Transthoracic Three-dimensional Echocardiography is as Good as Magnetic Resonance Imaging in Measuring Dynamic Changes in Left Ventricular Volume During the Heart Cycle in Children

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Aims: The purpose of the study was to assess the dynamic changes in left ventricular (LV) volume by transthoracic three-dimensional echocardiography (3DE) and to compare the results with those obtained by magnetic resonance imaging (MRI).

Methods and Results: Thirty healthy children were studied by digitized 3DE and Doppler, and by MRI. Three-dimensional echocardiography of LV was performed by using rotational acquisition from the transthoracic apical view with ECG gating and without respiratory gating. The acquisition of 3DE data took 10–15 s. Three-dimensional echocardiography gave similar values to MRI for EDV, ESV and LVM measurements, and the results correlated well. Peak emptying rates by 3DE and MRI were 236.6 and 169.6 ml/s and peak filling rates were 215.0 and 215.9 ml/s, respectively. Dynamic changes of LV volumes during the heart cycle were detectable with both methods.

Conclusion: Digitized 3DE performed in the outpatient clinic and MRI were both useful methods for studying the physiological volume changes in left ventricle in children. These methods may be used for further study of the systolic and diastolic function of the left ventricle in various clinical conditions.

Key Words: Three-dimensional echocardiography; magnetic resonance imaging; left ventricular volume; left ventricular mass; children.

Introduction

Accurate determinations of left ventricular (LV) volume and function are important in the management of patients with heart diseases. M-mode and two-dimensional (2D) echocardiography are widely used methods to assess the dimensions and systolic function of LV. These methods are of limited value due to the geometric assumptions made of the shape of left ventricle and the position and orientation of imaging planes. The examination of diastolic function has been based on the relation between changes in ventricular pressure and volume during cardiac catheterization. Doppler echocardiography has become an important non-invasive tool to assess LV filling. Normal values for diastolic filling parameters have been reported for children. However, left ventricular diastolic function consists of several variables that affect the Doppler echocardiographic recordings and there are limitations with the non-invasive assessment of LV diastolic function and filling pressures by Doppler echocardiography. Radionuclide angiography, and more recently magnetic resonance imaging (MRI), have been used to evaluate left ventricular systolic and diastolic function. With both methods a time-volume curve can be generated with a moderate temporal resolution. The disadvantages of these methods are their expense, patient discomfort and the need for injection of radiopharmaceutical agents in nuclear scans and the prolonged image acquisition time in MRI.

Three-dimensional echocardiography (3DE) is a new, non-invasive imaging technique that has been shown to be accurate in determining end systolic and end diastolic...
volumes of both left and right ventricles[9,10]. There are a few studies that have reported right and left ventricular volumes and ejection fraction in children with various heart diseases[11–14]. Most of these studies have used analogue data from the video output of the ultrasound machine. Thus the data acquisition time has been long and the temporal resolution too poor to allow adequate evaluation of the different phases of the heart cycle. In future, real-time 3DE will offer further advantages on cardiac measurements during single cardiac cycle[15,16]. To our knowledge, there are no published data on left ventricular volumes and mass in healthy children or on the dynamic changes of left ventricular volume in adults or in children assessed by 3DE. In the present study we performed these measurements in healthy children and compared the results achieved by digitized transthoracic 3DE to those achieved by MRI.

### Patients and Methods

The study was carried out in Kuopio University Hospital from April to November 1998. Written informed consent for the study was obtained from the parents or subjects. The study was approved by the research ethics committee of the hospital.

### Study Population

Thirty healthy children were enrolled in the study. The weight and height and of all subjects were recorded and body surface area (BSA) was calculated[17]. Clinical cardiovascular examination was performed. Blood pressure was recorded at phase I and V Korotkoff sounds. All children underwent MRI and two echocardiographic examinations on the same day without sedation. The clinical details of the children are shown in Table 1.

### Echocardiographic Examination

Transthoracic echocardiographic examination was performed with the patient lying supine or in the left lateral semi-recumbent position. Two independent observers performed examinations on the same day using a GE Vingmed System FiVe ultrasound scanner (Horten, Norway). The transducer frequency was 3-5 MHz or 5 MHz, either or both being used for each patient. Standard parasternal, apical and subcostal views were used to confirm the presence of normal cardiac anatomy. An ECG trace was recorded simultaneously with the echocardiogram. Echocardiographic data were saved in digital form on the hard disk of the ultrasound scanner for later analysis.

Three-dimensional echocardiography was performed by using rotational image acquisition from an apical view, with ECG gating and without respiratory gating. The subjects breathed normally during the scanning of 3D cine loops. The normal transducer was fixed to a lightweight, computer-controlled motorized carriage that was easy to hold in the hand. An optimal acoustic window was first selected by 2DE. Pressing a button in the motorized carriage initiated 3D data acquisition. The transducer rotated in a semicircle of 180° around the central axis of the imaging plane, producing a conical data set. Ten images were collected during the rotation. Scanning of a plane took place if pulse rate was within ±20 beats/min of average. Thus, automatic selection of scanning times by RR intervals allowed adequate recordings of the cardiac cross sections. Three-dimensional cine loops (10 views, median 55 frames/heart cycle, range 41–71 frames/heart cycle) were digitally stored.

### Analysis and Calculations: Doppler Echocardiographic Data

All recordings were independently analysed by two observers from digital cine loops previously saved on the patient archive of System FiVe.

Transmitral flow velocity patterns were recorded from the apical four-chamber view, with small sample volume being positioned between the tips of the mitral valve leaflets. The angle between the sampling beam and the mitral inflow was less than 20°. The diameter of mitral valve annulus was measured from the apical four-chamber view, and valve area was calculated assuming circular annular geometry (πd^2/4). Doppler peak filling rate was calculated as the peak early transmitral velocity multiplied by the mitral annular area. All measurements were made from three consecutive heart cycles. The means of measurements of three cardiac cycles were used for analysis.

### Analysis of 3D Echocardiographic Data

The three-dimensional (3D) datasets were analysed with a detached computer. Volume estimation in 3DE started with interactive manual contour tracing in the computer display. Planar contours were selected and drawn with a
mouse before the object was reconstructed and visualized in three dimensions. From the given set of contours a polyhedron was reconstructed by cubic spline interpolation (Fig. 1) and the volume calculated by disc summation\(^{18}\). Both observers analysed the two 3DE datasets of each child.

Tracing of the endocardium was performed on the white side of the black-white boundary. Papillary muscles were included as part of the cavity volume when they were noted to be discontinuous with the myocardium. The end diastolic volume was calculated from the frame at the beginning of R wave on the ECG. The mitral annulus was taken to be the atrioventricular border. The frame with the smallest cavity size when the mitral valve was still closed was chosen as the minimum volume. The LV boundaries at maximum and minimum size were traced manually. LV endocardial edges between these two extremities were interpolated automatically by the software. The accuracy of the interpolation was checked at every frame during the heart cycle, and approximately every fifth frame needed manual correction.

**Magnetic Resonance Imaging**

MRI was performed with a 1.5-T whole body imaging system (Magnetom Vision, Siemens Medical Systems, Erlangen, Germany), using a circularly polarized phase array coil. All scans were obtained during breath holding in deep inspiration, and electrocardiographic triggering was used. LV was imaged with cross-sectional, fast, low angle-shot (FLASH) type of gradient echo cine sequence, time of repetition (TR)=100 ms, time of echo (TE)=4.8 ms, field of view (FOV)=300 × 300 mm, imaging matrix=162 × 256, flip angle=20°. The sequence applied nine-fold k-space segmentation, four echoes were shared and a bandwidth of 195 Hz/pixel was used. In-plane resolution was 1.85 × 1.17 mm and two phase images were acquired in every TR interval. To ensure ECG triggering, after every R wave the number of phases was selected at the beginning of data acquisition so that the mean product of TR and the number of phases was 100 ms below the RR interval. Since the heart rate slowed down during data acquisition, the respective value was 200 ms at the end of the study. On average, 12 (9–17) slices were obtained during the heart cycle.

The long axis of the left ventricle was identified using the scout images obtained for imaging the left atrium and scout image centred through the apex of left ventricle to intersect the mitral valve plane. Based on the scout images, 8–12 slices without gaps were positioned perpendicular to the long axis of the LV to obtain images of LV in the short axis orientation. Slice thickness was 8 mm.

**Analysis of MRI Data**

LV boundaries were traced manually in every image acquired during the heart cycle. Volumes were achieved using the slice summation method, which is based on summation of the volumes of each of the slices, taking the slice thickness and interslice distance into account.

**Calculations Used to Analyse Volume Data of 3DE and MRI Scanning**

The maximum and minimum LV volumes of each subject were calculated as mean values of four analyses. Ejection fraction (EF) was calculated from end diastolic
volume (EDV) and end systolic volume (ESV). The left ventricular mass (LVM) was calculated as the difference between epicardial and endocardial end diastolic volumes multiplied by the specific gravity of myocardium (1.05).

Peak ventricular ejection rate (PER) represents the greatest volume change per time during three frame intervals in 3DE recording (on average 40 ms) in the ejection phase of the time-volume curve. Peak filling rate (PFR) represents the greatest volume change per time during three frame intervals in the filling phase of the time-volume curve. Time during three frame intervals was used in 3DE rate calculations in order to get a time resolution comparable to that in MRI. From MRI data PER and PFR were calculated as the volume change between two adjacent time points that were 50 ms apart. The rate of the volume change was normalized by left ventricular EDV, ESV and stroke volume (SV) (ml). Time to peak filling rate was measured from end systole to the time of peak left ventricular filling rate.

**Calculations to Produce Sum Curves**

Mean time-volume curves were calculated from individual curves to obtain a visually informative way of representing the volume changes in the 30 subjects. For each patient we first calculated the time intervals from R-wave to minimum volume and from minimum volume to the end of heart cycle. Both time intervals were divided into 20 equal parts (5%). The respective volumes were interpolated at each time point. Data on the 30 subjects were then averaged to obtain a sum curve that represents the times from R-peak in ECG (by 5% intervals before and after the maximum volume point) and the respective volumes.

**Statistical Analysis**

Interobserver and intraobserver variability of 3DE were determined. Bland–Altman analysis was used to determine possible bias (mean difference between the two methods) and the limits of agreement (2 SD of the difference)\(^1\). Interobserver variability was calculated between analysis made by observer 1 and observer 2. Intraobserver variability was calculated between analyses from two examinations made by observer 1. The echocardiographic data produced by the two observers, consisting of two separate examinations and four independent analyses, were averaged for further analysis. Volumes determined by echocardiography were then compared with MRI by Pearson’s correlation. Bland–Altman analysis was used to compare the results of 3DE and MRI recordings. Group means were compared with Student’s paired t-test in which the null hypothesis is that there is no difference between the groups. Bonferroni correction was used. Mitral inflow parameters and time-volume data were analysed by linear regression analysis. The data are given as the mean (SD) and, when considered informative, as the range of individual measurements.

**Results**

All 3DE examinations were carried out successfully, and manual tracing of images was possible. In some image planes the borders were not clearly detectable, but the endocardial borders could be traced with the aid of interpolated lines calculated according to adjacent image planes. The acquisition time for a 3DE data set was 10–15 s depending on the frame rate used and the heart rate. Image transfer to the computer took 2–3 min. Tracing of LV and determination of the volumes and the mass took 30–50 min per patient depending on image quality and number of frames. The acquisition time for a MRI data set was 10–15 min. Tracing and determination of the volumes of LV took 30–45 min.

**Data Reproducibility**

Table 2 shows the results of interobserver and intraobserver analysis for LVM, EF, EDV and ESV. Bias, limits of agreement (2 SD) and correlation coefficient \(r\) are calculated for 3DE using MRI as the reference. Intraobserver variability was generally lower than interobserver variability and the overall reproducibility was acceptable for 3DE.

**Left Ventricular Mass and Volumes by MRI and 3DE**

All the volumes calculated for left ventricle were normally distributed. Data on EDV, ESV and LVM

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**Table 2.** The results of Bland–Altman analysis for interobserver and intraobserver variability in 30 healthy children. The values are bias ± limits of agreement (2SD); \(r\)=correlation coefficient.

<table>
<thead>
<tr>
<th></th>
<th>LVM (g)</th>
<th>EF (%)</th>
<th>EDV (ml)</th>
<th>ESV (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intraobserver variability</strong></td>
<td>(0 \pm 3 \pm 15.6)</td>
<td>(-0.2 \pm 3.8)</td>
<td>(-1.0 \pm 13.0)</td>
<td>(-0.2 \pm 6.7)</td>
</tr>
<tr>
<td>(r)</td>
<td>0.93</td>
<td>0.43</td>
<td>0.92</td>
<td>0.85</td>
</tr>
<tr>
<td><strong>Interobserver variability</strong></td>
<td>(1.0 \pm 26.9)</td>
<td>(1.1 \pm 7.2)</td>
<td>(4.6 \pm 17.6)</td>
<td>(0.9 \pm 8.4)</td>
</tr>
<tr>
<td>(r)</td>
<td>0.79</td>
<td>0.28</td>
<td>0.83</td>
<td>0.82</td>
</tr>
</tbody>
</table>
results assessed by MRI and 3DE are summarized in Table 3.

**End diastolic volumes**

Three-dimensional echocardiography resulted in slightly higher end diastolic volumes than MRI. In agreement analysis between MRI and 3DE, the bias was $-0.15 \pm 19.6$ ml (Fig. 2), but this difference was not statistically significant ($P=0.1$). EDV/BSA was $54.2$ and $57.3$ ml/m² assessed by MRI and 3DE, and the respective correlation coefficients of EDV to BSA were $0.66$ and $0.83$.

**End systolic volume**

ESV/BSA was $22.1$ and $22.5$ ml/m² when assessed by MRI and 3DE, with the respective correlation coefficients being $0.74$ and $0.80$.

**LV mass**

LV mass assessed by MRI and 3DE correlated well with BSA (0.86 and 0.90, respectively), and the estimates

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**Table 3.** Left ventricular mass, volumes and indexes for systolic and diastolic function measured by MRI and 3DE in 30 healthy children aged 8–13 years. Results are compared by Student’s paired t-test.

<table>
<thead>
<tr>
<th></th>
<th>MRI</th>
<th>3DE</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVM (g)</td>
<td>74.4 (16.4)</td>
<td>75.3 (17.3)*</td>
<td>0.81</td>
</tr>
<tr>
<td>EDV (ml)</td>
<td>65.5 (15.5)</td>
<td>69.5 (15.0)*</td>
<td>0.80</td>
</tr>
<tr>
<td>ESV (ml)</td>
<td>26.8 (6.9)</td>
<td>27.3 (6.3)*</td>
<td>0.88</td>
</tr>
<tr>
<td>EF (%)</td>
<td>59.1 (3.8)</td>
<td>60.8 (1.8)*</td>
<td>0.20</td>
</tr>
<tr>
<td>SV (ml)</td>
<td>38.7 (9.3)</td>
<td>45.3 (12.3)†</td>
<td>0.67</td>
</tr>
<tr>
<td>LVM/EDV (g/ml)</td>
<td>1.2 (0.2)</td>
<td>1.1 (0.1)*</td>
<td></td>
</tr>
<tr>
<td>PER (ml/s)</td>
<td>-236.6 (52.9)</td>
<td>-169.6 (40.3)‡</td>
<td>0.49</td>
</tr>
<tr>
<td>PFR (ml/s)</td>
<td>215.0 (71.1)</td>
<td>215.9 (52.6)*</td>
<td>0.44</td>
</tr>
<tr>
<td>PFR/EDV (l/s)</td>
<td>3.4 (0.8)</td>
<td>3.1 (0.4)*</td>
<td></td>
</tr>
<tr>
<td>PFR/ESV (l/s)</td>
<td>8.5 (2.9)</td>
<td>8.0 (1.0)*</td>
<td></td>
</tr>
<tr>
<td>PFR/SV (l/s)</td>
<td>5.7 (1.2)</td>
<td>5.2 (0.7)†</td>
<td></td>
</tr>
<tr>
<td>Time to PFR (ms)</td>
<td>186.7 (29.1)</td>
<td>106.3 (18.6)‡</td>
<td></td>
</tr>
</tbody>
</table>

Values are mean (SD).

*ns.

‡$P \leq 0.001$, as compared to MRI.

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**Figure 2.** Bland–Altman agreement plots for estimation of left ventricular mass, ejection fraction, end diastolic volume and end systolic volume by three-dimensional echocardiography (3DE) in comparison with magnetic resonance imaging (MRI). The dotted line represents the mean difference (bias). Dashed lines represent $\pm 2$ SD from the mean between the two techniques.
obtained for LVM/BSA were 61·2 and 61·8 g/m², respectively. The LVM/EDV ratios averaged 1·1–1·2 g/ml by both methods.

**Systolic and Diastolic Function Assessed by Doppler, 3DE and MRI**

**Figure 3** shows a representative time-volume curve for LV estimated with 3DE. The different phases in ventricular volume changes are clearly seen in the curve. **Figure 4** shows the time-volume curves of 30 children estimated with 3DE (Fig. 4A) and MRI (Fig. 4B). The LV ejection phase took 48% of the heart cycle (0·35 s) in 3DE. The respective values for MRI were 43% and 0·24 s. The mean heart rate was 90 beats/min at the beginning of MRI examination, 80 beats/min at the end of MRI examination and 76 beats/min during 3DE scanning. The systolic and diastolic indexes calculated from time-volume data are presented in Table 3.

**Mitral inflow parameters**

The mean diameter of the mitral annulus was 2·3 (± 0·2) cm. The peak E and A waves were 1·0 (± 0·1) and 0·5 (± 0·09) m/s, respectively. The E/A ratio was 2·0 (± 0·4). The velocity time integral of E wave was 13·9 (± 1·7) cm, the velocity time integral of entire transmitial flow complex was 20·7 (± 2·8) cm and their ratio was 0·7 (± 0·03). The time to peak E was 78·3 (± 7·2) ms, and the time from peak E to baseline was 128·6 (± 12·4). The isovolumetric relaxation time was 69·4 (± 8·2) ms. A correlation was found between Doppler peak filling rate and PFR \((r=0·67)\) and also between the diameter of mitral annulus and PFR \((r=0·77)\). In a linear regression model, including also heart rate and BSA, the effect of mitral annular diameter for PFR was significant \((P<0·05)\). PFR values and TPFR did not correlate significantly with other mitral inflow parameters.

**Discussion**

The results of this study demonstrate that 3DE and MRI are equally good methods for assessing left ventricular
Left Ventricular Volume Changes in Children

In our study, EDV, ESV and LVM determined by MRI and 3DE agreed closely and correlated well with BSA. Previously, in a 2DE study in healthy children, the mean EDV was assessed as 57 ml/m², ESV 20 ml/m² and LVM 60 g/m² [21]. In an angiographic study in children over 2 years of age, EDV was estimated to be 73 ml/m² [21]. In a group of healthy children and children 2–3 years after aortic coarctation repair, the mean results of the study subjects for LVM/BSA were 69 g/m² with MRI and 64 g/m² with 2DE [22]. The LVM/EDV ratio was 1.2 g/ml in children over 7 years of age [23]. Left ventricular volumes and mass have not previously been defined by 3DE in children. However, MRI has been shown to be capable of accurate and reproducible measurement of right [24] and left [25] ventricular volumes. The good correlation of our data with MRI and 3DE, and with the very similar results published earlier, are evidence that 3DE is an accurate method for studying LV volumes and mass.

To our knowledge the present study is the first to provide time-volume data on LV by 3DE. Previously, left ventricular time-volume curves have been generated by MRI, radionuclide angiography [7,8] and magnetic resonance velocity mapping [26]. Accurate determination of PER and PFR requires a temporal resolution of less than 40 ms/frame [27]. In this study the temporal resolution was 50 ms in MRI examination (9–17 time points during the heart cycle). In 3DE examination the temporal resolution was on average 13 ms, corresponding to 41–71 frames during the heart cycle. Representative time-volume curves were produced from 3DE and MRI data on 30 children, and the different phases in ventricular volume changes were seen clearly.

We calculated indexes for left ventricular ejection and filling from both 3DE and MRI time-volume data. PFR values were equal with both methods, also with normalization for EDV and ESV. The mean PFR/EDV values by 3DE and MRI were 3.1 and 3.4 l/s, corresponding to the values in healthy adults in MRI and radionuclide angiography studies (2.6–3.4 l/s) [27–30]. In those studies TPFR varied between 139–160 ms. In our study in children, TPFR values by 3DE and MRI were 106 and 186 ms, respectively. The higher PER, shorter ejection time and significantly longer TPFR seen in MRI could be due to the higher heart rate during the MRI examination. The heart rate dependency of PER, PFR and TPFR has previously been shown in radionuclide angiography and angiography [8]. The higher heart rate was probably caused by the excitement and frequent breath holdings needed during the image acquisition.

The time-volume data obtained by MRI and radionuclide ventriculography have been used to evaluate right and left ventricular diastolic function in patients with hypertrophic and dilated cardiomyopathy [7,28,29]. With the use of these techniques, abnormal filling is demonstrated by reduced PFR, prolonged TPFR and increased contribution of atrial systole to left ventricular filling [31]. The most commonly used method in assessing left ventricular filling is Doppler echocardiographic analysis of transmitral flow. The relation between Doppler echocardiography and data from time-volume curves is still unclear. A good correlation between the deceleration of early Doppler diastolic flow and the radionuclide peak filling rate (r=0.79) and between the E/A ratio by Doppler and ratio of early to atrial filling (r=0.76) was found in a radionuclide study [32]. However, another study could detect no such correlation [33]. A similar relationship has been reported for PFR with contrast angiography and Doppler (r=0.87) [34]. We did find a moderate correlation between PFR with 3DE and Doppler peak filling rate (r=0.67). However, the results of Doppler echocardiography of mitral inflow are influenced by technical problems, such as sample volume positioning, and anatomical conditions, such as the size of the mitral annulus. In the future, the accurate and rapid volumetric estimation of LV filling in diastole may become the standard method for studying diastolic function.

In the MRI examination, the major limiting factors in young children are the need for breath holding and the long image acquisition time. However, in our study the youngest children were 8 years old and they co-operated well. Reconstruction of time volume curves involves manual tracing of images, which is time-consuming as in 3DE image analysis. As seen also in this study (Fig. 4B), MRI does not provide data during late diastole [25].

Despite this, it is obvious that, especially in patients with a poor echocardiographic window, MRI represents a valuable method for estimating LV cyclic volume changes.

Digitized transthoracic 3DE is a new, non-invasive method to assess LV function. The scanning is easy to perform at the bedside and the scanning time is short enough to study even children younger than evaluated in the present study. Our results for variability and reproducibility are acceptable, and they are close to those obtained in previous 3DE studies of left ventricle [14,35,36]. Ignoring respiratory gating during 3DE, image acquisition may affect the interpretation of the results in this study and the comparison of results gained in studies using different methodologies. The major limiting factor in clinical practice is the time needed for manual tracing of images. In our study, determining the 55 (range 41–71) instantaneous LV volumes during the heart cycle took on average 45 min per patient. The 2DE data of our study (not presented) correlated well with 3DE and MRI data in these healthy children, again confirming the value of 2DE as rapid basic method in assessing LV volumes in children. True real-time 3DE image acquisition will be needed before this new technique will gain widespread clinical acceptance. The method also awaits further validation in patients with distorted ventricles.

In conclusion, 3DE and MRI were found to be practical methods of studying LV volumes and function in children. The clinical value of accurately measuring
LV volume changes during the heart cycle will soon be evaluated in studies with patient groups. The experience gained during this study indicates that 3DE is a noteworthy alternative to MRI even today, owing to its easier image acquisition possibilities. Further improvements in technology will undoubtedly increase the role of 3DE as a routine tool in cardiological diagnosis in children and in adults.

Acknowledgement

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References


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