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Variability of M-mode versus two-dimensional echocardiography measurements in children with dilated cardiomyopathy.

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Variability of M-Mode Versus Two-Dimensional Echocardiography Measurements in Children With Dilated Cardiomyopathy

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Abstract

M-mode and 2-dimensional (2D) echocardio-graphic imaging are routinely used to quantify leftventricular (LV) size and function in pediatric patients with dilated cardiomyopathy (DCM). The reproducibility of and correlation between these techniques are unknown. This analysis sought to compare interreader, intrareader, and interacquisition reproducibility of M-mode versus 2D measurements in pediatric DCM patients. The Ventricular Volume Variability study of the Pediatric Heart Network is a multicenter, prospective, observational study assessing the course of chronic DCM in children. Two sonographers performed baseline image acquisitions locally, and two readers performed measurements at the echocardiographic core laboratory. One reader repeated measurements 1 month later. These data were used to assess reproducibility and agreement between M-mode and 2D measurements. One hundred sixty-nine subjects were enrolled. M-mode had similar or greater reproducibility in both intrareader and interreader settings for LV dimensions, shortening fraction (SF), and most wall thicknesses. In contrast, 2D reproducibility was similar or better for nearly all variables in the interacquisition setting but not for SF. Interacquisition variability was approximately twice the intrareader variability. LV dimensions by either modality consistently had high reproducibility and had the highest agreement between modalities. In pediatric DCM patients, variability of linear echocardiographic assessment could be minimized by relying on a single reader and using a consistent method (M-mode or 2D) for serial measurements, preferably M-mode when SF is the primary variable of interest. Except for LV dimensions, M-mode and 2D values should not be used interchangeably due to poor agreement.

Keywords

Cardiomyopathy; Ventricular function; Pediatrics; Echocardiography; Reproducibility

Introduction

Echocardiographic assessments of left-ventricular (LV) dimensions, mass, and function are an essential part of the diagnosis and ongoing management of pediatric patients with dilated cardiomyopathy (DCM). Echocardiographic measurements are commonly used in outcome studies of children with DCM [1, 5, 9, 10, 16] and as an end point to assess therapeutic drug interventions in pediatric heart failure patients [2, 14, 15]. In designing a study where an echocardiographic measurement is a variable or outcome, the sources and magnitude of variability should be identified and decreased when possible.

M-mode and 2-dimensional (2D) echocardiography allow simple linear measurements of LV dimensions and wall thickness, and these measurements enable calculation of LV shortening fraction (SF), mass, and other variables of systolic performance. There are few studies in the pediatric population evaluating the reproducibility of these measurements and rarely in the setting of DCM [4, 7, 11, 13]. There is also paucity of data examining the impact of regional wall motion abnormalities (RWMAs) and interventricular septal flattening (ISF) on the reproducibility of these measurements.

This analysis sought to (1) compare interreader and intrareader reproducibility of LV dimensions, SF, and mass in pediatric patients with DCM using M-mode versus 2D measurements; (2) determine the effect of interacquisition differences on reproducibility; (3) determine whether and how the presence of RWMA and/or ISF affect reproducibility; and (4) assess agreement between the two modalities.

Materials and Methods

This analysis uses the Pediatric Heart Network Ventricular Volume Variability (VVV) Study database. The VVV study is a multicenter, prospective, observational study assessing the longitudinal course of chronic DCM in children. The study design has previously been described in detail [3]. As part of the VVV study, data relevant to intrareader and interreader variability of multiple echocardiographic indices of LV dimensions, mass, and function in pediatric patients with DCM were collected. Subjects were enrolled at eight study centers between May 2005 and July 2007. The study was approved by the Institutional Review Committee at each study center. Consent was obtained from the patient (if of legal age), parent, or legal guardian.

Subjects

Patient-enrollment criteria included the following: age < 22 years, diagnosis of chronic DCM based on LV end-diastolic dimension >5.5 cm or *z*-score for body surface area (BSA) > 2 on the first study echocardiogram, LV ejection fraction <50 % or SF < 28 % (or *z*-score for age < −2) on the first echocardiogram, disease duration >2 months, anticipated ongoing evaluation at the same institution, and informed consent or assent. Exclusion criteria included other forms of cardiomyopathy, including LV noncompaction, congenital heart disease, frequent ectopy, and need for intravenous or mechanical hemodynamic support.

Demographics

Patient data, including age, length/height, weight, blood pressure, sex, race, and etiology of DCM, were obtained. BSA was calculated using the Haycock formula [8].

Echocardiographic Acquisition and Analysis

All clinical centers followed a standardized protocol for transthoracic image acquisition. Baseline echocardiograms performed at study enrollment included two identical protocol echocardiograms: The first acquisition was followed immediately by a second acquisition performed by another sonographer.

These studies were submitted to the echocardiographic core laboratory for central measurement of 150 echocardiographic variables (M-mode, 2D, Doppler, and tissue Doppler) by two experienced readers (termed primary and secondary readers) to assess interreader variability. To assess intrareader variability, the primary reader performed measurements on the first acquisition baseline study and repeated measurements on that study 1 month later. To examine interacquisition variability, measurements made by the primary reader on the first and second acquisition echocardiograms were compared. For each variable, measurements were performed on three sequential cardiac cycles. The presence of RWMAs and/or ISF was noted.

Of the 150 echocardiographic variables measured in each VVV study echocardiogram, 12 M-mode and the corresponding 12 2D variables and calculations from the baseline echocardiograms comprise the data set for this analysis. A previous VVV analysis of the impact of beat averaging on reproducibility of echocardiographic variables showed that use of three-beat averaging yielded better reproducibility, and thus three-beat average measurements were used in this analysis [3].

M-mode and 2D images of the LV short axis at the level of the papillary muscles from parasternal windows were used to measure LV end-diastolic and end-systolic dimensions (LVEDD and LVESD, respectively), end-diastolic interventricular septal thickness (EDIVST) and posterior wall thickness (EDPWT), and end-systolic interventricular septal thickness (ESIVST) and posterior wall thickness (ESPWT). Using these measurements, SF, LV thickness-to-dimension ratio, velocity of fiber shortening, end-systolic wall stress, and end-systolic fiber stress were calculated. Calculations of LV mass for both M-mode and 2D were based on the Devereux formula [6]. All echocardiographic measurements were performed using custom DICOM software (Echotrace; Marcus Laboratories, Boston, MA).

Statistical Methods

Reproducibility Analysis—The outcome measure of reproducibility for all variables was % error of the mean.

For interreader reproducibility:

 $\%$ error= $\frac{|(\text{Primary reader measurement} - \text{secondary reader measurement})| \times 100}{\sqrt{(\text{Primary說} - \text{decayed} + \text{measurement} + \text{secondary reader} + \text{measurement})}}$ Mean of primary and secondary reader measurements

For intrareader reproducibility:

 $|$ (Primary reader'simmediate measurement – Primary reader's1 – month measurement) $| \times 100$ $\%$ error= Mean of primary reader'simmediate and 1month measurements

For interacquisition reproducibility:

 $\%$ error= $\frac{|(\text{First acquisition measurement} - \text{second acquisition measurement})| \times 100}{\sqrt{2\pi}}$ Mean of first and second acquisition measurements

A mixed-effects model (fixed effect of mode and random effect for subjects) with estimates obtained by restricted maximum likelihood, unstructured covariance structure, was used to assess whether interreader and intrareader % errors significantly differed between measurements made by M-mode and 2D, and to assess the impact of RWMA and ISF on reproducibility.

Agreement Analysis—Based on the primary reader's immediate measurements, intraclass correlation coefficient (ICC) estimation from a random effects model and Bland– Altman analyses and plots were used to determine the level of agreement between M-mode versus 2D measurements.

Results

Demographics

During the study period, 169 subjects were enrolled. Patient demographic data at the time of baseline echocardiogram are listed in Table 1. Infants (age $<$ 1 year) comprised 11 % of the subjects ($N = 18$), and adolescents (age 12 years) comprised 39 % ($N = 66$).

Interreader Reproducibility

Table 2 summarizes interreader reproducibility (% error). Median % error was smallest for LVEDD and LVESD (2–3 %) and was 8–16 % for other measures. M-mode measurements had significantly greater interreader reproducibility (lower % error) for SF, LV mass, EDIVST and ESIVST, whereas 2D measurements had significantly greater interreader reproducibility for ESPWT and LV end-systolic stress. Reproducibility was similar for the two methods in measurements of LVEDD, LVESD, EDPWT, velocity of fiber shortening, and end-systolic fiber stress.

Intrareader Reproducibility

Table 3 summarizes intrareader reproducibility (% error). Median % error was also lowest for LVEDD and LVESD (<2 %), whereas the magnitude of median % error was 4–9 % for all other variables. Intrareader reproducibility was similar for the two methods for all measurements except SF and velocity of fiber shortening, which both had greater intrareader reproducibility (lower % error) by M-mode.

Interacquisition Reproducibility

The effect of acquisition on intrareader reproducibility was made by comparing measurements made by the primary reader of the first versus second acquisition. 2D measurements had significantly greater reproducibility (lower % error) than M-mode for 6 of the 12 variables: LVESD, EDIVST, EDPWT, ESPWT, thickness-to-dimension ratio, and end-systolic stress (Table 4). Conversely, M-mode had greater reproducibility for SF and velocity of fiber shortening. Overall, comparison of intrareader reproducibility using the same echocardiographic study evaluated 1 month apart versus using two consecutive image acquisitions shows that interacquisition variability results in approximately twice the % error (Tables 3, 4). Table 5 summarizes the comparison of interreader, intrareader, and

RWMAs and ISF

RWMAs were present in 20 % of baseline images ($N = 33$) and ISF in 10 % ($N = 17$). There were no significant interactions between RWMA or ISF and mode of measurement (Mmode vs. 2D), meaning that the differences in reproducibility between modes, where they exist, were present regardless of whether RWMA or ISF was used.

When RWMAs were present, there were variables that had significantly greater % error regardless of mode. In the interreader setting, these variables were EDPWT ($p = 0.002$), ESPWT ($p < 0.001$), LV thickness-to-dimension ratio ($p < 0.001$), LV end-systolic stress (p < 0.001) and LV end-systolic fiber stress ($p < 0.001$), and SF ($p = 0.033$). In the intrareader setting, these variables were EDIVST ($p = 0.003$), ESIVST ($p = 0.025$), SF ($p < 0.001$), and LV velocity of fiber shortening ($p = 0.001$). Mean % errors for SF when RWMA were present were 18–19 % in interreader and 11–16 % in intrareader settings, significantly greater than 12–16 % and 6–9 %, respectively, when RWMAs were not present. When ISF was observed, only one variable, ESIVST ($p = 0.026$), had greater % error in the interreader setting regardless of mode.

Agreement Analysis of M-mode Versus 2D

Table 6 displays the primary reader's immediate measurements made by M-mode versus 2D and the ICC between the two methods. The ICC was highest (best) for LV dimensions (0.97 for both LVEDD and LVESD) followed by LV mass (ICC 0.94) and SF (ICC 0.86). Figure 1 shows the scatter and Bland–Altman plots of 2D versus M-mode measurements of selected variables (LV dimensions and septal wall thicknesses). Bland–Altman plots are presented in two ways: with the absolute difference between 2D and M-mode measurements on the yaxis and with the % difference between measurements on the y-axis. These show that the confidence band (half the total width) is approximately 10–15 % for LV dimensions and 30– 35 % for septal wall thicknesses. For posterior wall thicknesses, SF, mass, and velocity of fiber shortening, the confidence band is 30–35 % and 50 % for end-systolic stress (Figures available in online supplement). Agreement analysis showed systematically lower mass by 2D methodology compared with M-mode at greater absolute mass values and also lower SF values by 2D methodology.

Discussion

In this analysis comparing linear echocardiographic measurements in pediatric DCM patients, intrareader reproducibility was consistently greater than interreader reproducibility for all variables regardless of whether measured in M-mode or 2D. This is an expected finding that has been shown in previous pediatric studies of M-mode measurements in healthy children [4, 7, 11].

In addition, similar to previous studies, we found that both interreader and intrareader reproducibility were highest (lowest % error) for LV dimensions [4, 7, 13]. Amongst all measurements, there was highest agreement between methods for LV dimensions.

Consistent measurement of LV dimensions requires accurate identification of the blood– endocardium interface, and the good spatial and temporal resolution provided by M-mode and recent improvements in resolution by 2D imaging may explain the low variability and high correlation between methods for LV dimensions.

An expected finding of the comparison between 2D and M-mode is that some measurements should be more reproducible by M-mode, which relates to the fact that one of the sources of variability, the reader-selected position of wall for measurement, is absent in M-mode. The analysis of the impact of interacquisition reproducibility provides some insight into this issue because the placement of the M-mode sample and the imaging plane for 2D image acquisition will vary between acquisitions by different sonographers. This analysis showed that interacquisition variability approximately doubled the intrareader variability even when the second set of images was obtained immediately after the first and was obtained according to the same protocol. In this comparison, 6 of 12 measurements had lower median % error by 2D than by M-mode methods, although both SF and velocity of shortening had lower median % error by M-mode. SF and velocity of shortening notwithstanding, the comparison of intraobserver analysis of the same versus different image acquisitions supports the concept that 2D imaging may permit the observer to overcome some of the limitations imposed by the fixed location for M-mode measurements. In clinical practice as well as in the conduct of clinical research, the effect of image acquisition contributes to the analysis of temporally related change in echocardiographic variables. Therefore, the results of this comparison may be more meaningful in this context than intraobserver or interobserver analysis of a single acquisition.

SF is the linear-derived echocardiographic variable most often used in both clinical practice and research of pediatric DCM patients. For SF, M-mode was more reproducible than 2D in the intrareader, interreader, and interacquisition analyses. M-mode tracings may allow for more consistency in SF measurements because end-diastole and end-systole are displayed on the same image, and the same border "line" representing the endocardium is followed over the cardiac cycle. In contrast, the 2D image displays end-diastole and end-systole on separate images, and thus these measurements are dependent on the reader to visually follow the specific border representing the blood–endocardium interface between images on a frame-by-frame basis.

Recently published guidelines by the American Society of Echocardiography on quantification in pediatric echocardiograms recommended that 2D imaging in parasternal or subxiphoid short-axis views be used instead of M-mode for LV short-axis measurements [12]. These expert opinion- based recommendations were justified based on the ability to confirm LV geometry on the same image on which the measurements are performed. Our results concerning reproducibility do not unequivocally indicate the superiority of one method or the other in pediatric DCM patients. Although M-mode appears to have an advantage compared with 2D methods for a number of linear LV measurements regarding inter and intraobserver variability, when the effect of sequential image acquisition is included in the analysis, there are advantages to the 2D technique with the exception of the derived variables related to function and velocity of shortening.

Implicit in the use of linear echocardiographic techniques, because they characterize the left ventricle in only one dimension, is that the short-axis diameter is circular [12]. Both RWMAs and ISF may result in a noncircular short-axis LV configuration, and thus their effect on reproducibilty was evaluated. Differences in reproducibility between 2D versus Mmode did not depend on whether RWMAs or ISF were present. Although ISF had little effect on reproducibility results, the reproducibility of multiple variables was affected by RWMAs regardless of mode. The most important finding was the significantly greater mean % error for SF when RWMAs were present. These results confirm that when RWMAs are present, it is inadvisable to use linear echocardiographic techniques.

There have been few reports concerning the agreement and interchangeability of M-mode and 2D measurements. In this analysis, there was very high correlation between both modes for LV dimensions (ICC = 0.97 for LVEDD and LVESD). Although there was also high correlation between modes for calculation of LV mass (ICC = 0.94), agreement analysis showed a systematically lower mass by 2D methodology compared with M-mode at greater absolute mass values. Similarly, although there is good correlation for SF (ICC = 0.86), agreement analysis showed lower values by 2D methodology compared with M-mode values. Clinical decisions are frequently based on echocardiographic LV systolic function assessment, and these findings caution that 2D assessment of SF may produce a worse impression of systolic function than if M-mode had been used. This systematic difference implies that method-specific normative ranges must be used for the clinical interpretation of these measurements.

The Bland–Altman analyses and plots showed poor agreement between M-mode and 2D measurements for all variables except LV dimensions. Even for LV dimensions, although the agreement between M-mode and 2D measurements was better, the limits of agreement ranged from 20 to 30 %. In clinical practice it would not be practical then to assume that the values obtained from one mode are interchangeable with the other. Thus, modality-specific normative data are required to enable comparison of values obtained by these different methods.

Limitations

Because the intent of this study was to evaluate patients with chronic, stable DCM, there were relatively fewer infants in this study population (11 %) compared with the proportion of infants reported in large population-based cohort studies of pediatric DCM (41–66 %) [5, 16]. Factors that may impact reproducibility of M-mode and 2D measurements, such as patient age, body size, disease severity, use of sedation, and technical factors regarding image acquisition, such as the use of harmonics, were not examined in this analysis.

Ultimately, although reproducibility is an important consideration when selecting a specific modality, the comparative accuracy of these measurements is important but not known because there is no "gold standard" for comparison. There may indeed be a tradeoff between reproducibility and accuracy. For example, 2D measurements allow the reader to select regions of the wall that are most representative of circumferential wall thickness and

therefore may provide a more accurate measurement but potentially at the expense of reproducibility.

From a clinical perspective, echocardiographic evaluation of LV function must be considered in the context of a patient's clinical status. Decisions on therapeutic intervention take into account both echocardiographic and clinical variables. Although our analyses showed statistically significant differences in reproducibility and agreement between echocardiographic modes and in different reader and acquisition settings, these may not be considered clinically significant.

Conclusion

In the evaluation of pediatric DCM patients by linear echocardiographic methods, M-mode has similar or greater reproducibility (lower % error) than the 2D method in both intrareader and interreader settings for the assessment of LV dimensions, SF, and most wall thicknesses. In contrast, 2D reproducibility was similar or better for nearly all variables in the interacquisition setting but not for SF. LV dimensions by either modality consistently had high reproducibility and had the highest agreement between modalities. However, for other variables, poor agreement precludes the use of 2D and M-mode interchangeably. Normative data for the two methods are needed to enable comparison of values obtained by these different methods. These findings have important implications for the design of future studies in pediatric DCM patients. Variability could be minimized by relying on a single reader and using a consistent method (M-mode or 2D) for serial measurements, preferably M-mode when SF is the primary variable of interest, because it had the greater reproducibility in intrareader, interreader, and interacquisition settings.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1.

Scatter plots and Bland–Altman plots of M-mode versus 2D measurements. **a** End-diastolic short-axis dimension (cm). **b** End-systolic short-axis dimension (cm). **c** End-diastolic septal thickness (cm). **d** End-systolic septal thickness (cm)

Patient demographic data at baseline echocardiogram acquisition (*N* = 169)

Interreader reproducibility in M-mode and 2D measurements Interreader reproducibility in M-mode and 2D measurements

Bold values are statistically significant $(p < 0.05)$ }
}

Pediatr Cardiol. Author manuscript; available in PMC 2015 December 16.

SD standard deviation, IQR interquartile range, SAX short-axis, LV left ventricle *SD* standard deviation, *IQR* interquartile range, *SAX* short-axis, *LV* left ventricle

Intrareader reproducibility in M-mode and 2D measurements Intrareader reproducibility in M-mode and 2D measurements

 $\text{tically sufficient}$ $(p < 0.05)$ Bold values are statistically significant $(p < 0.05)$ Bold value

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SD standard deviation, IQR interquartile range, SAX short-axis, LV left ventricle *SD* standard deviation, *IQR* interquartile range, *SAX* short-axis, *LV* left ventricle

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SD standard deviation, IQR interquartile range, SAX short-axis, LV left ventricle *SD* standard deviation, *IQR* interquartile range, *SAX* short-axis, *LV* left ventricle

Summary table of reproducibility Summary table of reproducibility

Correlation of measurements made by M-mode versus 2D Correlation of measurements made by M-mode versus 2D

SD standard deviation, IQR interquartile range, ICC intra-class correlation, SAX short-axis, LV left ventricle, circ circumferences *SD* standard deviation, *IQR* interquartile range, *ICC* intra-class correlation, *SAX* short-axis, *LV* left ventricle, *circ* circumferences