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ORIGINAL ARTICLES

Subclinical right ventricular dysfunction in juvenile systemic sclerosis: a cross-sectional echocardiographic study

Sarısoy O[1], Turkmen S[2], Sozeri B[2]

ABSTRACT

Objective: This study aimed to evaluate subclinical myocardial involvement in asymptomatic juvenile systemic sclerosis (JSSc) patients using conventional Doppler (CD), tissue Doppler imaging (TDI), and speckle tracking echocardiography (STE).

Methods: In this cross-sectional, retrospective study, nine asymptomatic JSSc patients and ten age- and gender-matched healthy controls were evaluated. All participants underwent echocardiographic assessment, including CD, TDI, and STE, according to standardized protocols. Right and left ventricular systolic and diastolic parameters were compared between groups.

Results: In JSSc patients, tricuspid E/A ratio was lower (p=0.012), deceleration time (DT) and ejection time (ET) were shorter (p=0.025, p=0.006), and myocardial performance index (MPI) was higher (p=0.025) compared to controls. TDI measurements also showed shorter ET (p=0.024) and increased MPI (p=0.002). Right ventricular end-diastolic and end-systolic volumes were significantly smaller (p=0.004, p=0.018), and right ventricular ejection fraction (RVEF) was lower (p=0.019) in JSSc patients. No significant differences were detected in right ventricular strain parameters or left ventricular global longitudinal strain (GLS) and circumferential strain (GCS) values between groups. However, TDI-derived MPI for the left ventricle was elevated in JSSc patients (p=0.018), suggesting early global dysfunction despite preserved left ventricular ejection fraction.

Conclusion: Subclinical right ventricular dysfunction occurs early in JSSc, even in asymptomatic patients without pulmonary hypertension. Routine use of advanced echocardiographic techniques such as STE and TDI-derived MPI assessment may facilitate earlier detection of cardiac involvement, enabling timely intervention to improve long-term outcomes.

Keywords: Juvenile systemic sclerosis; Speckle tracking echocardiography; Subclinical cardiac dysfunction.

INTRODUCTION

Systemic sclerosis (SSc) is a chronic autoimmune connective tissue disease characterized by progressive fibrosis, endothelial dysfunction, and microvascular damage[1-3]. Cardiac involvement is one of the most severe complications of the disease, significantly contributing to morbidity and mortality[1,2]. Myocardial fibrosis, resulting from microvascular changes, collagen deposition, and immune dysregulation, leads to both systolic and diastolic dysfunction.

Cardiac involvement in SSc often remains asymptomatic, complicating the estimation of its true prevalence[4]. Clinical studies have indicated that the incidence of cardiac involvement ranges from 15% to 35%, depending on diagnostic methods employed[4,5]. Importantly, cardiac complications are associated with a poor prognosis, contributing to 14–36% of overall mortality among SSc patients[5]. Even in the absence of overt clinical manifestations, subclinical myocardial dysfunction is frequent, emphasizing the necessity for sensitive diagnostic modalities[6].

Juvenile systemic sclerosis (JSSc), a rarer and potentially more aggressive form of SSc occurring in childhood, remains poorly understood, particularly regarding cardiac involvement[7]. Early detection of subclinical myocardial abnormalities is crucial to improving long-term cardiac outcomes.

This study aimed to perform a detailed cardiac assessment using conventional Doppler (CD), Tissue Doppler Imaging (TDI), and Speckle Tracking Echocardiography (STE) in asymptomatic JSSc patients to detect subclinical myocardial abnormalities and evaluate their potential clinical implications.

1. Umraniye Research and Training Hospital, Pediatric Cardiology Unit, Umraniye, Istanbul, Turkey
2. Umraniye Research and Training Hospital, Pediatric Rheumatology Unit, Umraniye, Istanbul, Turkey

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Correspondence to: Ozlem Sarisoy
E-mail: ozlemsarisoy@yahoo.com

MATERIALS AND METHODS

This cross-sectional and retrospective study included nine JSSc patients diagnosed and followed for at least six months at the Pediatric Rheumatology Clinic of the University of Health Sciences Ümraniye Training and Research Hospital between June 2016 and December 2023, along with 10 healthy children who were evaluated for various reasons at the Pediatric Cardiology Clinic of the same institution. The study adhered to the Declaration of Helsinki and was approved by the ethics committee of the University of Health Sciences Ümraniye Training and Research Hospital (Ethics committee no:B.10.1.THK.4.34.H.GP.0.01/415).

Patients with systemic sclerosis exhibiting no complaints and demonstrating normal cardiac examinations, without signs of heart failure or congenital heart disease, were included in the study, whereas individuals with previously diagnosed or known cardiac conditions were excluded from participation. The control group consisted of healthy children or adolescents matched in terms of gender and age, who had no cardiovascular disease or cardiac anomalies on echocardiography and who applied to the pediatric cardiology clinic for various reasons (sports license examination, innocent murmur, nonspecific chest pain, etc.) and volunteered for the study. All participants and their families were informed, and written informed consent was obtained.

Physical examination findings, height and weight measurements of both groups and diagnosis, follow-up period and treatments in the patient group were recorded.

Echocardiography was performed using a Philips Affinite 50 Echocardiography machine (Release 2.0.1 Philips Healthcare 3000, Minuteman Road, Andover, MA 01810, USA) equipped with 4.2 MHz transducers. Echocardiographic measurements for both the patient group and the control group were performed by a single experienced pediatric cardiologist. All patients underwent M-Mode, conventional and tissue doppler echocardiographic examinations, and these measurements were obtained using standard techniques according to the recommendations of the American Society of Echocardiography[8]. E and A wave velocity, deceleration time (DT), isovolumic contraction time (IVCT), isovolumic relaxation time (IVRT) and ejection time (ET) were measured with conventional and tissue doppler echocardiography. Right ventricular systolic functions were measured by Simpson's method, and left ventricular systolic functions were measured by the M-mode method. MPI was calculated by dividing the sum of IVCT and IVRT by ET[9].

Strain echocardiography is a new technique that analyzes movement by tracking natural acoustic reflections within an ultrasonic window. Deformation measurement has been achieved through the acquisition of suitable 2D images, allowing for deformation estimation. This new measure of regional and global contractility is made possible by the frame-by-frame tracking of unique speckles in the myocardium. The algorithm uses correlation criteria and the sum of absolute differences to track the position of speckles in sequential images. This process is carried out using the ultrasonic velocity vector tracking method. Algorithms are available that can create deformation curves in individual segments as well as average deformation across all chambers. One significant advantage is their angle independence in the obtained imaging plane; however, proper alignment of the image planes is still important. Two-dimensional strain is used to measure both left and right ventricular function. Initially, it was applied and validated on the left ventricle, and recent studies have increasingly focused on assessing right ventricular function[10,11].

Analyses were performed using the program loaded onto the echocardiography device for strain measurements. Left ventricular global longitudinal and circumferential strain and right ventricular strain were calculated. Standard images specified for both ventricles were recorded for strain analysis. After recording, analysis was performed using an automatic program. The obtained data were obtained consecutively by the same physician for all patients and the analyses were performed retrospectively.

Strain is defined as the percentage of reduction in the original length of a region of interest (ROI) and is typically expressed as a negative percentage (%). Deteriorating strain is represented by a smaller negative number (i.e., a lower absolute value) and is assessed relative to the expected value for a ROI or for longitudinal/circumferential or radial axis in the case of hypokinesia or reduced deformation area[10].

Statistical analysis

Statistical analysis was performed using SPSS for Windows, version 26.0 (IBM Corp., Armonk, NY, United States of America). Data are presented as mean ± SD for continuous variables. For comparisons between groups, t-test, $\chi 2$ test, and Mann–Whitney U were used, as appropriate. Correlation between variables was expressed using the Spearman rank correlation coefficient. A p-value <0.05 was considered statistically significant.

RESULTS

The study group consisted of 9 patients with JSSc, their ages ranged between 7 and 22 years with a mean ± SD of 15,44±4,61 (median 17 years), of whom 6 (66.6%)

were girls and 3 (33.3%) were boys. The control group, which consisted of 10 healthy children between 11 and 18 years of age with a mean ± SD of 14,30±2,21 (median 14,5) years contained 7(70 %) girls and 3 (30%) boys. Duration after diagnosis of SSc in patients ranged between 1-7 years (mean ± SD= 3,46±2,30 ; median: 2,2 years). When the control group and patients with SSc were compared in terms of age, weight, height, and body surface area there was no statistically significant difference.

Right ventricular measurements

In conventional doppler echocardiography measurements, tricuspid E/A was lower (p:0.012), DT and ET were shorter (p:0,025,p:0.006) and calculated MPI was higher (p:0.025) in the JSSc group. Tissue doppler echocardiography also showed that ET was shorter (p:0.024) and MPI value was higher (p:0.002) in patients with JSSc. No difference was found between the two groups for other measurements.

Right ventricular end-diastolic volume measured by echocardiography was found to be smaller in patients with JSSc compared to the control group (p:0,008). The echocardiography and Doppler measurements of the right ventricle are presented in detail in Table I.

The patients did not have significant tricuspid regurgitation and there was no high velocity measured here that would suggest pulmonary arterial hypertension.

In right ventricular strain measurements, end diastolic (EDV) and end systolic (ESV) volumes were found to be smaller in patients with JSSc (p: 0.004, 0.018). Right ventricular ejection fraction (RVEF) measured by strain echocardiography was found to be lower in the JSSc group (p: 0.019). There was no difference between the two groups in terms of right ventricular free wall, septum and endo peak strain measurements (Table II).

Left ventricular measurements

There was no difference between the two groups in all left ventricular measurements performed with conventional doppler, tissue doppler and strain echocardiography (Table 1). However, only the calculated TDI MPI value was found to be higher compared to the control group (p:0,018).No difference was found between global longitudinal (GLS) and circumfrencial strain (GCS) values in the two groups (Table II).

The significant differences between JSSc patients and healthy controls in echocardiographic parameters are summarized in Figure 1.

DISCUSSION

This study presents comprehensive cardiac evaluation results in asymptomatic JSSc patients using conventional and advanced echocardiographic techniques. Our findings demonstrate that right ventricular (RV) dysfunction begins at a subclinical level early in the disease

TABLE I. Right and left ventricular doppler echocardiography measurements

	JSSc (meanSD)		Control (meanSD)		P	
CD	LV	RV	LV	RV	LV	RV
E/A	1,69	1,16	1,79	1,17	0,449	**0,012**
DT	123,6749,81	116,2250,85	138,9026,23	167,5039,90	0,409	**0,025**
IVRT	44,229,36	44,005,36	39,90 9,67	41,8013,14	0,338	0,646
IVCT	37,00 8,27	35,33 4,55	32,106,52	33,007,58	0,168	0,434
ET	343,1173,62	337,8972,40	377,4039,10	429,2052,36	0,215	**0,006**
MPI	0,24	0,06	0,19	0,05	0,051	**0,025**
TDI						
E/A	1,93	0,72	1,69	0,43	0,398	0,902
S	1,8	3,59	1,64	1,32	0,508	0,083
IVRT	47,674,58	47,678,13	42,307,22	40,008,40	0,074	0,060
IVCT	39,223,80	39,679,28	34,605,75	33,905,66	0,057	0,116
ET	334,0077,44	312,7864,73	376,7059,93	376,8047,65	0,194	**0,024**
MPI	0,04	0,06	0,05	0,04	**0,018**	**0,002**
EF	70,568,01	5,23	73,307,00	56,428,82	**0,437**	0,446
EDd	36,22 7,54	4,38	4,50	7,19	**0,124**	**0,008**

CD: Conventional Doppler DT: Decerelation time IVRT: Interventricular relaxation time IVCT: Interventricular contraction ET: Ejection time MPI: Myocardial performance index TDI: Tissue doppler imaging EF: Ejection fraction EDd: End diastolic diameter

TABLE II. Right and left ventricular strain echocardiography measurements

	JSSc (meanSD)	Kontrol (meanSD)	p
GLS	-21,703,46	-23,913,26	0,171
GCS	-24,81	-28,144,14	0,116
LVEF	56,983,13	58,383,68	0,390
LVEDV	50,8416,77	**61,41**28,68	0,348
LVESV	7,43	11,14	0,425
RV EndoPikStrain	7,86	3,35	0,709
RVEF	5,82	3,28	**0,019**
RVEDV	6,78	8,59	**0,004**
RVESV	3,33	4,02	**0,018**

GLS: Global longitudinal strain GCS: Global circumferential strain LVEF:Left ventricular ejection time LVEDV: Left ventricular end diastolic volüme LVESV: Left ventricular end systolic volüme RVEF: Right ventricular ejection time RVEDV: Right ventricular end diastolic volume RVESV: Right ventricular end systolic volume

course. Specifically, increased MPI values, shortened DT and ET intervals, decreased tricuspid E/A ratios, and reduced RV volumes were observed, suggesting early impairment of RV function even before the onset of clinical symptoms.

The myocardial performance index (MPI), which combines systolic and diastolic time intervals, serves as a valuable marker for assessing global myocardial function and has demonstrated prognostic significance across various cardiac conditions, including SSc[5,12]. Studies using CD and TDI have shown reasonable correlations between these modalities and global ventricular performance[13,14].

Assessment of RV function poses particular challenges due to the complex geometry of the right ventricle. The Right Ventricular Myocardial Performance Index is considered a reliable measure due to its independence from heart rate, blood pressure, and pulmonary pressure levels, while also being a useful and reproducible parameter[15]. Our analysis revealed a significant elevation in the MPI in our patients, as measured by both CD and TDI. Furthermore, both modalities demonstrated notable impairments in systolic and diastolic parameters. It is postulated that the deterioration of both systolic and diastolic myocardial functions in SSc arises from the development of microvascular ischemia and fibrotic remodeling. Our findings align with previous studies that suggest intrinsic myocardial fibrosis and microvascular dysfunction, key characteristics of SSc, play a significant role in the progression of myocardial impairment[16].

Prior research has demonstrated that RV dysfunction may develop early, even preceding pulmonary arterial hypertension (PAH) onset[17,18]. Furthermore, the elevated TDI-derived MPI values we observed align with previous studies suggesting that TDI-MPI is sensitive for detecting early myocardial dysfunction in SSc[19]. This elevation of MPI, even in asymptomatic patients, underlines the silent progression of myocardial disease in JSSc.

Regarding left ventricular (LV) function, no significant differences were observed in systolic or diastolic parameters by conventional Doppler or STE in our cohort. However, the increased MPI value indicates potential early global LV dysfunction. Previous studies have indicated that LV involvement tends to occur at later stages following the progression of RV dysfunction[20,21].

Advances in cardiac imaging, particularly the development of myocardial deformation imaging through STE, have significantly enhanced the early detection of myocardial involvement in SSc[22]. Although none of the patients in our study showed clinical or echocardiographic signs of PAH, it should be noted that mild or early intermittent pulmonary hypertension might be underestimated using Doppler echocardiography based on tricuspid regurgitation gradients[23].

STE has proven to be a highly sensitive method for identifying subclinical myocardial fibrosis by quantifying subtle changes in myocardial strain[24-26].

The importance of early diagnosis and intervention has been highlighted by previous studies, stressing that timely identification of myocardial involvement in systemic sclerosis may offer opportunities for earlier therapeutic strategies and improved outcomes[27,28].

The main limitations of our study include the small sample size and the cross-sectional design, limiting our ability to assess disease progression longitudinally. Nevertheless, the demonstration of early RV dysfunction in asymptomatic JSSc patients highlights the need for regular cardiac surveillance and supports the use of sensitive echocardiographic techniques such as STE for early myocardial assessment.

In conclusion, our study suggests that subclinical ri-

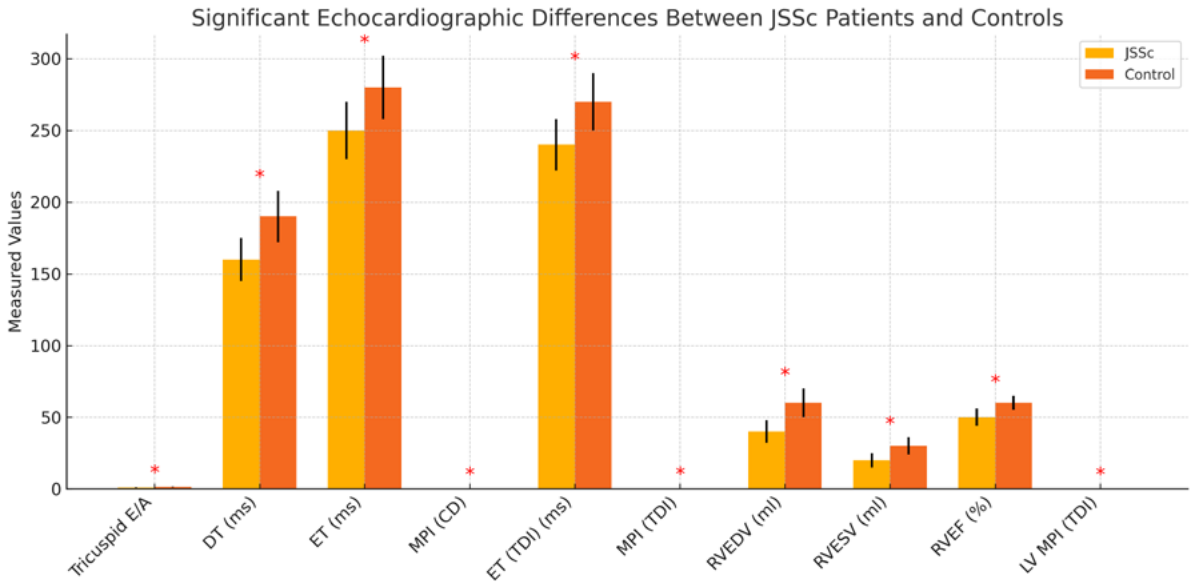

Figure 1. Comparison of significant echocardiographic parameters between juvenile systemic sclerosis (JSSc) patients and healthy controls.

The bar plot illustrates the mean values and standard deviations (SD) of right and left ventricular systolic and diastolic parameters as well as volumetric measurements obtained by conventional Doppler, tissue Doppler imaging, and speckle tracking echocardiography. Parameters showing statistically significant differences ($p<0.05$) between JSSc patients and controls include tricuspid E/A ratio, deceleration time (DT), ejection time (ET) by conventional Doppler and TDI, myocardial performance index (MPI) by conventional Doppler and TDI, right ventricular end-diastolic volume (RVEDV), right ventricular end-systolic volume (RVESV), right ventricular ejection fraction (RVEF), and left ventricular MPI by TDI. An asterisk () denotes statistically significant differences ($p<0.05$).*

ght ventricular dysfunction occurs early in JSSc, even before the onset of clinical symptoms or pulmonary hypertension. Routine use of advanced echocardiographic modalities such as STE may facilitate earlier detection, improve risk stratification, and guide timely therapeutic interventions to optimize long-term outcomes in these patients.

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