Normal Values for Left Ventricular Strain and Synchrony in Children Based on Speckle Tracking Echocardiography

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Strain and synchrony are associated with clinical outcomes in children with heart diseases. Robust normative data for these values, measured by 2-dimensional speckle tracking echocardiography (2DSTE), are limited. Therefore, we aimed to derive normal ranges and z-scores of 2DSTE strain and synchrony parameters in children. Subjects were <21 years old with structurally and functionally normal hearts. High frame-rate 2-dimensional echocardiographic images were retrospectively analyzed to measure longitudinal (LS) and circumferential (CS) strain and synchrony; views used were apical 4, 2, and 3-chamber (AP 4, 2, 3) and mid-papillary short-axis (SAX-M). Synchrony measures included standard deviation of time to peak strain, maximal wall delay, and cross-correlation mean segmental delay; these were calculated without and with heart rate (HR) correction (divided by $\sqrt{RR}$). Z-score equations were created for AP4 and SAX-M strain components. n = 312 subjects (40% female) were included (age 3 days to 20.5 years). Mean strain values (%) were: AP4 −24.4 ± 3.2, AP2 −24.2 ± 3.3, AP3 −24.6 ± 3.4, SAX-M −25.8 ± 3.4. Significant differences between ages were present for all strain components (AP4 $p < 0.001$; AP2 $p = 0.003$; AP3 $p = 0.014$; SAX-M $p = 0.01$). LS components decreased with increasing age and body surface area ($p < 0.001$ for all); CS did not. Longitudinal, but not circumferential, synchrony parameters decreased with age; however, these were nonsignificant after HR correction. In conclusion, normal pediatric 2DSTE strain and synchrony parameters and z-scores are reported to provide a foundation for incorporation into clinical practice. LS decline with age whereas CS does not. Age-related decreases in LS synchrony were mostly nonsignificant when corrected for HR. **(Am J Cardiol 2019;123:1546−1554)**

Myocardial strain measured by 2-dimensional speckle tracking echocardiography (2DSTE) is increasingly being adopted into clinical practice. Impaired strain indices have been shown to be associated with adverse clinical outcomes in a variety of congenital and acquired heart diseases.[1−5] In addition, ventricular synchrony measures derived from strain are associated with life-threatening arrhythmias, heart failure, and mortality in both adult and pediatric populations.[6−8] Robust normative data for a variety of strain components are well established in adult populations. Data in pediatric patients, however, are much less well developed, for normal strain as well as synchrony; before publications have been based on relatively small cohorts and have used echocardiographic platforms with limited adoption in the pediatric community.[9−13] As normal adult ranges of synchrony do not apply in the pediatric population,[14] appropriate age-based measures are needed in this population. For the Philips echocardiographic platform, which is widely used in pediatrics, normal ranges are scarce and based on small numbers of participants, and no published z-scores are available.[15−17] Therefore, the objective of this study was to report left ventricular (LV) longitudinal (LS) and circumferential strain (CS) and synchrony parameters in a large normal pediatric cohort, using Philips ultrasound equipment and analysis tools.

Methods

Data were included from subjects referred for a clinical echocardiogram at our institution beginning in October 2015, when a protocol including strain data acquisition as part of routine clinical care was instituted. All included echocardiograms were performed in unsedated subjects <21 years old in the outpatient or well-baby nursery setting, and all were interpreted by staff pediatric cardiologists as normal studies (structurally normal heart with normal function). Patients were excluded for any of the following: noncardiac co-morbidity with potential cardiovascular impact; weight-for-age or heart rate (HR) z-score >2.5 or <−2.5; hypertension (systolic or diastolic blood pressure >95% for age or that is being medically treated); any 2-dimensional

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echocardiographic (2D-echo) measurement z-score >2.5 or <−2.5 (including ventricular volumes and ejection fraction); family history of cardiomyopathy in a first-degree relative; or poor image quality.

Demographic and clinical parameters were recorded, including: age at echocardiogram, gender, height, weight, blood pressure, HR, and 2D LV size and function measurements. The echocardiogram indication was recorded as well. Body surface area (BSA) was calculated according to the Haycock formula.[18] LV ejection fraction was recorded based upon volumes calculated using the 5/6 × Area × Length method.

This study was approved by The Committee for Clinical Investigation at Boston Children's Hospital, with a waiver of the requirement for informed consent given the retrospective nature of the research.

Echocardiograms were all performed using the Philips EPIQ platform (Philips Healthcare, Andover, Massachusetts). Image quality and temporal resolution were optimized using standard techniques. LV Images were acquired in some or all of the following views: apical 2, 3 and 4-chamber (AP2, AP3, and AP4, respectively) and parasternal short-axis (SAX) view at the mid-papillary level (SAX-M). Images were all acquired in Philips native data format (also referred to as "acquisition frame rate"), which retains all frames from the original image, maximizing temporal resolution for subsequent analyses. Images were included only if tracking of all segments were considered to be adequate.

QLAB v.10.5 (Philips Healthcare, Andover, Massachusetts) was used to evaluate longitudinal (AP4, AP2, AP3 views) and circumferential LV peak strain (SAX-M view). Of note, this software version preceded the release of the "Strain Task Force" consensus document.[19] Figure 1 presents LV segments used and Figure 2 presents strain versus time curves. These curves were produced for each segment and for the entire contour, and their peak endocardial strain values were recorded (these values were typically end-systolic, but were not expressly defined as such; aortic valve closure time was not recorded).

Three synchrony measures were calculated using the segmental curves:

1. *Standard deviation of time to peak strain* (TTP-SD): Calculated automatically by QLAB as the standard deviation of the time to peak strain value of the included segments.
2. *Maximal wall delay* (MWD): Time difference between segments with the longest and shortest times to peak strain; this was calculated from the exported data from QLAB.
3. *Cross-correlation of segmental strain-time curves*: Cross-correlation mean delay (XCMD) was calculated using custom software (National Instruments Labview, Austin, Texas). Briefly, as previously described,[13,20] cross-correlation analysis identifies the temporal shift between 2 time series based on a survey of all correlations between 2 signals computed at all possible delays, with the eventual selection of the temporal shift that demonstrates the maximum correlation result (as such, the advantage of this technique is that it may be less sensitive to noise than time-to-peak strain analysis); this value is referred to as the cross-correlation delay. In this study, the mean cross-correlation delay was calculated as the average of the cross-correlation delays between each segment and all of the other constituent segments.

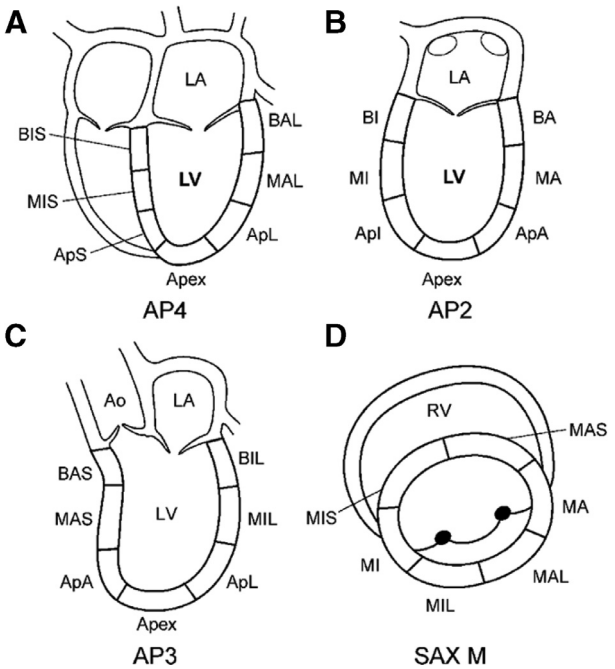

Figure 1. **Left ventricular segments used for analysis**. (*A*) AP4 (apical 4-chamber) view. BIS = Basal inferoseptal, MIS = Mid inferoseptal, ApS = Apical septal, Apex = Apical, ApL = Apical lateral, MAL = Mid anterolateral, BAL = Basal anterolateral. (*B*) AP2 (apical 2-chamber) view. BI = Basal inferior, MI = Mid inferior, ApI = Apical inferior, Apex = Apical, ApA = Apical anterior, MA = Mid anterior, BA = Basal anterior (*C*) AP3 (apical 3-chamber) view. BAS = Basal anteroseptal, MAS = Mid anteroseptal, ApA = Apical anterior, Apex = Apical, ApL = Apical lateral, MIL = Mid inferolateral, BIL = Basal inferolateral (*D*) SAX-M (short axis mid papillary) view. MIS = Mid inferoseptal, MI = Mid inferior, MIL = Mid inferolateral, MAL = Mid anterolateral, MA = Mid anterior, MAS = Mid anteroseptal.

Synchrony parameters were analyzed with and without HR correction, using Bazett's formula (i.e., the time parameter was divided by $\sqrt{RR}$, as previously described).[13]

Intra- and interobserver variability were evaluated by estimation of the intraclass correlation coefficient (ICC) and Bland-Altman analysis. Interobserver variability was assessed by measurement of LV strain in 30 randomly selected participants by 2 observers (AA and DMH), blinded to each other's results. Intraobserver variability was assessed by repeated measurement of 30 participants by the primary observer (AA) at least 3 months apart to minimize recall bias.

The study sample was divided into 6 age groups: <1 year, 1 to 5 years, >5 to 10 years, >10 to 14 years, >14 to 18 years, and 18 to 21 years. Results are presented as mean ± standard deviation (SD) for strain, demographic parameters and 2D-echo characteristics, and as median and interquartile range (IQR) for synchrony variables, due to the right-skewed nature of

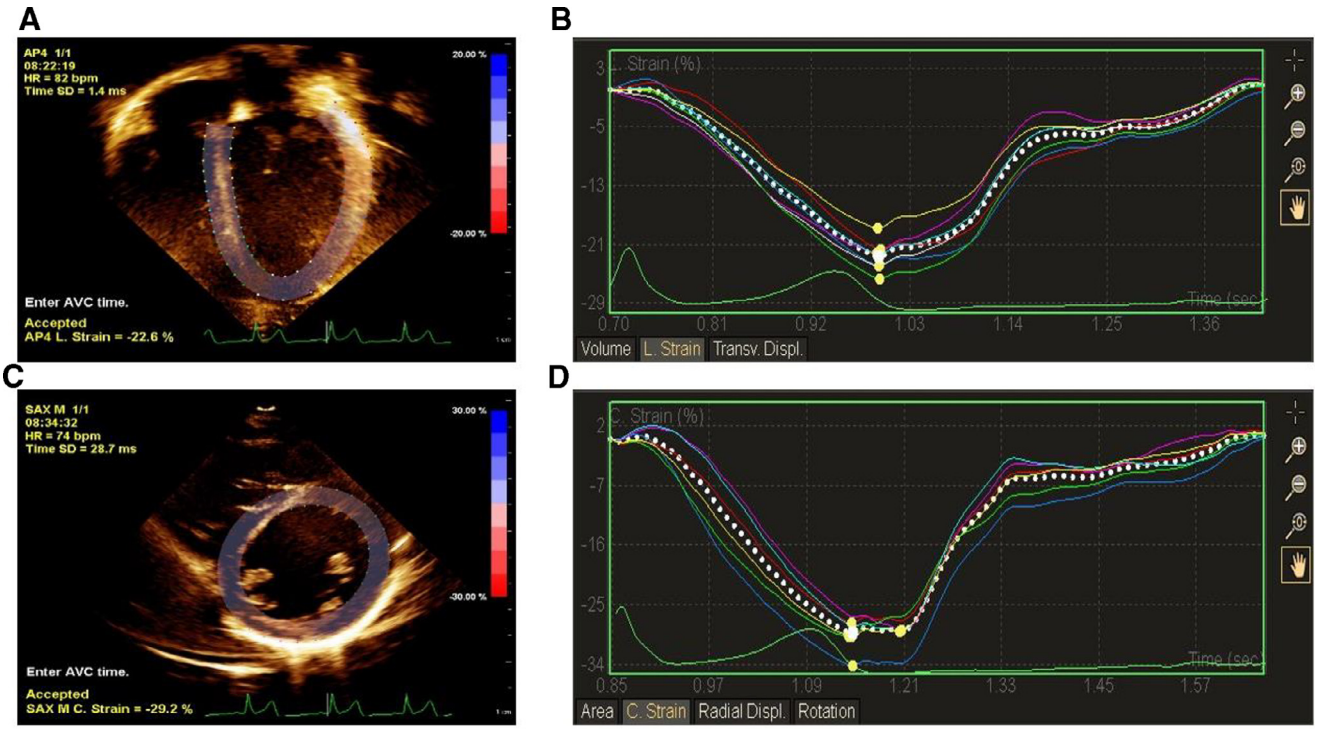

Figure 2. **Example of left ventricular strain versus time plots**. Example of a strain versus time curve from a normal 10-year-old boy referred due to a murmur. The analysis is produced by the QLAB software from AP4 (panels A+B) and SAX-M (panels C+D) views: Strain versus time curves for each segment (colored curves); average endocardial strain contour (*white dotted curve*) is calculated by the software. Segmental time-to-peak strain values (TTP; *yellow dot* on each segmental curve) allow the standard deviation of TTP calculation. Cross-correlation of these segmental strains versus time curves is used to calculate mean segmental delay. AP4 = apical 4-chamber; AVC = aortic closure time; bpm = beats per minute; C. Strain = circumferential strain; HR = heart rate; Ao = Aorta; LA = left atrium; LV = left ventricle; L. Strain = longitudinal strain; Sec = seconds; SAX M = sort axis mid-papillary; Time SD = time to peak strain standard deviation.

these time-related measures. Associations with age were assessed using age groups and continuous age without HR correction for descriptive purposes, and again after HR correction. Associations with age groups were evaluated using analysis of variance for strain measures and the Kruskal-Wallis test for synchrony measures, and with age as a continuous variable using the Spearman correlation. Generalized additive modeling was used to assess whether the relations between strain and synchrony variables versus age or BSA were nonlinear. Z-scores for AP4 and SAX-M strain were computed using generalized additive models for location, scale and shape, with selection according to the Schwartz Bayesian criterion. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Inc., Cary, North Carolina) and R version 3.2.1. A p value of ≤ 0.05 was considered statistically significant.

Results

The study population included 312 subjects. Mean age was 10.2 ± 5.8 years, age range 3 days to 20.5 years; 40% were female. Demographic and 2D echo data are presented by age group in Table 1. Indications for echocardiogram were: murmur (18%), chest pain and/or shortness of breath (14%), possible connective tissue disorder (without confirmatory echocardiographic findings; 12%), syncope (12%), family history of bicuspid aortic valve and/or congenital heart disease (11%), family history of arrhythmia and/or sudden cardiac death (8%), palpitations (6%), concern for abnormal electrocardiogram with later interpretation as normal and with normal echocardiogram (4%), and other (15%).

Of the 312 subjects, the number of subjects with images that were available and analyzable by view was as follows: AP4 292, AP2 121, AP3 102, and SAX-M 275. Median imaging frame rate was 74 Hz (IQR 66 to 87; range 29 to 202 Hz).

Overall, mean ± SD longitudinal strain (LS) values in the AP4, AP2, and AP3 views were −24.4 ± 3.2%, −24.2 ± 3.3%, and −24.6 ± 3.4%; mean circumferential SAX-M strain was −25.8 ± 3.4%. Strain values by age group are presented in Table 2. Significant differences were present between age groups for all 4 mean strain parameters. LS parameters became progressively less negative with age. SAX-M strain also varied significantly by age group, but the trend was not uniform; the 1 to 5 year age group had the least negative mean strain. LS versus BSA curves are presented in Figure 3, with modest but statistically significant correlations for all longitudinal components. Correlations for LS versus age were similar but slightly weaker ($R = 0.54$ for AP4; $R = 0.34$ for AP2; $R = 0.32$ for AP3). SAX-M strain (Figure 3) was not correlated with BSA or age ($p = 0.07$ for both). The infant age group (<1 year, $n = 36$) included 19 (53%) neonates

Table 1
Demographic and 2-dimensional echocardiographic characteristics of participants by age group in years

Variable	<1 (n = 36)	1–5 (n = 35)	>5–10 (n = 65)	>10–14 (n = 76)	>14–18 (n = 83)	18–21 (n = 17)	p
Age (years)	0.2 ± 0.2	3.4 ± 1.0	7.5 ± 1.6	12.0 ± 1.2	15.9 ± 0.9	19.2 ± 0.7	
Female	11 (31%)	14 (40%)	22 (34%)	32 (42%)	36 (43%)	10 (59%)	0.377
Height (cm)	54.7 ± 6.8	97.5 ± 7.9	124.9 ± 11.4	153.8 ± 12.0	170.1 ± 8.8	172.6 ± 12.1	**<0.001**
Weight (kg)	4.8 ± 1.6	15.7 ± 3.0	26.5 ± 7.7	45.4 ± 10.6	64.6 ± 10.6	67.3 ± 11.1	**<0.001**
BSA (m^2)	0.27 ± 0.06	0.65 ± 0.09	0.95 ± 0.18	1.39 ± 0.20	1.74 ± 0.16	1.79 ± 0.20	**<0.001**
BMI (kg/m^2)	15.5 ± 2.2	16.4 ± 1.5	16.6 ± 2.1	19.0 ± 3.1	22.2 ± 3.0	22.5 ± 2.6	**<0.001**
SBP (mmHg)	89 ± 12	94 ± 11	103 ± 8	109 ± 10	115 ± 9	115 ± 8	**<0.001**
DBP (mmHg)	51 ± 12	55 ± 8	57 ± 8	58 ± 8	60 ± 8	62 ± 9	**<0.001**
Heart rate (bpm)	139 ± 15	99 ± 12	83 ± 12	70 ± 11	66 ± 12	68 ± 13	**<0.001**
LVEF (%)	61 ± 4	65 ± 4	64 ± 4	63 ± 4	62 ± 4	61 ± 4	**<0.001**
LVEDV (ml)	11.3 ± 3.6	41.3 ± 9.0	67.9 ± 14.1	109.8 ± 27.4	147.5 ± 31.1	151.8 ± 36.1	**<0.001**
LVESV (ml)	4.3 ± 1.4	14.2 ± 3.3	24.4 ± 6.2	41.1 ± 11.9	55.5 ± 12.9	58.8 ± 15.0	**<0.001**

Values are presented as mean ± SD. BMI = body mass index; BSA = body surface area; DBP = diastolic blood pressure; LVEDV = left ventricular end diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end systolic volume; SBP = systolic blood pressure.

Table 2
Left ventricular strain by view and age group in years

View	<1	1–5	>5–10	>10–14	>14–18	18–21	p
AP4	−27.2±3.2 (32)	−26.06±2.29 (35)	−25.36±2.73 (64)	−23.94±2.84 (70)	−22.41±2.57 (76)	−22.63±2.61 (15)	**<.001**
AP2	−26.20±2.42 (10)	−24.21±2.43 (10)	−25.93±3.53 (27)	−23.86±3.17 (30)	−22.98±2.60 (36)	−23.01±4.76 (8)	**0.003**
AP3	−26.51± 4.02 (10)	−25.42 ± 2.88 (10)	−25.52±2.48 (24)	−24.79±3.78 (26)	−22.71±2.94 (26)	−23.89±4.19 (6)	**0.014**
SAX-M	−25.62±3.96 (25)	−23.89±3.72 (32)	−25.74±2.92 (56)	−26.68±3.38 (70)	−25.78±3.36 (78)	−25.52±2.09 (14)	**0.010**

Values listed are mean ± SD in % (number of patients). AP2 = apical 2-chamber view; AP3 = apical 3-chamber view; AP4 = apical 4-chamber view; SAX-M = short-axis at mid-papillary level view.

(defined as <1 month of age). No statistically significant differences were found in strain values of neonates versus non-neonate infants, for either longitudinal or CS. LS was highly correlated with LV length (less negative with increasing length; $p < 0.001$, $R = 0.57$), but not with LV length z-score ($p = 0.16$).

Z-score equations for strain parameters versus BSA are:

$$\text{Longitudinal(AP4)}:$$

$$Z = \frac{(Strain - (-0.283995 + 0.033356 * BSA))}{0.026202}$$

$$\text{Circumferential(SAX-M)}:$$

$$Z = \frac{(Strain - (-0.248082 - 0.00763 * BSA))}{0.033668}$$

(Note that the strain variable is formatted as a raw value in these equations; for example, '−0.25').

Results of synchrony assessment by all 3 methods (TTP-SD, MWD, and XCMD) by age group are presented in Table 3. Significant differences in age groups were present for all methods, for nearly all longitudinal components. No differences between age groups were present for SAX-M synchrony measures. After HR correction, significant differences remained in only a small subset of the parameters (AP4 MWD, AP4 TTP-SD, AP3 TTP-SD, and SAX-M MWD, $p < 0.05$ for all).

Figure 4 shows the TTP-SD versus continuous age for all views. Longitudinal TTP-SD varied significantly with age in a nonlinear fashion as it increased up until age 8 years, after which the slope flattened ($p < 0.05$ for all views); SAX-M TTP-SD did not vary with age as a continuous variable. Similar associations were found for the other synchrony parameters as well (MWD and XCMD) when plotted versus age ($p < 0.05$ for all, except for AP2 MWD). With HR correction, only 3 longitudinal synchrony parameters retained a statistically significant, weak correlation with age in the continuous analysis (AP4 MWD, AP3 TTP-SD, and AP3 MWD; $p < 0.05$ for all, with $R \leq 0.26$). SAX-M synchrony parameters showed weak age associations after HR correction ($p < 0.05$ for all, with $R \geq -0.17$).

When analyzed versus BSA instead of age, longitudinal synchrony parameters showed a similar positive but weak correlation with increasing value (TTP-SD: AP4 $R = 0.28$, $p < 0.001$; AP2 $R = 0.21$, $p = 0.02$; AP3 $R = 0.34$, $p = 0.001$; MWD: AP4 $R = 0.24$, $p < 0.001$; AP3 $R = 0.26$, $p = 0.009$). When HR-corrected, AP4 and AP3 parameters continued to have a significant but weak correlation with BSA (TTP-SD: AP4 $R = 0.13$, $p = 0.04$; AP3 $R = 0.26$, $p = 0.013$; MWD: AP4 $R = 0.17$, $p = 0.005$; AP3 $R = 0.22$, $p = 0.041$). As with age, SAX-M synchrony parameters showed significant but very weak correlations with BSA only after HR correction (TTP-SD $R = -0.17$, $p = 0.006$; MWD $R = -0.15$, $p = 0.016$). As for strain, no gender differences were found for all synchrony parameters.

Interobserver and intraobserver variability of strain and synchrony measurements are presented in Table 4. ICC estimates for strain variables were generally good or very good (ICC > 0.7), except for AP2 interobserver variability

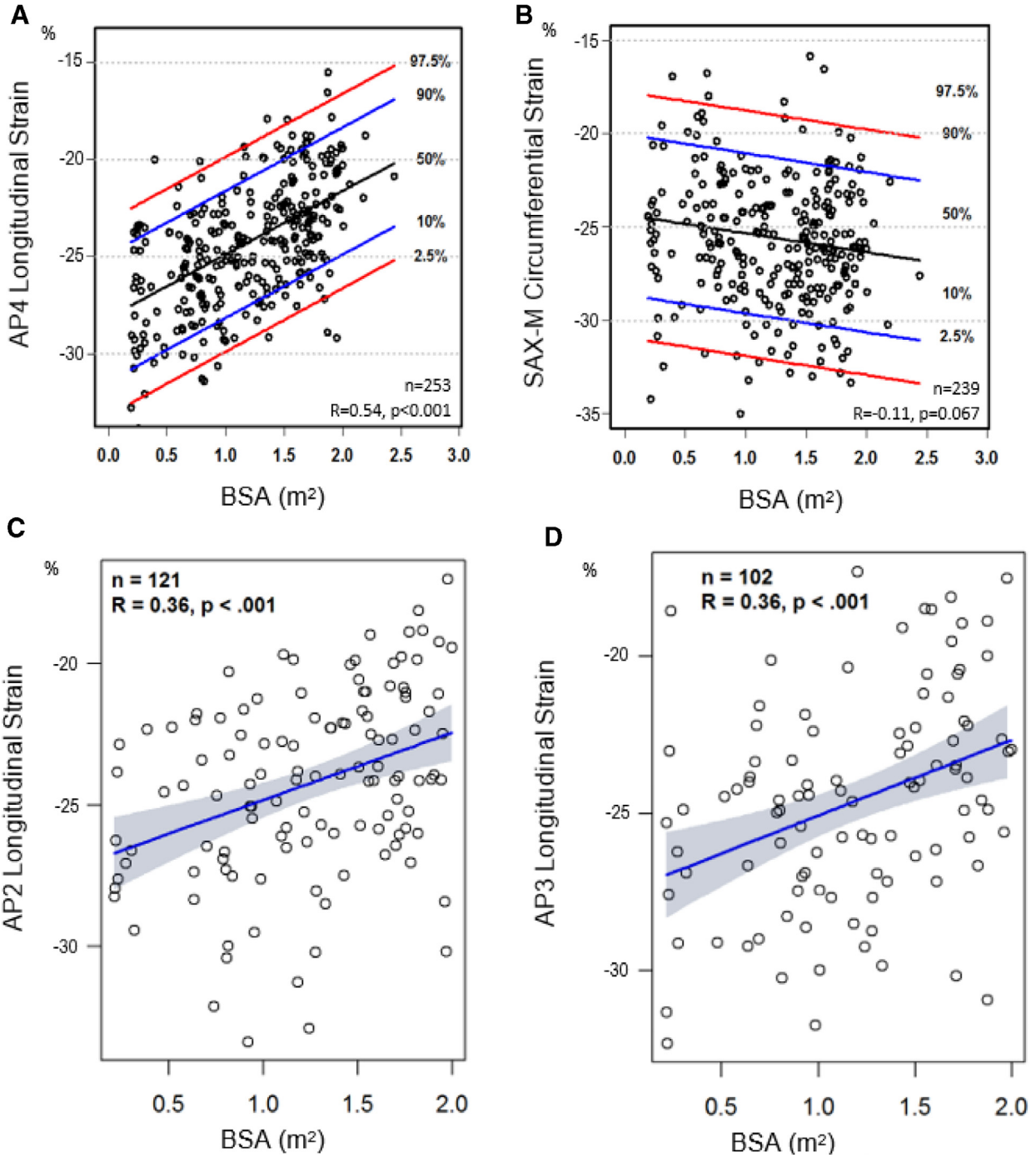

Figure 3. **Strain versus BSA**. (*A*) AP4 (= apical 4-chamber) view; (*B*) SAX-M (= short axis at mid-papillary level); (*C*) AP2 (= apical 2-chamber) view; (*D*) AP3 (= apical 3-chamber) view. Circles represent individual values. In panels A+B (views for which z-scores were calculated): the black line represents the 50th percentile, the blue lines represent the 10th and 90th percentiles, and the red lines represent the 2.5th and 97.5th percentiles. In panels C+D (no z-scores calculated): the blue line represents the predicted mean using generalized additive modeling and linear regression, respectively. The shaded areas represent 95% pointwise confidence bands for the mean. Strain values are in %. Statistically significant changes with BSA are present for the longitudinal, but not circumferential, strain components. AP2 = apical 2-chamber; AP3 = apical 3-chamber; AP4 = apical 4-chamber; BSA = body surface area.

(ICC = 0.66). Mean differences for all strain parameters were small (≤1%). ICC values were generally very good for synchrony as well, particularly for interobserver measurements (ICC ≥ 0.7 for all); they were less robust for intraobserver measurements (ICC > 0.7 for 8 out of 12 measurements).

Discussion

This study provides normal values for LS and CS and mechanical synchrony in children. In contrast with before reports based upon the GE platform,[15,16] our data are based entirely upon the Philips system, one of the most

Table 3
Left ventricular synchrony by view and age group in years

View	Method	<1	1−5	>5−10	>10−14	>14−18	18−21	p
AP4	TTP-SD	2.3 (0.95, 7.9)	9.6 (2.1, 16.5)	17.4 (4.6, 24.3)	12.8 (2.0, 23.9)	17.8 (3.1, 27.6)	15.1 (1.7, 20.8)	**<0.001**
	MWD	3.0 (0.0, 14.0)	25.0 (0.0, 49.0)	49.5 (17.5, 62.0)	34.5 (12.0, 63.0)	48.5 (14.5, 69.5)	47.0 (16.0, 63.0)	**<0.001**
	XCMD	6.0 (4.5, 9.0)	7.0 (6.0, 10.0)	10.5 (7.0, 14.0)	11.0 (8.0, 15.0)	11.0 (8.0, 15.0)	9.0 (7.0, 11.0)	**<0.001**
AP2	TTP-SD	1.1 (0.5, 10.1)	14.2 (3.0, 19.1)	22.9 (8.9, 27.1)	10.2 (2.0, 27.2)	16.3 (3.0, 29.0)	20.0 (6.9, 35.9)	**0.011**
	MWD	0.0 (0.0, 34.0)	38.0 (0.0, 60.0)	58.0 (26.0, 76.0)	55.0 (15.0, 82.0)	24.5 (7.0, 74.0)	39.0 (13.5, 74.5)	0.066
	XCMD	4.5 (3.0, 8.0)	10.0 (8.0, 14.0)	9.0 (5.0, 12.0)	9.5 (5.0, 13.0)	9.5 (8.0, 13.5)	9.0 (5.5, 13.0)	0.119
AP3	TTP-SD	1.4 (0.8, 6.6)	3.3 (1.5, 16.0)	15.1 (8.3, 23.2)	11.4 (2.5, 17.0)	15.1 (4.1, 27.3)	29.7 (17.5, 32.1)	**0.002**
	MWD	7.5 (0.0, 20.0)	22.0 (0.0, 45.0)	47.0 (24.0, 60.0)	37.5 (0.0, 54.0)	40.0 (15.0, 79.0)	78.5 (47.0, 82.0)	**0.026**
	XCMD	6.0 (3.0, 8.0)	8.0 (6.0, 9.0)	8.5 (7.0, 13.0)	10.5 (8.0, 14.0)	11.0 (7.0, 19.0)	9.0 (8.0, 12.0)	**0.004**
SAX-M	TTP-SD	12.1 (1.9, 21.8)	15.4 (1.0, 22.2)	6.2 (1.2, 25.9)	1.3 (0.9, 6.8)	2.4 (1.0, 27.3)	2.2 (0.9, 8.6)	0.066
	MWD	34.0 (8.0, 53.0)	43.0 (5.5, 56.0)	21.0 (0.0, 66.0)	0.0 (0.0, 32.0)	14.0 (0.0, 56.0)	0.0 (0.0, 28.0)	0.093
	XCMD	11.0 (7.0, 14.0)	11.0 (9.0, 17.0)	12.0 (9.5, 16.0)	10.5 (7.0, 17.0)	10.5 (7.0, 21.0)	12.0 (10.0, 19.0)	0.785

Values are presented as median (IQR); all listed values are in milliseconds. Number of patients is as listed in Table 2. Values are not heart rate corrected. Association assessed with Spearman correlation. AP2 = apical 2-chamber view; AP3 = apical 3-chamber view; AP4 = apical 4-chamber view; MWD = maximal wall delay; SAX-M = short-axis at mid-papillary level view; TTP-SD = Time-to-peak strain standard deviation; XCMD = cross-correlation mean segmental delay.

commonly used echocardiography platforms in pediatrics. Overall, we found that LS changed modestly with patient size and age, whereas CS remained relatively constant. HR uncorrected synchrony parameter values differed between age groups and views, with shorter longitudinal peak strain differences in the younger subjects up to age 8 years. After HR-correction, however, most values showed no age association. We provide reference ranges and z-scores for LS and CS, in order to facilitate the incorporation of strain measurements into clinical practice in pediatric echocardiographic laboratories. These data are intended to supplement existing LS data and to establish foundational data for 2DSTE CS, which are nearly nonexistent at present.[9,15−17]

With increasing age and BSA, changes observed for the 2 strain components were different: LS values became less negative, whereas CS did not change in a systematic fashion. This difference in the behavior of longitudinal versus circumferential fibers may reflect LV architecture, where longitudinal and circumferential fibers are not interspersed, but instead, are thought to be regionally distinct. That is, the fibers of the midwall are predominantly circumferential, whereas those of both the subendocardium and subepicardium are mostly longitudinal.[21] Before reports of maturational changes of strain have been conflicting, with some reports showing no association[10,11,15] and others describing relations of varying strength.[9,17,22,23] These differences may be related to vendor-based differences in measurement or analysis, or to the specific age range in each age group, such as more neonates versus infants included in the age group under 1 year. Our infant age group included about 50% neonates (<1 month old), potentially explaining some of the differences from before reported values of neonatal strain.[15,16]

Coordinated myocardial contraction contributes importantly to ventricular systolic function in congenital heart disease patients.[6] Reference values for normal pediatric synchrony parameters, however, are scarce, and use of adult ranges of synchrony parameters may be inappropriate or misleading.[14] Before studies describing the normal pattern of contraction in children have shown inconsistent results.[12,13,24] We found a significant association between age groups and most longitudinal synchrony measures when analyzed without HR correction. With HR correction, however, most of the age-related differences were eliminated, suggesting that the HR-uncorrected findings may reflect normal maturational changes in conduction time rather than actual differences in patterns of myocardial conduction.

Small numbers of participants in each group and a lack of available AP2-chamber, AP3-chamber, and apical and basal SAX images precluded their analysis, as these were not part of our lab standard protocol and were not routinely acquired. We also do not have data on the number of patients who were excluded due to technical issues such as poor LV tracking or imaging. Nonetheless, this is one of the largest pediatric multiaged cohort of normal LV strain and synchrony measurement reported to date. Included patients were referred for an echo exam and might be considered to be abnormal on that basis; however, subjects were rigorously screened and excluded from the present study on the basis of even minor abnormalities with potential cardiovascular impact. The use of a single vendor analysis tool does not permit comparison to other vendors, and may limit the generalizability of these data. Nonetheless, Philips is one of the most common echocardiographic platforms in use in pediatric echo laboratories, and this methodology allowed for a single large dataset and z-score generation. The use of custom-made software for cross-correlation assessment limits this tool's generalizability and incorporation into routine clinical use; for this reason, other common synchrony measures were included as well. The primary software tool used for this current analysis, QLAB, remains in development. As such, its strain algorithm can be expected to change in the future, requiring regeneration of the data contained within this report in a systemic fashion. Still, this software package and version have been widely adopted on an international scale and can be expected to retain relevance for a number of years. Finally, ethnicity data was not a part of our original database. This may have partially affected our results, though with no direct bias, and would be a valuable addition in future studies.

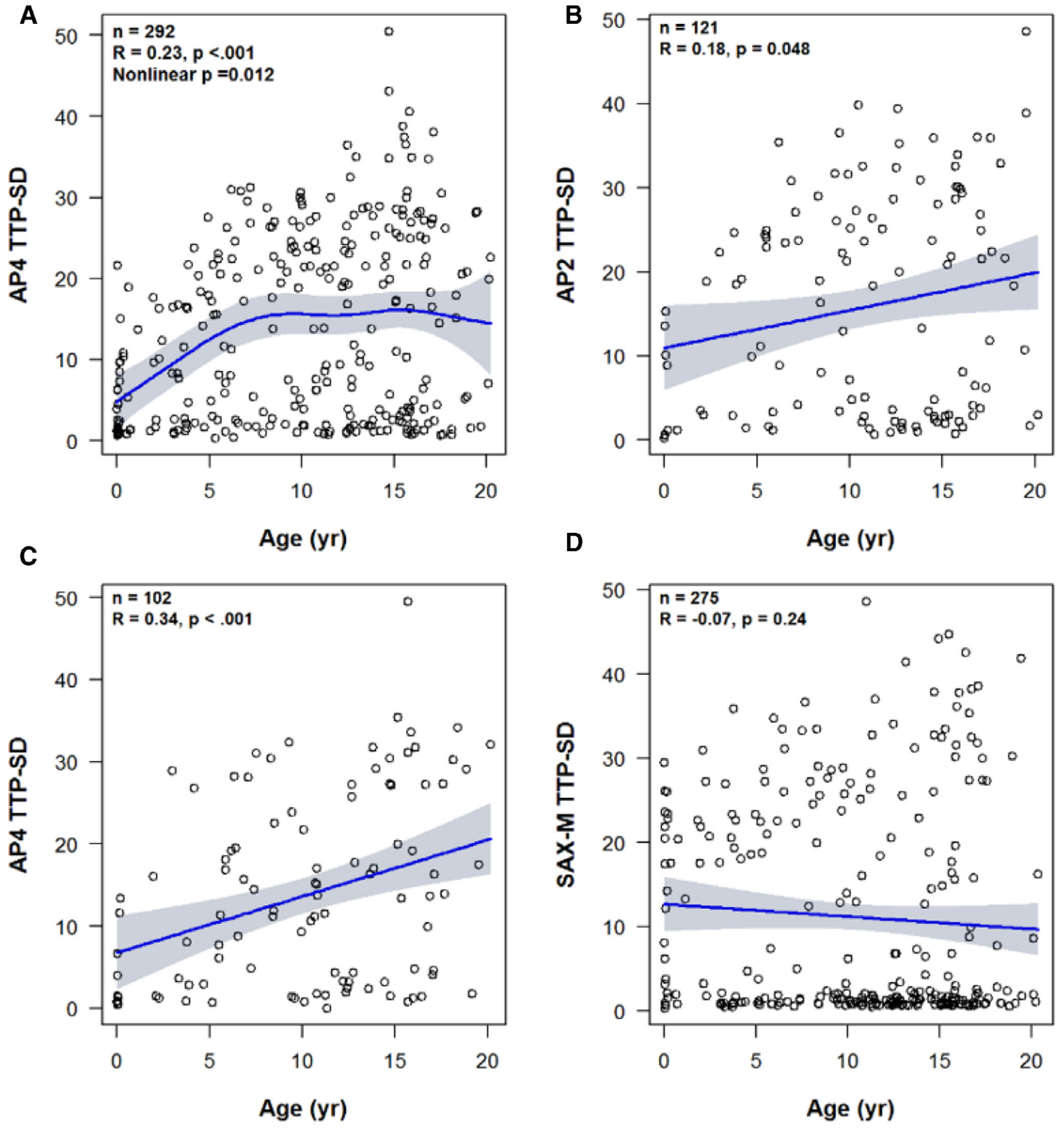

Figure 4. **Time to peak strain standard deviation versus age in years (yr)**. (*A*) AP4 (= apical 4-chamber) view; (*B*) AP2 (= apical 2-chamber) view; (*C*) AP3 (= apical 3-chamber) view; D. SAX-M (= short axis at mid-papillary level) view. TTP-SD (= time to peak strain standard deviation). The blue line in each panel represents the predicted mean using linear regression. The shaded areas represent 95% pointwise confidence bands for the mean. TTP-SD values are in milliseconds. Values are not corrected for heart rate.

In summary, we report normal values for strain and synchrony parameters in children based upon the most commonly used echocardiography platform. Z-scores are presented for LS and CS. LS became less negative with increasing age and BSA; CS did not. Age-related differences in synchrony parameter values were present in longitudinal views primarily when uncorrected for heart rate. Data such as these may be incorporated into pediatric echocardiography laboratories to facilitate future assessment of ventricular function and synchrony in children with congenital and acquired heart diseases.

Table 4
Inter- and intraobserver variability analysis

	N pairs	ICC (95% CI)	Mean difference ± SD Reading 1-Reading 2	Absolute mean difference ± SD |Reading 2 − Reading 1|	% error mean ± SD*	Bland and Altman 95% CI
Interobserver						
AP4 LS	28	0.88 (0.76, 0.94)	−0.8 ± 2.0	1.8 ± 1.2	7.03 ± 4.58	−4.7, 3.2
AP2 LS	12	0.66 (0.21, 0.88)	−1.0 ± 3.3	2.6 ± 2.2	10.52 ± 10.20	−7.5, 5.5
AP3 LS	15	0.74 (0.41, 0.90)	−0.1 ± 2.9	2.0 ± 2.0	8.01 ± 7.81	−5.7, 5.5
SAX-M CS	23	0.93 (0.84, 0.97)	−0.5 ± 1.6	1.2 ± 1.1	4.68 ± 3.99	−3.6, 2.6
AP4 TTP-SD	28	0.70 (0.46, 0.85)	−2.2 ± 10.4	7.7 ± 7.2		−22.6, 18.1
AP2 TTP-SD	12	0.98 (0.93, 0.99)	2.3 ± 4.9	3.8 ± 3.8		−7.4, 11.9
AP3 TTP-SD	15	0.70 (0.33, 0.88)	−0.5 ± 10.5	6.1 ± 8.3		−21.0, 19.9
SAX-M TTP-SD	23	0.80 (0.59, 0.91)	−2.9 ± 9.8	4.0 ± 9.4		−22.2, 16.2
AP4 MWD	28	0.78 (0.59, 0.89)	−10 ± 25	19 ± 19		−59.0, 40.0
AP2 MWD	12	0.96 (0.88, 0.99)	−3 ± 16	10 ± 13		−35.0, 28.0
AP3 MWD	15	0.83 (0.59, 0.94)	2 ± 24	15 ± 18		−45.0, 49.0
SAX-M MWD	23	0.77 (0.53, 0.89)	−10 ± 29	13 ± 27		−66.0, 47.0
AP4 XCMD	28	0.80 (0.61, 0.90)	−2.1 ± 3.7	3.6 ± 2.2		−9.4, 5.1
AP2 XCMD	12	0.82 (0.52, 0.94)	2.2 ± 4.2	3.3 ± 3.3		−6.1, 10.4
AP3 XCMD	15	0.82 (0.56, 0.93)	1.7 ± 4.8	2.4 ± 4.5		−7.7, 11.2
SAX-M XCMD	23	0.74 (0.49, 0.88)	−4.1 ± 7.7	6.5 ± 5.6		−19.1, 10.8
Intraobserver						
AP4 LS	28	0.92 (0.83, 0.96)	−0.4 ± 1.5	1.2 ± 1.0	3.28 (2.14, 5.93)	−3.3, 2.5
AP2 LS	17	0.84 (0.63, 0.94)	−0.2 ± 1.9	1.3 ± 1.3	4.24 (2.69, 5.96)	−3.8, 3.5
AP3 LS	11	0.92 (0.75, 0.97)	−0.2 ± 1.7	1.4 ± 0.9	5.61 (3.38, 8.64)	−3.6, 3.2
SAX-M CS	26	0.97 (0.93, 0.99)	−0.0 ± 1.1	0.8 ± 0.8	1.90 (0.88, 4.43)	−2.3, 2.2
AP4 TTP-SD	28	0.61 (0.32, 0.79)	−2.9 ± 10.8	6.5 ± 9.1		−24.1, 18.3
AP2 TTP-SD	17	0.78 (0.52, 0.91)	−1.9 ± 10.0	5.2 ± 8.7		−21.6, 17.6
AP3 TTP-SD	11	0.97 (0.89, 0.99)	−0.7 ± 4.3	3.1 ± 3.0		−9.1, 7.8
SAX-M TTP-SD	26	0.98 (0.96, 0.99)	−0.3 ± 3.3	1.7 ± 2.8		−6.7, 6.2
AP4 MWD	28	0.68 (0.43, 0.84)	−5.5 ± 26.9	15.1 ± 22.8		−58.3, 47.0
AP2 MWD	17	0.77 (0.48, 0.90)	−6.2 ± 26.4	12.3 ± 24.0		−57.9, 45.3
AP3 MWD	11	0.90 (0.70, 0.97)	−1.5 ± 16.8	10.4 ± 12.9		−34.5, 31.4
SAX-M MWD	26	0.98 (0.95, 0.99)	1.1 ± 9.3	5.5 ± 7.5		−17.1, 19.2
AP4 XCMD	28	0.82 (0.65, 0.91)	−0.1 ± 4.0	2.8 ± 2.9		−8.1, 7.7
AP2 XCMD	17	0.50 (0.07, 0.78)	−0.6 ± 5.3	3.2 ± 4.3		−11.1, 9.8
AP3 XCMD	11	0.86 (0.58, 0.95)	0.7 ± 4.5	2.7 ± 3.6		−8.2, 9.6
SAX-M XCMD	26	0.67 (0.39, 0.83)	0.2 ± 5.2	3.5 ± 3.7		−9.9, 10.2

All listed strain values are in %, all listed synchrony parameters (TTP-SD, MWD, XCMD) are in milliseconds. AP2 = apical 2-chamber view; AP3 = apical 3-chamber view; AP4 = apical 4-chamber view; CS = circumferential strain; ICC = intraclass correlation coefficient; LS = longitudinal strain; MWD = maximal wall delay; SAX-M = short-axis at mid-papillary level view; TTP-SD = time-to-peak strain standard deviation; XCMD = cross-correlation mean segmental delay.

* Mean % errors are provided for strain variables but not for synchrony parameters, as the denominators for this calculation for synchrony variables trended toward zero (calculated as: %error = [Reader 2 − Reader1]/[mean of Reader 1 and Reader 2]).

Disclosures

The authors have not conflict of interests to disclose.

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