Left Atrial Volumes and Strain in Healthy Children Measured by Three-Dimensional Echocardiography: Normal Values and Maturational Changes

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Background: Assessment of left atrial (LA) size and function is important in a number of pediatric cardiac conditions including those affecting the diastolic performance of the left ventricle. Measurements of LA volume and strain by two-dimensional echocardiography rely upon inaccurate geometric assumptions and are hampered by out-of-plane motion. The objective of this study was to characterize LA volumes and strain by three-dimensional echocardiography in healthy children.

Methods: LA volumes and strain were retrospectively measured by three-dimensional echocardiography in healthy children with no known structural or functional heart disease using a commercial speckle-tracking package applied to the LA to compute maximum volume (V_{max}), minimum volume (V_{min}), ejection volume (LAEV), ejection fraction (LAEF), and the following components of global strain: 3D principal (3DS), longitudinal (GLS), and circumferential (GCS).

Results: The study population included 196 normal subjects (median age, 12 years; range, 4 days to 20.9 years). V_{max}, V_{min}, and LAEV increased with age and body surface area. Significant age-related declines were present in all measured functional indices including LAEF, 3DS, GLS, and GCS. Analysis of a subset of 50 subjects showed excellent agreement between V_{max} derived by three-dimensional and two-dimensional biplane area-length method. Regression equations with standard deviations were generated to enable calculation of Z scores.

Conclusions: LA volume and functional indices can be reliably calculated using a commercial three-dimensional analysis software. All components of LA strain decline modestly with age. Normative data generated in this study have the potential to greatly enhance the utility of three-dimensional echocardiography-derived measurements in a wide range of cardiac pathologies. (J Am Soc Echocardiogr 2017;■:■-■.)

Keywords: Left atrial volume, Left atrial function, Strain, Three-dimensional echocardiography

Left atrial (LA) size is a well-established indicator of left ventricular diastolic function and has been shown to be an important prognostic marker in adults with ischemic heart disease, heart failure, and atrial fibrillation.[1-3] In children, assessment of LA size is useful in a variety of conditions including mitral valve disease, left-to-right shunting lesions, and conditions affecting left ventricular diastolic performance. A number of techniques exist for the calculation of LA size. Determination of LA volume is preferred over measurement of linear dimensions and area because the volumetric calculation allows for more accurate assessment of the asymmetric geometry of the chamber and has been shown to have stronger association with disease progression than linear models.[4-6] Indices of LA function such as strain and ejection fraction (LAEF) have also been shown to be sensitive markers of poor prognosis, for example, in adults with ischemic heart disease, hypertension, and atrial arrhythmias.[7,8]

Two-dimensional (2D) echocardiographic methods for the calculation of chamber volumes and speckle-tracking-derived strain rely upon geometric assumptions that are known to be inaccurate; their

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Abbreviations

2D = Two-dimensional

3D = Three-dimensional

3DS = Three-dimensional (principal) strain

BSA = Body surface area

EF = Ejection fraction

GCS = Global circumferential strain

GLS = Global longitudinal strain

ICC = Intraclass correlation coefficient

IQR = Interquartile range

LA = Left atrium, atrial

LAEF = Left atrial ejection fraction

LAEV = Left atrial ejection volume

V_{max} = Maximum left atrial volume

V_{min} = Minimum left atrial volume

accuracy is impaired further by out-of-plane motion. Three-dimensional (3D) measurements have been shown to have superior accuracy for the assessment of left ventricular volumes when compared with 2D echocardiography using magnetic resonance imaging as the gold standard.[9] Recent studies have explored the assessment of LA function using 3D echocardiography in adults; however, reports of 3D-based normal LA volumes in children are scarce.[10-17] Moreover, to our knowledge, no published data exist on normal LA 3D strain values in this cohort. Therefore, the present study used 3D echocardiography to measure LA strain and volumes in normal children and assessed maturational changes in these measurements.

METHODS

Study Design

This study was a single-center, retrospective, cross-sectional analysis. The Institutional Review Board approved this study and waived the requirement for informed consent.

Patients

Inclusion criteria for this study were age < 21, study performed in the outpatient cardiology clinic or well-baby nursery, body surface area (BSA) ≥ 0.2 m^2 (average for a healthy newborn), structurally and functionally normal heart by standard 2D echocardiogram (patent foramen ovale and trivial branch pulmonary artery stenosis permitted in the newborn period), and available 3D data set for the left heart (note that 3D LA/left ventricular volumes have been acquired in our laboratory since January 2014 as part of routine clinical practice). Patients were excluded from analysis if they had evidence of acquired heart disease (e.g., Kawasaki disease or myocarditis), systemic comorbidities with potential cardiac impact (e.g., anemia, hypertension, body mass index >30 kg/m^2), or family history of cardiomyopathy; more than trivial stenosis or regurgitation of any heart valve; arrhythmia (other than rare atrial or ventricular premature beat); brady- or tachycardia (heart rate Z score < -2 or > 2); probable or definite connective tissue disorder; or poor image quality or incomplete capture of the LA.

Image Acquisition and Analysis

Three-dimensional volumetric data sets were acquired from the apical view with the Philips IE33 machine with X5/X7 probes using two beat loops and four beat volumes. These data sets were analyzed using a commercial 3D speckle-tracking analysis package (4D left ventricular Analysis 3.1; Tomtec Imaging Systems, Unterschleissheim, Germany). The analysis software is natively designed to analyze one complete ventricular cardiac cycle defined by the two adjacent QRS complexes. To ensure the inclusion of a complete atrial cycle, containing maximal and minimal atrial volumes within the same continuous clip, the markers defining the beginning and end of the analysis cycle were both shifted to the right by 1/3 of the R-R interval. The atrial appendage was excluded from analysis, and the contour of the LA wall was extended across the pulmonary vein orifices. The following volume and strain components were recorded: maximum LA volume (V_{max}); minimum LA volume (V_{min}); global 3D (principal) strain (3DS); global longitudinal strain (GLS); and global circumferential strain (GCS; Figure 1, Video 1, available at www.onlinejase.com). Longitudinal strain measures the shortening along the long axis of the chamber, while circumferential strain measures shortening along the circumference in a short axis. Principal (3D) strain component estimates deformation in the direction in which shortening primarily develops with no shear and represents a direct result of change in myocardial fiber length. Detailed discussion regarding estimation of various strain components using semiautomated endocardial speckle-tracking has been published elsewhere.[18]

Comparison with 2D Measurements

A subset of 50 subjects were chosen at random to compare V_{max} measured by 3D analysis with commonly used 2D techniques. For this analysis, V_{max} was calculated by a single observer using 2D apical four- and two-chamber views from the same echocardiogram as the 3D acquisition using the following four methods: (1) biplane area-length, (2) ellipsoid, (3) single plane area-length using apical four-chamber view, and (4) single plane area-length using apical two-chamber view.[6]

Statistical Analysis

Data are presented as medians with interquartile ranges (IQRs) unless otherwise specified. Relationships between age or BSA and LA measurements were modeled using linear and fractional polynomial regression analysis with log transformation. For each measurement, multiple potential models were explored to determine the statistical best fit and compared using the F-statistic. Residuals analysis demonstrated heteroskedasticity for virtually all models, and therefore standard deviations and Z scores were calculated using absolute residuals as described by Altman.[19] Agreement between 3D measurement of V_{max} and different 2D methods was assessed estimating Lin's concordance correlation coefficient (Rc), mean differences, and mean ratios between the methods.[20] Inter- and intraobserver reproducibility for 3D measurements was assessed on a random subset of 20 subjects. Intraobserver measurements were made at least 1 month from the initial measurements. Reproducibility was quantified using the intraclass correlation coefficient (ICC), which was generated using the two-way model for absolute agreement for average measures. In addition, mean relative difference (%) was calculated as the mean of the ratio of absolute difference and average of each pair of observations expressed as a percentage for intraobserver and interobserver measurements. Analysis was performed using IBM SPSS version 23.0 (IBM, Armonk, NY), SAS version 9.2 (SAS Institute, Cary, NC), and STATA version 13.1 (StataCorp, College Station, TX).

RESULTS

Of 251 eligible subjects, 55 (22%) were excluded due to inadequate imaging data. The most common reasons for exclusion were lack of inclusion of the entire LA in the 3D volume and presence of a stitch artifact.