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Assessment of Right Ventricular Function and Structure in Children with Idiopathic Dilated Cardiomyopathy

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Dilated cardiomyopathy (DCM) refers to dilating the ventricles and dysfunction of their systolic functions (predominantly the left ventricle) with or without congestive heart failure. In children, it is the most common form of heart muscle disease. We aimed to evaluate the right ventricular functions and structure using speckling tracking echocardiography in children with dilated cardiomyopathy and correlate this parameter with other echocardiographic findings.
Methods: This observational Case-Control Study was carried out on 75 subjects. They were subdivided into two groups: *Group 1:* 50 patients with dilated cardiomyopathy *Group 2:* 25 healthy children matched for age and sex. Patients were evaluated by M-mode echocardiography, Transthoracic 2DE Examination (TTE), Tissue Doppler Examination (TDE) and Speckling Tracking Technique.
Results: Left ventricle (LV) and right ventricle (RV) systolic dysfunction was evidenced by a significant decrease of mitral and tricuspid annular systolic velocities and a significant decrease of LV and RV global systolic strain and a significant decrease of LV and RV Ejection fraction (EF). LV and RV diastolic dysfunction were evidenced by a significant decrease of mitral and tricuspid

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annular diastolic velocities (E'/A') and a significant increase of LV and RV Myocardial Perfusion Imaging (MPI). LV and RV global strains were significantly reduced in comparison to controls, suggesting that the dilated cardiomyopathy is a diffuse disease.

Conclusion: In DCM patients, RV had significant systolic and diastolic dysfunction mainly elicited by the Tissue Doppler imaging (TDI) beside LV affection secondary to the interventricular interaction. TDI and 2D-STE add value to interpreting the findings and the dependency of RV systolic and diastolic functions on each other in DCM patients.

Keywords: Right ventricular function; idiopathic dilated cardiomyopathy.

1. INTRODUCTION

Dilated cardiomyopathy (DCM) refers to dilating the ventricles and dysfunction of their systolic functions (predominantly the left ventricle) with or without congestive heart failure. In children, it is the most common form of heart muscle disease [1].

Injury to the myocardial cell is the initiating factor that leads to cell death. If a significant loss of cells occurs, the myocardium fails to generate sufficient contractile force to produce adequate cardiac output. This results in activation of the renin-angiotensin-aldosterone system, antidiuretic hormone production, sympathetic stimulation, and release of atrial natriuretic peptide. These compensatory mechanisms help to maintain cardiac output in the initial phase; however, as myocardial damage progresses, continuous and excessive activation can be detrimental to cardiac function, resulting in overt congestive heart failure [2].

The work aimed to evaluate the right ventricular functions and structure using speckling tracking echocardiography in children with dilated cardiomyopathy and correlate this parameter with other echocardiographic findings.

2. SUBJECTS AND METHODS

This observational Case-Control Study was carried out at Pediatric Cardiology Unit, Tanta University Hospital between March 2018 and March 2019. A total of 75 subjects were enrolled in this study. They were subdivided into two groups:

Group (1): 50 patients with dilated cardiomyopathy aged from 6 months up to 8years, those patients attended the Cardiology Unit Pediatric Department, Tanta University Hospital.
Group (2): 25 healthy children matched for age and sex.

Inclusion Criteria: Children with primary dilated cardiomyopathy.

Exclusion Criteria: Children with congenital or acquired heart diseases and children with dilated cardiomyopathy secondary to systemic diseases.

Collection of Data: All studied individuals were subjected to the following:

1. **Clinical Evaluation:** Full history taking, general, regional and systemic examination such as body weight, height, and vital signs; heart rate, blood pressure. Cardiac examination for detection of cardiomegaly and evidence of murmur.
2. **Echocardiographic Examination:** Infants and young children received chloral hydrate (50-100mg /kg orally). Echocardiographic studies were performed using a commercially available ultrasound transducer and equipment (*Vivid 7 or Vivid 9, GE Healthcare, Horten, Norway*), data acquisition was performed with a 3.5-MHz transducer, S7, and V3 matrix real-time 3-dimensional probes, and digital loops were stored on the hard disk of the echocardiography machine, and transferred to a workstation for offline analysis.

A- M-mode measurements

- **RV Systolic Function:** Tricuspid annular plane systolic excursion **(TAPSE)** was determined by the total excursion of the tricuspid annulus from its highest position after atrial ascent, to the lowest point of descent during ventricular systole.

B- Transthoracic 2DE Examination (TTE): Examination was performed for all patients using the standard apical, parasternal, and subcostal views.

C- Tissue Doppler Examination (TDE)

- **Systolic and diastolic mitral and tricuspid annulus velocities:** PW-TDI sample volume is placed at the level of the septal tricuspid annulus. Tissue Doppler imaging (TDI) display shows an antegrade systolic wave S', and two retrograde waves, E' (passive LV filling) and A' wave (atrial contraction) [3].

- **RV Myocardial Performance Index (MPI):** The MPI was calculated as Tei SE'-wave and b' the time from the onset to the end of the S'-wave [4].

D- Speckling Tracking Technique: Right Ventricular Longitudinal Systolic Strain Analysis

- **2D Strain:** Image acquisition was performed using a 3.5-MHz transducer at a depth of 16 cm in the standard apical view (4-chamber image).
- **Auto EF for LV and RV systolic function:** End-diastolic and end-systolic volumes are calculated based on the tracings and serve as the basis for the Ejection fraction (EF) calculation.

2.1 Statistical Analysis

Statistical analysis was done using IBM SPSS version 19 **(**Armonk, NY: IBM Corp**).** For quantitative data, the range, mean and standard deviation was calculated. Boxplots were performed to illustrate the median, first and third quartiles of the quantitative data. For qualitative data, which describes a categorical set of data by frequency, percentage, or proportion of each category, comparison between two groups and more was done using the Chi-square test ($\chi2$). For comparison between means of two groups of parametric data of independent samples, the student t-test was used. For comparison between percent (%), testing of proportion was done (Z test). Correlation between variables was evaluated using Pearson's correlation coefficient. P < 0.05 was accepted as significant and P > 0.05 was non-significant.

3. RESULTS

The study included 50 children with dilated cardiomyopathy with a mean± SD age of 4.90±2.25, a mean ±SD weight of 17.92±5.95, they were 27 male and 23 female. The healthy control group had a mean ±SD age of 5.56±2.31, a mean ±SD weight of 20.60±5.97, they were 14 males and 11 females. There is no statistically significant difference was found between studied groups regarding age, sex, and weight (Table 1).

As regard to LV results, we evaluated *sphericity index (SI)* by Conventional Echo and our results showed that there was a significant reduction of sphericity index (SI) in patients with a mean (1.197 ±0.345) when compared with controls with mean (1.566±0.272) with P-value <0.001*.

Also, as regards to tissue doppler examination there was a significant reduction of mitral annulus systolic velocity (S') in patients with mean (3.667±1.061) when compared with controls with mean (6.933±0.785) with p-value <0.001*.

There was a significant reduction of (E'/A' ratio) in patients with mean (1.147±0.401) when compared with controls with mean (1.540±0.246) with p-value <0.001* and there was a significant increase in LV MPI in patients with mean (1.876±0.233) when compared with controls with mean (0.407± 0.078) with p-value <0.001* (Table 2).

Left ventricle evaluation by Speckling tracking showed that there was a significant reduction of EF in patients with a mean (43.360±11.7600) when compared with controls with a mean (65.234±7.589) with P-value <0.001*, and there was a significant reduction of LV global longitudinal systolic strain in patients with a mean (-12.667±4.943) when compared with controls with a mean (-24.400±1.610) with P-value <0.001* (Table 2).

As regard to RV results, we evaluated *Tricuspid annular plane systolic excursion (TAPSE)* by M-mode and our results showed that there was a significant reduction of RV TAPSE in patients with mean (12.00±3.56) when compared with controls with mean (19.00±1.72) with p-value 0.0001*****, also as regards to tissue doppler examination there was a significant reduction of Tricuspid annulus systolic velocity (S') in patients with mean (4.42±0.82) when compared with controls with mean (6.88±0.82) with P-value 0.0001*****, there was a significant reduction of RV E'/A' in patients with mean (1.17±0.25) when compared with controls with mean (1.52±0.27) with p-value <0.001* and there was a significant increase in RV Myocardial Performance Index (*MPI)* in patients with mean (0.86±0.16) when compared with controls with mean (0.40±0.08) with P-value <0.001* (Table 3).

Right ventricle evaluation by Speckling tracking showed that there was a significant reduction of RVEF in patients with a mean (32.18±10.47) when compared with controls with a mean (46.23±4.22) with p-value <0.001*, and there was a significant reduction of RV global longitudinal systolic strain in patients with a mean (10.04±5.28) when compared with controls with a mean (-24.50±1.61) with p-value <0.001* (Table 3).

As regard correlation between longitudinal strain (LS) of the right ventricle and other echocardiographic parameters among the studied children with dilated cardiomyopathy, there is a significant positive correlation between RV LS and RV S and TAPSE (Table 4).

4. DISCUSSION

Echocardiography can adequately assess right ventricular structure and function and also suggest prognosis for patients with dilated cardiomyopathy especially using modern imaging techniques [5].

This work aimed to evaluate the right ventricular functions and structure using speckling tracking echocardiography in children with dilated cardiomyopathy and correlate this parameter with other echocardiographic findings.

The present work showed that the sex distribution was 27 (54%) males, so male to female ratio for cases of dilated cardiomyopathy was 3:2.5 which agreed with Towbin et al. and Cox et al. explained that boys have a higher DCM incidence than girls, related to X-linked genetic causes [6,7].
As regard to LV evaluation S' wave Mitral Annulus, systolic velocity was significantly lower in cases compared to control, which agreed with previous studies (Yu et al., McMahon et al., Zamorano & Lennie, and Mohammed & Friedberg) confirming usefulness for measuring the S' as a tool for assessment of systolic function and clarifying the effect of the left ventricular systolic impairment on LV diastolic function [8-11].

Table 1. Demographic data of the studied groups

Variables	The study group (with dilated cardiomyopathy) (n=50)	Control group (n=25)	P-value
Age (years) Mean±SD	4.90±2.25	5.56±2.31	0.239
Sex (male:female)	27:23	14:11	0.870
Weight (kg) Mean±SD	17.92±5.95	20.60±5.97	0.070

Table 2. Left ventricle parameters

Variables	The study group	Control group	P-value
LV SI Mean±SD	1.197 ±0.345	1.566±0.272	<0.001*
S' Mean±SD	3.667±1.061	6.933±0.785	<0.001*
E'/A' Mean±SD	1.147±0.401	1.540±0.246	<0.001*
MPI Mean±SD	1.876±0.233	0.407± 0.078	<0.001*
LVEF Mean±SD	43.360±11.760	65.234±7.589	<0.001*
LV GLSS Mean±SD	-12.667±4.943	-24.400±1.610	< 0.001*

SI: sphericity index, *S': Mitral Annulus systolic velocity, E'=Early diastolic mitral annulus tissue velocity and A'= Late diastolic mitral annulus tissue velocity, MPI: myocardial performance index, EF: ejection fraction, LV GLSS: left ventricular global longitudinal systolic strain*

Table 3. Right ventricle parameters

Variables	The study group	Control group	P-value
TAPSE Mean±SD	12.00±3.56	19.00±1.72	0.0001*
S' Mean±SD	4.42±0.82	6.88±0.82	0.0001*
E'/A' Mean±SD	1.17±0.25	1.52±0.27	0.0001*
MPI Mean±SD	0.86±0.16	0.40±0.08	0.0001*
RVEF Mean±SD	32.18±10.47	46.23±4.22	0.0001*
RV GLSS Mean±SD	10.04±5.28	-24.50±1.61	0.0001*

TAPSE: *Tricuspid annular plane systolic excursion*, *S': Tricuspid Annulus systolic velocity, E'=Early diastolic Tricuspid annulus tissue velocity and A'= Late diastolic Tricuspid annulus tissue velocity, MPI: myocardial performance index, EF: ejection fraction, RV GLSS: right ventricular global longitudinal systolic strain*

Table 4. Correlation between longitudinal strain (LS) of the right ventricle and other echocardiographic parameters among the studied children with dilated cardiomyopathy

Variables	LS (%) of the right ventricle among the studied children with dilated cardiomyopathy
	P
Age (years)	0.057
Weight (kg)	0.058
Tricuspid annulus systolic velocity (S') (cm/sec)	0.008*
RV E'/A' ratio	0.059
RV MPI	0.084
RV EF (%)	0.435
TAPSE (mm)	0.0001*

LS: Longitudinal strain, *S': Mitral Annulus systolic velocity, E'=Early diastolic mitral annulus tissue velocity and A'= Late diastolic mitral annulus tissue velocity, MPI: myocardial performance index, EF: ejection fraction,* TAPSE: *Tricuspid annular plane systolic excursion*

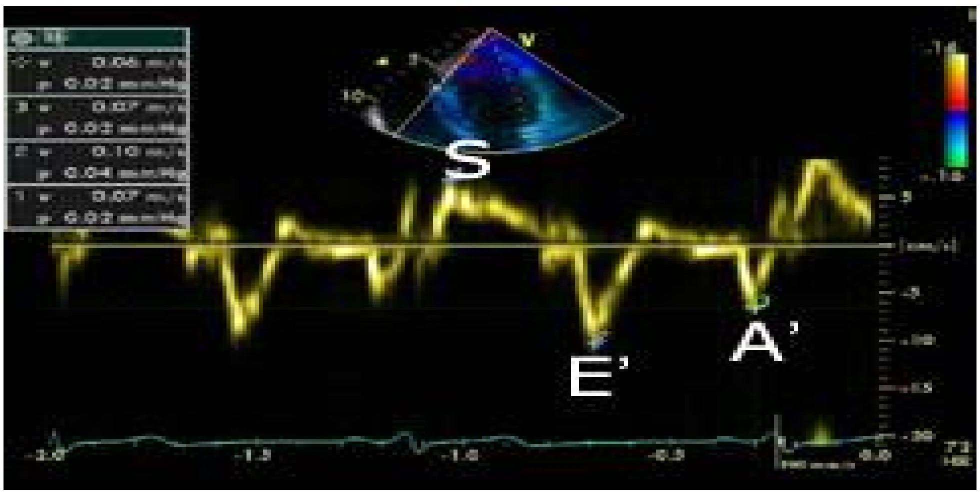

Fig. 1. Estimation of S, E', and A' with tissue doppler imaging

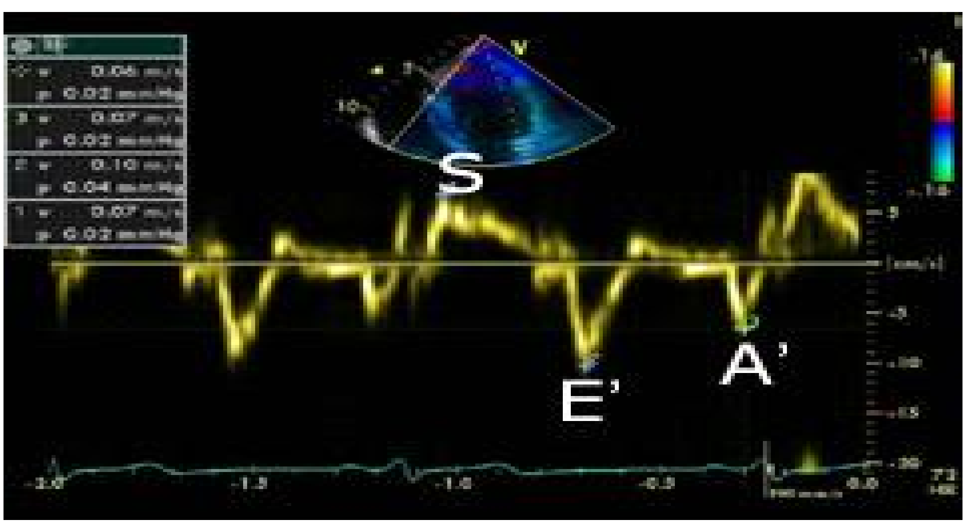

Fig. 2. Myocardial performance index measured by TDI

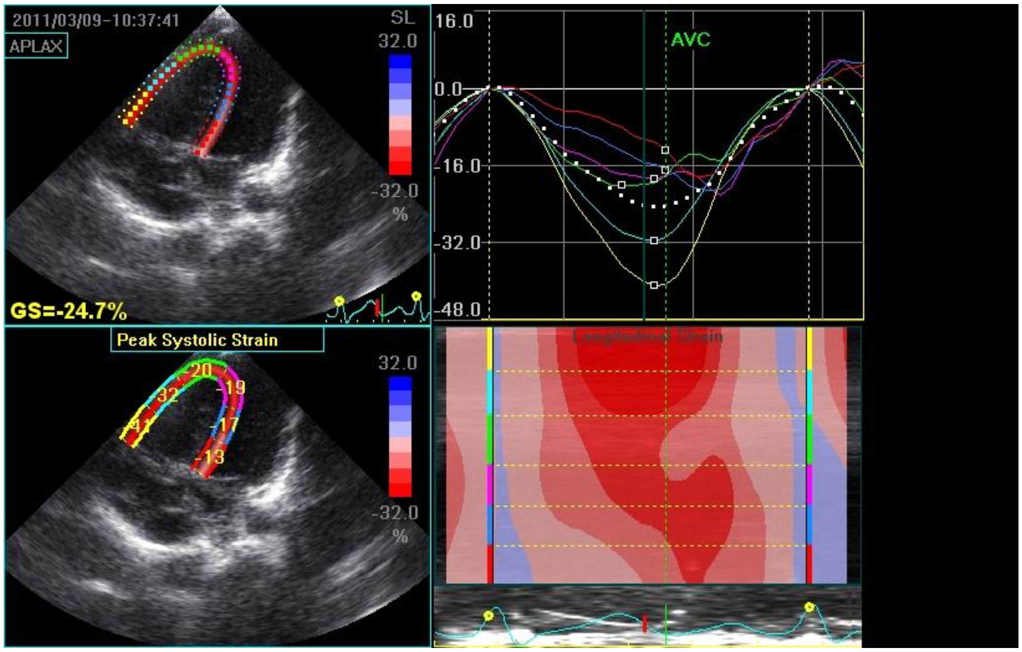

Fig. 3. RV LSS (%) measured by speckling tracking

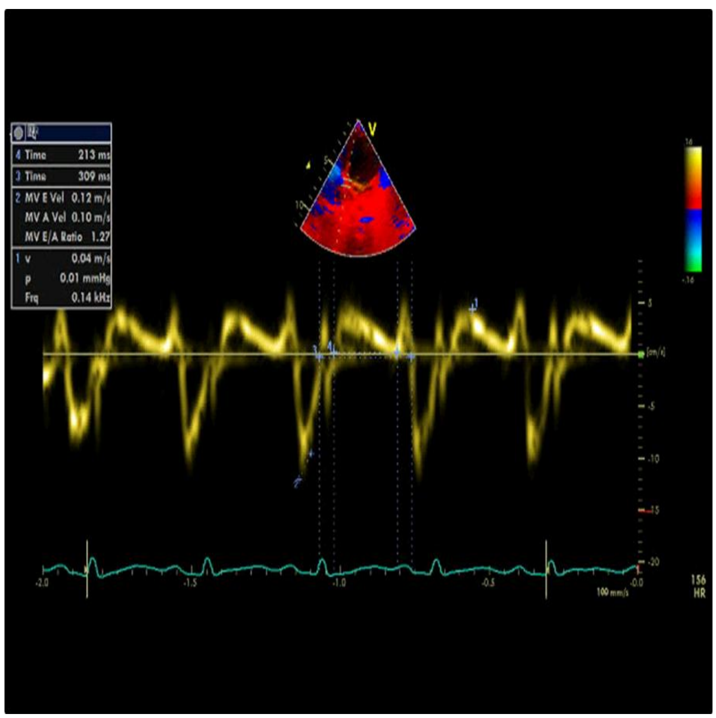

Fig. 4. Pulsed-wave tissue Doppler velocity measurement of a patient with IDC, from the left lateral atrioventricular plane from the apical four-chamber view. The ultrasound system records the velocities from the area between the two calipers (the two white solid lines in the upper left panel). The dotted line denotes the direction of the ultrasound beams assessing the velocities

S=4 cm/s E'/A'= 1.4 LV MPI=0.51

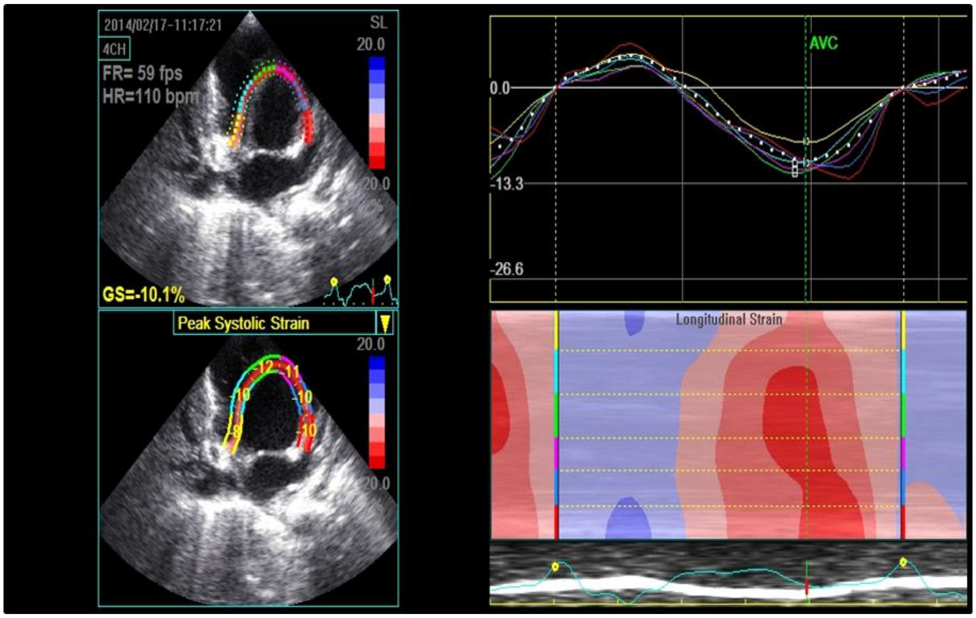

Fig. 5. Example of LV global longitudinal strain measures of a child with dilated cardiomyopathy from the 4 standard apical views. The upper left quadrant shows tracking. Right half shows color-coded segmental strain curves and average strain curve (dashed line).Lower left quadrant depicts anatomic M-mode. Dashed yellow line=Time to peak (from R-wave to maximum systolic strain. AVC=Aortic Valve Closure

LV GLSS=-10.1%

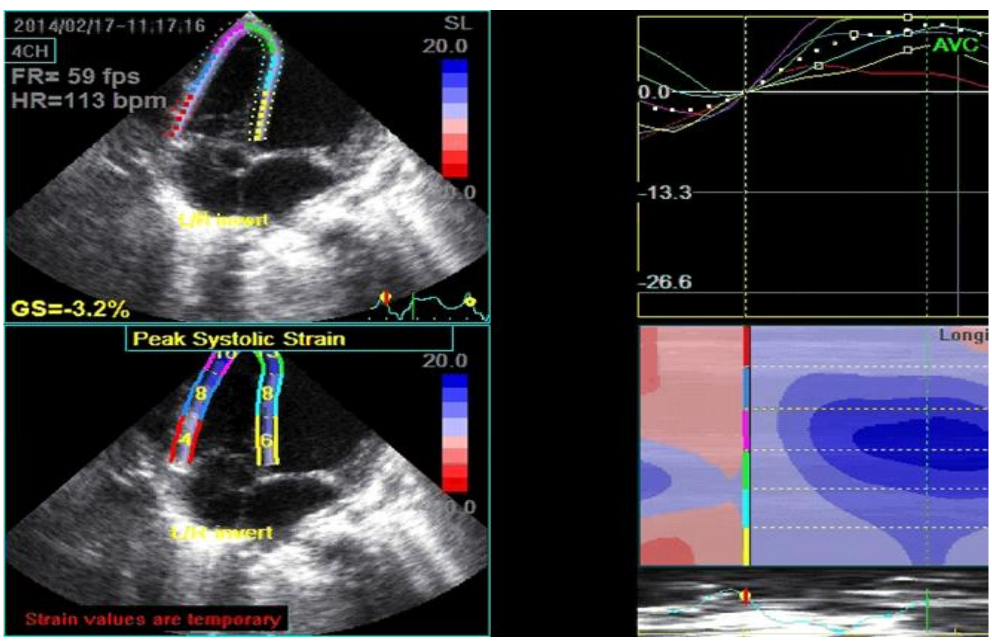

Fig. 6. Example of RV global longitudinal strain measures of a child with dilated cardiomyopathy from the 4 standard apical views. The upper left quadrant shows tracking. Right half shows color-coded segmental strain curves and average strain curve (dashed line).Lower left quadrant depicts anatomic M-mode. Dashed yellow line=Time to peak (from R-wave to maximum systolic strain. AVC=Aortic Valve Closure

RV GLSS=-3.2%

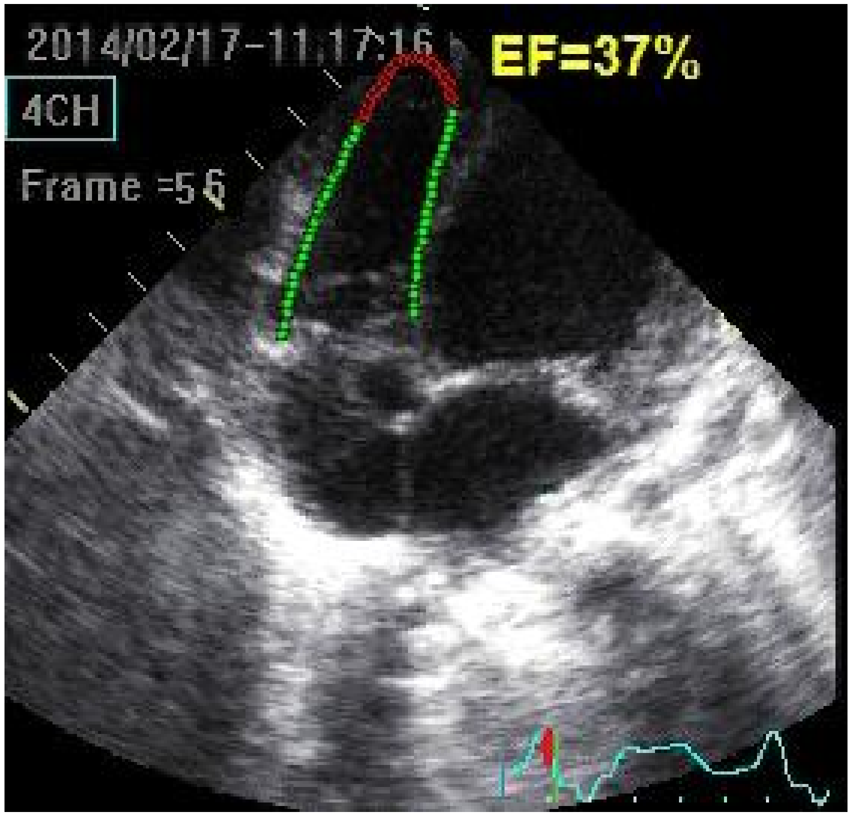

Fig. 7. RV EF measured by auto EF child with DCM
RV EF=37%

Also, Ciuca et al. reported that all pediatric patients hospitalized for heart failure due to DCM had coexistent left ventricular systolic dysfunction [12].

There was a significant reduction of the mean value of LV (E'/A' ratio) LV in cases compared to control. These data confirmed the diastolic dysfunction in dilated cardiomyopathy patients with impaired LV filling. Similar findings were reported by Friedberg et al. [13].

Like other previous studies McMahon et al. and Eto et al., in the current study, the tissue Doppler-derived MPI of LV in DCM cases was significantly prolonged compared to control. This could be explained due to LV systolic and diastolic dysfunction that reported in our patients, as the MPI reflects both the systolic and diastolic function of the ventricles [9,14].

Patients in this study showed a marked decrease of LV ejection fraction (EF) measured by auto LV EF compared to the control, similar findings were reported by Koestenberger et al., Bergenzaun, and Taşolar et al. [15], this may support that EF is an easy, sensitive tool for evaluation of LV systolic function [16,17,15]. In the current study speckling tracking echocardiography was used to measure the sphericity index of the left ventricle. There was a significant reduction in the sphericity index of patients when compared with controls. Similar findings were reported by van Dalen et al and this is due to Left ventricular (LV) remodeling which manifests as a change in chamber geometry to a more spherical shape and has been considered to be a consequence of heart failure [18].

Strain can be determined by either tissue Doppler, two-dimensional speckle tracking which determines LV Global Longitudinal systolic strain (LV GLSS). The tissue Doppler method is angle-dependent. Unlike Doppler derived strain, Two-dimensional speckle tracking (2DSTE) is angle independent, which measures the strain by tracking speckles, which are acoustic backscatter generated by ultrasound interactions with the myocardium [19].

In the current study left ventricular longitudinal systolic strain was significantly decreased in cases compared to control, this is in agreement with several publications reporting the decrease of the different types of systolic strain in cases of dilated cardiomyopathy [20,21].

The RV is usually missed during the echocardiographic assessment of DCM patients. This is due to its complex shape that does not fit with any geometrical assumption; subsequently, the majority of the studies were focusing on LV assessment. In the present study, we studied the right as well as the LV systolic and diastolic functions combining TDI and 2D-STE with the other echocardiographic parameters. RV dysfunction among patients was evident in the present study; the RV dysfunction among this study was explained by the relationship between both ventricles and secondary to the disease itself that may affect both ventricles but in different patterns [22].

The RV in the current study had significant systolic dysfunction compared to controls, as TAPSE and S′ were reduced, RV dysfunction may be due to the close link between LV and RV function. The RV has mainly transverse muscle fibers in its free wall in addition to sharing oblique fibers in the IVS with the LV, subsequently, its contraction augments RV contraction; a condition defined as systolic ventricular interaction. The impaired LV systolic and diastolic functions in DCM together with MR lead to pulmonary venous congestion and pulmonary hypertension increasing the RV afterload thus making RV contraction more dependent on the oblique septal fibers which are mechanically more efficient than the free wall transverse fibers. As the global LV deformation is markedly diminished (including the IVS containing these oblique fibers) this leads to decreased systolic ventricular interaction and reduction of RV deformation. Moreover, as the LV acquires a more spherical shape, the septal fibers become less oblique decreasing their mechanical efficiency with more and more deterioration of RV deformation.

The RV diastolic function in our study was also impaired compared to controls. These findings could be interpreted as the IVS is in common share, RV systolic dysfunction leads to an increase in RV diastolic pressure and LV dilatation might compress the RV cavity reducing the filling of RV and hence adding to the elevation of end-diastolic pressure and diastolic dysfunction.

The RV MPI measured by TDI was significantly prolonged in cases compared to controls, Krenning et al. reported similar findings [23]. Most of the RV parameters like TAPSE, S′, E′ A′ velocities are load-dependent varying with respiration and different loading conditions, unlike MPI which is load-independent. So, this index might be used on routine echocardiographic evaluation in such patients.

Patients in this study showed a decrease of RV ejection fraction (EF) measured by auto RV EF compared to the control, this may support that EF is an easy, sensitive tool for evaluation of RV systolic function. Also, the right ventricular longitudinal systolic strain was significantly decreased in cases compared to control, this is in agreement with several publications reporting the decrease of the longitudinal systolic strain in cases of dilated cardiomyopathy [1,24].

The present study reported a significant positive correlation between RV LS and RV S and between RV LS and TAPSE, while there was no significant correlation between RV LS and diastolic echo parameters (RV E'/A') and RV EF. It is logical because RV LS, RV S, and RV TABSE are denoting RV systolic function. RV EF although it represents a systolic function, it is a load-dependent parameter [25-28].

5. CONCLUSION

In DCM patients, RV had significant systolic and diastolic dysfunction mainly elicited by TDI beside LV affection secondary to the interventricular interaction. TDI and 2D-STE add value to interpreting the findings and the dependency of RV systolic and diastolic functions on each other in DCM patients in children.

CONSENT AND ETHICAL APPROVAL

Written Informed consent was obtained from the parents or guardians of studied infants. The study was approved by the Ethics Committee of the Faculty of Medicine, Tanta University.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by the personal efforts of the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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