Assessment of Cardiac Function in Children by Strain Imaging and its Correlation with Conventional Echocardiographic Parameter

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ABSTRACT

Background: The objectives of this study were to find out of normal reference value for age-dependent longitudinal strain values in children and find its correlation with conventional echocardiographic parameters.

Methods: In total, 100 healthy normal children aged between 2 and 15 years were enrolled and divided into three age groups, namely, 2–5 years, 5–10 years, and 10–15 years. Using the GE Vivid 7 ultrasound platform with 4 or 7 MHz probes, both LV and RV global longitudinal strains and conventional echocardiographic parameters were acquired.

Results: In normal healthy children, left ventricular GLS values were –20.10 to –19.68 (mean: –19.89), –21.93 to –21.02 (mean: –21.48), and –20.87 to –20.41 (mean: –20.64)) in children aged 2–5 years, 5–10 years, and 10–15 years and right ventricular GLS values were –16.80 to –16.44 (mean: –16.62), –27.85 to –27.27 (mean: –27.56), –28.44 to –27.93 (mean: –28.19) in the above three groups, respectively. No significant increase was noted in the left ventricular strain value from basal to the apical segment from age group 2 years to 15 years and no gender differences were seen. None of the conventional echocardiographic parameters commonly used to assess the left or right ventricular systolic function had a significant correlation with LVGLS and RVGLS.

Conclusions: The mean LVGLS values were –19.89, –21.48, and –20.64 and RVGLS were –16.62, –27.56, and –28.19 in healthy normal children aged 2–5 years, 5–10 years, and 10–15 years, respectively, and conventional echocardiographic parameters did not have any significant correlation with these values.

Keywords: Children, echocardiography, global longitudinal strain, left ventricle, right ventricle

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INTRODUCTION

Echocardiography has become the most important non-invasive technique for the diagnosis and follow-up of heart disease in children. The diagnostic accuracy of echocardiography for describing cardiac morphology is extremely high, with a reported incidence of diagnostic errors

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of only 87 errors in more than 50,660 echocardiograms in an established pediatric echocardiography laboratory.^[1] Tissue Doppler echocardiography and speckle tracking-based strain imaging provide direct quantitative information of both global and regional myocardial function and several characteristics of this technique make them

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attractive tools for the assessment of ventricular function in both adults and children.^[2-4] The new methods also allow quantification of myocardial motion and deformation in different directions (longitudinal, radial, and circumferential), whereas conventional methods mainly rely on the assessment of radial function. It has been shown to be accurate in detecting subclinical myocardial dysfunction when most of the conventional echocardiographic parameters were normal or reported inconsistent results.^[5] Likewise, detailed analysis of LV myocardial deformation in a three-dimensional fashion carries the potential of providing a clearer understanding of segmental and regional function interaction in different diseases.^[6,7] However, routine application of myocardial strain in clinical practice requires a clear definition of normal values and variables that may influence strain measurements. The objectives of the present study were to find out the normal reference value for age-dependent longitudinal strain/strain rate values in children and assessment of global ventricular systolic function by strain imaging echocardiography (2D STE) and its correlation with conventional Echocardiographic parameters.

MATERIALS AND METHODS

After approval from the institutional ethics committee, this observational study was undertaken. With the written consent of guardians, 100 children aged between 2 and 15 years without any congenital or acquired heart disease or any other systemic disorder attending the department of cardiology between September 2016 to January 2018 were enrolled. They had been referred to the cardiology department to exclude any cardiac problem but were found normal on echocardiography. We divided the whole population into three age groups named, 2–5 years, 5–10 years, and 10–15 years of age.

Inclusion criteria

Children aged between 2 and 15 years.

Exclusion criteria

- 1. Children having congenital cyanotic or acyanotic heart disease
- 2. Children with acquired heart disease (e.g., rheumatic heart disease, pericardial disease, myocarditis, cardiomyopathy)
- 3. Children with severe non-cardiac diseases such as malignancy, renal problem (nephritic or nephrotic syndrome), severe respiratory problem, growth or developmental anomaly
- 4. We did not include the infant in our study because the infant needs special technical support and a

special infant echocardiographic probe. Also, there are some important issues regarding infant cardiologic hemodynamics.

All echocardiograms were acquired on a General Electric (GE) Vivid 6 (GE Medical Systems) ultrasound platform using 4 or 7 MHz probes. Strain analysis was performed offline using customized computer software (EchoPAC, Vingmed, General Electronics, Horten, Norway). For longitudinal strain analysis, gray-scale images were recorded from apical four-, two-, and three-chamber views [Figure 1]. A frame rate of 80 to 100 frames/s was used for storage and analysis. The images were optimized to visualize the myocardial walls. In brief, the endocardial border was manually traced at end-systole. Tracking was automatically performed and the analysis was accepted after visual inspection and when the software indicated adequate tracking. If tracking was suboptimal, the endocardial border was retraced. If satisfactory tracking was not accomplished within 5 min, the non-tracking segments were excluded from the analysis. The end-systolic strain values were measured at aortic valve closure. Following analysis of all three LV apical views, a "bulls-eye" was generated with regional strain measurements consistent with standardized myocardial segmentation and nomenclature.^[8] A total of 18 regional segments were produced comparable to VVI measurements. The global longitudinal strain of LV (including the septum) and RV (free wall only) longitudinal strain was calculated by averaging all measured segmental values. The RV global longitudinal strain was also determined in the apical four-chamber view [Figure 2]. Conventional echocardiographic parameters were also acquired for correlation with strain parameters.

Sample size determination

Sample size determination was based on the number of patients needed to show the difference in the width of the limits of agreement (LOA; as defined by Bland–Altman

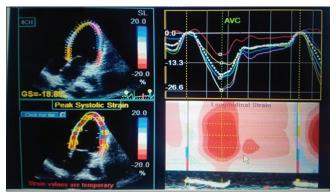


Figure 1: Normal LVGLS curve obtained from a standard apical four-chamber (A4C)

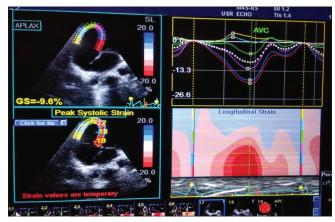


Figure 2: Normal RVGLS curve obtained from a standard apical four-chamber (A4C)

analysis 8) between pediatric subjects studied. Our sample size was calculated to have a power of 80% (assuming a two-tailed alpha of 0.05) to detect if one group had a 50% larger width of LOA than the other. We obtained a sample size of 30 subjects per group using the Statistica 8.0 software.

Statistical methods

Continuous variables are expressed as descriptive statistics with a 95% confidence interval. The association between continuous variables was determined using Spearman's rank correlation coefficient. The statistical software SPSS version 20 was used for the analysis. An alpha level of 5% was taken, i.e., if any *P*-value is less than 0.05 it has been considered as significant.

RESULTS

In normal healthy children, the mean left ventricular GLS values are -19.89 (male: -20.06 and female: -19.72) (95% CI: -20.10 to -19.68, SD of 0.559), -21.48 (male: -21.73 and female: -21.23) (95% CI, -21.93 to -21.02, SD of 1.21) and -20.64 (male: -21.03 and -20.25) (95% CI, -20.87 to -20.41, SD of 0.613) in children aged 2–5 years, 5-10 years, and 10-15 years, respectively. In normal healthy children, the mean right ventricular GLS values were -16.62 (male: -17.17 and -16.07) (95% CI, -16.80 to -16.44, SD of 0.486), -27.56 (male: -28.27 and female: -26.85) (95% CI, -27.85 to -27.27, SD of 0.775), -28.19 (male: -27.59 and female: -28.79) (95% CI, -28.44 to -27.93, SD of 0.693) in children aged 2–5 years, 5-10 years, and 10-15 years, respectively.

The mean left ventricular basal strain values are -19.67 (95% CI, -19.88 to -19.45, SD of 0.566), -20.93 (95% CI, -21.33 to -20.54, SD of 1.06), -21.95 (95% CI, -21.25 to -20.66, SD of 0.789) among different age group respectively. In

the midbasal level, the mean left ventricular strain values were -20.37 (95% CI, -20.54 to -20.19), -21.13 (95% CI, -21.34 to -20.32), and -20.17 (95% CI, -20.49 to -19.84) among three above age groups. At the apical level, mean left ventricular strain values are -22.32 (95% CI, -23.71 to -20.92), -21.17 (95% CI, -20.49 to -19.84), and -20.52 (95-% CI, -20.80 to -20.24) among different age group respectively [Table 1].

The conventional echocardiographic parameters of the left ventricle that assess the systolic functions were also studied [Table 2]. The mean values of left ventricular ejection fraction were 68.56% (95% CI: 67.76 to 69.37 with SD of 2.16), 68.4% (95% CI: 67.39 to 69.40 with SD of 2.69), and 69.06% (95% CI: 68.45 to 69.67 with SD of 1.63), and the mean values of left ventricular fraction shortening (FS) were 37.75% (95% CI: 37.29 to 38.20 with SD of 1.23), 37.76% (95% CI: 37.08 to 38.44 with SD of 1.88), and 37.7% (95% CI: 37.40 to 37.99 with SD of 0.783) in three different age group, respectively. The mean values of left ventricular "Tei" index were 0.48 (95% CI: 0.47 to 0.48 with SD of 0.015), 0.489 (95% CI: 0.47 to 0.50 with SD of 0.041) and 0.497 (95% CI: 0.49 to 0.50 with SD of 0.018) in above three age groups. Septal and lateral MAPSE were measured and average values were taken. The mean values of "MAPSE" were 13.96 mm (95% CI: 13.71 to 14.21 with SD of 0.669), 14.66 mm (95% CI: 14.19 to 15.13 with SD of 1.262) and 15.46 mm (95% CI: 15.13 to 15.80 with SD of 0.90) and the mean values of LVS' are 0.078 cm/sec (95% CI: 0.076 to 0.080 with SD of 0.005), 0.090 cm/sec (95% CI: 0.086 to 0.093 with SD of 0.010) and 0.09 cm/sec (95% CI: 0.084 to 0.096 with SD of 0.016) in three different age groups, respectively.

Regarding the conventional right ventricular echocardiographic parameters that are commonly used for right ventricular systolic function, The mean values of RVOT fraction shortening (FS) were 51.76% (95% CI: 50.50 to 52.59 with SD of 2.22), 52.50% (95% CI: 51.68 to 53.31 with SD of 2.19) and 55.53% (95% CI: 54.48 to 56.47 with SD of 2.52) in three different age groups, respectively. The mean values of "TAPSE" were 16.06 mm (95% CI: 15.74 to 16.38 with SD of 0.858), 19.16 mm (95% CI: 18.62 to 19.71 with SD of 1.46) and 20.80 mm (95% CI: 20.20 to 21.40 with SD of 1.60) and the mean values of right ventricular "Tei" index were 0.454 (95% CI: 0.449 to 0.460 with SD of 0.015), 0.485 (95% CI: 0.474 to 0.497 with SD of 0.031) and 0.478 (95% CI: 0.472 to 0.483 with SD of 0.015) in three different age groups, respectively. The mean values of RVS were 0.075 cm/sec (95% CI: 0.071 to 0.078 with SD of 0.009), 0.086 cm/sec (95% CI: 0.081 to 0.092 with SD

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	2–5 years		5-10 years			10–15 years			
	95% CI	Mean	SD	95% CI	Mean	SD	95% CI	Mean	SD
LVGLS	-20.10 to -19.68	- 19.89	0.559	21.93 to -21.02	-21.48	1.212	-20.87 to -20.41	-20.65	0.613
LV Basal strain	– 19.88 to – 19.46	- 19.67	0.566	-20.54 to -20.33	-20.94	1.062	-20.66 to -20.25	-20.96	0.789
LV mid basal strain	-20.55 to -20.19	-20.37	0.471	-21.13 to 20.32	-20.73	1.087	-20.49 to -19.88	-20.17	0.865
LV apical strain	-23.72 to -20.93	-22.32	3.735	-21.82 to -20.52	-22.17	1.729	-20.80 to -20.24	-20.52	0.750
LV GLS PLAX	-22.36 to -22.01	-22.18	0.470	-22.67 to -21.69	-22.18	1.309	-23.73 to -23.30	-23.51	0.576
LV GLS A4C	– 17.74 to – 17.19	- 17.47	0.740	-22.41 to -22.99	-21.70	1.899	-27.47 to -27.17	-27.32	0.411
LV GLS A2C	-20.36 to -20.02	-20.19	0.451	-24.68 to -23.61	-24.14	1.419	-26.95 to -26.51	-26.73	0.578
RV GLS	– 16.81 to – 16.44	-16.62	0.486	-27.86 to -27.28	-27.57	0.775	-28.45 to -27.93	-28.19	0.693

Table 1: LV and RV	strain values in children	according to their age groups
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Table 2: Conventional echocardiographic parameters of LV and RV in children according to their respective age groups

ECHO Parameters	2-5 years			5-10 years			10-15 years		
	95% CI	Mean	SD	95% CI	Mean	SD	95% CI	Mean	SD
LVEF (%)	67.76-69.37	68.57	2.161	67.39-69.41	68.40	2.699	68.46-69.68	69.07%	0.783
LVFS	37.29-38.21	37.75	1.230	37.09-38.45	37.77	1.818	37.41-37.99	37.70	0.783
MAPSE	13.18-14.22	13.97	0.669	14.19-15.14	14.67	1.262	15.13-15.80	15.47	0.900
LV Tei index	0.474-0.485	0.48	0.015	0.473-0.504	0.49	0.041	0.491-0.504	0.50	0.018
LVS	0.076-0.080	0.08	0.005	0.086-0.093	0.09	0.010	0.084-0.096	0.09	0.016
RVOT FS	50.94-52.60	51.77	2.223	51.68-53.32	52.50	2.193	54.59-56.48	55.53	2.529
TAPSE	15.75-16.39	16.07	0.858	18.62-19.71	19.17	1.454	20.20-21.40	20.80	1.606
RV Tei Index	0.449-0.460	0.45	0.015	0.474-0.0497	0.49	0.031	0.472-0.483	0.48	0.015
RVS	0.07-0.08	0.07	0.009	0.081-0.092	0.09	0.015	0.084-0.090	0.09	0.007

of 0.015) and 0.087 cm/sec (95% CI: 0.084 to 0.090 with SD of 0.007) in above three different age groups.

DISCUSSION

Deformation parameters can detect early subclinical dysfunction of the left ventricle and right ventricle in various congenital and acquired heart diseases in children.^[5] However, a lack of a normal range of values and associated variation hinder their use for everyday clinical evaluation. This is a study among Indian children that defines left ventricle (LV) and right ventricle (RV) normal strain values of children in different age groups and that evaluates demographic, clinical, and echocardiographic parameters as possible confounding factors through an observational study. The base-to-apex LS gradient seems to emerge as children grow up.^[9] Even though a base-to-apex gradient can be noticed from early infancy, significant differences in segmental myocardial strain appear only in 5-9 and 10-14 years age groups. In this study, we also compared the global longitudinal strain value of LV and RV with the conventional echocardiographic parameters individually, generally used during systolic function evaluation.

In this study, the left ventricular GLS varied from -19.68 to -21.93 (mean: -20.81) in normal healthy children, which was consistent with other studies conducted across the globe. The mean left ventricular GLS value is a meta-analysis published in *Cardiovascular Ultrasound* 2015 by Jashari *et al.*^[10] showed longitudinal strain (LS) normal mean values varied from -12.9 to -26.5 (mean: -20.5; 95% CI, -20.0

to -21.0). In normal healthy children, right ventricular GLS values were -16.44 to -28.45 (mean: -22.45). Zhang *et al.*^[11] reported normal values for mean RV strain ranging from -16 to -24.8 among different age groups in children.

The mean left ventricular strain values at basal level (-19.67, -20.93, and -21.95), midbasal level (-20.37, -21.13, and -20.17), and apical level (-22.32, -21.17, and -20.52) among different age groups were similar. That means, in this study, no significant increase was noted in the left ventricular strain value from basal to the apical segment from age group 2 years to 15 years and no significant difference in LVGLS or RVGLS was found among males and females.

A small study by Bussadori *et al.*^[12] demonstrated an increase in circumferential strain from the base to the apex, (base $-22 \pm 4\%$, midventricle $-24 \pm 6\%$, and apical $-32 \pm 7\%$); however, these data are somewhat limited by low numbers. Although other studies such as that by Marcus *et al.*^[13] have demonstrated an increase in strain toward the apex, the gradient has not been as large as reported in the Bussadori study. However, in our study, we did not find any significant increment in the regional strain value of the left ventricle from the basal to the apical segment.

In this observation, left ventricular ejection fraction were 67.39–69.68% (mean: 68.54%) and fraction shortening (FS) are 37.09–38.45% (mean: 37.77%), left ventricular "Tei" index are 0.47–0.50 (mean: 0.49), "MAPSE" are

13.18-15.80 (mean: 14.49) and the mean values of LVS were 0.076-0.096 cm (mean: 0.086 cm) in normal healthy children. A study by Eto et al.[14] published in the journal of American Society of Echocardiography conducted in children below 18 years old found LVEF 78 \pm 6%, LVFS $40 \pm 6\%$, peak E/A 1.77 ± 0.53 , Tei index 0.40 ± 0.09 (in less than 3 years) and 0.33 ± 0.02 (in more than 3 years). None of the above conventional echocardiographic parameters commonly used to assess the left ventricular systolic function had a significant correlation with left ventricular global longitudinal strain value (LVGLS). Table 3 shows the correlation pattern of each conventional left ventricular systolic parameter with the LVGLS with a P-value more than 0.05 in each aspect, except some correlation of MAPSE with LVGLS in age group more than 5 years to 10 years of age with a P-value of 0.01.

The present study shows the values of "TAPSE" (15.75-21.40, mean 18.56), RV "Tei" index (0.449-0.497, mean, 0.473), and RVS (0.07-0.092, mean 0.08) that are consistent with other related studies. Uys al et al. determined the mean TAPSE value in Turkish children and it was found to be 19.56 \pm 5.54 mm (9.09 \pm 1.36 mm in newborns and 25.91 ± 3.60 mm in the 13–18 years age group) and no significant difference was identified between male and female children.^[15] Ishii et al. showed the RV Tei index was not affected by age in healthy children (0.24 ± 0.04) .^[16] None of the above conventional echocardiographic parameters commonly used to assess the right ventricular systolic function had a significant correlation with right ventricular global longitudinal strain value (RVGLS). Table 4 shows the correlation pattern of each conventional right ventricular systolic parameter with the RVGLS with a P-value of more than 0.05 in each aspect. It confirms that though there are numerous methods to measure the left ventricular systolic function, 2D strain echo is very useful for the proper evaluation of systolic function and superior to the conventional parameter.

CONCLUSIONS

We tried to find out the age-dependent longitudinal strain value of both left ventricle and right ventricle among children of different age groups and correlation between the strain values with the conventional echocardiographic systolic parameter of both ventricles. In normal healthy children, the mean left ventricular GLS values were –19.89, –21.48, –20.64 and the mean right ventricular GLS values were –16.62, –27.56, –28.19 in children aged 2–5 years, 5–10 years, and 10–15 years, respectively. There was no significant correlation between conventional normal echocardiographic systolic parameters and global

Table 3: Correlation of LVGLS with conventional left ventricular systolic parameters

	Groups		Correlations	
Age 2 to 5	Spearman's	LVEF™	Correlation coefficient	-0.310
	rho		Р	0.095
		LV tei index	Correlation coefficient	0.179
			Р	0.343
		LVS	Correlation coefficient	-0.045
			Р	0.815
		LVFS	Correlation coefficient	-0.106
			Р	0.577
		MAPSE	Correlation coefficient	-0.041
			Р	0.832
More than	Spearman's	LVEF™	Correlation coefficient	-0.136
5 to 10 y	rho		Р	0.475
		LV tei index	Correlation coefficient	0.358
			Р	0.052
		LVS	Correlation coefficient	-0.241
			Р	0.200
		LVFS	Correlation coefficient	0.063
			Р	0.741
		MAPSE	Correlation coefficient	-0.587
			Р	0.001
More than	Spearman's	LVEF™	Correlation coefficient	-0.005
10 to 15 y	rho		Р	0.979
		LV tei index	Correlation coefficient	-0.263
			Р	0.160
		LVS	Correlation coefficient	0.259
			Р	0.167
		LVFS	Correlation coefficient	-0.049
			Р	0.797
		MAPSE	Correlation coefficient	-0.347
			Р	0.061

Table 4: Correlation of RVGLS with conventional right ventricular systolic parameters

	Groups		Correlations	
Age 2 to 5 y	Spearman's rho	RVOT FS	Correlation coefficient	-0.205 0.276
•)		RV tei index	Correlation coefficient	-0.105
		RVS	Correlation coefficient	-0.356
		TAPSE	Correlation coefficient	0.168
More than 5 to 10 y	Spearman's rho	RVOT FS	Correlation coefficient	0.116 0.543
,		RV tei index	Correlation coefficient	-0.080 0.676
		RVS	Correlation coefficient	-0.057 0.764
		TAPSE	Correlation coefficient	0.358
More than 10 to 15 y	Spearman's rho	RVOT FS	Correlation coefficient	-0.180 0.342
5		RV tei index	Correlation coefficient	-0.031
		RV S'	Correlation coefficient	-0.213 0.259
		TAPSE	Correlation coefficient	

longitudinal strain of left or right ventricle. There was no significant increase in the left ventricular strain value from the basal to the apical segment in the age group 2 to 15 years and no significant difference in LVGLS or RVGLS among males and females.

There were a few limitations of our study. Circumferential and radial strain of left ventricle measurements were not investigated for comparison, and infants were excluded from our study. Another limitation was the sole use of VVI as the vendor-neutral DICOM-based strain analysis software when several analysis systems were potentially available for analysis. We must say that further long-term, multi-centric, multi-arm studies involving larger groups are necessary for this field. Our study was just an observational cross-sectional study, should be compared 16 with metaanalysis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient (s)/ caregiver (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patient (s)/ caregiver (s) understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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