Cardiac MRI Volumetric Assessment by Short-Axis Orientation has Better Reproducibility than the Axial Orientation in Functionally Single Right Ventricle Hearts Prior to Bidirectional Cavopulmonary Anastomosis

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Abstract

Background: Cardiovascular Magnetic resonance imaging (CMR) is the standard for assessment of ventricular volumes and function. However, few reports exist regarding methodology for measurements of functionally single right ventricular (RV) volumes in congenital heart disease. This study aims to determine which imaging plane, the short axis oblique (SAO) or the axial orientation (AX), provides greater reproducibility in evaluation of RV volumes and function in patients with hypoplastic left heart syndrome (HLHS) prior to bidirectional cavopulmonary anastomosis (BCPA).

Methods: CMR was performed under general anesthesia in 23 patients (5 ± 3.4 months) with single RV prior to BCPA to obtain ventricular volumes from the axial and/or short-axis cine orientations. Post-processing (cmr42 - Circle Imaging, Calgary, Alberta) was performed by two independent observers to obtain end-diastolic (EDV), end-systolic (ESV) volumes and ejection fraction (EF) in both SAO (n=23) and AX (n=16) planes. Absolute differences (mean ± SD), repeatability values, intraclass correlation coefficients (ICC), coefficient of variation, and Bland Altman plots were used to assess the reproducibility between methods, and interobserver and intraobserver variability.

Results: Comparisons of SAO versus AX volumes revealed small absolute differences, with better repeatability for ESV (4.6 ml) compared to EDV (8.5 ml), and high agreement between the 2 methods. Interobserver variability showed high correlations and narrow limits of agreements for SAO and AX measured ESV. However, AX EDV had poorer repeatability (11 ml) and wider limits of agreement than SAO EDV (6.4 ml). Intraobserver testing showed higher correlations for all measurements, but SAO EDV (2.7 ml) showed better repeatability than AX EDV (5.7 ml).

Conclusion: CMR assessment of single RV volumes showed better inter and intraobserver reproducibility for the SAO than the AX methods suggesting that the addition of an axial stack does not provide any benefit over the short axis orientation in the assessment of single RV volumes and function.

Keywords
Single right ventricle; Hypoplastic left heart; Short-axis oblique orientation; Axial orientation Cardiovascular MRI

Abbreviations: LV: Left Ventricle; CMR: Cardiac Magnetic Resonance Imaging; Pre-BCPA: Pre-Bidirectional Cavopulmonary Anastomosis; SAO: Short-Axis Oblique Orientation; AX: Axial Orientation; ESV: End Systolic Volume; EDV: End Diastolic Volume

Background

Hypoplastic left heart syndrome is a congenital heart defect in which the left ventricle (LV) is underdeveloped and a single right ventricle (RV) supports both the pulmonary and systemic circulation [1]. There is a shift now from cardiac catheterization to Cardiovascular Magnetic Resonance Imaging (CMR) in the pre-operative evaluation of these patients prior to the second stage bidirectional cavopulmonary anastomosis (BCPA) surgery, where the success and outcome of BCPA depends on accurate preoperative anatomical and functional assessment, specifically RV ejection fraction (EF) [2-4]. Due to the complex, crescentic shape of the single RV, conventional echocardiographic methods for assessing normal biventricular hearts do not apply to the single RV [5]. CMR being non-invasive is able to evaluate the entire cardiac anatomy and is considered the gold standard for measuring ventricular volumes and function [6]. Unlike echocardiography, CMR is not limited by the complex geometry of the right ventricle [7]; furthermore, it is a reproducible method of assessment in various forms of congenital heart disease [8-13].

The accuracy and reproducibility of CMR measurements of ventricular volume, EF and mass have been demonstrated [9,14-16]. Two imaging planes are commonly used to determine volumetric function: the short axis oblique orientation (SAO) or the axial (transverse) orientation (AX). The SAO is typically obtained with the plane of imaging parallel to the plane of the mitral valve annulus and is the standard method for measuring LV volumes; whereas the AX is obtained with the plane of imaging perpendicular to the long axis of the body. The current literature shows conflicting data as to the ideal imaging orientation for measuring RV volumes [6,9,11,12]. While the AX method was found to be more reproducible for RV measurements in normal hearts [17], in a variety of congenital heart diseases [11], and corrected TOF [13], others have found no difference between the imaging planes [18]. While reference ranges for normal RV volumes are obtained from the SAO orientation, Alfakih et al. found lower intra- and interobserver variability in the AX compared to SAO [17]. Since ejection fraction (EF=(EDV-ESV)/EDV) is calculated from the volumetric measurements, accurate volume assessments in the single RV is vital as small errors in measurement may lead to large errors in EF in these small infants, which is important in the pre-BCPA assessment. To our knowledge, there are no reports about the best method, SAO or AX, for assessing RV volume and function, in the single RV hearts specifically at the pre-BCPA stage. Both orientation planes have distinct advantages; SAO has been validated in the LV, there is familiarity among observers, and in general has a shorter image acquisition time, which in turn is more comfortable for patients. When comparing with traditional SAO, the AX plane should not have the same difficulty in assessing the basal border of the RV as the SAO does; therefore, in theory eliminating error. Given these potential advantages, there is still no consensus or guidelines as to the best imaging plane for assessment of single RV function of structure. This study aims to determine which imaging plane, the
SAO or the AX is the most reproducible method to measure single RV volumes in HLHS patients at the pre-BCPA stage.

Methods

Study population

We performed a retrospective study of 23 patients with HLHS and its variants who had survived a prior Norwood procedure from 2007–2011 (age: 5 ± 3.4 months, weight: 5.3 ± 0.7 kg, 61% male). CMR was routinely performed prior to bidirectional cavopulmonary anastomosis (BCPA) procedure to evaluate the intracardiac and extracardiac anatomy, and ventricular function from a SAO stack. Among the 23 patients who had SAO stack, 16 of these patients had an additional AX stack performed to obtain further evaluation of anatomy at the discretion of the supervising physician. Exclusion criteria included incomplete CMR protocols or poor image quality. Studies were conducted at the Stollery Children’s Hospital, Edmonton, and the Alberta Children’s Hospital, Calgary, with all images analyzed at the Stollery Children’s Hospital. The Health Research Ethics Board at both institutions approved the study.

Cardiac magnetic resonance imaging

CMR studies were performed with the Siemens Sonata or Avanto 1.5 Tesla MRI scanner (Siemens Healthcare, Erlangen, Germany) with the patient intubated and ventilated under general anaesthesia, using a head coil for infants <4 kg and a 32 channel knee or thoracic coil if 4-10 kg, depending on the site of imaging. Standard protocol was applied to evaluate the cardiac anatomy and RV volumes and function. After a 2 and 4 chamber localizer, a contiguous short-axis stack was obtained with the plane of imaging parallel to the plane of the tricuspid valve annulus, using steady state free precession (echo time 1.5-1.8 ms, repetition time 3.0-3.6 ms, 22-30 phases, flip angle 56°, matrix size 192-256, field of view (155-225) × (123-256) mm², time 1.5-1.8 ms, repetition time 3.0–3.6 ms, 22-30 phases, flip angle function. After a 2 and 4 chamber localizer, a contiguous short-axis stack was obtained with the plane of imaging parallel to the plane of the tricuspid valve annulus, using steady state free precession (echo time 1.5-1.8 ms, repetition time 3.0-3.6 ms, 22-30 phases, flip angle 56°, matrix size 192-256, field of view (155-225) × (123-256) mm², slice thickness 5 mm, 10% gap, and 3–4 averages). Axial stacks were performed perpendicular to the long axis of the body from just below the diaphragm to the pulmonary artery bifurcation.

Image analysis

CMR volumetric analysis was performed offline using cmr42 software (Circle Cardiovascular Imaging, Calgary, Alberta, Canada) by 2 independent observers. A medical student (observer 1) received instruction on the anatomy of normal and single ventricular hearts by a cardiologist experienced in CMR (observer 2), and then was trained in post processing analysis on 15 normal biventricular hearts first. Then 8 practice cases of functionally single ventricle at other surgical stages were analyzed. After achieving competence in the analysis, 5 cases of single ventricles at other surgical stages were analyzed by both observers where the difference in volumes between them was ≤ 10%. Analysis of study patients commenced after the preceding training protocol. For a given patient, analysis of the short axis and axial images were performed at different times so that each observer did not recall the results during analysis. Intraobserver variability was examined by observer 1 reanalyzing 10 randomly selected studies after a minimum of 14 days.

The method of volumetric assessment was standardized as described: By scrolling through a mid-ventricular slice, the end-diastolic (largest volume) and end-systolic (smallest volume) phases were selected and marked. Endocardial and epicardial borders were then manually traced in each ventricular slice where there was myocardium, to obtain end-diastolic volume (EDV) and end-systolic volume (ESV). The individual phase selection for EDV and ESV of both observers was also noted. The cmr42 software displays a reference image in a plane perpendicular to the slice in view, which aids in determining ventricular margins from the plane of the tricuspid valve to the right ventricular outflow tract (Figure 1) [19]. Slices were considered to be in the atrium, and thus excluded, if the myocardial wall was thin and did not thicken in systole. Using the principle of conservation of mass, the observer reviewed, and if necessary, revised the contours, ensuring that the myocardial mass difference was <10% between end-diastolic and end-systolic phases. Ventricular septal muscle was included in the right ventricular mass measurements. However, papillary muscles were excluded from ventricular myocardial mass measurements and included in the blood pool and thus volume measurements. Due to the highly trabeculated systemic right ventricle, we pre-determined that if 2 or less trabeculations were present they would be included in the blood pool. However, if 3 or more trabeculations were present, then contours were drawn through the middle of the trabeculations, such that half were included in the volume and half in the mass measurements. The ‘middle’ is defined as the mid-way point between the base of the trabeculation at the endocardium and the tip of the trabeculae extending into the blood pool. Semi-automated contouring option was not utilized as the software is designed for a normal RV. EF was calculated as (EDV-ESV)/EDV and expressed as a percentage. RV mass was not reported as it is not used in decision making when assessing suitability for BCPA.

Statistical methods

Volumetric data was expressed as mean and standard deviation. Shapiro-Wilk test was conducted on the volumetric data to assess for normal distribution. The interobserver and intraobserver variability of EDV, ESV and EF, as well as differences between SAO and AX measured mean EDV, ESV and EF were assessed using the absolute difference (mean difference ± SD of the difference), 1.96 × within subject SD, repeatability (2.77 × within subject standard deviation), limits of agreement, coefficient of variation (standard deviation of the difference of the 2 measurements divided by the mean of the 2 measurements, %), intra-class correlation coefficients, and Bland-Altman analysis [20,21]. Student’s t-test was performed to see if the calculated Bland-Altman biases were significantly different from zero. The effect of phase selection on the volumetric results between the two observers was also assessed by comparison of volumes from the same phase versus those measured from different phases using absolute differences and paired t-tests.

Results

Of the 23 patients who underwent CMR, all had a SAO stack, and 16 of them had an AX stack performed resulting in a total of 78 volumetric assessments between both observers. Studies contained a range of 8-13 slices and 22-30 phases. The results of EDV, ESV and EF for both observers are displayed in Table 1.

SAO vs. AX

Comparisons of SAO versus AX volumes revealed small absolute differences between ESV and EDV (2.8 ± 1.5 ml and 2.8 ± 1.9 ml, respectively), with better repeatability for ESV (4.6 ml) compared to EDV (8.5 ml). EF showed small absolute differences (6.2 ± 4.4%) but poorer repeatability (12.4%) and wider limits of agreement (−14.3 to 7.5). (Table 2) The SAO and AX methods showed high ICC for EDV, ESV and EF (0.92, 0.97, 0.82, respectively) indicating a high agreement.
between the 2 methods, and providing some internal validation for our volume analysis. Shapiro-Wilk test demonstrated p value 0.074 and 0.061 for SAO and AX respectively, both greater than the alpha of 0.05; therefore, normal distribution of data cannot be rejected.

**Interobserver variability**

Measurements of EDV between observers showed a smaller absolute difference and narrower limits of agreement in the SAO (2.2 ± 2.4 ml, C.I: -7.1 – 5.6 ml) compared to the AX method (4.2 ± 3.9 ml C.I: -12.4 – 5.5 ml) (Figure 2). ICC for SAO measured EDV (0.92) showed good correlation, but AX EDV (0.64) showed only a moderate correlation between observers. For ESV and EF, the interobserver variability was similar for both methods, with good correlation between observers. Repeatability for SAO EDV (6.4 ml), SAO ESV (3.2 ml), and AX ESV (3.5 ml) were good, however AX EDV had poorer repeatability (11 ml) (Table 3). The Bland-Altman plots for interobserver variability are displayed in Figure 2, showing the mean difference and limits of agreements for EDV, ESV and EF. It can be seen from the graphs that the SAO EDV had narrower limits of agreement than AX EDV (C.I: -7.1 – 5.6 ml and -12.4-5.5 ml, respectively). Student t-test of the bias significance for SAO EDV, ESV, and EF showed p=0.39, 0.35, and 0.17 while AX values were p=0.008, 0.47, and 0.22, respectively.

**Intraobserver variability**

Intraobserver variability demonstrated smaller absolute differences for SAO derived EDV (1.1 ± 0.9 ml) and ESV (1.2 ± 0.6 ml), and AX ESV (1.5 ± 1.0 ml) compared to AX EDV (2.3 ± 1.9 ml). Although all showed good intraclass correlations, the SAO had better ICC values for EDV (0.96) when compared to AX method EDV (0.88). Limits of agreement were narrow for all measurements except AX EDV (C.I: -6.6-3.0 ml) (Figure 3). Repeatability for SAO EDV (2.7 ml), SAO ESV (2.7 ml), and AX ESV (3.5 ml) were good, however AX EDV had significantly poorer repeatability (5.7 ml). (Table 4) Bland-Altman plots for intraobserver variability are shown in Figure 3. Student t-test of the bias significance for SAO EDV, ESV, and EF showed p=0.40, 0.77, and 0.38 while AX values were p=0.27, 0.30, and 0.38, respectively.

**Effect of phase selection**

Out of a total of 78 volumetric measurements, observers selected the same phase 42% of the time (Table 5). Phase selection differed by 1 in 35%, by 2 in 13% and by 3-4 phases in 10% of the measurements. Thus 77% of the analyses were performed with 0-1 phase difference between observers. When examining the volumetric data for studies examined within the same phase, compared with analyses ≥ 1 phase difference between observers, there were no significant differences between the mean...
EDV and ESV, or absolute differences by SAO or AX methods. As seen in Table 5, choosing a different phase for analysis did not account for larger differences in volumetric or EF results. It can also be seen that differences in volumes and EF was seen whether there was a phase difference or not.

### Discussion

The results of this study show that although the SAO and AX methods were highly correlated, the SAO method demonstrated lower intraobserver variability and interobserver variability for EDV, compared to the AX method in the evaluation of single RV volumes.
Table 3: Interobserver variability.

<table>
<thead>
<tr>
<th>Variable</th>
<th>SAO (n=23)</th>
<th>AX (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDV (ml)</td>
<td>2.2 ± 2.4</td>
<td>4.2 ± 3.9</td>
</tr>
<tr>
<td>ESV (ml)</td>
<td>1.2 ± 1.1</td>
<td>1.2 ± 1.0</td>
</tr>
<tr>
<td>EF (%)</td>
<td>6.2 ± 4.5</td>
<td>6.4 ± 4.0</td>
</tr>
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<table>
<thead>
<tr>
<th> </th>
<th>Absolute difference Mean ± SD</th>
<th>1.96 x within subject SD</th>
<th>Repeatability</th>
<th>Limits of Agreement</th>
<th>Coefficient of variation</th>
<th>ICC (R)</th>
</tr>
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<tbody>
<tr>
<td>EDV (ml)</td>
<td>2.2 ± 2.4</td>
<td>4.5</td>
<td>6.4</td>
<td>-7.1 – 5.6</td>
<td>8.0</td>
<td>0.92</td>
</tr>
<tr>
<td>ESV (ml)</td>
<td>1.2 ± 1.1</td>
<td>2.3</td>
<td>3.2</td>
<td>-3.6 – 2.2</td>
<td>8.0</td>
<td>0.97</td>
</tr>
<tr>
<td>EF (%)</td>
<td>6.2 ± 4.5</td>
<td>10.6</td>
<td>15</td>
<td>-17 – 9.5</td>
<td>8.2</td>
<td>0.92</td>
</tr>
</tbody>
</table>

Figure 2: Interobserver variability showing the Bland Altman analysis between observers. The dashed line indicates the mean difference, and dotted lines indicate 95% limits of agreement.


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Table 4: Intraobserver variability.

<table>
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<tr>
<th></th>
<th>n=10</th>
<th>Absolute difference Mean ± SD</th>
<th>1.96 x within subject SD</th>
<th>Repeatability</th>
<th>Limits of Agreement</th>
<th>Coefficient of variation</th>
<th>ICC (R)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>SAO</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>EDV (ml)</td>
<td>1.1 ± 0.9</td>
<td>1.9</td>
<td>2.7</td>
<td>-3.2 – 2.0</td>
<td>2.0</td>
<td>0.96</td>
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<tr>
<td>ESV (ml)</td>
<td>1.2 ± 0.6</td>
<td>1.9</td>
<td>2.7</td>
<td>-3.2 – 1.8</td>
<td>2.9</td>
<td>0.96</td>
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<tr>
<td>EF (%)</td>
<td>3.6 ± 2.7</td>
<td>6.1</td>
<td>8.6</td>
<td>-7.0 – 10.0</td>
<td>4.4</td>
<td>0.92</td>
<td></td>
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<tr>
<td>AX</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>EDV (ml)</td>
<td>2.3 ± 1.9</td>
<td>4.1</td>
<td>5.7</td>
<td>-6.6 – 3.0</td>
<td>4.4</td>
<td>0.88</td>
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<tr>
<td>ESV (ml)</td>
<td>1.5 ± 1.0</td>
<td>2.5</td>
<td>3.5</td>
<td>-3.7 – 0.9</td>
<td>3.8</td>
<td>0.95</td>
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<tr>
<td>EF (%)</td>
<td>2.3 ± 3.0</td>
<td>5.1</td>
<td>7.2</td>
<td>-5.0 – 8.5</td>
<td>4.2</td>
<td>0.95</td>
<td></td>
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Figure 3: Intraobserver variability showing the Bland Altman analysis for observer 1. The dashed line indicates the mean difference, and dotted lines indicate 95% limits of agreement.
Table 5: Effect of phase selection on volumetric data.

<table>
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<th>Method</th>
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<th>≥ 1 phase difference</th>
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<td></td>
<td></td>
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<tr>
<td>EDV (ml)</td>
<td>32.7 ± 9.6</td>
<td>28.3 ± 7.1</td>
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<tr>
<td></td>
<td>1.9 ± 1.7</td>
<td>2.5 ± 2.9</td>
</tr>
<tr>
<td>ESV (ml)</td>
<td>12.7 ± 1.7</td>
<td>15.0 ± 6.0</td>
</tr>
<tr>
<td></td>
<td>1.5 ± 1.4</td>
<td>1.0 ± 0.9</td>
</tr>
<tr>
<td>EF (%)</td>
<td>52 ± 4</td>
<td>58 ± 2</td>
</tr>
<tr>
<td></td>
<td>6.3 ± 6.8</td>
<td>6.2 ± 3.5</td>
</tr>
<tr>
<td><strong>AX</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EDV (ml)</td>
<td>31.4 ± 6.8</td>
<td>28.1 ± 6.5</td>
</tr>
<tr>
<td></td>
<td>5.1 ± 5.4</td>
<td>3.5 ± 2.2</td>
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<tr>
<td>ESV (ml)</td>
<td>12.1 ± 6.7</td>
<td>13.1 ± 4.1</td>
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<tr>
<td></td>
<td>1.3 ± 1.1</td>
<td>1.6 ± 1.0</td>
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<tr>
<td>EF (%)</td>
<td>60 ± 4</td>
<td>54 ± 1</td>
</tr>
<tr>
<td></td>
<td>5.2 ± 2.8</td>
<td>7.1 ± 4.5</td>
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</table>

and function prior to BCPA. Previous studies that examined the interobserver and intraobserver reproducibility of the AX versus SAO have focused on adults with biventricular hearts, with relatively fewer studies in congenital heart defects, and even less data in young infants with functionally single ventricles. While Luijnenburg et al. assessed all types of congenital heart disease (CHD), their study only included 3 subjects with a single RV [13]. Margossian et al. examined the reproducibility of MRI measurements in a large population of older single ventricle Fontan patients, however only 15 of these included a single RV [10].

Although previous studies advocate the AX orientation for RV measurements, these have all been described in biventricular hearts, where planning for ventricular volumes is aligned to the plane of the LV, not the RV, and when the RV happens to be within the imaging field [11,12,17]. In comparison, when planning the SAO stack in a single RV, the imaging slice is aligned exactly parallel to the plane of the tricuspid annulus and the stack continues along the long-axis plane of the RV, perpendicular to the tricuspid annulus, resulting in a true RV volumetric short-axis stack. The difficulty in identifying the basal boundary has been cited as a limitation of the SAO orientation [11,17]. This difficulty is overcome by analysis software which displays a reference image (Figure 1) [19], and has been used by us and others [9,11,22] to facilitate delineation of the atrio-ventricular boundary by identifying the tricuspid valve plane, eliminating a large source of potential error as the basal slice constitutes a large area of volume. Comparatively, in the AX orientation the tricuspid valve lies obliquely; therefore appears on two slices and selection of which slice to include in the RV analysis could be a contributing source of variability in the AX method. The oblique nature of the captured images, compounded by a significant outlier, may also be contributing to a fixed bias of the interobserver AX EDV calculations (p<0.05); however, this is not seen in other AX analysis. Furthermore, the AX orientation has been advocated as a preferred method because it is easy to plan, and can be performed without any understanding of the anatomy [12]. However, accurate planning of the SAO stack requires knowledge and understanding of the anatomy, which may be a pitfall of previous studies that favor the AX method due to unfamiliarity with the anatomy of complex forms of congenital heart disease. Furthermore, our images were obtained using free-breathing technique as per our institution protocol, which we have not found to alter image quality. Although this may decrease the image quality and accuracy, Valsangiacomo et al. have demonstrated that contour tracing was not impeded in free-breathing normal children of all ages [23].

Our interobserver and intraobserver reproducibility was generally better for ESV than EDV measurements. This is in contrast to previous studies reporting higher variation in the ESV than EDV in both LV and RV [9,13,24-27]. This finding, as well as our narrower limits of agreement compared to previous studies, is likely due to the ventricular volumes being smaller in small infants and therefore a smaller absolute error. However, when dealing with small infants, even small changes in ventricular volumes make a substantial difference in whether a ventricle is considered normal or dilated. For example, although a 3 ml volume difference in an adult heart may still be within the margin of measurement error, a 3 ml difference in our subjects would represent a 10% change in EDV, and a 5% change in EF.

As expected, EF between observers was highly correlated; however, the reproducibility was poor with wider limits of agreement. A 1.96 x within subject SD of 10% implies that the difference in the subject’s EF from the true measurement is less than 10% for 95% of observations, and 15% repeatability implies that the difference between 2 measurements of EF is expected to be less than 15%, in 95% of the measurements [20,21]. Thus despite the high correlations of single RV volumes and EF, the variability in EF and wide limits of agreement seem unacceptably wide. This is particularly important when ventricular dysfunction, being a risk factor for worse outcome in single ventricle, impacts on risk stratification and timing of BCPA [4,28]. While RVEF may be more critical in the pre-BCPA assessment, the EF is simply a calculated measurement from EDV and ESV, and a known load dependent measure of ventricular function. For this reason, we chose to focus on the volumetric parameters, as errors in these volumetric data are compounded in small infants. Many studies have attributed the variability in EF to the magnified variability when 2 individual parameters are subtracted then divided, which are only magnified in smaller ventricles where even small changes in volume measurements can have a large effect on EF [9,10]. Given the better repeatability of volume measurements, it may be that ESV, rather than EF, should be considered the more robust method to help in the overall assessment of single ventricular function in this population. In fact, ESV has been shown to be a marker of pre-load reserve and is well recognized to be associated with clinical outcome due to its relationship to function and afterload [29]. White et al. found that LVEF was a greater predictor than EDV and LVEF, of survival after myocardial infarction [30], and Geva et al. found a curvilinear relationship between RVEF and RVESVi in 100 patients with repaired tetralogy of Fallot, suggesting that ESV may become important in decision making in the future [31].

The number and size of trabeculations and papillary muscles may be a source of variation in volume measurements as extensive trabeculations in the systemic RV can potentially lead to higher observer variability compared to the RV under normal loading conditions [13,22]. This is mainly attributed to the fact that extensive trabeculation, as often seen in the single RV in pre-BCPA patients, leads to complex and irregular shapes which make for difficult
measurements of RV volume and function in normal and dilated
observer for 9 months before measuring the data sets for the study.
2. In Fratz’s TOF study, the first investigator trained the second
also, analysis of our study patients did not begin until observer 1 had
our study, observer 1 had more training and more practice cases, and
performed 5 practice cases before the study cases were analyzed. In
students in Mooij et al.’s study initially received 1:1 training, but only

increase in RV volume measurements. However, this would not alter
muscle can become quite hypertrophied and may contribute to
blood pool measurements. In HLHS patients the anterior papillary
and endocardial borders, the papillary muscle was included in the
RV mass in this plane [8,9,17]. Furthermore, in contouring epicardial
and myocardium on the inferior wall makes it more difficult to define
harder to measure in the AX method so this may explain some of the

systole, we applied the conservation of mass principle to improve
volume overloaded RVs. Therefore, since these methods are fraught
the exclusion of trabeculae resulted in substantial differences of
semi-automated contouring with exclusion of trabeculae; however,
trabeculae inclusion had lower reproducibility when compared to

showed that manually contouring endo- and epicardial borders with
trabeculae inclusion had lower reproducibility when compared to
semi-automated contouring with exclusion of trabeculae; however,
the exclusion of trabeculae resulted in substantial differences of
EDV, ESV, EF and RV mass in patient populations with pressure and
volume overloaded RVs. Therefore, since these methods are fraught
with their own limitations, we decided on an alternative approach of
contouring through the middle of multiple trabecule.

By contouring the epicardium in both end-diastole and end-
stylole, we applied the conservation of mass principle to improve
reproducibility and accuracy of volume measurements. Geva and
Mooij [8,9] used the conservation of mass principle and thus mass
did not differ between stylole and diastole. It is known that mass is
harder to measure in the AX method so this may explain some of the
observed differences. This is because the partial volume effect of blood
and myocardium on the inferior wall makes it more difficult to define
the epicardial and endocardial borders, thus limit measurements of
RV mass in this plane [8,9,17]. Furthermore, in contouring epicardial
and endocardial borders, the papillary muscle was included in the
blood pool measurements. In HLHS patients the anterior papillary
muscle can become quite hypertrophied and may contribute to
increase in RV volume measurements. However, this would not alter
estimated EF since both EDV and ESV contouring would apply the
same principles.

Another source of variability in assessing CMR reproducibility is
the amount of training received prior to contour analysis. The medical
students in Mooij et al.’s study initially received 1:1 training, but only
performed 5 practice cases before the study cases were analyzed. In
our study, observer 1 had more training and more practice cases, and
also, analysis of our study patients did not begin until observer 1 had
demonstrated a <10% difference in measurements from observer 2. In Fratz’s TOF study, the first investigator trained the second
observer for 9 months before measuring the data sets for the study.
Mooij et al. indicated that the minimal training represented the ‘worst
case scenario’ and thus despite this, the high reproducibility of CMR
measurements of RV volume and function in normal and dilated
RVs, serves to establish its utility in the longitudinal follow up of these
patients [9]. In addition to Fratz et al. demonstrated that medical
students and inexperience observers with minimal coaching have reproducible measurements for LV and RV in normal hearts [36]. Whatever the time period of training undertaken, or the experience of the observer it is shown that with proper training, adherence to
clear guidelines, and constant exposure, CMR reproducibility can be obtained at any level of experience.

The selection of which phase to use for contouring may be an
additional source of variability. EDV and ESV phases were selected
through mid-ventricular slices by looking for the largest and smallest
blood pools, respectively. However, the complex crescentic shaped RV
does not uniformly contract, which can lead to variability in selected
phases. However, our results round that only 10% of all volumetric
measurements had a >3 phase difference in selection. Furthermore, it
was demonstrated that the selection of different phases did not cause a
significant difference in the volumetric measurements (Table 5),
indicating that the source of variability is due to individual variation
in contouring rather than different phase selection.

This study is the first to examine CMR orientation planes in a
homogeneous group of anesthetized, free-breathing infants with a
functionally single RV. With the expanding indications for, and
beneﬁts of CMR, more studies in the younger age group are needed.
Most normal CMR values are adopted from older, non-sedated,
children [30,31,34,37] with few in anesthetized infants [23]. Despite
this, normal volumetric data in biventricular hearts do not apply
to the functionally single ventricle which carries the combined
ventricular output. Our results can provide normal reference values
for single RV volumes prior to BCPA surgery, which are expected to
be larger than RV volumes in a normal biventricular circulation. The
shift from cardiac catheterization to performing CMR prior to the
BCPA requires standardized protocols and normative data in order to
develop CMR criteria to determine suitability for BCPA.

Study Limitations

The limitations of this study include its retrospective nature and thus not all patients had an AX stack performed. The selection of
patients who had an AX stack was at the discretion of the reading
physician at the time of the scan; as such, there may be a tendency
that the AX stacks were performed in more anatomically complicated patients which can contribute to variability. However, given the rarity of pediatric cardiac anomalies such as HLHS, we chose not to limit
the sample sizes by reducing those who only underwent both imaging
planes and thus decreasing the power of the analysis. Additionally,
since observer 2 trained observer 1, the possibility of a bias exists.
However, this is necessary in order to establish standardized methods
for measurement of complex single RV hearts [22], and should be
the way to standardize CMR measurements when establishing a
CMR unit. Our sample size was small, consisting of 23 SAO and
16 AX stack assessments at the pre-BCPA stage. Future studies can
expand upon our data by assessing a larger number of patients at
different stages of HLHS palliative surgery. A further limitation is
that different technicians and different centers were involved with
image acquisition, which can provide variability between the studies.
We also do not have flow quantification data for which to validate
our results, however flow measurements in the single RV, which
have previously undergone the Norwood procedure, can be difficult
to accurately quantify, as it requires summation of the neo-aortic
and shunt flow creating another source of error. While tricuspid
valve inflow is another potential flow validation option, this may be
complicated by regurgitation which is often seen in these patients.
Lastly, we are lacking inter-study reproducibility. Grouthes et al.
demonstrated that CMR has good inter-study reproducibility for
RV function parameters in biventricular hearts [6], and this can be further explored in CHD and single RVs.

Conclusion

In conclusion, our data suggests that the SAO orientation is the more reproducible method for assessing RV volumes and function in patients with HLHS at the pre-BCPA stage, suggesting that the addition of an axial stack does not provide any benefit over the short axis orientation. The availability of a reference imaging during analysis and accurate planning of imaging planes parallel to the tricuspid valve annulus are reasons which may explain better reproducibility of the SAO orientation in functionally single RVs. Our results also show that with proper training, clear guidelines for contour analysis, and an understanding of the anatomy, CMR can be a highly reproducible method for evaluating the functionally single right ventricle.

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