

Subtle myocardial effects of rheumatic heart disease in children are revealed earlier with two-dimensional speckle tracking echocardiography

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ABSTRACT

Objective. Rheumatic heart disease (RHD) is the most common cause of acquired heart disease in developing countries and remains a serious public health problem. In the subclinical course of carditis, the absence of typical symptoms and the normal range of classical echocardiographic measurements used to evaluate cardiac functions have required new echocardiographic methods and parameters. Previous studies regarding rheumatic heart disease in children and adults have shown that strain patterns obtained by speckle tracking echocardiography, are in fact affected although left ventricular systolic functions are preserved, yet some studies have suggested otherwise. The aim of our study is to compare the use of speckle tracking echocardiography with conventional methods in the evaluation of cardiac functions and myocardial involvement in children with subclinical RHD.

Materials and Methods. The study group consisted of 24 patients with asymptomatic cardiovascular who had no history of acute rheumatic fever, but had definite or probable rheumatic valve disease. This study group was determined according to the World Heart Federation guidelines by an echocardiographic examination performed for different reasons, as well as the control group of 22 healthy children. In order to evaluate the left ventricular regional myocardial functions of the patients, tissue Doppler echocardiography (TDE) and speckle tracking echocardiographic parameters were compared with the control group.

Results. The mean ages of the patient and control groups were 14.1±2.7 years and 13.9±2.3 years, respectively. There was no statistically significant difference between the two groups in terms of conventional methods ($p>0.05$) but global longitudinal strain and strain rate values were found to be significantly lower in the patient group ($p<0.01$). These changes appeared to be relevant throughout the duration of the illness.

Conclusion. In patients with subclinical rheumatic heart disease, conventional echocardiographic evaluations are likely negative, whereas two-dimensional speckle tracking echocardiography reveal systolic and diastolic dysfunctions of the disease.

Key words: children, speckle tracking echocardiography, rheumatic heart disease

Rheumatic heart disease (RHD) is still one of the leading causes of morbidity and mortality in developing countries, which makes early diagnosis and management of the disease of prime importance.¹

Conventional echocardiography can yield valuable information on the morphology of the atrioventricular valves, degree of valvular involvement and functional evaluation. Unfortunately, these evaluations can fail because of their dependence on geometric assumptions.² Two-dimensional speckle tracking echocardiography (2D-STE) has been designed to detect cardiac deformation by tracking myocardial speckles throughout the cardiac cycle.

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Primary advantages of this technique are being independent of geometric angles and translational movements of the heart.³ Disadvantages of 2D-STE are noted as not being as accurate as three-dimensional speckle tracking echocardiography and having lower temporal resolution.⁴

The main objective of our study is to evaluate cardiac functions and find out whether subtle myocardial impairment in subclinical RHD can be detected by using 2D-STE and also compare our findings with conventional echocardiography.

Methods

The study was designed as a retrospective cross-sectional study. After the approval of the Health Sciences University Gulhane Training and Research Hospital Scientific Investigations Ethical Committee (approval number: 46418926), 24 asymptomatic patients, admitted with a variety of symptoms and diagnosed with rheumatic valvular disease were reevaluated with speckle tracking echocardiography. Patients with a history of congenital heart disease, non-sinus rhythm, systemic disease

state or medication were excluded. Patients were also classified as borderline and definite rheumatic heart disease according to the 2012 American Heart Association Criteria for echocardiographic evaluation of rheumatic heart diseases.⁵ Their medical records were examined and compared to a control group of 22 healthy children.

The children in both groups were examined using a Philips Epiq 7C echocardiography system with a 5 μHz transducer (Philips, Andover, MA, USA). Left ventricular function analysis was done with conventional echocardiography, tissue Doppler and two-dimensional speckle tracking echocardiography. Using short-axis and apical views, real-time strain and strain rate values were obtained. The Philips Epiq 7C software was used for post-processing of the findings (Fig. 1). Obtained data were interpreted according to reference values for age, gender and body mass index.⁶

The data were statistically analyzed with IBM SPSS version 23.0. The Shapiro-Wilk test was used to detect normal distribution and chi-square test for comparing gender among groups. Variables with normal distribution

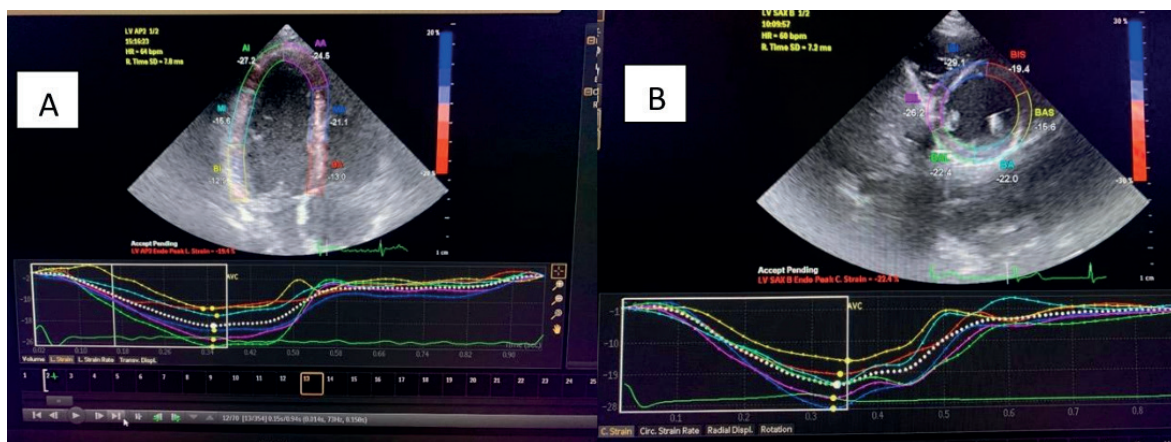


Fig. 1. A shows the evaluation of global longitudinal strain measurement. B shows radial and circumferential strain measurements.

were compared with independent samples t-test and variables without normal distribution were compared with Mann-Whitney U test. Quantitative data are presented as mean \pm standard deviation or median (minimum - maximum). Categorical data are presented as frequency (percent). P value <0.05 is accepted statistically significant.

Results

The patient group consisted of 24 children aged 14.1 ± 2.7 years (range 8-18), 14 girls and 10 boys and the control group consisted of 22 healthy children, aged 13.7 ± 2.3 years (range 8-18), 14 girls and 8 boys. There were no statistically significant differences between the study and control groups in terms of age, weight, height, body mass index (BMI) and heart rate variables ($p>0.05$) as seen in Table I. Table II summarizes the major complaints, valvular dysfunction, RHD type and disease duration in the patient group.

There were no statistically significant differences between M-mode values and Doppler parameters calculated by conventional echocardiography, as outlined in Table III ($p>0.05$). However, 2D-STE measurements yielded significant differences; left ventricle apical 4-chamber, 3- chamber and 2-chamber (LVAP4, LVAP3, LVAP2, respectively) strain and strain rate values were significantly lower

in the patient group as compared to the control group ($p<0.001$). Circumferential measurements showed the papillary muscle plane (SAXM) strain and strain rate did not differ significantly between the two groups ($p>0.05$), whereas that the parasternal short axis views at the mitral valve plane (SAXB) strain and strain were higher in the study group ($p=0.01$). Table IV summarizes the strain and strain rate measurements.

Table II. Clinical characteristics of our patient group

	Number and frequency (%)
Chief complaint at application	
Chest pain	3 (13.6)
Palpitation	2 (9.1)
Heart murmur	1 (4.5)
Sports participation	4 (18.2)
Other	13 (54.1)
Valvular dysfunction	
Mitral	20 (83.3)
Mitral+Aortic	4 (16.7)
Degree of valvular regurgitation	
Mild	20 (83.3)
Severe	4 (16.7)
Rheumatic heart disease type	
Borderline	12 (50.0)
Definite	12 (50.0)
Mean disease duration for patient group (month)	34.1 ± 28.6

Table I. Clinical properties of the patient and control groups

	Patient	Control	P
Age	14.1 ± 2.7	13.9 ± 2.3	0.726
Body weight (kg)	51.8 ± 14.8	49.9 ± 10.5	0.621
Height (cm)	159.5 ± 14.3	156.7 ± 10.0	0.461
Body mass index (kg/m ²)	19.9 ± 3.5	20.0 ± 2.7	0.967
Heart rate (beats per minute)	83.5 ± 14.2	81.8 ± 15.2	0.765

Table III. Comparison of conventional M-mode and Doppler echocardiographic parameters

	Patient	Control	P
LVEDS (mm)	25.4 ± 3.5	25.1 ± 4.7	0.830*
IVSS (mm)	11.2 ± 2.0	11.4 ± 1.2	0.696*
LVPWD (mm)	7.5 ± 1.1	7.7 ± 1.1	0.539*
LVEDD (mm)	42.3 (7.6- 50.8)	43.2 (31.1- 249.1)	0.185**
IVSDD (mm)	8.1 ± 1.6	8.2 ± 0.9	0.762*
LVMASS (gr)	107.6 ± 35.0	111.7 ± 27.4	0.666*
FS (%)	41.8 ± 4.3	44.3 ± 5.9	0.120*
EF (%)	72.8 ± 5.0	75.2 ± 6.6	0.186*
Mitral E (msn)	85.8 ± 15.3	87.5 ± 15.1	0.722*
Mitral A (msn)	59.3 ± 10.0	59.2 ± 10.0	0.994*
Mitral E/A	1.4 (1.2- 2.1)	1.5 (1.2- 1.8)	0.374**

2D-STE: two-dimensional speckle tracking echocardiography; A: peak velocity of late diastolic filling, E: peak velocity of early diastolic filling, EF: ejection fraction, FS: fractional shortening, IVSDD: interventricular septum end-diastolic thickness, IVSS: interventricular septum end-systolic thickness, LV mass: left ventricular mass, LVEDD: left-ventricular end-diastolic dimension, LVEDS: left ventricular end-systolic dimension, LVPWD: left ventricular posterior wall dimension.

*Independent samples t-test **Mann-Whitney U test. Data presented as median (minimum-maximum), or mean ± standard deviation

Table IV. Comparison of 2D-STE parameters between patient and control groups

	Patient group	Control group	P value
LVAP2	-16.9 (-27.3- -13.1)	-20.0 (-22.3- -17.2)	<0.001**
LVAP2 Rate	-1.0 (-1.7- -0.7)	-1.4 (-2.6- 0.8)	<0.001**
LVAP3	-17.4 ± 2.3	-19.4 ± 1.7	0.002*
LVAP3 Rate	-1.1 ± 0.3	-1.5 ± 0.4	<0.001*
LVAP4	-17.2 ± 2.9	-20.2 ± 1.2	<0.001*
LVAP4 Rate	-1.0 (-2.1- -0.7)	-1.6 (-2.4- -0.8)	0.003**
SAXM	-20.5 ± 2.9	-20.9 ± 2.0	0.638*
SAXM Rate	-1.2 (-1.8- -0.8)	-1.6 (-2.1- -0.9)	0.065**
SAXB	-20.8 ± 3.7	-21.6 ± 1.8	0.381*
SAXB Rate	-1.2 (-1.58- -0.7)	-1.8 (-2.5- -1.0)	0.010**
LV Longitudinal Strain	-17.3 ± 2.2	-19.8 ± 1.1	<0.001*
LV Longitudinal Strain Rate	-1.1 ± 0.2	-1.5 ± 0.5	0.001*
Circumferential Global Strain	-20.6 ± 2.5	-21.2 ± 1.4	0.359*
Circumferential Global Strain Rate	-1.3 (-8.6- -0.8)	-1.5 (-2.3- -0.9)	0.025**

2D-STE: two-dimensional speckle tracking echocardiography; LVAP2: Left ventricle apical 2-chamber; LVAP3: left ventricle apical 3- chamber; LVAP4: left ventricle apical 4-chamber; SAXM: circumferential measurements from papillary muscle plane; SAXB: parasternal short axis views at the mitral valve plane; Strain: % Strain rate: 1/Sec).

*Independent samples t-test **Mann-Whitney U test. Data presented as mean ± standard deviation, or median (minimum – maximum)

Four of our cases had severe valve insufficiency. Overall, speckle tracking measurements revealed minimally higher strain values of global measurements but not at all investigation plane distorted strain values were found.

Parameters between borderline and definite RHD did not show any significant difference either, as seen in Table V. 2D-STE values were also compared between definite, borderline and control groups. Table VI demonstrates

Table V. Comparison of 2D-STE parameters between the types of RHD

	Borderline RHD	Definite RHD	P
LVAP2	-17.61 ± 4.25	-17.05 ± 2.31	0.706*
LVAP2 Rate	-0.98 ± 0.23	-1.05 ± 0.30	0.517*
LVAP3	-17.79 ± 2.54	-16.96 ± 2.04	0.401*
LVAP3 Rate	-1.21 ± 0.33	-0.98 ± 0.29	0.103*
LVAP4	-17.10 (-22.90- -11.40)	-16.50 (-25.50- -14.70)	0.786**
LVAP4 Rate	-1.02 ± 0.29	-1.15 ± 0.42	0.415*
SAXM	-21.30 (-26.20- -16.00)	-18.65 (-25.20- -17.10)	0.203**
SAXM Rate	-1.34 ± 0.24	-1.07 ± 0.28	0.023*
SAXB	-21.50 ± 3.82	-19.88 ± 3.64	0.324*
SAXB Rate	-1.20 (-15.80- -0.70)	-1.31 (-1.80- -0.82)	0.771**
LV Long Strain	-17.42 ± 2.48	-17.21 ± 2.03	0.829*
LV Long Strain Rate	-1.07 ± 0.18	-1.06 ± 0.25	0.934*
Circumferential Global Strain	-21.31 ± 2.33	-19.82 ± 2.68	0.178*
Circumferential Global Strain Rate	-1.28 (-8.64- -0.89)	-1.19 (-1.75- -0.81)	0.314**

2D-STE: two-dimensional speckle tracking echocardiography; LVAP2: Left ventricle apical 2-chamber; LVAP3: left ventricle apical 3- chamber; LVAP4: left ventricle apical 4-chamber; RHD: rheumatic heart disease; SAXM: circumferential measurements from papillary muscle plane; SAXB: parasternal short axis views at the mitral valve plane.

*Independent samples t-test **Mann-Whitney U test. Data presented as mean ± standard deviation, or median (minimum – maximum)

Table VI. Adjusted significance values of comparison of 2D-STE parameters between the types of RHD and control group

	Borderline-Definite RHD	Borderline RHD-Control	Definite RHD-Control
LVAP2	1	0.031	0.006
LVAP2 Rate	1	0.004	0.023
LVAP3	1	0.289	0.026
LVAP3 Rate	0.624	0.092	0.001
LVAP4	1	0.000	0.003
LVAP4 Rate	1	0.005	0.075
SAXM	0.158	0.158	0.158
SAXM Rate	0.174	1	0.007
SAXB	0.412	0.412	0.412
SAXB Rate	1	0.087	0.114
LV Long Strain	1	0.020	0.003
LV Long Strain Rate	1	0.008	0.008
Circumferential Glob-al Strain	0.191	0.191	0.191
Circumferential Glob-al Strain Rate	0.912	0.375	0.028

2D-STE: two-dimensional speckle tracking echocardiography; LVAP2: Left ventricle apical 2-chamber; LVAP3: left ventricle apical 3- chamber; LVAP4: left ventricle apical 4-chamber; RHD: rheumatic heart disease; SAXB: parasternal short axis views at the mitral valve plane; SAXM: circumferential measurements from papillary muscle plane.

*The significance level is 0.05. Significance values were adjusted by Bonferroni correction for multiple tests.

global longitudinal strain and strain rate values, also circumferential strain rate values were significantly lower in borderline group compared to control group.

Disease duration and LVAP4 strain values were found to be negatively related as can be seen in Table VII ($r=-0.521$; $p=0.038$). Other strain parameters were non-related with disease duration ($p>0.050$).

Table VII. Correlations of 2D-STE measurements with disease duration

	Disease duration	
	r	P
LVAP2	-0.232	0.387
LVAP2 Rate	-0.223	0.406
LVAP3	-0.199	0.459
LVAP3 Rate	-0.193	0.473
LVAP4	-0.521	0.038
LVAP4 Rate	0.134	0.621
SAXM	0.014	0.960
SAXM Rate	-0.276	0.319
SAXB	-0.248	0.373
SAXB Rate	-0.201	0.472
LV Long Strain	-0.463	0.071
LV Long Strain Rate	-0.106	0.695
Circ. Global Strain	-0.118	0.675
Circ. Global Strain Rate	-0.248	0.374

2D-STE: two-dimensional speckle tracking echocardiography; LVAP2: Left ventricle apical 2-chamber; LVAP3: left ventricle apical 3- chamber; LVAP4: left ventricle apical 4-chamber; r: Spearman's rho correlation coefficient; RHD: rheumatic heart disease; SAXB: parasternal short axis views at the mitral valve plane; SAXM: circumferential measurements from papillary muscle plane.

Discussion

Widespread usage of conventional echocardiography has aided in the detection of subclinical RHD, which shows that RHD has been affecting more patients than previously predicted.⁷ Clinical studies have revealed that 2D-STE could be beneficial for detecting diastolic dysfunction, postoperative mitral regurgitation and ischemia of myocardial tissue.⁸⁻¹⁰ Dorobantu et al. have suggested that similar usage of 2D-STE can benefit children with acquired cardiomyopathy.¹¹ Also diminished radial strain values may reveal systolic dysfunctions earlier than conventional Doppler studies. Therefore, 2D-STE can facilitate early detection of RHD and institution of penicillin therapy to prevent valvular involvement. On the other hand, Sobhy et al. studied 30 children with RHD and preserved left ventricular systolic functions and 23 healthy controls with 3-dimensional speckle tracking echocardiography. They found 3D-derived left ventricular end-diastolic

volume and sphericity index among patients were significantly increased when compared to controls. 3D-derived EF and longitudinal strain did not differ significantly. 3D-derived global circumferential strain was higher in patients when compared to controls. They also had cardiac magnetic resonance imaging of the patient group but none of the patients demonstrated late enhancement myocardial fibrosis.¹² In our study we only used 2D-STE, 3D-STE and magnetic resonance imaging, which may be more accurate yet hard to reach in daily clinical use. Pamuk et al. reported some significant changes in the strain measurements with 2D-STE in the acute phase of rheumatic fever and relieving with treatment.¹³

Acute rheumatic fever affects both genders equally but RHD tends to be more common in females; similarly, 58% of our study group was female.^{14,15} Especially studies in developing countries have shown that subclinical rheumatic valvular disease or RHD without a known history of acute rheumatic fever could actually be a widespread form of the disease in endemic regions.¹⁶ In our study, eighteen percent of our patient (n=4/24) group had been evaluated for sports participation.

Mitral valvulitis was observed in 83.3 % of our patient group; none of our patients had sole aortic valvulitis, which was always associated with mitral valvulitis (16.7%), similar to other reports.^{17,18} Cantinotti et al. studied 544 healthy children to outline standardized Doppler values.¹⁹ Our conventional Doppler studies showed that mitral and tricuspid E velocities, as well as E/A ratios, were normal in both study and control groups. We also observed longer E and A times and decreased A velocity as children got older.

In recent studies, speckle tracking echocardiography is seen to have a wide range of clinical uses. Harrington et al. evaluated 577 healthy children and composed normal left ventricular systolic and diastolic strain and strain rate values as well as Z scores.⁶ Although we did not examine Z scores, our findings in both groups were within normal ranges according to

these values. Levy et al. evaluated 2325 healthy children and found GLS ranges between -16.7-23.6% (mean: -20.2; 95% CI, -19.5 to -20.8%).²⁰ We found average GLS values of -17.3% in the study group and -19.8% in the control group. Our findings support the observation that RHD causes decreased systolic functions. Also, Koopman et al. studied normal ranges of 2D-STE findings; the primary advantage of this study is the resemblance of average ages of participants to those of our study and approximately 10 percent of their participants being Turkish.²¹ Their average values were $-20.9 \pm 2.7\%$ for LPA2, $-21.0 \pm 2.7\%$ for LPA3, $-20.6 \pm 2.6\%$ for LPA4 and $-24.2 \pm 3.5\%$ for SAXB. These figures show that our study group patients have decreased myocardial functions as compared to healthy children.

Beaton et al. first studied myocardial strain in a cohort of children with RHD in 2017.²² They compared 14 definite and 13 borderline RHD patients with 112 healthy children and found no significant difference between left ventricle volumes and ejection fraction. However, GLS values were decreased in 57% of definite RHD and 44% of borderline RHD cases (p: 0.03, p: 0.002; respectively), similar to our results.

Limitations

Our study was conducted on a relatively small number of study patients. Another limitation might be omission of Z scores; however, the pediatric population is hard to standardize. These limitations may be overcome with further studies on larger cohorts that also include Z scores.

Conclusion

Routine conventional echocardiographic evaluations can benefit high-risk populations with rheumatic heart disease and we suggest that it is possible to determine myocardial dysfunction with 2D-STE earlier and more accurately than conventional echocardiography and the detection of subclinical myocardial dysfunction can help in risk stratification and

also prognostic stratification of RHD. These patients might benefit from a change in heart failure treatment or of timing of surgery before irreversible myocardial damage occurs. Larger studies are needed for further investigation of this hypothesis.

Ethical approval

The study was approved by Health Sciences University, Gulhane Training and Research Hospital Scientific Investigations Ethical Committee (date: 06.01.2022, number: 46418926).

Author contribution

The authors confirm contribution to the paper as follows: study conception and design: ŞK, AK; data collection: HIB; analysis and interpretation of results: İT, ŞK; draft manuscript preparation: İT, AK. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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