroke volume

$TomTec_{30}$ = TomTec with low contour-finding activity

$TomTec_{75}$ = TomTec with high contour-finding activity

essential role in daily echocardiographic examination and decision making.[5,6]

Real-time three-dimensional echocardiography (RT3DE) with matrix transducer technology has become widely available for the assessment of cardiac anatomy and function and has been proven to be superior to conventional two-dimensional methods with regard to accuracy and reproducibility of LV volume calculations.[2,7-11] Further improvement of matrix technology with transducers of small aperture and improved near-field resolution by X7-2 and X5-1 transducers (Philips, Andover, MA) have led to the increased application of 3DRTE in children. However, although there is widespread clinical need for the calculation of 3D-related volumes, pediatric reference values derived from a large normal population are currently lacking.

For 3D volume calculation, several clinical software programs with a variety of postprocessing options and different benefits have been developed.[12] Currently, the most commonly used software programs for 3D quantification of the pediatric left ventricle are the vendor-independent software TomTec (TomTec, Unterschleissheim, Germany) and the vendor-specific QLab (Philips, Andover, MA), which can only be used for 3D volume data sets obtained by Philips ultrasound scanners. Both apply semiautomatic endocardial border-tracking algorithms and offer the opportunity to calculate values quickly, reproducibly, and in a practical workflow. Up until now, data regarding the intervendor agreement and consistency between the two software types have been limited to a small number of healthy children, as well as children with a single ventricle.[13,14]

The primary aim of our study is to provide reference values for LV indices in a large cohort of healthy children. In order to investigate whether a set of universal reference values could be applicable for both quantification software algorithms, intervendor agreement and the influence of different contour-finding adjustments were assessed for QLab as well as TomTec.

METHODS

Study Design and Data

In a prospective multicenter design, 497 children and adolescents from birth to 18 years of age were enrolled to undergo RT3DE of the left ventricle between April 2011 and November 2013. Normal cardiac anatomy and function as well as sinus rhythm were a precondition and confirmed by physical examination and echocardiography, according to standard recommendations.[1] The study was approved by the local ethics institutional review committee (Registration No. 226/06) and representative boards of all participating centers and conformed to the principles of the Declaration of Helsinki as well as German law. Written consent was given by the legal guardian or in person by young adults. Examinations were performed at three different centers by five different operators with five different sonographic units from the same manufacturer (iE33, Philips, using the transducers X7-2, $n = 285$; X5-1, $n = 6$; and X3-1, $n = 6$). Prior to the start of the study, standardization of the acquisition procedure including presets and operator training took place. Insights regarding the use of real-time 3D matrix transducers[15] and restrictions in spatiotemporal accuracy of RT3DE in pediatrics[16] were incorporated into the acquisition procedures. Measurement accuracy of the ultrasound scanners was validated using calibrated, static, tissue-mimicking phantoms[17] as well as moving phantoms.[16] In the core lab in Bonn, all data were reviewed and quantified. Results were compared to the gold standard, cardiovascular magnetic resonance imaging (CMR), performed on volunteers (22 cases: 20 children, mean age 12.3 years, and two adults, ages 22 years and 43 years). Due to ethical reasons, CMR on young healthy children requiring sedation was not performed.

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Image Acquisition. Image acquisition was implemented from an apical window based on standard recommendations.[18] A full-volume scan was acquired from four to seven R-wave triggered subvolumes during end-expiratory breath holding when necessary. Blinded 3D data sets were stored in a DICOM format on a DVD and sent to the core lab. In the core lab, the quality of the 3D data was rated, and any data sets containing artefacts due to movement, arrhythmia, or incomplete depiction of the left ventricle were excluded. Only those data sets that could be interpreted sufficiently, with complete delineation of the left ventricle and without disturbing artefacts, were processed and transferred to two different offline workstations (Figure 1A, 1B).

Data Analysis with QLab 9.0. Three-dimensional data sets of the LV were analyzed using offline QLab Version 9.0 (3DQ Advanced software, Philips). After initially adjusting a proper four-chamber view, the end-diastolic frame, presented by the one with maximum LV volume, was first determined. Ventricular trabeculae and papillary muscles were included in the LV cavity. Next the end-systolic frame showing the smallest volume, respectively the frame before mitral valve opening, was selected. After subsequently setting five points, at the apex, septal, lateral, anterior, and mitral annulus (Figure 1C), the cardiac cycle as well as minimal end-systolic volume (ESV), maximal end-diastolic volume (EDV), EF, and stroke volume (SV) were semiautomatically computed and the LV cavity was displayed as a 3D model. If delineation of the LV endocardial borders was unsatisfactory (Figure 1D), the operator manually adjusted the initial endocardial contour at the apex, septum, and mitral valve and repeated the automatic tracking throughout the cardiac cycle. Data analysis was performed by two raters who were blinded to results derived from TomTec (K.K. and U.H.).

Data Analysis with TomTec. TomTec 4DLV analysis software 2.7 (Image-Arena version 4.1; Build 4.1.1.30, TomTec, Unterschleißheim, Germany) was used to perform offline LV data analysis. All operators followed a standardized protocol for analysis of the data after interinstitutional operator training based on previous findings.[15,19] The data sets were adjusted in order to acquire maximal long-axis dimension. Using the four- and two-chamber views as well as the apical long-axis view, the end-systolic and end-diastolic delineations were traced manually. Ventricular trabeculae and papillary muscles were included in the LV cavity. EDV, ESV, and EF were calculated semiautomatically. Manual adjustments were made to the initial endocardial