Comparing knowledge-based 3D Reconstruction to Conventional MRI Algorithms Measuring Left Cardiac Chamber Volumes in Pediatrics

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Research Article

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Abstract

Objectives: Compare accuracy of 3D knowledge-based reconstruction (3D KBR) algorithm to standard measurement of left atrial (LA) and left ventricle (LV) volumes.

Background: Accurate measurement of LV and LA volume is essential in assessing cardiac function. Cardiac magnetic resonance imaging (CMR) is the gold standard, but analysis is relatively time consuming. Our study compared analysis time and agreement of 3D KBR algorithm to conventional CMR.

Methods: CMR studies of children aged 3-17 years with iron-overload were analyzed. DiCOM data was uploaded into the 3D KBR software calculated the LA and LV volumes in end systole and diastole, and ejection fraction. LA volumes were calculated using biplane method. LV measurements were calculated using Simpson's method (using a short axis stack) (SAX) technique. These methods were compared using intraclass coefficients (ICC) and Bland-Altman plots.

Results: 71 CMR studies of 31 patients were analyzed. No mean bias between SAX and VMS (Ventripoint software) measurement of LV end diastolic volume (EDV), biplane and VMS measurements of LA end systolic volume (ESV) or LA EDV were found. A small positive bias in VMS LV ESV; with moderate agreement in LV EDV, LA ESV and LV ejection fraction (EF)/ LA EF and wider limits of agreement in LV ESV and LA EDV. Excellent correlation between SAX and VMS in measuring LV volumes, biplane and VMS LA volumes. Interobserver agreement for VMS LV and LA volumes were excellent. VMS LV analysis time was 2.43 min and VMS LA analysis time was 1.46 min.

Conclusion: 3DKBR offers a time efficient alternative with comparable accuracy to the current LV and LA measurements used in clinical practice.

1. Introduction

Accurate measurement of cardiac chamber volumes is essential to determine cardiac function in children. Left ventricular (LV) volume and function provides important information that aids diagnosis and prognostication in a variety of clinical conditions[1-4]: Left atrial enlargement (LAE) is an important indicator of diastolic dysfunction due to congenital or acquired left heart disease, volume overload due to left to right shunting, a marker of severity of mitral stenosis and regurgitation, and a risk factor for atrial arrhythmias[5-7].

Cardiac MRI (CMR) has been used and validated for measurement of cardiac chamber volumes and ejection/emptying fractions in pediatric populations[8], and normal reference values for the pediatric population exist⁶. CMR is also currently considered the reference standard in both pediatric and adult populations in measuring cardiac chamber volumes. However, the current short axis stack algorithm for measuring cardiac chambers is often labor intensive, time consuming and requires specialized software and expertise for its use. In a study by Child and colleagues, the time for short axis analysis of LV
volumes was nearly 9 minutes by an experienced reader, and over 13 minutes by a less experienced reader. These were adult healthy volunteers and patients referred for clinical assessment[9].

Ventricpoint medical system software (VMS+ 3.0), (Ventricpoint Diagnostics Ltd., Toronto ON), contains a knowledge-based reconstruction (KBR) piecewise smooth subdivision surface algorithm which utilizes an MRI-derived catalogue of heart datasets to reconstruct a unique cardiac chamber rendering for each patient. Unlike other software, the VMS software includes specific algorithms for all four cardiac chambers. VMS has been previously validated for right and left ventricular volume measurements using a proprietary console in echocardiography[10, 11]. The most recent VMS software released enables import of 3-dimensional CMR and echocardiography derived DICOM datasets, enabling VMS measurement of cardiac chambers from CMR. We hypothesized that this would offer an alternative volumetric measurement technique for cardiac chambers using a semiautomated software algorithm with accuracy comparable to conventional MRI methods and reduced time for analysis. The aim of our study was to compare a 3D reconstruction algorithm software (VMS) to conventional CMR LV and LA volumetric measurement.

2. Methods

Cardiac MRI studies of consecutively examined patients aged 3 to 17 years with iron overload who were followed at our cardiac center were retrospectively collected and analyzed. Many of the patients had serial CMR at different ages as part of their surveillance for iron overload. Age, height, weight, and BSA were recorded at the time the MRI study was completed. Ethics approval at our institution was obtained prior to commencing this project.

2.1 CMR acquisition protocol:

CMR examinations were performed using a 1.5 Tesla Scanner (Avanto; Siemens Medical Systems, Erlangen, Germany) following a standardized protocol, which included a short axis (SA) cine stack for ventricular volume measurements. The SA cine stack was acquired using a steady state free precession technique during multiple breath holds with a temporal resolution adjusted to allow for 25 true phases per cardiac cycle, slice thickness 7 mm, 10-12 slices, gap adjusted to cover both ventricles. Using similar settings cine two (2C), three (3C) and four chamber (4C) views were acquired.

2.2 Conventional CMR analysis:

The images were analyzed using commercially available software (CMR 42; Circle Cardiovascular Imaging Inc, Calgary, Canada). The LV volumetric data were extracted from the cine short-axis stack by contouring the endocardial borders as per routine clinical practice. LA measurements were calculated from the standard 2C, 3C, and 4C CMR cine sequences. LA maximum end-systolic and diastolic diameters and areas were measured. LA volume analysis included delineation of the atrial endocardial
borders, including atrial appendage, in all planes in end systolic and diastolic cardiac phases. The biplane area-length method was also used to measure LA end systolic volume (ESV) and end diastolic volume (EDV)[12]. The following were formula used to calculate LAEF; Stroke volume (SV) = ESV-ESV, and ejection fraction (EF) = SV/EDV x 100%. The atrial appendage was included while pulmonary veins excluded when measuring LA volumes.

2.3 Ventripoint (VMS) CMR analysis:
CMR DICOMs were imported to VMS software from cine images acquired from 2C, 3C and 4C views. Reference points for each of LA and LV chamber’s walls, aortic valve (AoV), and mitral valve (MV) were placed on these images as per the VMS protocol at both end systole and end diastole. The software generates a KBR-derived ESV and EDV and ejection fraction for each chamber (figure 1, figure 2). The time taken to complete LA and LV volume VMS analysis, and LA biplane analysis was recorded.

2.4 LV and LA analysis time:
We used published analysis time by Child et al for SAX of LV volumes that had a mean (SD) of 8:42 (4:38) minutes by an experienced reader, and 13:08 (7:14) minutes by less experienced reader; for comparison to VMS LV time analysis[10]. Difference in mean analysis time for VMS and biplane LA measures was tested using a paired t-test (n paired=15). Differences in mean analysis time was tested using a non-paired t-test for VMS vs Childs et al. paper (LV measures (n VMS=71, n Child’s=46) for both less experienced and more experienced readers.

2.5 Statistical Methods:
Data are presented as means and standard deviation (SD) for LA and LV volumes and EF, and 95% confidence intervals. All analyses were performed using GraphPad Prism 9.3.1 (GraphPad Software, San Diego, CA). Students T-test and p-values measured the difference in analysis time between VMS and SAX. Linear regression models and intraclass correlation coefficient (ICC) were used to compare the different methods of measurement of LV and LA systolic and diastolic volumes, LV EF and LA ejection fractions. Intraclass coefficient was measured for interobserver variability for VMS and biplane and triplane methods in 22% of the CMR studies.

3. Results
3.1 Population:
Seventy-one CMR studies (n=71) performed in thirty-one patients (age 3-17 years) who were serially followed for iron overload were included in the analysis. The serial CMR studies for each subject used in
this study ranged from 1 up to 6; with the majority having between 1 (38.7%), 2 (19.3%) or 3 (16%) studies. Of the subjects, 13 (42%) were female and 18 (58%) were male. The mean (SD) height, weight, and body surface area (BSA) were 142 (16.6) cm, 38.3 (14.1) kg, and 1.22 (0.288) kg/m² respectively. The majority had either beta thalassemia (10, 32.2%) or sickle cell disease (18, 58%), while 2 had Diamond Blackfan anemia and 1 aplastic anemia. The population characteristics are outlined in Table 1.

### 3.2 Reliability and agreement:

LV Volumes: There was no mean bias between SAX and VMS measurement of LVEDV (mean difference -0.84% (95% CI -2.7, 1.09), with 95% of values falling within a 17% range of variation. There was a small bias in mean LVESV (6.94%, (95% CI 6.47, 13.4), with 95% of values falling within 35% to -20% range of variation. There was excellent correlation in SAX and VMS LV volumes (LVEDV ICC 0.97 (95% CI 0.96, 0.98); LVESV ICC 0.92 (95% CI 0.86, 0.95)).

LA Volumes: There was no mean bias between Biplane and VMS measurements of LAESV (mean difference -1.67% (95% CI -0.36, -3.0) or LAEDV (mean difference -1.36 (95% CI -2.2, -0.54) , with 95% of LAESV values within a 20% range, and 95% of LAEDV values within an 18% range. There was excellent correlation in mean LA volumes between biplane and VMS (LAESV ICC 0.96 (95% CI 093, 0.97); LAEDV ICC 0.93 (95% CI 0.87, 0.96)). The results are presented in Figures 2, 3 and 4.

### 3.3 Analysis of time spent contouring/Efficiency:

Average analysis time using VMS for LV / VMS and Biplane for LA are presented in Table 3.

LV analysis time of VMS vs SAX analysis time (using Childs et al.’s reported “less experienced” analysis time data reported above) had an estimated difference of 10.56 minutes (95% CI 8.32, 12.82). The analysis time for LV analysis (VMS Vs SAX) estimated difference was 6.13 minutes (95% CI 4.68, 7.58) For the LA analysis time, the estimated difference between VMS and BP for the LA analysis was 0.2 minutes (95% CI -0.06, 0.45). The results are reported in Table 3.

### 3.4 Reproducibility:

Inter-observer Agreement (IOA): We used a two-way agreement model with 95% confidence interval to report IOA. Initial assessment was completed by AA (fellow) and IOA agreement was off 22% of the CMR studies (n=16) was completed by JW (attending with 10 years’ imaging experience) There was excellent IOA for VMS LA and LV volumes (LVEDV ICC 0.95 (95% CI 0.1, 0.99), LVESV 0.97 (0.84, 0.99); LAESV ICC 0.96 (95% CI 0.42,0.99), LAEDV ICC 0.94 (0.73, 0.98)). There was also excellent IOA for BP LA volumes (LAEDV ICC 0.95 (95% CI 0.88, 0.98, LAESV 0.98 (0.91, 0.99)). Results are represented in Table 5.
LA and LV ejection fraction reliability and reproducibility: The LVEF bias when comparing VMS to SAX was 2.34% with SD of 4.1%. While the LAEF bias was 1.71% with a SD of 9.94% when comparing VMS to BP method. There was modest correlation between VMS and SAX in measuring LVEF with ICC of 0.58 (95% CI 0.31, 0.75). There was also modest correlation between VMS and BP in measuring LAEF with ICC of 0.55 (95% CI of 0.36, 0.7). The inter-observer agreement was modest in measuring LAEF in both VMS and BP methods with VMS ICC of 0.77 (CI 0.32, 0.92) and BP ICC of 0.78 (95% CI 0.49, 0.92). For the VMS LVEF, the IOA was also modest with an ICC of 0.64 (95% CI 0.21, 0.86). Results are represented in Tables 3 and 4 and Figure 6.

4. Discussion

CMR is an important tool in risk stratification, pre-procedural planning, and assessment of treatment in pediatric and adult cardiac populations[13]. In pathologies such as Tetralogy of Fallot, CMR has become an integral part of the longitudinal follow up. CMR derived measures of RV dilation with LV or RV dysfunction have been shown to predict adverse outcomes[14]. CMR is gradually becoming an alternative to cardiac catheterization in assessing anatomic and functional information in single ventricle pathologies, particularly in the pre-bidirectional Glenn evaluation[13-15]. Unfortunately, current conventional CMR volumetric analysis is usually time consuming[9].

This study, to the best of our knowledge, is the first to compare VMS software to conventional CMR methods in measuring left cardiac chambers. The technique has been used previously in assessing RV volumes in patients after the arterial switch operation for dextro-transposition of the great arteries. RV volumes were assessed using both KBR and Simpson's method. Good correlation between KBR and Simpson's method was noted and the intraobserver and interobserver variability for KBR showed excellent agreement [10]. CMR is considered the reference standard imaging technique for volumetric analysis; here we provide an alternative software algorithm to that currently available, with comparable accuracy in measuring left cardiac chambers that is significantly less time consuming compared to current modalities. This is especially important in reporting clinically relevant CMR volumetric results in a timely fashion.

Software such as VMS offers a tool to analyze LV volumes that is as accurate but also more time-efficient than what is currently commonly used. In our comparison of the time difference for analysis, LV volume analysis using VMS was 6.13 to 10.56 minutes faster than the standard SAX analysis. We acknowledge that this should be interpreted with caution given studies were performed on two different cohorts and by different investigators. In measurement of the LA, VMS is systematically larger than Biplane, However, as biplane is not a 3D method in MRI, we have not really compared it with a gold standard, and that may be different than if comparison was with SAX for LA which is considered the gold standard[7]. Unfortunately, SAX LA stacks were not available in the datasets for comparison. With regards to ejection fraction, the two methods had only modest correlation and interobserver agreement in measuring LVEF and LAEF.
5. Limitations

Several significant limitations must be acknowledged. We did not prospectively re-measure LV volumes in SAX analysis but depended on the clinical report. That said, we did complete interobserver analysis and found that the measurements were reproducible, and previous studies have reported good reproducibility for the left ventricle using CMR[3, 9]. We used studies on patients who had iron overload, meaning that they did not all have normal volumes and function. This was by design, to provide a wider range of volumes indexed to BSA to test the analysis software, and the goal of this study was not to generate data on normal volumes of the heart by VMS.

We also had a relatively small number of patients with a narrower range of body surface areas and ages than in some pediatric studies and included repeated studies from the same patients who had CMR at different ages. Quality of CMR datasets is relatively independent of patient-related factors such as body habitus and sex, so it is unlikely that repeated studies would bias the data. Another limitation is that we did not directly measure time to analyze SAX LV volumetric analysis, as clinically reported values were used. We therefore compared VMS to previously published data. As these values were derived in different cohorts, there might be differences in quality of datasets, expertise of the readers or other factors which we cannot account for. It would have been interesting to compare LA volumetric analysis in SAX to VMS however these slices are not routinely acquired in clinical studies.

6. Conclusions

Ventripoint software offers a time efficient alternative with comparable accuracy to the current standard algorithms used in clinical practice for measurement of LV and LA volumes derived from cardiac MRI.

7. Future Directions

Compare VMS to standard CMR methods for right sided structures and in patients with congenital heart disease.

Abbreviations

SD: standard deviation
min: minimum
max: maximum
BSA: body surface area
VMS: ventripoint software
SAX: short axis stacks
BP: biplane
TP: triplane
LV: left ventricle
LA: left atrium
EDV: end diastolic volume
ESV: end systolic volume
EF: ejection fraction
AoV: aortic valve
MV: Mitral valve
ICC: inter class correlation coefficient
IOA: interobserver agreement

Declarations

Funding:

Dr. Ahmad received a subspecialty resident Grant by Women's and Children's Health Research Institute (WCHRI).

References


Tables

Table 1: CMR study subject characteristics.
Demographics

<table>
<thead>
<tr>
<th>Total CMR studies (N=71)</th>
<th>Total patients (n=31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>18 (58%)</td>
</tr>
<tr>
<td>Female</td>
<td>13 (42%)</td>
</tr>
<tr>
<td>Height</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>142 (16.6)</td>
</tr>
<tr>
<td>Median [Min, Max]</td>
<td>142 [98.0, 174]</td>
</tr>
<tr>
<td>Weight</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>38.3 (14.1)</td>
</tr>
<tr>
<td>Median [Min, Max]</td>
<td>36.0 [15.0, 77.0]</td>
</tr>
<tr>
<td>BSA</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>1.22 (0.288)</td>
</tr>
<tr>
<td>Median [Min, Max]</td>
<td>1.20 [0.640, 1.85]</td>
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<tr>
<td>Diagnosis</td>
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<tr>
<td>Aplastic anemia</td>
<td>2 (6.4%)</td>
</tr>
<tr>
<td>Beta thalassemia</td>
<td>10 (32.2%)</td>
</tr>
<tr>
<td>Diamond Blackfan anemia</td>
<td>2 (6.4%)</td>
</tr>
<tr>
<td>Sickle cell disease</td>
<td>18 (58%)</td>
</tr>
</tbody>
</table>

SD: standard deviation, min: minimum, max: maximum, BSA: body surface area.

Table 2: LV and LA volumes and Ejection Fraction

<table>
<thead>
<tr>
<th>VMS mean (SD)</th>
<th>SAX mean (SD)</th>
<th>BP mean (SD)</th>
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</thead>
<tbody>
<tr>
<td>LVEDV /BSA</td>
<td>95.40 (20.92)</td>
<td>94.63 (20.92)</td>
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<tr>
<td>LVESV/BSA</td>
<td>50.70 (10.82)</td>
<td>38.07 (10.46)</td>
</tr>
<tr>
<td>LAESV/BSA</td>
<td>39.58 (11.52)</td>
<td></td>
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<tr>
<td>LAEDV/BSA</td>
<td>17.79 (9.49)</td>
<td>16.58 (6.28)</td>
</tr>
<tr>
<td>LVEF</td>
<td>57.5 (4.46)</td>
<td>59.9 (5.31)</td>
</tr>
<tr>
<td>LAEF</td>
<td>55.1 (4.63)</td>
<td>56.8 (6.71)</td>
</tr>
</tbody>
</table>


Table 3: Measurement times for LV and LA volume measurements.
<table>
<thead>
<tr>
<th></th>
<th>Mean (SD) minute</th>
<th>Median [Min, Max] minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>VMS LA</td>
<td>1.46 (0.198)</td>
<td>1.41 [1.23, 2.14]</td>
</tr>
<tr>
<td>BP LA</td>
<td>1.22 (0.326)</td>
<td>1.10 [1.00, 2.28]</td>
</tr>
<tr>
<td>VMS LV</td>
<td>2.43 (0.438)</td>
<td>2.33 [1.54, 4.09]</td>
</tr>
</tbody>
</table>

Mean, median and standard deviations presented. SD: standard deviation, min: minimum, max: maximum, VMS: ventripoint software, BP: biplane, LV: left ventricle, LA: left atrium

Tables 4-6 are not available with this version.

Table 4: Analysis of the time differences between different methods in measuring LA and LV volumes and ejection fractions.

Table 5: Inter-technique agreement for Ventripoint vs other methods for left cardiac chambers.

Table 6: Inter-observer Agreement for VMS, biplane and triplane in measuring left cardiac chambers.

**Figures**

Figure 1
Measurement of left atrial volume analysis using the Ventripoint software. Analysis of four (A), two (B) and three (C) four chamber views allows for reconstruction of the left atrial volume (D). Here shown in end-systole.

Figure 2

Measurement of left ventricular volume analysis using the Ventripoint software. Analysis of four (A), two (B) and three (C) four chamber views allows for reconstruction of the left ventricular volume (D). Here shown in end-diastole.

Figure 3

3a, 3b, and 3c: Scatterplots with y~x Regression Lines for LV measurements comparing ventripoint to SAX, and LA ventripoint to biplane, and triplane methods. solid line denotes a simple linear regression line. Dashed line is plotted at perfect agreement (y=x).
Figure 4.

Bland-Altman Plots for Ventripoint Agreement vs. short axis stack in measuring LV volumes. Solid line at exact agreement (difference = 0). Dashed lines at bias and limits of agreement (1.96 * SE), with shading around confidence intervals for these estimates.

Figure 5.

Bland-Altman Plots for Ventripoint Agreement vs. biplane in measuring LA volumes. Solid line at exact agreement (difference = 0). Dashed lines at bias and limits of agreement (1.96 * SE), with shading around
confidance intervals for these estimates.

Figure 6.

Bland-Altman Plots for Ventripoint Agreement vs. biplane in measuring LA ejection fraction and Ventripoint Vs. short axis stacks agreement in measuring LV ejection fraction. Solid line at exact agreement (difference = 0). Dashed lines at bias and limits of agreement (1.96 * SE), with shading around confidence intervals for these estimates.

Figure 6
Figure 7

Bland-Altman Plots for interobserver Agreement Ventripoint vs. biplane in measuring LA volume and Ventripoint Vs. short axis stacks agreement in measuring LV volume. Solid line at exact agreement (difference = 0). Dashed lines at bias and limits of agreement (1.96 * SE), with shading around confidence intervals for these estimates.