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The Reproducibility and Absolute Values of Echocardiographic Measurements of Left Ventricular Size and Function in Children are Algorithm Dependent

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Abstract

Background—Several quantification algorithms for measuring left ventricular (LV) size and function are used in clinical and research settings. We investigated the effect of the measurement algorithm and beat averaging on the reproducibility of measurements of the LV and assessed the magnitude of agreement among the algorithms in children with dilated cardiomyopathy (DCM).

Methods—Echocardiograms were obtained on 169 children from 8 clinical centers. Inter- and intra-reader reproducibility were assessed on measurements of LV volumes using biplane Simpson, modified Simpson (MS), and 5/6 x area x length (5/6AL) algorithms. Percent error (%error) was calculated as the inter- or intra-reader difference / mean x 100. Single beat measurements and the 3-beat average (3BA) were compared. Intra-class correlation coefficients (ICC) were calculated to assess agreement.

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Results—Single beat inter-reader reproducibility was lowest (%error was highest) using biplane Simpson; 5/6AL and MS were similar but significantly better than biplane Simpson ($p < .05$). Single beat intra-reader reproducibility was highest using 5/6AL ($p < .05$). 3BA improved reproducibility for almost all measures ($p < .05$). Reproducibility in both single and 3BA values fell with greater LV dilation and systolic dysfunction ($p < .05$). ICCs were > 0.95 across measures, although absolute volume and mass values were systematically lower for biplane Simpson compared to MS and to 5/6AL.

Conclusions—The reproducibility of LV size and function measurements in children with DCM is highest using the 5/6AL algorithm, and can be further improved by using 3BA. However, values derived from different algorithms are not interchangeable.

INTRODUCTION

Echocardiographic measures of left ventricular (LV) size and systolic function are widely used as endpoints in clinical trials. However, the limited availability of data concerning the reproducibility of quantitative indices of ventricular function in pediatric dilated cardiomyopathy (DCM) is an impediment to controlled trials of therapy for ventricular dysfunction in children. Several algorithms for measuring LV volumes using 2-dimensional echocardiographic methods are common in clinical and research use. These methods include the 5/6 x area x length (5/6AL), modified Simpson (MS) and biplane Simpson algorithms. While the American Society of Echocardiography (ASE) has recommended the biplane Simpson (also known as the biplane method of disks) algorithm as the approach of choice for LV volume quantification in adults (1), the applicability of this recommendation to pediatric populations is unknown.

The objectives of this analysis were to: 1) determine the impact of the method of calculating LV volumes on inter-reader and intra-reader reproducibility of measured and calculated variables in children with DCM; 2) determine whether averaging multiple beats improves reproducibility; 3) assess the agreement among measurements by algorithm; and 4) determine whether the severity of cardiomyopathy impacts the reproducibility of LV volumes.

METHODS

The Ventricular Volume Variability Study (VVV) was a multi-center observational study of pediatric subjects with stable dilated cardiomyopathy undertaken by the NHLBI-sponsored Pediatric Heart Network (PHN). Enrolled subjects were followed for 18 months, and a study protocol echocardiogram was obtained at each clinical visit during this time. Inclusion and exclusion criteria are listed in the online appendix. The study was conducted in accordance with the guidelines of the PHN's Data and Safety Monitoring Board and of each center's Institutional Review Board. Full details of the study design have been previously published (2).

The primary aim of the VVV study was to evaluate the longitudinal variance of echocardiographic indices of LV size and function. Subjects with a history of dilated cardiomyopathy by chart review were approached for consent for participation at the time of

a clinical evaluation. Those subjects who met full inclusion criteria based on the baseline study echocardiogram were eligible for follow-up echocardiograms to determine longitudinal variability. The data from baseline echocardiograms obtained in patients who did not meet exclusion criteria, but who also did not meet the dilation and/or dysfunction criteria (in other words, data obtained in those subjects whose echocardiograms had improved sufficiently to not meet entrance criteria for dilation and/or dysfunction since the diagnosis of dilated cardiomyopathy was made) were retained in the database and represent a normalized or near-normalized population. Inclusion of these exams permitted the analyses to be performed across a broader range of disease severity. For purposes of this report, only baseline evaluations are included.

Consented subjects underwent a study echocardiogram performed by sonographers at each site who were specifically trained on the standardized protocol for image acquisition. At least three cardiac cycles were recorded for each parameter. Height and weight were measured and body surface area (BSA) was calculated using the Haycock formula (3). All baseline echocardiograms were submitted to the data coordinating center and forwarded to the echocardiography core laboratory (ECL).

At the ECL, two readers performed measurements on each echocardiogram to assess inter-reader reproducibility. The protocol specified 150 measured and derived parameters on each study (2). One ECL reader repeated all measurements one month later to assess intra-reader reproducibility. All measurements were performed using custom DICOM software (Echotrace, Marcus Laboratories, Boston, MA).

Left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), LV mass, and LV ejection fraction (LVEF) were calculated using three common algorithms. The ASE recommended biplane Simpson method (1) utilized areas from apical 4-Chamber and apical 2-Chamber views (Figure 1A). For the MS approach (4) we used an apical 4-chamber area and a parasternal short axis area (Figure 1B). The 5/6AL algorithm (5) required the length of the LV from the apical 4-chamber and a parasternal short axis area (Figure 1C).

Statistical Methods

Definitions

Inter- and intra-reader reproducibility: In these analyses, the outcome measure is the percent (%) error of the mean. In order to evaluate inter-reader reproducibility, the absolute difference ('error') between the measurements made by the primary and secondary readers was divided by the mean of those two measurements. In order to evaluate intra-reader reproducibility, the difference ('error') between the immediate and 1-month repeat measurements made by the primary reader was divided by the mean of those two measurements. Single-beat %error was based on the measurements obtained from the first beat and three-beat average (3BA) %error was based on the average of all three measurements.

Reduction in error: In order to quantify the reduction in error that was due to beat averaging, a ‘% reduction in %error’ term (abbreviated to error reduction) was calculated using 3BA as compared to single-beat averages as:

$$(\text{Single beat \%error} - 3BA \%error) / \text{Single beat \%error} \times 100\%$$

We fit a mixed regression model (fixed effect for method and random effect for subject) to assess whether reduction in error occurs using 3BA vs. single-beat.

Impact of Disease Severity, Age and Body Size on Reproducibility: Tests of interaction in the respective regression models were utilized to assess whether differences in reproducibility (%error) among the three algorithms were altered by disease severity (LVEDV, LVEF), age, and body surface area.

Z-scores: To adjust LV measurements to account for the effect of body size and age in this cohort of children, z-score values were used as recommended by ASE (5). The z-score normative relationships for LVEDV were based on 5/6AL values (i.e. they are not algorithm-specific) and they were therefore calculated only for the 5/6AL volumes (LVEDVz) and were used only for entry criteria and severity stratification.

To determine the level of agreement between the absolute measurements yielded by each of the algorithms, intra-class correlation coefficients (ICC) and Bland-Altman plots were used, based on the initial reading by the primary core laboratory reviewer. The ICC ranges from 0 to 1, with a value of 1 indicating that all of the variability in the measurement is due to random measurement error for a subject and is not due to the algorithm utilized. From Bland-Altman analyses and plots, the bias (systematic difference between the measurements) and limits of agreement (average difference \pm 2 standard deviations of the differences) were used to determine the level of agreement between algorithms.

RESULTS

Screening baseline echocardiograms were obtained on 169 children with a history of dilated cardiomyopathy at eight clinical centers. Demographic data, the causes of DCM in this cohort, and baseline ventricular size and function data (based on the 5/6AL algorithm) are presented in Table 1. Almost two-thirds (63%) of the baseline studies had an LVEDVz >2, and 79% of the echocardiograms demonstrated an LVEF z-score <-2 (see online appendix for inclusion and exclusion criteria).

The %error values for single beat measurements by the three algorithms are presented in Figure 2. For all parameters and for all of the algorithms, inter-reader %error was higher than intra-reader. For inter-reader values, the overall p-values for the main effect of algorithm ranged from <0.001 for EF to 0.05 for LVEDV. There was no difference in inter-reader reproducibility between the 5/6AL and MS approaches; both of these algorithms had lower %error than the biplane Simpson method, i.e. they had higher reproducibility. For intra-reader comparisons, the overall p-values for the main effect of algorithm were all

<0.001. The 5/6AL algorithm measurements demonstrated lower %error compared to both MS and biplane Simpson, which were not statistically different from each other.

The reduction in error that resulted from averaging 3 beats compared to a single beat is shown in Figure 3. 3BA improved reproducibility across most of the parameters, although the magnitude of the effect was variable for each parameter and algorithm. Notably, the effect of 3BA on LVEF was similar for all of the algorithms: approximately 20% error reduction for inter-reader reproducibility and 30-40% error reduction for intra-reader. LV mass was an exception to the improvement seen with 3BA, with negligible error reduction, particularly for inter-reader reproducibility. This association was true regardless of volume algorithm, supporting the finding of no interaction.

To determine whether disease severity had an impact upon the reproducibility of measuring LVEF, the data were analyzed using indices of dilation (LVEDV) and dysfunction (LVEF) calculated using the 5/6AL method as both continuous variables and categorical variables by dividing the cohort into tertiles.

Figure 4 demonstrates the inter-reader single beat and 3BA reproducibility in LVEF measurement relative to the degree of LV dilation and dysfunction (tertiles). Both single beat and 3BA measurements of LVEF manifested higher %error in subjects with higher LVEDVz and in subjects with lower LVEF. However, the %error of EF for 3BA was significantly lower for both LVEDV and LVEF compared to the single beat. The impact of 3BA was largest in the tertiles with the most dilated LVs ($p < .001$ for LVEDV) and the most dysfunctional LVs ($p = .04$ for LVEF, based on severity as a continuous measure). In other words, the benefit of 3BA on reproducibility is greatest in those with the most severe disease.

The same analysis was performed with intra-reader reproducibility of LVEF. The tertile with the most dilated LVs and the tertile with the lowest LVEF demonstrated a similar tendency of improvement in reproducibility (3BA compared to single beat), reaching statistical significance for LVEF tertile ($p = .001$) but not for LVEDVz tertile (Figure 5).

Using the three-beat-averaged data, we also examined whether differences in inter- and intra-reader reproducibility according to algorithm depended on patient age or body surface area (BSA). There were no interactions between algorithm and age or BSA with respect to intra-reader reproducibility (all $p > 0.16$). For inter-reader reproducibility, there was an interaction between algorithm and continuous age ($p = 0.034$), and algorithm and continuous BSA ($p = 0.007$), for one of the five outcomes: LVESV. At older ages and larger BSA, the biplane Simpson algorithm yielded higher %error (lower inter-reader reproducibility) for LVESV than the other two algorithms. For example, in patients age 5 years or younger, estimated %error was 10.2% to 10.9% for the three algorithms. In patients over age 13 years, the %error was 8.7% for 5/6AL, 10.4% for MS, and 14.5% for biplane Simpson. Similarly, for BSA above 1.5 m², the %error was 9.7% for 5/6AL, 12.0% for MS, and 16.1% for biplane Simpson. Thus, for inter-reader reproducibility of LVESV only, %error was roughly constant with age and BSA for 5/6AL, but increased with age and BSA for MS and increased with age and BSA to an even greater degree for biplane Simpson.

To assess the agreement among the raw measurements obtained by each of the three algorithms, ICC and Bland Altman analyses were assessed. Summary data of LVEDV, LVESV, LV mass and LVEF are presented in Table 2 along with ICC values. Although the ICC values for all of the measurements were high, with LVEDV, LVESV and mass ICCs of 0.99 and LVEF ICC of 0.95, Bland Altman analyses did not show good agreement between methods. For LVEDV, LVESV and mass, the data showed evidence of bias, as the 5/6AL algorithm returned larger values than MS, which were in turn larger than biplane Simpson values. Further, the 95% limits of agreement are wide for all of the LVEDV comparisons (e.g., measurements may be different by 40 ml at an LVEDV of 140 ml and still be within the broad limits of agreement) (Figure 6.A.1). For evaluations of LVEF, while there was no bias between MS and 5/6AL, there was bias when biplane Simpson was compared to the other methods, with both MS and 5/6AL yielding LVEF values larger than those calculated by biplane Simpson. Further, the limits of agreement between biplane Simpson and 5/6AL for LVEF were broad, such that a 15 point difference in measurements at an EF of ~35% would still be within the limits of agreement. Figure 6 includes scatter plots and Bland-Altman comparisons for LVEDV and LVEF. The plots for LVESV and LV mass were similar to those of LVEDV: MS produced larger measurements than biplane Simpson and smaller than 5/6AL. Both MS and biplane Simpson demonstrated non-systematic bias compared to 5/6AL, meaning as the volume or mass increases, the magnitude of bias increases. There was no non-systematic bias for LVEF measurements.

Previously published analyses of the VVV study data investigated the impact of variable type on variability (2). Of the types of variables (e.g. 2-D dimensions or areas, Doppler slopes or velocities, calculated variables that used 2, 3 or 4 measurements) calculated variables had higher variability, resulting from compounding the error of the individual components. The LV algorithms used data from the following measured variables to calculate a volume, listed below with their respective intra- and inter-observer variabilities (mean %error values).

- 5/6AL: short axis area (0.93%, 6.7%) and LV length (0.71%, 4.0%)
- MS: apical 4-chamber LV area (1.4%, 5.6%) and short axis area (0.93%, 6.7%)
- Biplane Simpson: apical 4-chamber LV area (1.4%, 5.6%) and apical 2-chamber LV area (2.1%, 8.0%)

Thus, the higher variability seen with the biplane Simpson algorithm was due to relatively higher variability in the apical 2-chamber LV area compared to the short axis area or LV length.

DISCUSSION

This multi-center observational study demonstrated that the 5/6AL method of assessing LV size and systolic function in pediatric patients was significantly more reproducible than the biplane Simpson algorithm recommended by ASE for adult patients, with intermediate reproducibility of the MS approach. Intra-reader reproducibility was higher than inter-reader for all parameters regardless of the algorithm chosen, and utilizing an average of three beats improved both intra and inter-reader reproducibility. The greatest benefit of using beat

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averaging occurred in the most dilated and/or dysfunctional LVs. In other words, even though parameters became less reproducible as the degree of disease severity increased, utilizing a three beat average mitigated the effect. Conversely, the closer to normal the size and systolic function are, the less likely that beat averaging improves reproducibility of LVEF. Although the ICCs were high, the broad limits of agreement on Bland-Altman analysis indicate differences among the algorithms that are highly significant. In other words, while correlation among the algorithms was high, agreement was not.

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The study has several important implications. The clinical management of this population over time relies on serial assessment of LV size and function, and our results imply that comparison of serial echocardiograms may not be valid if different measurement algorithms are used, either between laboratories or in the same patient between visits. Also, because the absolute values were different among the approaches, algorithm-specific normal values are required. These method-specific results for LV mass and volume calculations are parallel to the previously reported differences noted between imaging modalities, with cardiac magnetic resonance imaging (CMR) yielding ventricular volumes that are highly correlated with echocardiographic values obtained using the 5/6AL method, but are on average 14% larger (6). It is worth noting that in the current study, the 5/6AL algorithm yielded the largest volumes of the three algorithms, indicating that the other methods would be expected to underestimate CMR methods by an even larger proportion.

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The added benefit of 3BA is also a significant finding. The clinical care of pediatric patients may be affected by the 20-40% difference between single and 3BA performance, even though this is the percentage difference (%error) in EF rather than absolute LVEF percentage points. For example, even though the absolute difference between an EF measured as 40% versus 36% is 4 percentage points, the %error is 11% [difference in values divided by the mean x 100: $(40-36)/38 \times 100$]. The improved reproducibility using a single-reader approach mirrors observations from other studies, but implementing reliance on longitudinal measurements by a single observer in the clinical setting presents nearly insurmountable logistical obstacles. However, from the standpoint of research study design, we have demonstrated that the utilization of echocardiographic endpoints in this population benefits from a single reader approach, using multi-beat averaging of values. Given the challenges of achieving sufficient sample size in such rare-disease populations, the enhanced reproducibility of data would allow for a smaller sample size and therefore overall cost savings in clinical trials. Additionally, for most research in pediatric populations, patient recruitment is the primary obstacle to study success; therefore, reducing the variance in endpoint measurements is a particularly important consideration.

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The superior reproducibility of the 5/6AL method over the biplane Simpson method in children can be explained by the fact that the short axis area measurement was more reproducible than the 2-chamber apical long axis area and is likely related to the generally readily available short axis window in younger patients. The short axis view may be especially advantageous in this setting, because of the systolic lateral motion of the LV that can occur in children. In fact, the short axis is preferred in many studies involving children, which utilize linear dimension assessment of the LV (7, 8). Additionally, the apical 2-

chamber view is less frequently utilized in pediatric laboratories, in part because the small rib spaces in children makes the view more technically challenging.

Although the importance of reproducible quantitative data on LV size and function is widely recognized, it is equally widely acknowledged that such data are not currently available in pediatrics(5). Recommendations for adults are commonly applied to pediatric populations without acknowledgement of the limitations. A recent review of general echocardiographic nomograms available for use in pediatric populations (9) examined the currently available literature and described the significant limitations faced in the field, including a lack of standardized approaches to measurements (as highlighted in this report), as well as the lack of a robust database of measurements based on a large population of healthy children. In fact, most of the available nomograms for evaluation of LV size and function rely on m-mode dimensions, with occasional assessment of areas(10). Interest in this aspect of pediatric echocardiography is growing, however. Normative values in children based on the 5/6AL method as used in this study have been published(11), and Lytrivi and colleagues recently published normal values for the 5/6AL method, utilizing subcostal imaging planes rather than parasternal/apical planes, as this study used (12). Nielsen described good correlations between the 5/6AL method with CMR in a small series of children under 10 years of age (13). Utilizing parasternal/apical planes in larger patients may be superior to subcostal planes, however, due to decreased subcostal window availability.

Limitations

While these analyses assessed reproducibility of assessments, the study was not designed to assess accuracy. It should be kept in mind, however, that clinical management of patients rarely requires accuracy, but instead relies on the assessment of trends, making reproducibility important. Additionally, the core laboratory approach used in this study may not be applicable to clinical laboratories. Pediatric readers in general may be more experienced with the 5/6AL method versus the others, which may impact findings. Although we did not see a significant impact of age or BSA on the overall reproducibility of the majority of these measures, other important factors that may impact reproducibility of measurements, (e.g. specific diagnosis, treatment status or technical factors regarding image acquisition such as use of harmonics), were not examined in this analysis and will be investigated in further VVV study reports.

Conclusion

Reproducibility of LV size and function measurements in children with DCM is highest using the 5/6AL algorithm. Reproducibility can be further improved by using beat averaging, particularly as the severity of the disease increases. These findings have implications for endpoint choice and study design for future clinical trials in pediatric patients with DCM: utilizing a single reader core laboratory structure, the 5/6AL method of LV assessment, and reliance on 3BA results in increased reproducibility.

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Appendix

Appendix

Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
• Age <22 years	• Other forms of cardiomyopathy (e.g. HCM, restrictive cardiomyopathy)
• Diagnosis of dilated cardiomyopathy	• LV noncompaction
• Disease onset > 2 months	• Suspected acute myocarditis
• Anticipated follow-up at same institution	• Ventricular paced or other non-sinus rhythm
• Informed consent	• Congenital heart disease
• LVEDD>5.5cm (or z-score for BSA >2) on baseline study	• Heart transplant waiting list status 1A or 1B
• LVEF < 50% (or z-score for age <-2) or LVFS <28% (or z-score for age <-2) on baseline study	• Hemodynamic instability, including intravenous inotropic support, current LVAD or ECMO support

BSA: body surface area, ECMO: extracorporeal membrane oxygenator, HCM: hypertrophic cardiomyopathy, LV: left ventricle, LVAD: left ventricular assist device, LVEDD: left ventricular end-diastolic dimension, LVEF: left ventricular ejection fraction, LVFS: left ventricular fractional shortening.

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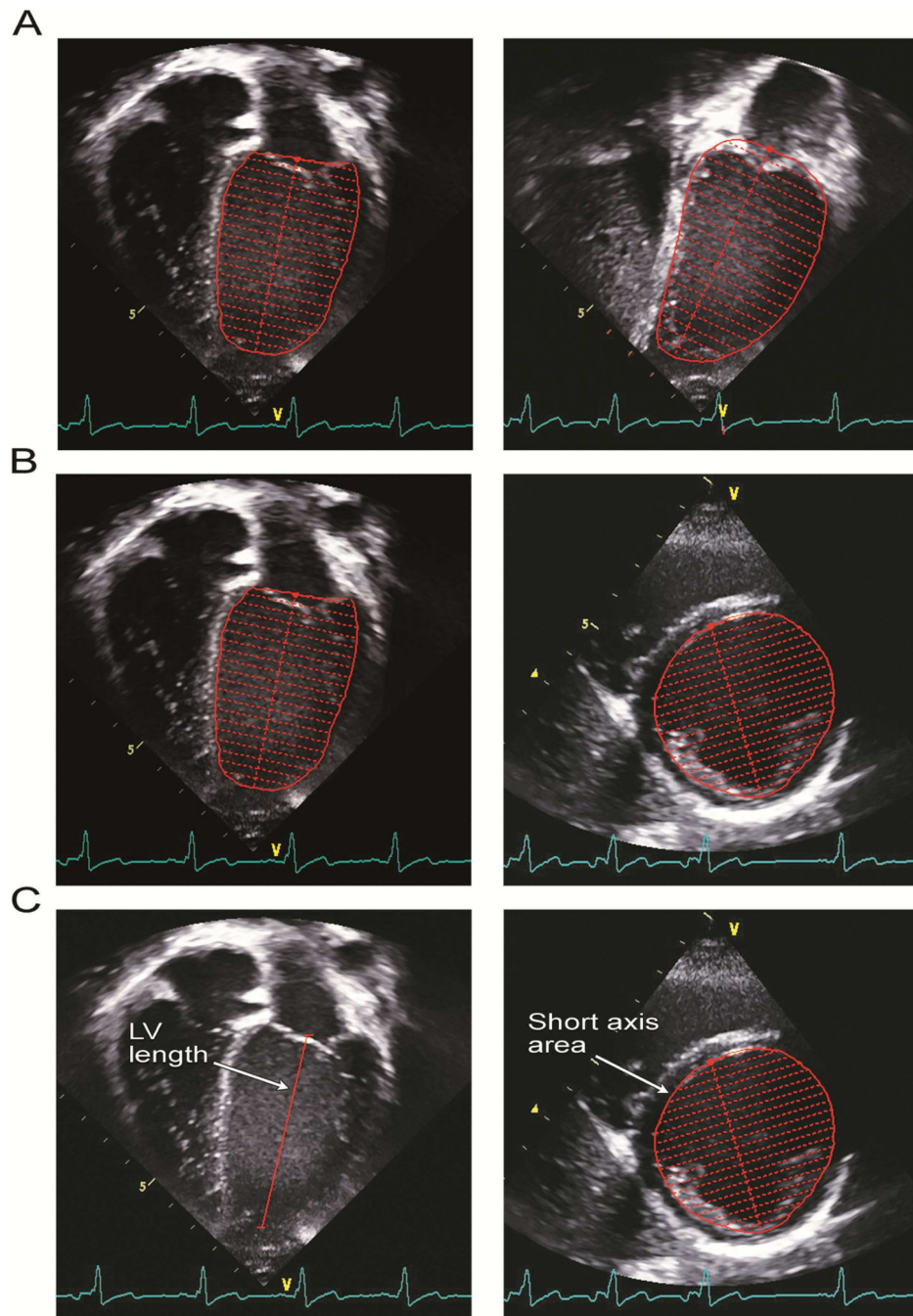


Figure 1. Representative images demonstrating the measurements obtained for each calculation method. A. Biplane Simpson, B. Modified Simpson, C. $\frac{5}{6} \times \text{Area} \times \text{Length}$, area and length measurements demonstrated.

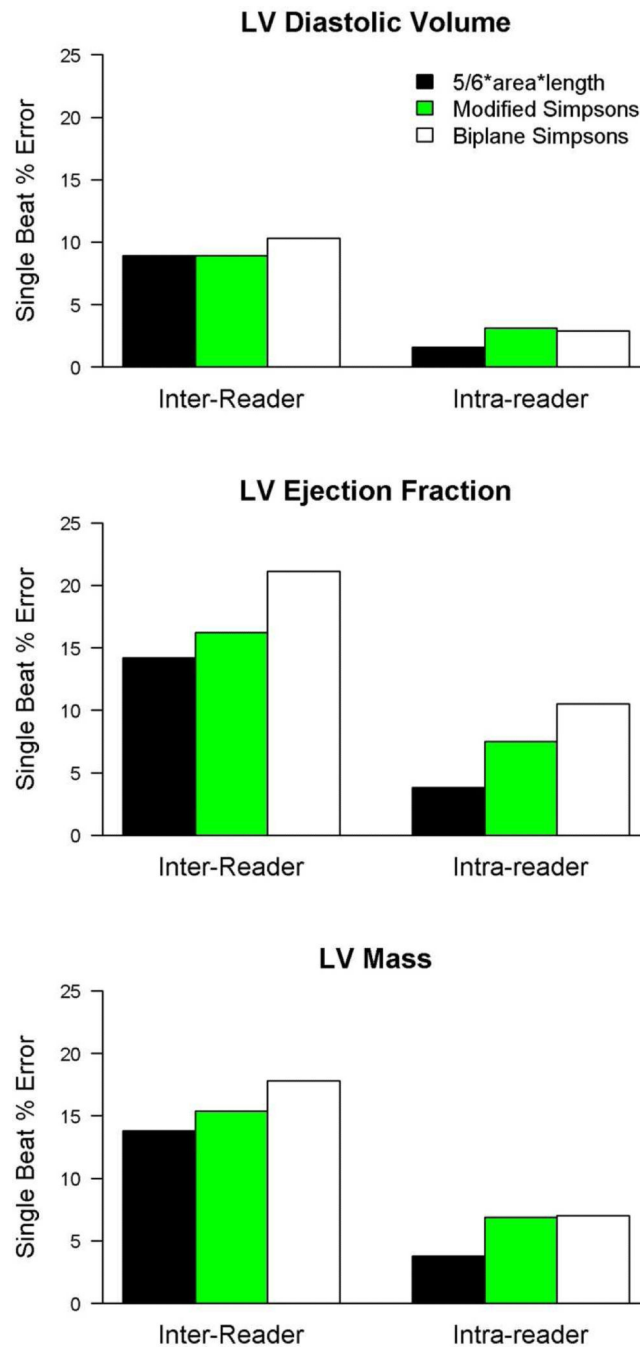


Figure 2.

Single Beat %error for three measurement algorithms. p values for *inter-reader* %error comparisons: all 5/6*area*length vs. Modified Simpson, p=n.s.; for Modified Simpson or 5/6*area*length vs. Biplane Simpson, p 0.01. p values for *intra-reader* %error comparisons: all 5/6*area*length vs. Modified Simpson or Biplane Simpson, p<0.001; LVEDV and LV mass Modified Simpson vs. Biplane Simpson p=n.s.; LVEF Modified Simpson vs. Biplane Simpson p<0.001

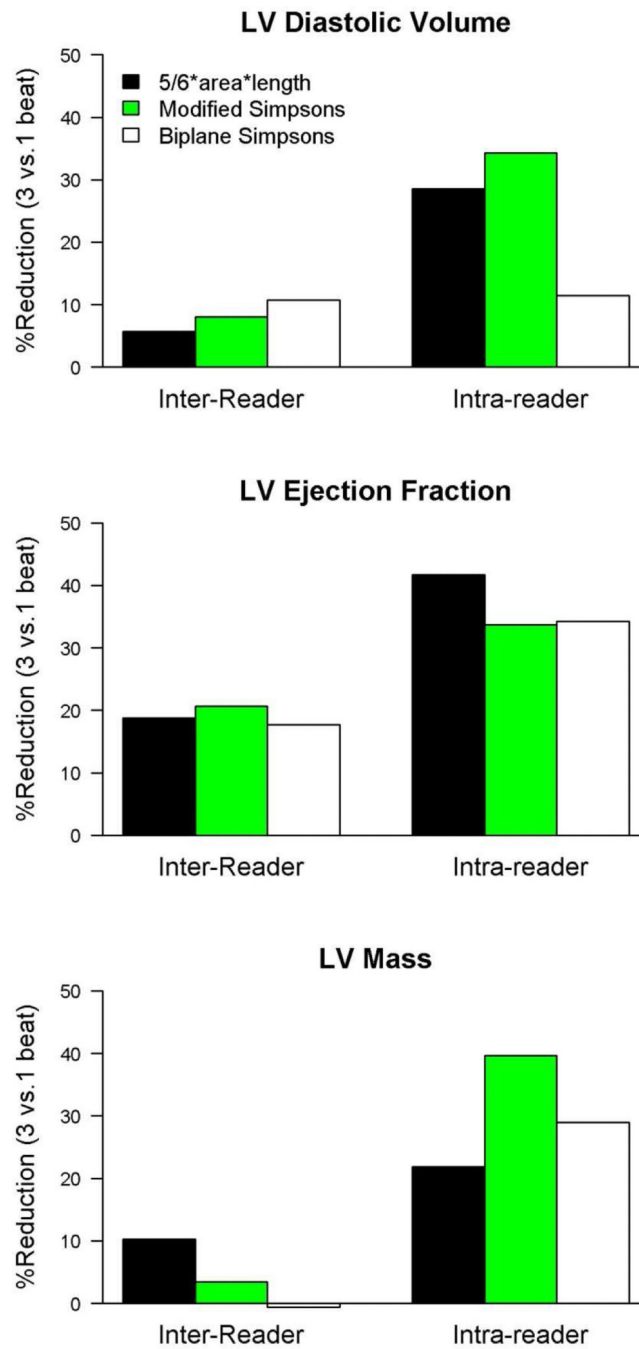


Figure 3.
Reduction in Error: 3 beat average relative to single beat.

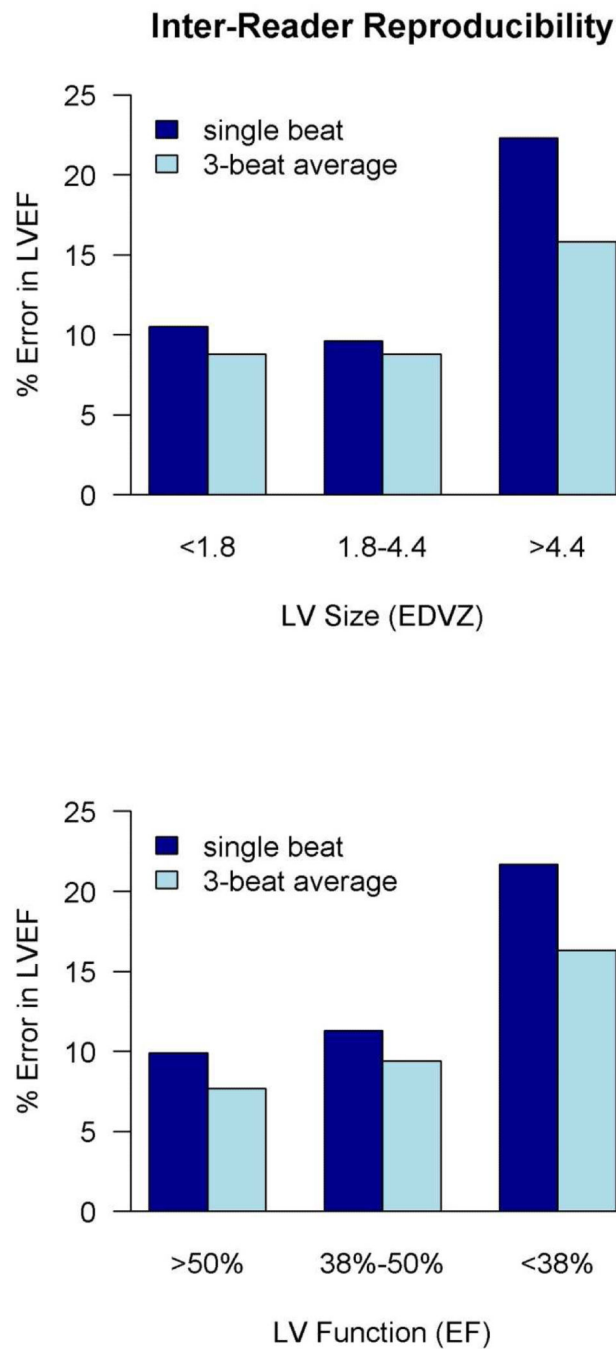


Figure 4. Effect of left ventricular size and function on Inter-reader Reproducibility of LVEF. LV size and function expressed in tertiles: LVEDV z-scores <1.8, z-scores 1.8 - 4.4, and z-scores >4.4; LVEF >50%, 38-50% and <38%.

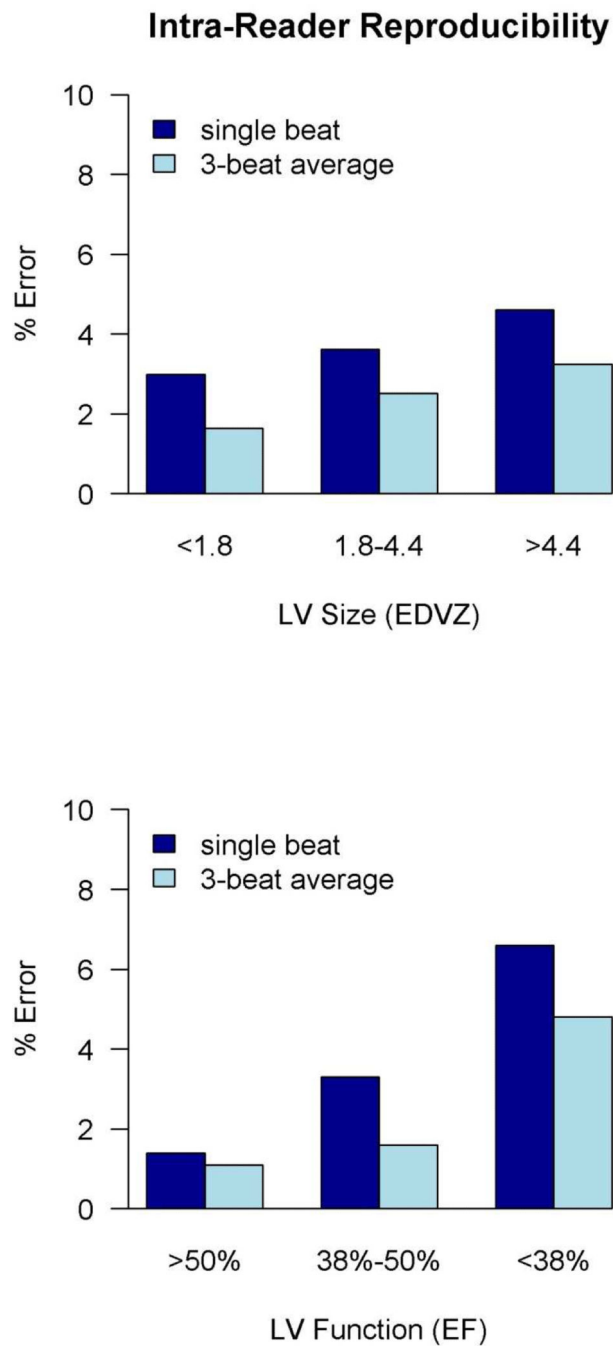
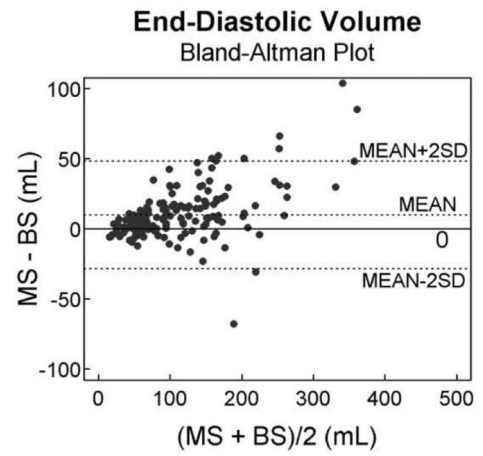
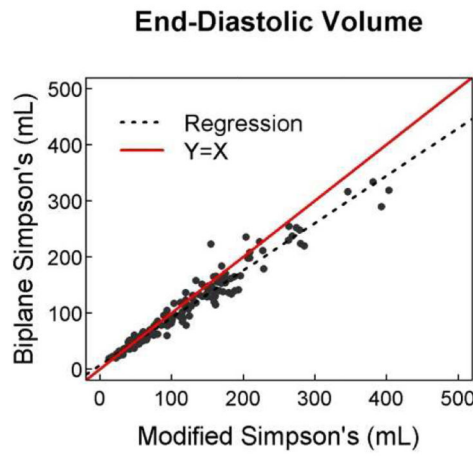


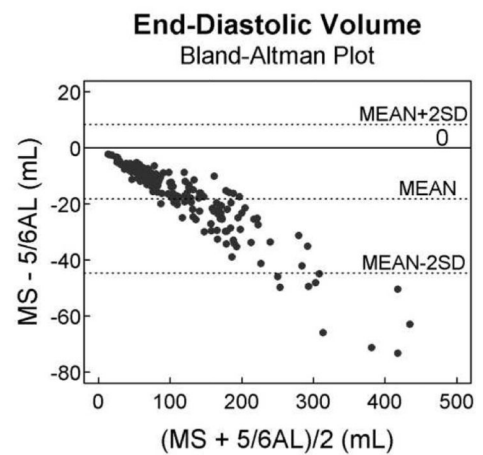
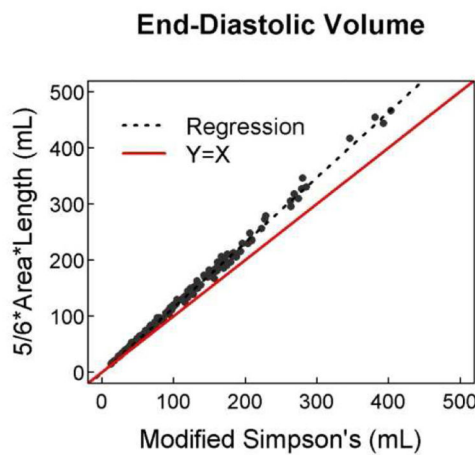
Figure 5. Effect of LV Size and Function on Intra-reader Reproducibility of LVEF. LV size and function expressed in tertiles: LVEDV z-scores <1.8, z-scores 1.8 - 4.4, and z-scores >4.4; LVEF >50%, 38-50% and <38%.

A. LV EDV, mL

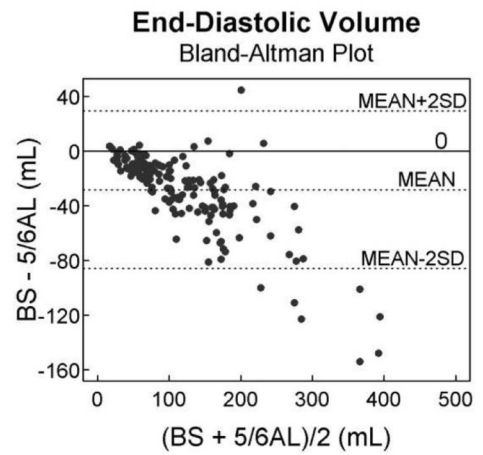
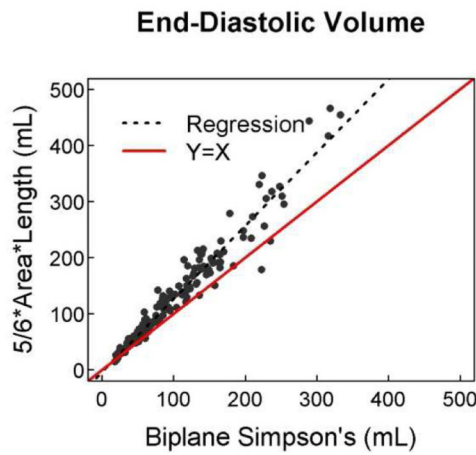
1. Modified Simpson vs. Biplane Simpson



2. Modified Simpson vs. 5/6*area*length

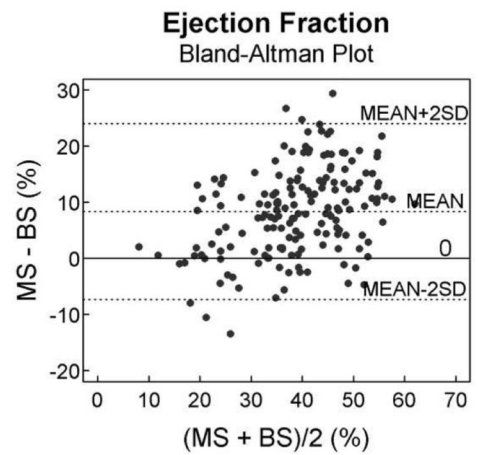
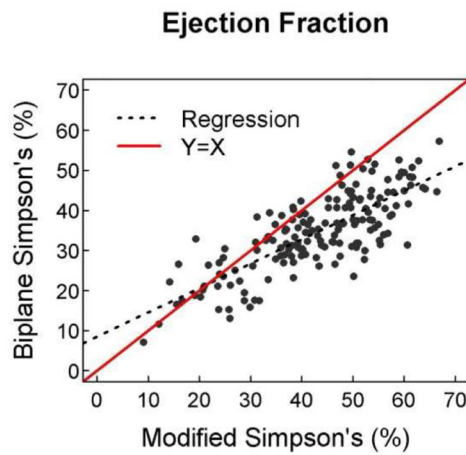


3. Biplane Simpson vs. 5/6*area*length

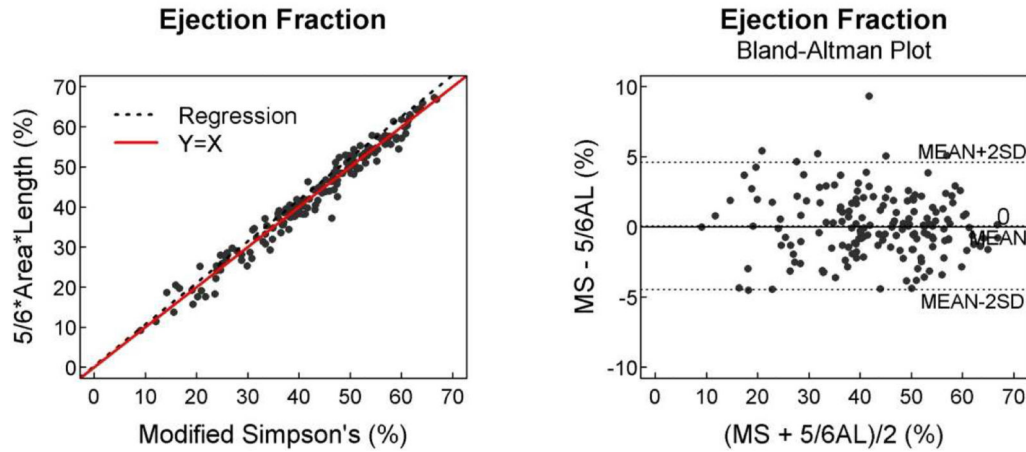


B. LVEF, %

1. Modified Simpson vs. Biplane Simpson



2. Modified Simpson vs. $5/6 \cdot \text{area} \cdot \text{length}$



3. Biplane Simpson vs. $5/6 \cdot \text{area} \cdot \text{length}$

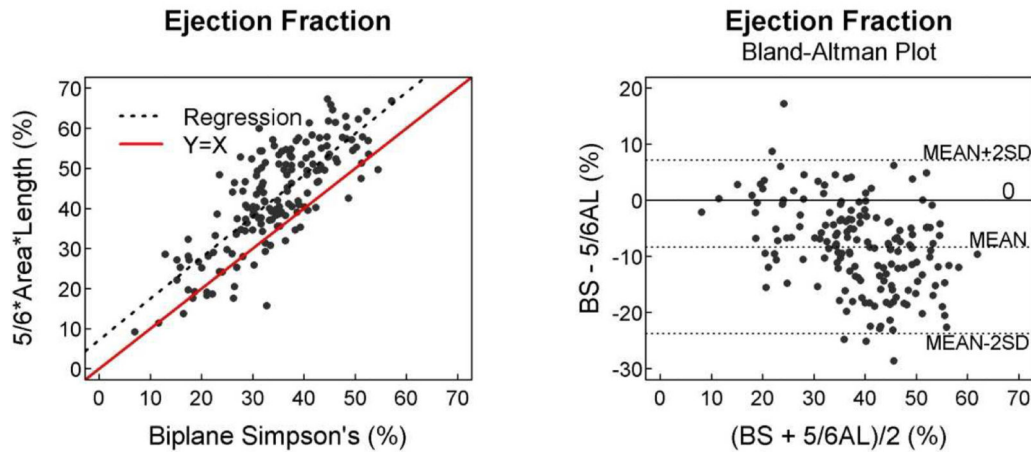


Figure 6. Scatter plots and Bland-Altman plots between Modified Simpson, Biplane Simpson and $5/6AL$ using 3-BA. A. LV EDV, mL 1. Modified Simpson vs. Biplane Simpson, 2. Modified Simpson vs. $5/6 \cdot \text{area} \cdot \text{length}$, 3. Biplane Simpson vs. $5/6 \cdot \text{area} \cdot \text{length}$. B. LVEF, % 1. Modified Simpson vs. Biplane Simpson, 2. Modified Simpson vs. $5/6 \cdot \text{area} \cdot \text{length}$, 3. Biplane Simpson vs. $5/6 \cdot \text{area} \cdot \text{length}$.

Table 1

Baseline demographic and diagnostic data

Characteristic	Median (range) or %
Age at echocardiogram (years)	9.5 (0.2 - 20.6)
Height (cm)	136.0 (58.0 - 195.5)
Weight (kg)	30.5 (4.4 - 136.5)
BSA (m ²)	1.1 (0.3 - 2.6)
Male	50.2%
Age at diagnosis of cardiomyopathy (years)	2.7 (0.0, 19.2)
Cause of Dilated Cardiomyopathy	N (%)
Idiopathic	104 (62%)
Anthracycline-associated	25 (15%)
Neuromuscular disease	6 (4%)
Single gene defect	5 (3%)
Metabolic disorder	4 (2%)
Mitochondrial disorder	2 (1%)
Other	23 (14%)
Baseline LV characteristics	Median \pm SD or %
EDVz	3.4 \pm 3.2
EDVz > 2	104 (63%)
LVEF, %	43.0 \pm 12.6
LVEFz	-4.4 \pm 2.7
LVEFz > -2	135 (80%)

BSA: body surface area, LVEDVz: left ventricular end-diastolic volume z-score (calculated by the 5/6 area/length method), LVEF: left ventricular ejection fraction (calculated by the 5/6 area/length method), LVEFz: left ventricular ejection fraction z-score.

Table 2

Measurement Agreement by Modified Simpsons, Biplane Simpsons and 5/6AL

	Modified Simpsons			Biplane Simpsons			5/6*Area*Length		
	Mean±SD	Median (IQR)	Mean±SD	Median (IQR)	Mean±SD	Median (IQR)	Mean±SD	Median (IQR)	ICC
LVEDV, mL	113.5±75.7	96.0 (53.7,157.2)	103.3±65.8	85.0 (52.7, 140.0)	131.8±88.2	111.4 (63.9, 181.4)	0.990		
LVESV, mL	68.8±58.7	52.1 (28.2,86.2)	70.0±52.8	56.2 (31.1, 91.3)	79.8±67.7	59.8 (33.7, 102.4)	0.989		
LV Mass, g	84.7±52.9	74.3 (43.2,119.8)	75.0±46.3	63.2 (37.1, 107.0)	96.8±60.4	83.9 (48.5, 137.2)	0.989		
LVEF, %	42.9±12.6	44.6 (35.4,52.0)	34.9±9.9	35.2 (29.0, 41.7)	43.0±12.6	43.9 (35.5, 52.8)	0.953		

ICC, intra-class correlation coefficients; IQR, interquartile range; LVEDV: left ventricular end-diastolic volume, LVEDV: left ventricular end-diastolic volume, LVEF: left ventricular ejection fraction, LVESV: left ventricular end systolic volume.