Comparison of Echocardiographic and Cardiac Magnetic Resonance Imaging Measurements of Functional Single Ventricular Volumes, Mass, and Ejection Fraction (from the Pediatric Heart Network Fontan Cross-Sectional Study)†

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Assessment of the size and function of a functional single ventricle (FSV) is a key element in the management of patients after the Fontan procedure. Measurement variability of ventricular mass, volume, and ejection fraction (EF) among observers by echocardiography and cardiac magnetic resonance imaging (CMR) and their reproducibility among readers in these patients have not been described. From the 546 patients enrolled in the Pediatric Heart Network Fontan Cross-Sectional Study (mean age 11.9 ± 3.4 years), 100 echocardiograms and 50 CMR studies were assessed for measurement reproducibility; 124 subjects with paired studies were selected for comparison between modalities. Interobserver agreement for qualitative grading of ventricular function by echocardiography was modest for left ventricular (LV) morphology ($\kappa = 0.42$) and weak for right ventricular (RV) morphology ($\kappa = 0.12$). For quantitative assessment, high intraclass correlation coefficients were found for echocardiographic interobserver agreement (LV 0.87 to 0.92, RV 0.82 to 0.85) of systolic and diastolic volumes, respectively. In contrast, intraclass correlation coefficients for LV and RV mass were moderate (LV 0.78, RV 0.72). The corresponding intraclass correlation coefficients by CMR were high (LV 0.96, RV 0.85). Volumes by echocardiography averaged 70% of CMR values. Interobserver reproducibility for the EF was similar for the 2 modalities. Although the absolute mean difference between modalities for the EF was small (<2%), 95% limits of agreement were wide. In conclusion, agreement between observers of qualitative FSV function by echocardiography is modest. Measurements of FSV volume by 2-dimensional echocardiography underestimate CMR measurements, but their reproducibility is high. Echocardiographic and CMR measurements of FSV EF demonstrate similar interobserver reproducibility, whereas measurements of FSV mass and LV diastolic volume are more reproducible by CMR. **(Am J Cardiol 2009;104:419–428)**

The National Heart, Lung, and Blood Institute–sponsored Pediatric Heart Network Fontan Cross-Sectional Study was a prospective multicenter study designed to evaluate the relation between health status and clinical measures in patients with functional single ventricles (FSVs) who had undergone Fontan procedures for the palliation of congenital heart disease.[1] As part of this study, echocardiographic and cardiac magnetic resonance imaging (CMR) evaluations of FSV size and function were performed. The purposes of this study were to define observer-related variability of echocardiographic and CMR-derived measures of ventricular mass, volume, and ejection fraction (EF) and to determine the levels of agreement for these measures between modalities.

Methods

A detailed description of the design and inclusion and exclusion criteria of the Pediatric Heart Network Fontan

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Table 1
Demographic, anatomic, and image quality data

Variable	Echocardiography (n = 100)	CMR (n = 50)	Echocardiography/CMR Comparison (n = 124)
Age at evaluation (yrs)	11.9 ± 3.4 (6.4–18.9)	11.7 ± 3.4 (6.8–18.9)	12.2 ± 3.3 (6.7–18.9)
Age at last Fontan procedure (yrs)	3.8 ± 2.6 (1.2–17.5)	3.1 ± 1.5 (1.4–8.9)	3.5 ± 2.2 (0.8–12.8)
Male	62 (62%)	31 (62%)	77 (62%)
Race			
White	75 (75%)	41 (82%)	102 (82%)
Black	12 (12%)	5 (10%)	12 (10%)
Asian	5 (5%)	1 (2%)	3 (2%)
Other	8 (8%)	3 (6%)	7 (6%)
Hispanic*	5 (5%)	0 (0%)	4 (3%)
Ventricular type			
LV	53 (53%)	26 (52%)	71 (57%)
RV	38 (38%)	15 (30%)	39 (31%)
Mixed	9 (9%)	9 (18%)	14 (11%)
Echocardiographic image quality			
Excellent	17 (17%)		22 (18%)
Good	66 (66%)		79 (64%)
Fair	17 (17%)		23 (19%)
CMR image quality			
Excellent		3 (6%)	23 (19%)
Good		25 (50%)	49 (40%)
Fair		22 (44%)	52 (42%)

Data are expressed as mean ± SD (range) or as number (percentage).
* Nonmissing totals for Hispanic status: echocardiography, n = 95; CMR, n = 48; echocardiography and CMR comparison, n = 118.

Table 2
Intra- and interobserver agreement for selected categorical echocardiographic findings

Variable	κ (95% CI)	Concordant	1-Grade Difference	2-Grade Difference	n*
Image quality†					
Intraobserver	0.19 (0.04–0.34)	48 (48%)	49 (49%)	3 (3%)	100
Interobserver	0.16 (0.01–0.31)	44 (44%)	54 (54%)	2 (2%)	100
LV dysfunction grade‡					
Intraobserver	0.58 (0.31–0.85)	53 (90%)	6 (10%)	0 (0%)	59
Interobserver	0.42 (0.12–0.71)	49 (83%)	9 (15%)	1 (2%)	59
RV dysfunction grade‡					
Intraobserver	0.25 (0.01–0.50)	34 (74%)	10 (22%)	2 (4%)	46
Interobserver	0.12 (−0.12–0.36)	29 (62%)	18 (38%)	0 (0%)	47

* Number of pairs of observations in which the 2 observers agreed that the structure was present and evaluable. In patients with mixed ventricular type, LV and RV measurements were included in their respective ventricular morphology group.
† Graded as excellent, good, or fair.
‡ Graded as none, mild, moderate, or severe.

Cross-Sectional Study has been published.[2] Briefly, subjects aged 6 to 18 years were enrolled from March 2003 through April 2004 at 7 pediatric clinical centers in the United States and Canada. Prospective data collection for each subject occurred within a 3-month period and included health status questionnaires, 2-dimensional and Doppler echocardiography, CMR, exercise, and other laboratory tests. The institutional review board of each center approved the study protocol, and written informed consent and assent were obtained according to local guidelines.

Two-dimensional and Doppler echocardiography were performed at participating centers according to the study protocol. None were performed under sedation. The studies were forwarded by the data coordinating center to the echocardiographic core laboratory for analysis by 1 of 2 echocardiographers (R.M., M.L.S.). Studies judged as acceptable for analysis were assigned an image quality grade of fair, good, or excellent on the basis of subjective assessments of short- and long-axis images. Ventricular morphology was characterized as left ventricular (LV) dominant (e.g., tricuspid atresia), right ventricular (RV) dominant (e.g., hypoplastic left-sided cardiac syndrome), or mixed (e.g., unbalanced atrioventricular canal defect).

FSVs were analyzed from the apical (ventricular long-axis) and parasternal short-axis views. The endocardial border of the FSV was traced at end-diastole and end-systole, and the epicardial border was traced at end-diastole in both planes. End-diastolic volume, end-systolic volume, and mass were calculated using a biplane-modified Simpson's rule.[3] The EF was calculated as (end-diastolic volume − end-systolic volume)/end-diastolic volume. Ventricular mass was calculated as myocardial end-diastolic volume (epicardial volume −

Table 3
Intra- and interobserver variability

Variable	Echocardiography Intraobserver			Echocardiography Interobserver			CMR Interobserver		
	n	ICC	Within-Subject SD (% Mean)	n	ICC	Within-Subject SD (% Mean)	n	ICC	Within-Subject SD (% Mean)
LV EDV (ml)	59	0.95	11.3 (16%)	59	0.92	15.9 (24%)	35	0.99	6.5 (7%)†
LV ESV (ml)	59	0.91	5.1 (18%)	59	0.87	6.5 (24%)	35	0.95	6.8 (18%)
LV EF (%)	59	0.54	7.6 (13%)	59	0.56	8.2 (14%)	35	0.46	6.2 (10%)
LV mass (g)	59	0.83	17.6 (22%)	59	0.78	24.8 (31%)	35	0.96	13.2 (17%)†
RV EDV (ml)	46	0.88	14.3 (20%)	47	0.85	19.6 (26%)	24	0.94	16.4 (17%)
RV ESV (ml)	46	0.86	7.0 (21%)	47	0.82	9.6 (28%)	23	0.90	7.4 (19%)
RV EF (%)	46	0.35	8.7 (15%)	47	0.43	8.2 (15%)	24	0.50	6.4 (12%)
RV mass (g)	46	0.78	19.1 (22%)	48	0.72	35.5 (40%)	24	0.85	23.2 (34%)*

* p value for likelihood ratio test of equality between echocardiography and CMR of within-subject SD <0.05.
† p value for likelihood ratio test of equality between echocardiography and CMR of within-subject SD <0.001.
EDV = end-diastolic volume; ESV = end-systolic volume; ICC = intraclass correlation coefficient.

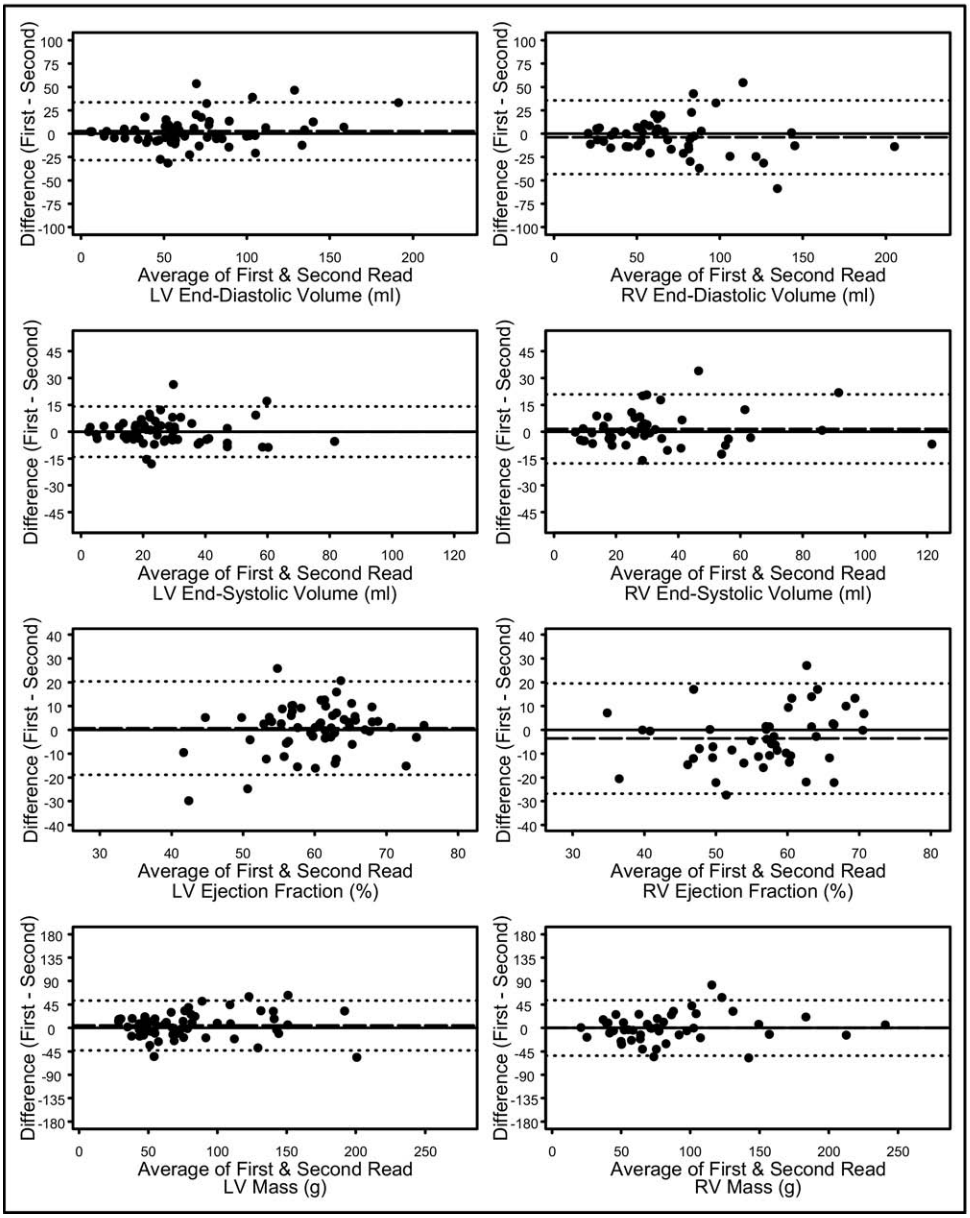

Figure 1. Intrarater comparison of echocardiographic measures. The *solid line* indicates perfect agreement; the *dashed line* indicates mean difference; *dotted lines* indicate 95% limits of agreement.

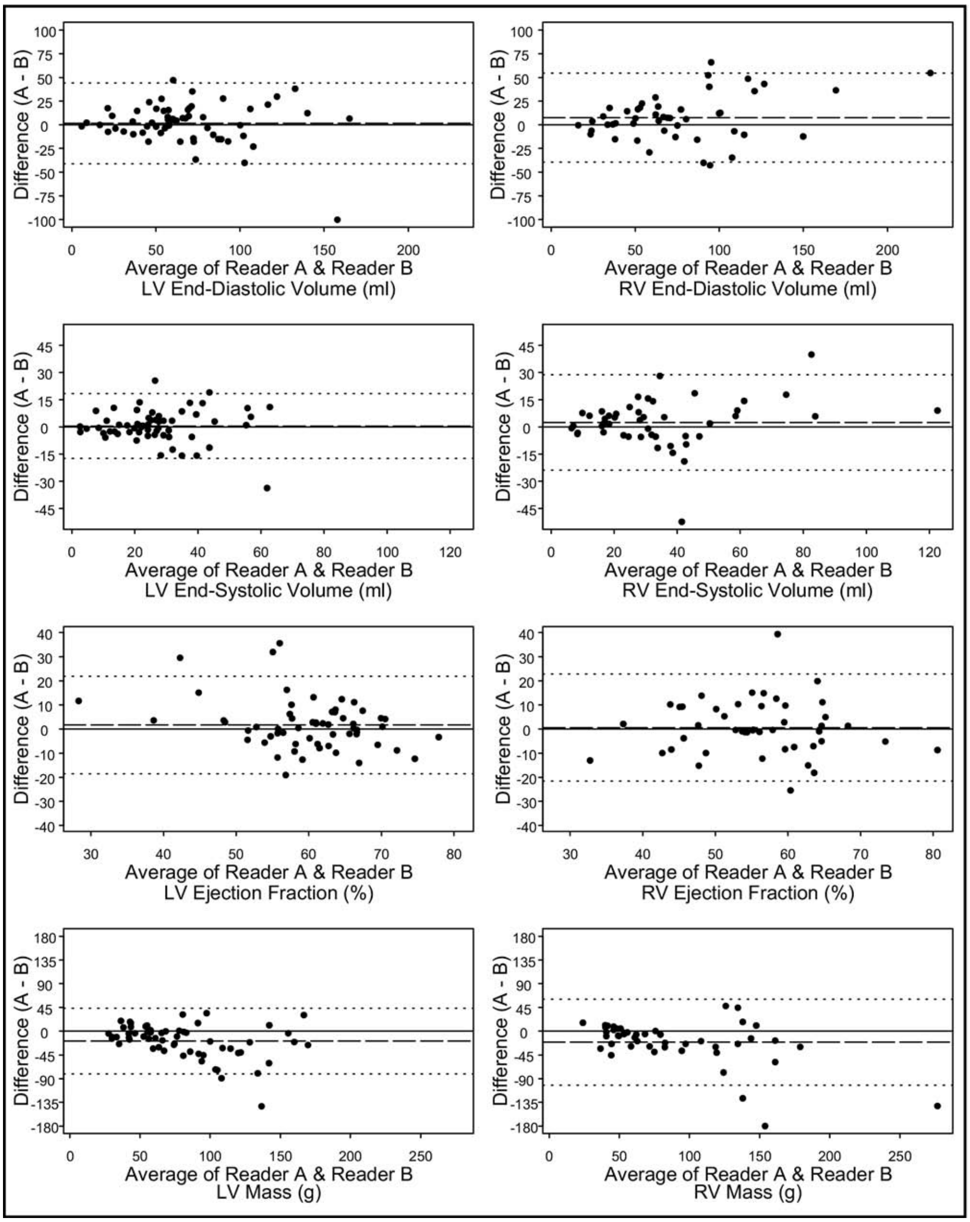

Figure 2. Interrater comparison of echocardiographic measures. The *solid line* indicates perfect agreement; the *dashed line* indicates mean difference; *dotted lines* indicate 95% limits of agreement.

endocardial volume) × myocardial density (1.05 g/ml). For the mixed-morphology group, the volume and mass of each ventricle were measured separately, and the values for each ventricle were included in their respective morphologic groups. Global ventricular systolic function was qualitatively graded as normal function or mild, moderate, or severe dysfunction. Echocardiographic data were reviewed and measurements made using custom software (Marcus Laboratories, Boston, Massachusetts).

CMR studies were performed at each participating center on 1.5-T scanners using a standard imaging protocol. Study subjects did not undergo CMR as part of their assessments if they met any of the following criteria: (1) unable to cooperate without sedation; (2) had a pacemaker, defibrillator, permanent pacemaker lead, or implanted device considered a contraindication according to institutional guidelines; (3) had intravascular occlusion coils deemed to result in excessive image artifact; or (4) were <6 weeks from endovascular device implantation.

The standardized imaging protocol included electrocardiographically gated segmented k-space fast (turbo) gradient (14% of studies) or steady-state free precession (86% of studies) cine magnetic resonance acquisitions in the vertical and horizontal long-axis planes and contiguous short-axis cine imaging from the atrioventricular junction through the cardiac apex. Deidentified CMR data were analyzed using commercially available software (MASS; MEDIS Medical Imaging Systems, Leiden, The Netherlands) at the core CMR laboratory. LV and/or RV end-diastolic (maximal) and end-systolic (minimal) volumes and mass at end-diastole were measured in the ventricular short-axis plane, as described by Lorenz.[4]

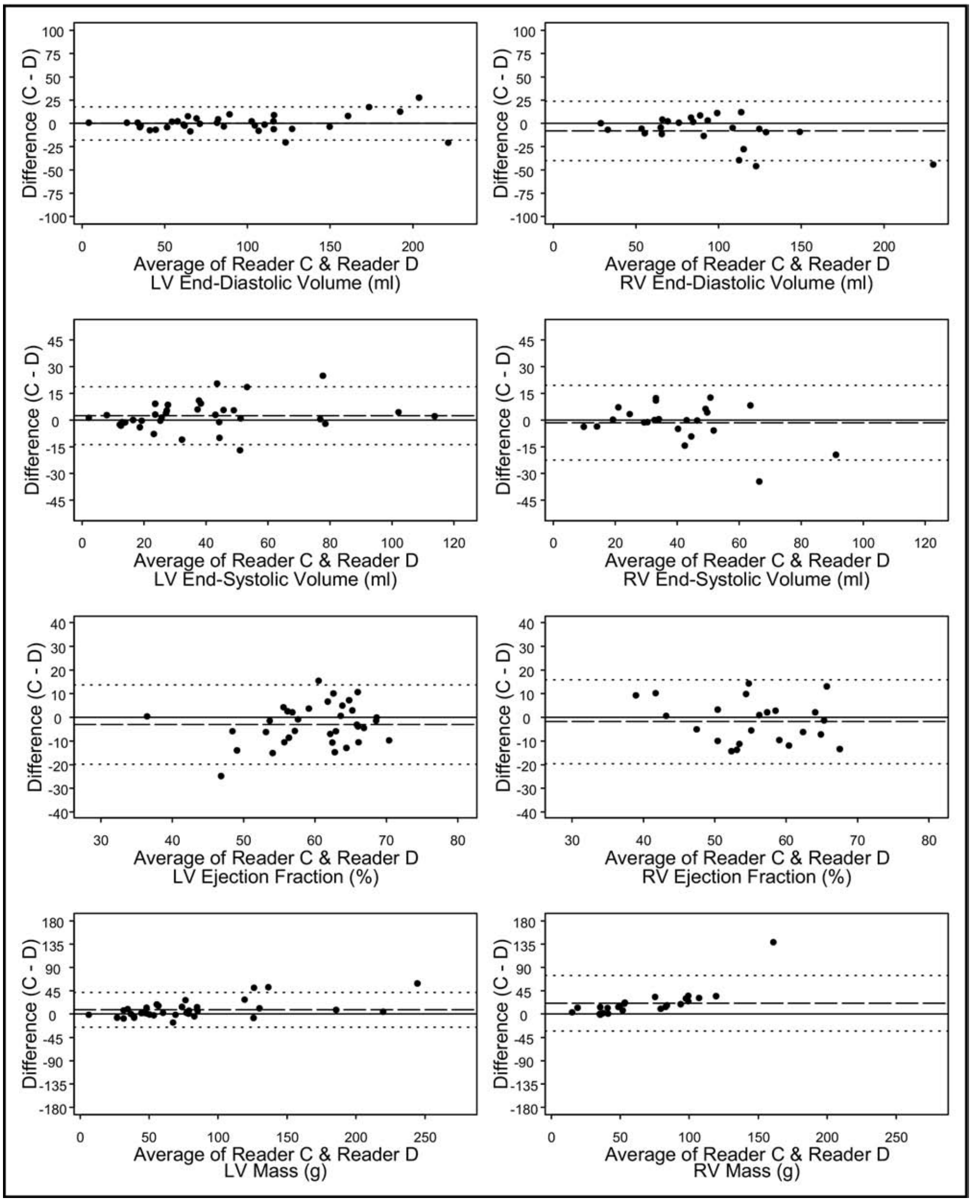

Figure 3. Interrater comparison of CMR measures. The *solid line* indicates perfect agreement; the *dashed line* indicates mean difference; *dotted lines* indicate 95% limits of agreement.

Stroke volumes, the EF, and the mass/volume ratio were calculated.

To evaluate inter- and intraobserver variability for echocardiograms and interobserver variability for CMR, eligible examinations were randomly selected for repeat analysis. To be eligible, the initial study was required to be rated as acceptable (of at least fair quality) and have complete assessment of FSV volumes and EFs by the initial reader. Of the 546 subjects enrolled in the study, 404 (74%) patients had echocardiograms and 159 (29%) had CMR studies that met these criteria. From this pool, 100 echocardiograms and 50 CMR studies were randomly selected for observer variability analysis. Sampling was stratified on the basis of ventricular morphology type and echocardiographic image quality grade. The echocardiographic analysis data set consisted of 3 readings per echocardiogram: 2 by the same core laboratory reviewer for intraobserver variability and 1 by the other reader for interobserver variability. The CMR data set consisted of 2 readings per CMR study: the original core laboratory review (T.G.) and a repeat evaluation (A.P.) for interobserver variability. Intraobserver variability was not assessed for CMR, because the relatively small number of studies resulted in a degree a familiarity with the images such that repeat contouring would not have resulted in a de novo analysis.

To compare between echocardiographic and CMR measurements of mass, volumes, and the EF, all 124 subjects with complete data sets for the 2 modalities rated as acceptable were selected.

Kappa statistics with Cicchetti-Allison weights and frequencies of concordance were calculated for the assessment of intra- and interobserver agreement for echocardiographic

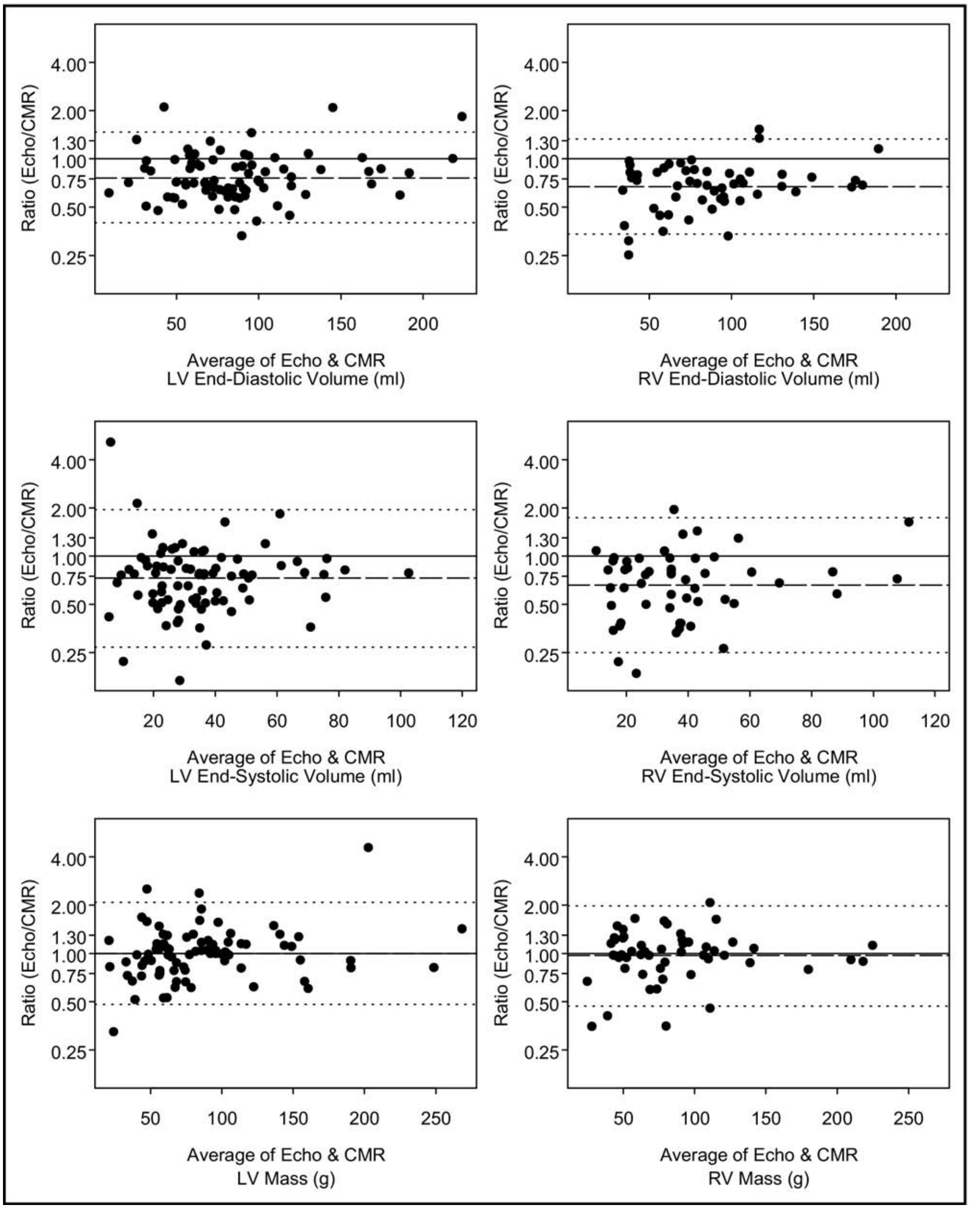

Figure 4. Comparison of echocardiographic and CMR-derived values for end-diastolic volume, end-systolic volume, and ventricular mass. The *solid line* indicates perfect agreement; the *dashed line* indicates mean difference; *dotted lines* indicate 95% limits of agreement. Ratios are plotted on a log scale.

image quality and FSV functional grade. This analysis was performed only when both readers agreed that the structure was present and evaluable. Weighted κ statistics were used to determine the agreement between echocardiographic quantitative and qualitative approaches to FSV systolic function grade using CMR-based FSV functional grade as reference standard.

The intra- and interobserver variability of continuous variables was assessed using the intraclass correlation coefficient estimated with variance component models.[5] The intraclass correlation coefficient can be interpreted as the proportion of variability explained by subject differences as opposed to rater differences and random error. To meet the normality and constant variance assumptions of this model, log transformations were used for end-diastolic volume, end-systolic volume, and mass. Because the estimation of intraclass correlation coefficients can be imprecise when the number of raters is small, within-subject SD was also used to assess intra- and interobserver variability.[6] Plots of differences versus mean values were produced to graphically examine variability and magnitude of the differences. Likelihood ratio tests were used to test differences in interobserver within-subject SD between echocardiography and CMR and among subgroups stratified by image quality grade. Bland-Altman 95% limits of agreement with log transformation were calculated to assess agreement between echocardiographic and CMR measurements. To examine the relation between the level of agreement and echocardiographic image quality, geometric mean ratios and 95% limits of agreement were calculated to assess agreement between echocardiographic and CMR measurements. Log transformations were used and geometric mean ratios re-

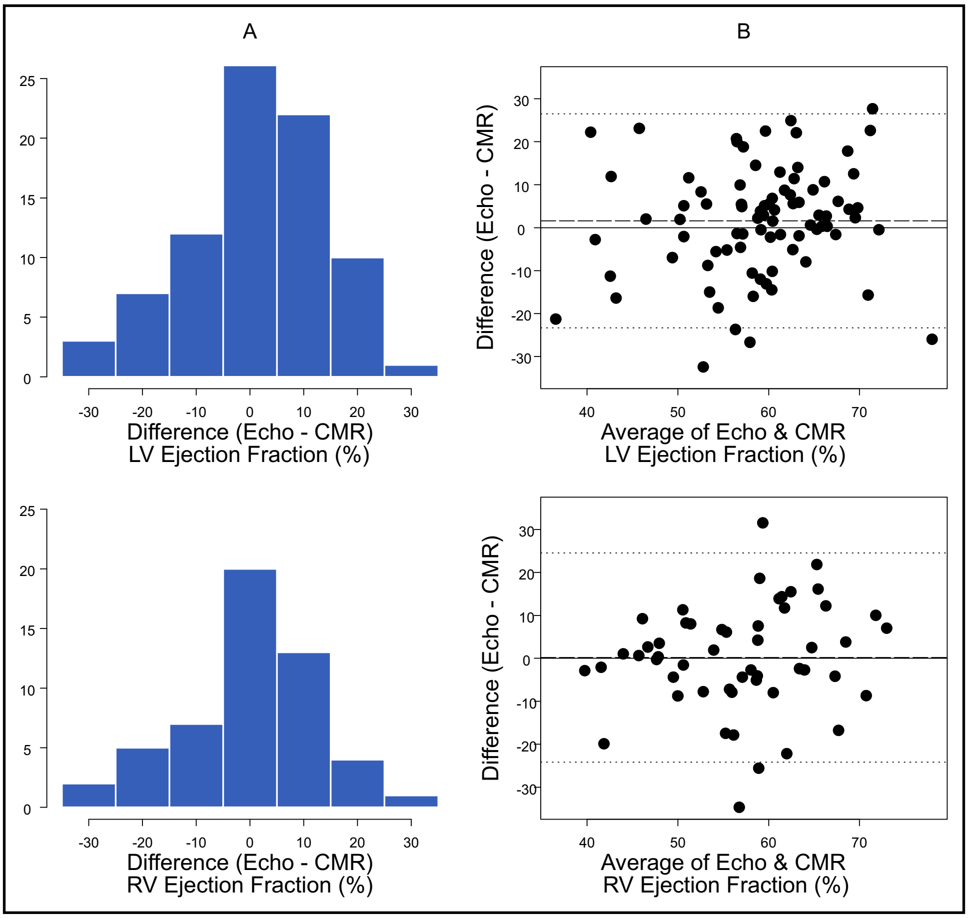

Figure 5. Comparison of echocardiographic and CMR-derived values LV and RV EFs. *(A)* Bar graphs demonstrating the frequency of differences between echocardiographic and CMR measures of the EF. *(B)* Comparison of echocardiography and CMR for the EF. The *solid line* indicates perfect agreement; the *dashed line* indicates mean difference; *dotted lines* indicate 95% limits of agreement.

ported for end-diastolic volume, end-systolic volume, and mass. One outlier was excluded from CMR RV end-systolic volume and RV EF interobserver analyses. For all analyses, differences were considered significant at a p value <0.05. Statistical analysis was performed using SAS version 9.1.3 (SAS Institute Inc., Cary, North Carolina), and figures were produced using S-plus version 6.2 (Insightful Corporation, Seattle, Washington).

Results

The demographic, anatomic, and image quality data for the echocardiography and CMR groups are listed in Table 1. The groups were similar with respect to age, gender, race, and ventricular type.

Table 2 lists intra- and interobserver agreement for echocardiographic image quality and ventricular function grade. Although the confidence intervals (CIs) are wide, the data suggest that agreement for overall image quality grade was weak, with readers' assessments of quality being concordant less than half the time. Agreement regarding FSV functional grade was moderate for LV morphology and weak for RV morphology.

FSV systolic function was categorized by echocardiography as normal function or mild, moderate, or severe dysfunction on the basis of EF measurements (quantitative approach) and by qualitative assessment ("eyeball" approach). For the quantitative approach, the EF was classified as indicating normal (>55%), mild (41% to 55%), moderate (31% to 40%), or severe (≤30%) dysfunction, and for the qualitative approach the same categories were used. CMR-based FSV functional grade was used as reference standard, also using the same quantitative categorization. The agreement in FSV functional grade between categorization on the basis of quantitative echocardiographic measurements and CMR was weak (LV: weighted $\kappa = 0.13$, 95% CI -0.03 to 0.30, 58% concordant; RV: weighted $\kappa = 0.34$, 95% CI 0.07 to 0.61, 60% concordant). The agreement in FSV functional grade between categorization on the basis of qualitative echocardiographic assessment and CMR was similarly weak (LV: weighted $\kappa = 0.28$, 95% CI 0.09 to 0.46, 65% concordant; RV: weighted $\kappa = 0.30$, 95% CI 0.144 to 0.45, 61% concordant). When only studies with echocardiographic image quality rated as good or excellent were included in the analysis, the level of agreement was slightly improved for the qualitative approach (LV: weighted $\kappa = 0.33$, 95% CI 0.14 to 0.51, 66% concordant; RV: weighted $\kappa = 0.32$, 95% CI 0.13 to 0.51, 63% concordant) but did not improve for the quantitative approach

Table 4
Comparison between echocardiography and CMR measurements in 124 subjects

Variable*	Echocardiography		CMR		Mean Difference (95% CI)	Mean Ratio (95% CI)
	Mean ± SD (Range)	Median	Mean ± SD (Range)	Median		
LV EDV (ml)	76.8 ± 46.3 (6.8 to 289.6)	62.8	97.5 ± 45.8 (11.1 to 233.2)	94.0	−20.7 (−86.6 to 45.1)	0.76 (0.40 to 1.47)
LV ESV (ml)	31.9 ± 27.1 (3.3 to 214.7)	24.9	41.1 ± 22.5 (2.0 to 114.9)	38.3	−9.3 (−51.3 to 32.7)	0.73 (0.27 to 1.95)
LV EF (%)	59.9 ± 10.8 (25.9 to 85.3)	61.0	58.3 ± 9.4 (29.3 to 91.0)	58.6	1.6 (−23.3 to 26.5)	1.02 (0.65 to 1.61)
LV mass (g)	88.2 ± 55.9 (11.9 to 332.8)	68.2	84.8 ± 47.5 (19.0 to 273.9)	76.2	3.4 (−74.3 to 81.1)	1.00 (0.48 to 2.08)
RV EDV (ml)	71.6 ± 39.1 (15.1 to 203.0)	67.1	101.9 ± 44.4 (38.5 to 213.0)	93.0	−30.3 (−83.5 to 23.0)	0.67 (0.34 to 1.33)
RV ESV (ml)	31.5 ± 23.7 (6.3 to 138.3)	24.1	44.4 ± 24.9 (9.9 to 125.2)	38.7	−12.9 (−50.0 to 24.2)	0.66 (0.25 to 1.74)
RV EF (%)	56.9 ± 11.0 (26.2 to 76.8)	56.2	56.7 ± 9.5 (8.6 to 76.1)	55.5	0.2 (−24.2 to 24.6)	1.00 (0.65 to 1.53)
RV mass (g)	84.7 ± 47.2 (14.6 to 237.7)	67.8	86.2 ± 48.0 (29.6 to 230.4)	74.6	−1.4 (−55.1 to 52.2)	0.97 (0.47 to 1.98)

* For LV comparisons, n = 83; for RV comparisons, n = 53.
Abbreviations as in Table 3.

(LV: weighted κ = 0.17, 95% CI −0.01 to 0.34, 57% concordant; RV: weighted κ = 0.25, 95% CI −0.03 to 0.52, 61% concordant).

Table 3 lists intra- and interobserver variability for echocardiographic measurements and interobserver variability data for CMR. Plots of differences versus mean values demonstrating the variability and magnitude of the differences between readers are shown in Figures 1 to 3. Intraobserver agreement was high for echocardiographic measurements of LV volumes and for RV volumes. Intraobserver agreement was moderate for FSV mass and modest for the EF. Patterns for interobserver echocardiographic variability mirrored those for intraobserver variability, with lower or similar intraclass correlation coefficients.

For CMR measurements of LV and RV volumes, the level of agreement between readers was high. A high level of interobserver agreement was also noted for LV and RV mass measurement, but, similar to echocardiography, the agreement for the EF was modest. Compared with echocardiography, CMR within-subject SDs tended to be lower, reaching statistical significance for LV end-diastolic volume, LV mass, and RV mass (Table 3).

The comparison between echocardiographic and CMR-derived measurements is shown in Figures 4 and 5 and listed in Table 4. Compared with CMR, echocardiographic measurements of ventricular volume were smaller (70% to 79%), and the limits of agreement were wide. For example, echocardiographic measurement of LV end-systolic volume ranged from approximately a quarter to twice that of CMR measurement. Although on average, the measurements of the EF and mass were similar between modalities (e.g., a mean difference of 1.6% for the LV EF and 0.2% for the RV EF), the limits of agreement were wide (Figure 5, Table 4).

Discussion

The results of this study reveal several important findings regarding the noninvasive assessment of FSV size and function. Although the qualitative assessment of LV function by 2-dimensional echocardiography was moderately reproducible between observers, assessment of the right ventricle was poorly reproducible. In contrast, quantitative echocardiographic measures of ventricular volumes were quite reproducible for LV and RV morphologies. Although 2-dimensional echocardiographic measurements systematically underestimated CMR-derived ventricular volume measurements, the reproducibility of EF measurements was comparable on the 2 modalities. Interobserver reproducibility of CMR measurements was generally better than that of echocardiography, reaching statistical significance for measurements of LV end-diastolic volume and for LV and RV mass. Finally, qualitative and quantitative echocardiographic assessments of FSV functional grade agreed relatively weakly with CMR, with no clear advantage to either approach.

The limitations inherent to 2-dimensional as opposed to 3-dimensional imaging techniques were demonstrated by Chuang et al,[7] who showed that biplane 2-dimensional measurements of LV volume and EF were less accurate and reproducible than 3-dimensional volumetric measurements, regardless of imaging modality, echocardiography or CMR, in adult patients with dilated cardiomyopathy. Difficulties in acquiring "true" long- and short-axis imaging planes using 2-dimensional techniques were believed to be a key weakness of the biplane method. This limitation has been shown to be even more pronounced in the assessment of RV volume, for which the prediction of volume on the basis of linear and cross-sectional measurements is more difficult.[8–10] Extrapolation from these studies to FSVs should yield similar results, because chamber geometry and orientation within the thorax are often unpredictable, and imaging of the anterior, retrosternal free wall is often challenging. Although 3-dimensional echocardiography holds promise for the more accurate assessment of ventricular volume in biventricular circulation,[11–15] its accuracy and reproducibility in patients with FSVs await confirmation. Soriano et al[16] recently demonstrated that measurements of FSV volumes, EF, and mass by 3-dimensional echocardiography correlate well with CMR measurements. However, their study included a relatively small number of young patients (29 infants; median age 7 months) whose studies were performed under general anesthesia. The reproducibility of 3-dimensional echocardiographic measurements of FSV size and function in older patients with all forms of FSV requires further validation. Another alternative to 2-dimensional echocardiography for the assessment of ventricular function is based on Doppler techniques.[17,18] However, as with 3-dimensional echocardiography, the precise role of these techniques in patients who have undergone Fontan palliation awaits further investigation.

Although this study demonstrated low agreement for the qualitative assessment of RV systolic function, this method is in prevalent use at most echocardiographic laboratories. Poor reproducibility of the qualitative assessment of RV function was also demonstrated in patients with right-sided congenital heart disease and 2-ventricle circulation[19] but has not been reported in single-ventricle physiology.

Lower reproducibility of FSV EF measurements was noted for echocardiography and CMR despite a high intraclass correlation coefficient of end-diastolic volume and end-systolic volume measurements. The most likely explanation is that the variability of measuring individual parameters (end-diastolic volume and end-systolic volume) is magnified when they are subtracted and then divided. Similar observations were made in the studies of Lipshultz et al[20] (echocardiography) and Mooij et al (CMR).[21]

The results of this study agree with previous studies that demonstrated the accuracy and reproducibility of CMR measurements of ventricular volume, EF, and mass.[21–24] However, several practical limitations restrict the use of CMR in patients after the Fontan procedure. The presence of a pacemaker or cardiac defibrillator (13% in this cohort) is considered a strong relative contraindication for CMR. Image artifacts from metallic implants precluded quantitative volumetric analysis in 20% of patients with Fontan palliation reported by Garg et al[25] and were the primary reason for a lower image quality score in this cohort. Overall, the CMR data were inadequate or incomplete in 30% of patients in whom the test was performed, predominantly because of metallic artifacts. However, in patients who are able to cooperate with the examination, have no metallic artifacts that obscure the ventricular mass, and have no contraindications to CMR, this modality offers an advantage in terms of reproducible assessment of ventricular size and function. Moreover, the lower interobserver SDs of some CMR-derived measurements (LV end-diastolic volume and LV and RV mass) found in this study suggest that the sample size required to demonstrate a treatment effect or a change over time would be smaller with CMR compared with 2-dimensional echocardiography.[24]

Several limitations of this study merit attention. Our findings are conditional on having acceptable CMR and echocardiographic studies for analysis. In this highly heterogenous population, the success rate for obtaining adequate quality studies may vary by modality because of a variety of patient- and operator-related factors. CMR reproducibility may have been affected by the use of 2 cine magnetic resonance imaging techniques, although the percentage studies not using steady-state free precession was small. The number of patients with systolic ventricular dysfunction was small, which limited our ability to detect a possible trend between echocardiography and CMR agreement and the EF. The sample size for subgroup analyses was small, which might have precluded the detection of subtle associations with image quality. It should be noted that on the basis of the inclusion criteria, the study group included only patients aged 6 to 18 years. Extrapolation to older patients may not be accurate, because of worsening acoustic windows and a higher prevalence of ventricular dysfunction. Extrapolation to younger patients may also not be accurate, because of potentially better acoustic windows. Nonetheless, the results of this study are derived from a contemporary cohort of young patients studied at 7 different institutions, representing a relatively large group of patients with Fontan palliation.

Appendix

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