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Using Doppler Tissue Imaging among Children with End-Stage Renal Disease for Assessment of Cardiac Complications

Ahmed Hassan Mahmoud Hassan*, Shaimaa Ibrahim Ahmed Mohamed, Abd Elhamid Abd Allah Abd Allah, Raafat Salama

Department of Pediatrics, Al Ahrar Teaching Hospital, Zagazig, Sharkia, Egypt

***Corresponding author:** Ahmed Hassan Mahmoud Hassan, **Mobile:** (+20) 01022128882, **E-Mail:** drahmhassan@gmail.com

ABSTRACT

Background: Children with chronic renal disease can experience heart difficulties as a result of their condition. **Objective:** To evaluation of cardiac complications using Doppler tissue imaging among Children with end-stage renal disease.

Subject and Methods: This study was conducted on 40 children with chronic renal failure (17 male and 23 female) their ages ranged from 8 years to 17 years attending the Nephrology Unit of the Pediatric Hospital Zagazig University. All children were subjected to thorough history taking, complete detailed clinical examination, and laboratory investigations. All cases and control were assessed by tissue Doppler velocity and strain imaging before and after dialysis**.**

Results: Tissue Doppler Imaging (TDI) assessment of systolic functions using lateral and septal mitral velocity (S) in cases is decreased significantly in predialysis cases more than control but did not show significant change after dialysis, also septal S of tricuspid is reduced significantly in cases predialysis than control but did not show significant change after dialysis. TDI assessment of septal mitral & tricuspid E′ &E′/A′ showed a significant reduction in predialysis cases more than control but did not show any change after dialysis, also lateral mitral &tricuspid E′&E′/A′ is decreased significantly in cases more than control but showed a significant decrease after dialysis.

Conclusion: children with chronic renal failure (CRF) have significant cardiac abnormalities, TDI is a superior diagnostic method than conventional echocardiography in the diagnosis of systolic dysfunction as in our cases that appeared normal by conventional echocardiography. Also, TDI is less load-dependent in septal mitral & tricuspid E′&E′/A′

Keywords: End Stage Renal Disease, Doppler tissue imaging.

INTRODUCTION

Renal dysfunction is classified into chronic renal failure (CRF) phases, with moderate impairment (glomerular filtration rate [GFR] 75 ml/min/1.73 m2) progressing to severe impairment (GFR 10 ml/min/1.73 m2). This is the stage during which medications and biologicals are used to treat the effects of renal dysfunction, end-stage renal disease (ESRD) is a condition in which a patient's renal failure is so severe that they require dialysis or a kidney transplant to maintain their homeostasis and eventually their lives [(1)]**.**

Multiple factors contribute to the complexity of CVD development in CRF. Important and potentially modifiable risk factors for the development of CVD in this patient population appear to be present early in the course of CKD [(2)]. Several factors contribute to the complexity of cardiovascular disease development in CRF. Furthermore, it appears that significant risk factors for developing CVD in this patient population emerge early in the course of CKD and are amenable to intervention [(2)]**.**

Ejection phase indices are the most used echocardiographic markers of left ventricular systolic performance. These indices are used to evaluate the efficiency with which the left ventricle pumps blood and are affected by the heart's preload, after load, and contractility. The left ventricle's ability to pump oxygenated blood to the body's tissues is essential. For this reason, the ventricle's pump efficiency may be measured in part by its stroke volume [(3)].

The purpose of this research was the evaluation of cardiac complications using Doppler tissue imaging among Children with end-stage renal disease.

PATIENTS AND METHODS

Data were gathered pre- and post-dialysis from 40 children (8-17 years old) with chronic renal failure visiting the Nephrology Unit of the Pediatric Hospital at Zagazig University. The ratio of males to females was approximately equal.

Inclusion Criteria: Diagnosed children with chronic renal failure and ongoing dialysis.

Exclusion Criteria: Refusal of the parents, and age more than 18.

Methodology:

All participants in the research underwent a thorough clinical evaluation (history and physical) before inclusion.

Full History: Name, age, sex, date of admission, the chronology of symptoms, and social and family history. **Clinical examination:** General: Wt, Ht, BMI. Neurological: level of consciousness, headache. Respiratory: tachypnea, rapid shallow breathing, and cardiovascular.

Tissue doppler imaging: The four-chamber view was used for tissue Doppler imaging, and the mitral annular

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planes were oriented so that they were perpendicular to the ultrasound beam. To do this, samples were taken from the lateral mitral annular and septal mitral annular surfaces, as well as the lateral tricuspid annular surface, using a pulsed TD sample volume of 5 mm. The average velocities of the six LV walls were used to determine the global systolic and diastolic functions. It was possible to calculate the early diastolic to the aortic ratio (Ea/Aa) and the in-valve regurgitation time (IVRT) of the aortic valve. Heart rates during systole, early diastole, and late diastole were also assessed. The filling pressure of the LV was determined using the E/E' velocity ratio.

Ethical consent:

The study was authorized by Zagazig University's Ethical Institutional Review Board. All study participants provided written informed permission after being informed of our research's goals. The Declaration of Helsinki for human beings, which is the international medical association's code of ethics, was followed during the conduct of this study.

Statistical Analysis

The research was conducted on a computer with the help of SPSS 20 (Statistical Package for Social Services) (SPSS). Tables and graphs illustrated the results. Our presentation of the quantitative data includes measures of central tendency (mean, median, and standard deviation) and confidence intervals (CIs). Stats like frequency and percentage were used to make points. To examine data with numeric independent variables, the Student's t-test (T) is typically applied. Analyses of qualitatively different data sets were performed using Chi-Square with Linear Trend and Pearson Chi-Square (X^2). At the 5% probability level of significance.

RESULTS

Forty patients aged between 8 and 17 years and twenty control were included in the study, their data were collected pre & post-dialysis, and the proportion of boys to girls was nearly equal **(Table 1).**

Table (1): Demographics data.

Gender	**Frequency**	**Percentage**
Male	**17**	**42.5**
Female	**23**	**57.5**
Total	**40**	**100**
	Range	**Mean±SD**
Age(Yrs)	17- 8	12.3± 2.3
Dry weight(Kg)	20- 41	30.64± 5.5
Height(Cm)	157-110	130.7± 13.8

Table (2) shows a significant reduction in the weight of cases after dialysis (p<0.001).

Table (2): Weight change in cases with ESRD before and after dialysis:

	Predialysis n=40		**Post dialysis n=40**		**t-value**	**p-value**
	Mean	**SD**	**Mean**	**SD**		
Weight (Kg)	31.82	5.5	30.64	5.5	8.2	<0.001

Tables (3 a, b, c) show that lateral mitral E′&E′/A′ is less in cases pre & post-dialysis than those of control (P<0.001), and also shows a significant decrease after dialysis(P <0.001). The lateral mitral A′ value shows a non-significant difference between cases & control and also a non-significant change after dialysis (P >0.005). Lateral mitral S is less diseased than the control(P<0.001) and shows non-significant change after dialysis(P>0.05).

Table (3): Comparison of lateral mitral annular Tissue Doppler velocity among control, cases before and after dialysis

Table(3a) :

		Control n=20	**Predialysis N=40**	**t-value**	**P-value**
		Mean±SD	**Mean±SD**		
Lateral Mitral (cm/sec.)	**S**	**7.0±0.7**	**6.1±0.8**	**4.1**	**< 0.001**
	E′	**19.95±2**	**12.4±1.5**	**15.8**	**< 0.001**
	A′	**10.85±0.07**	**10.2±1.4**	**1.87**	**0.11**
	E′/A′	**1.85±0.2**	**1.24±0.21**	**4.3**	**< 0.001**

Table(3b) :

		Control n=20	**Post dialysis n=40**	**t-value**	**P-value**
		Mean±SD	**Mean±SD**		
Lateral Mitral (cm/sec.)	**S**	**7.0±0.7**	**6.6±1.2**	**1.2**	**0.2**
	E′	**19.95±2**	**10.1±1.5**	**20.9**	**< 0.001**
	A′	**10.85±0.07**	**10.8±1.87**	**0.11**	**0.9**
	E′/A′	**1.85±0.2**	**0.96±0.2**	**11.2**	**< 0.001**

Table(3c) :

		Predialysis n=40	**Post dialysis n=40**	**t-value**	**P-value**
		Mean±SD	**Mean±SD**		
Lateral Mitral (cm/sec.)	**S**	**6.1±0.8**	**6.6±1.2**	**1.67**	**0.1**
	E′	**12.4±1.5**	**10.1±1.5**	**6.7**	**< 0.001**
	A′	**10.2±1.4**	**10.8±1.87**	**1.6**	**0.14**
	E′/A′	**1.24±0.21**	**0.96±0.2**	**5.9**	**< 0.001**

Tables (4 a, b, c) show that the medial mitral E′& E′/A′ decreased significantly in cases than control(P<0.05&<0.001)respectively & E′/A′ decreased non-significantly after dialysis(P>0.05). Medial mitral S shows a significant decrease in cases than control both pre&postdialysis (P <0.001) and shows a non-significant decrease after dialysis (P>0.05).

Table (4): Comparison of medial mitral annular Tissue Doppler velocity among control, cases before and after dialysis

Table(4a):

		Control n=20	Pre-dialysis n=40	t-value	P-value
		Mean±SD	Mean±SD		
Medial (cm/sec.)	S	19.6±2.2	12.3±1.9	12.9	< 0.001
	E′	12±0.6	10.6±1.5	1.42	0.01
	A′	6.85±0.9	5.8±1.0	6.4	0.01
	E′/A′	1.62±0.17	1.08±0.24	3.6	< 0.001

Table(4b):

		Control n=20	Post dialysis n=40	t-value	P-value
		Mean±SD	Mean±SD		
Medial Mitral (cm/sec.)	S	19.6±2.2	12.0±1.7	14.0	< 0.001
	E′	12±0.6	10.8±1.7	0.071	0.01
	A′	6.85±0.9	6.4±1.49	1.2	0.08
	E′/A′	1.62±0.17	1.04±0.21	2.9	< 0.001

Table(4c):

		Pre-dialysis n=40	Post dialysis n=40	t-value	P-value
		Mean±SD	Mean±SD		
Medial mitral (cm/sec.)	S	12.3±1.9	12.0±1.7	0.6	0.56
	E′	11.6±1.5	11.8±1.7	0.63	0.71
	A′	5.8±1.0	6.4±1.49	1.8	0.15
	E′/A′	1.08±0.24	1.04±0.21	7.3	0.4

Lateral tricuspid E′& E′/A′ values are less in cases than in control both pre & post-dialysis (P<0.001) **(Tab.5a&b).** Also lateral tricuspid E′/A′ shows a significant decrease after dialysis(P<0.05)(**Tab.5c**). Lateral Tricuspid A′ value shows a significantly decreased after dialysis (P= <0.001). Lateral tricuspid S shows a non-significant difference between cases and controls and also after dialysis(P>0.05).

Table (5): Comparison of lateral tricuspid annular Tissue Doppler velocity among control, cases before and after dialysis

Table (5a):

		Control n=20	Predialysis n=40	t-value	P-valu
		Mean±SD	Mean±SD		
Lateral Tricuspid (cm/sec.)	S	6.8±0.6	6.55±1.4	0.72	0.47
	E′	14.95±1.1	12.2±1.8	6.4	< 0.00
	A′	12.2±0.9	11.7±1.1	1.7	0.08
	E′/A′	1.23±0.09	1.05±0.21	16.0	< 0.00

Table (5b):

		Control n=20	Post dialysis N=40	t-value	P-value
		Mean±SD	Mean±SD		
Lateral tricuspid (cm/sec.)	S	6.8±0.6	6.55±1.4	0.84	0.44
	E′	14.95±1.1	11.1±1.69	6.9	< 0.001
	A′	12.2±0.9	10.2±1.4	5.7	< 0.001
	E′/A′	1.23±0.09	1.01±0.28	15.1	<0.001

Table (5c):

		Predialysis n=40	Post dialysis n=40	t-value	P-value
		Mean±SD	Mean±SD		
Lateral tricuspid (cm/sec.)	S	6.55±1.4	6.55±1.4	0.003	0.84
	E′	12.2±1.8	11.1±1.69	0.23	0.01
	A′	11.7±1.1	10.2±1.4	5.3	< 0.001
	E′/A′	1.05±0.21	1.01±0.28	0.46	0.011

Tables (6 a, b, c) show a highly significant decrease of longitudinal strain in all segments in diseased more than control (P< 0.001)either in pre or post dialysis cases. Also, the table shows a highly significant increase (P <0.001) of Septal Longitudinal strain in all segments after dialysis.

Table (6): Septal longitudinal strain imaging measurements of control, cases before & after dialysis

Table(6a):

		Control n=20	Predialysis n=40	t-value	P-value
		Mean±SD	Mean±SD		
Septum (%)	Base	27.3±2.4	16.1±1.5	22.6	< 0.001
	Mid	28.2±3.0	17.2±1.4	19.8	< 0.001
	Apex	31.4±2.8	19.3±1.7	20.8	< 0.001

Table (6b):

		Control n=20	Post dialysis n=40	t-value	P-value
		Mean±SD	Mean±SD		
Septum (%)	Base	27.3±2.4	17.6±1.5	19.5	< 0.001
	Mid	28.2±3.0	19.1±1.5	16.2	< 0.001
	Apex	31.4±2.8	21.2±1.7	17.3	< 0.001

Table (6c):

		Predialysis n=40	Post dialysis n=40	t-value	P-value
		Mean±SD	Mean±SD		
Septum (%)	Base	16.1±1.5	17.6±1.5	4.46	< 0.001
	Mid	17.2±1.4	19.1±1.5	5.52	< 0.001
	Apex	19.3±1.7	21.2±1.7	5.06	< 0.001

Tables (7 a, b, c) show a highly significant decrease of longitudinal strain in diseased more than control (P< 0.001) either in pre or post dialysis cases. Also, the table shows a highly significant increase (P <0.001) of Posterior wall Longitudinal strain in all segments after dialysis.

Table (7): Left ventricular (posterior wall) Longitudinal strain imaging measurements of control, cases before & after dialysis

Table (7a):

		Control n=20	Predialysis n=40	t-value	P-value
		Mean±SD	Mean±SD		
Post.Wall (%)	Basal	28.3±3.7	17.0±1.7	16.06	< 0.001
	Lateral	27.5±3.3	19±1.6	13.3	< 0.001

Table (7b):

		Control n=20	Post dialysis n=40	t-value	-value
		Mean±SD	Mean±SD		
Post. Wall (%)	Basal	28.3±3.7	18.6±1.7	14.0	0.001
	Lateral	27.5±3.3	20.4±1.7	11.02	0.001

Table (7c):

		Predialysis n=40	Post dialysis n=40	t-value	P-value
		Mean±SD	Mean±SD		
Post.Wall (%)	Basal	17.0±1.7	18.6±1.7	3.89	< 0.001
	Lateral	19±1.6	20.4±1.7	3.07	< 0.001

Tables (8 a, b, c) show a highly significant decrease of longitudinal strain in diseased more than control (P< 0.001) either in pre or post dialysis cases. The Anterior wall (Basal and Lateral) Longitudinal strain shows a significant increase (P <0.05, P=0.01) respectively after dialysis.

Table (8): Right ventricular (Anterior wall) Longitudinal strain imaging measurements of control, cases before & after dialysis

Table (8a):

		Control n=20	Predialysis n=40	t-value	P-value
		Mean±SD	Mean±SD		
Ant.Wall (%)	Basal	29.2±2.8	20.5±1.5	15.6	< 0.001
	Lateral	30.1±2.8	21.9±1.4	15.05	< 0.001

Table (8b):

		Control n=20	Post dialysis n=40	t-value	P-value
		Mean±SD	Mean±SD		
Ant. Wall (%)	Basal	29.2±2.8	21.7±1.3	14.04	0.001
	Lateral	30.1±2.8	22.7±1.1	14.4	0.001

Table (8c):

		Predialysis n=40	Post dialysis n=40	t-value	P-value
		Mean±SD	Mean±SD		
Ant. Wall (%)	Basal	20.5±1.5	21.7±1.3	2.07	< 0.05
	Lateral	21.9±1.4	22.7±1.1	2.81	0.01

Tables (9 a, b, c) show a significant decrease of longitudinal SR in diseased than control (P<0.001). The basal Septal Longitudinal SR. shows a high significance increase (P <0.001) after dialysis and a significant increase of (Mid, Apex) of Septal Longitudinal SR. (P <0.05).

Table (9): Septal Longitudinal Strain Rate measurements in control, cases before & after diaysis:

Table (9a):

		Control n=20	Predialysis n=40	t-value	P-value
Septum (s^{-1})		Mean± SD	Mean±SD		
	Basal	-1.35± 0.1	-0.88± 0.15	12.4	< 0.001
	Mid	-1.4± 0.08	-1.0± 0.13	12.6	< 0.001
	Apex	-1.46± 0.06	-1.05± 0.1	9.7	< 0.001

Table(9b):

		Control n=20	Post dialysis n=40	t-value	P-value
Septum (s^{-1})		Mean±SD	Mean±SD		
	Basal	-1.35±0.1	-0.96±0.1	11.7	< 0.001
	Mid	-1.4±0.08	-1.1±0.1	13.1	< 0.001
	Apex	-1.46±0.06	-1.1±0.08	14.7	< 0.01

Table(9c):

		Predialysis n=40	Post dialysis n=40	t-value	P-value
Septum (s^{-1})		Mean±SD	Mean±SD		
	Basal	-0.88±0.15	-0.96±0.1	2.76	< 0.001
	Mid	-1.0±0.13	-1.1±0.1	2.75	< 0.007
	Apex	-1.05±0.1	-1.1±0.08	2.8	0.006

DISCUSSION

Most noninvasive evaluations of systolic and diastolic ventricular function are significantly affected by loading conditions. Conventional echocardiographic measures of systolic function, such as shortening fraction and ejection fraction, and Doppler measurements of left ventricular diastolic functions are significantly affected by changes in LV preload [(4)].

Doppler tissue imaging (DTI) is an exciting new non-invasive echocardiographic method for quantifying

systolic and diastolic velocities in the ventricle. Some adult investigations have indicated that DTI velocities are unaffected by loading circumstances. There is still some mystery about how lowering preload affects LV and RV function as measured by tissue Doppler measurements [5].

In the current study, ventricular performance was evaluated using the novel Doppler-derived Tei index. For the assessment of global left ventricular function, we were motivated by the fact that measurements of ventricular function derived from the M mode echocardiography as the ejection fraction and fractional shortening reflect regional rather than global ventricular performance. Because it allows visualization of a larger area of the heart at one time than does M-mode echocardiography, two-dimensional echocardiography provides a better estimate of global ventricular function even in the presence of regional wall motion abnormalities. However, most of the two-dimensional echocardiographic measurements of ventricular performance are based on assumptions concerning ventricular geometry that may not be accurate. On the other hand, Doppler echocardiography evaluates intracardiac blood flow and thus, provides an estimate of global ventricular performance that is independent of assumptions about ventricular geometry **[6].**

In our study, both LV and RV Tei index values are significantly higher in diseased cases with ESRD than in the controls (P< 0.001).

And regarding the effect of dialysis, there was no significant difference observed in the Tei index values of either the left or the right ventricles after dialysis (P >0.05). In our study, the net fluid loss or (preload reduction) as detected by weight loss of our cases was < 1 Kg post dialysis.

Following our results, **Ouali *et al.*** [7] reported that The LV Tei Index did not significantly shift after HD. **Koga and colleagues** [8] indicated that substantial changes in the Tei index were only seen before and after HD in the group who dropped more than 1.5 kg of weight.

While both the PDE- and TDE-Tei indices are preload-dependent indicators, the impact of HD on tissue Doppler TDE-Tei index is different when a considerable volume of fluid is removed by HD. In patients who lose more than 3 kg of body weight due to HD, however, the TDI-Tei index is a more accurate measure of global left ventricular function because it is less dependent on preload **[9].**

Conventional echocardiographic studies of the immediate effects of HD on heart function have yielded contradictory results. This may be because traditional Doppler echocardiography has limitations in assessing systolic and diastolic function in HD patients for many reasons. The most significant drawback of using standard indices from conventional Doppler echocardiography to evaluate LV systolic and diastolic function, including cardiac output, fractional shortening (FS) percent, ejection fraction (EF), and the Doppler filling parameter, is the impact of different loading conditions on the measurements obtained. Tissue Doppler echocardiography records and shows the velocities of moving objects, and tissue Doppler imaging (TDI) is a unique use of ultrasound for visualizing tissue motion. Erythrocytes are the focus of Doppler echocardiography for determining blood flow velocity [10].

Concerning TDI systolic functions are demonstrated by the peak systolic velocity of the mitral annulus (S), we found in our study a significant reduction of S of lateral and septal mitral annuli in cases pre-dialysis as compared to control (P<0.001), thus reflecting the presence of LV systolic dysfunction despite normal EF and FS.

In agreement, **Pirat *et al.*** [11], demonstrated that tissue systolic measures, like as peak systolic velocity (S wave) when comparing ESRD patients and healthy controls using Doppler echocardiography of the septal mitral annulus, the ESRD group revealed lower values. According to these findings, ESRD patients may have reduced systolic myocardial performance.

On the other hand, in our study, we reported hemodialysis to improve slightly Peak systolic velocity of mitral annuli, yet the difference was not statistically significant (<0.05), implying that TDI-derived systolic velocity is not preload dependent.

In concordance with our results **Lee *et al.*** [12]**,** showed that despite a significant decrease in intravascular effective volume after HD, there was no change in myocardial peak systolic velocity, demonstrating that Mitral annular velocity "S" is preload independent.

Drighil *et al.* [5], found that in HD patients, The LV and RV TDI velocities during systole and diastole are both sensitive to the stress on the heart. Preload resistance is higher in the lateral mitral annulus, though.

Early diastolic mitral inflow velocity (E) to early diastolic mitral annular velocity (E'), calculated with either septal E' or the average of septal and lateral E', has been described by several authors as the greatest non-invasive predictor of increased LV filling pressure and a hemodynamic catheter's ultimate diastolic pressure **[12].**

Similarly, **Kim and Sohn** [13] showed a correlation between E/E' and LV diastolic pressure, while **Ommen *et al.*** [14] found E/E' to be most predictive of LV filling pressures in those with LV dysfunction, where LV dysfunction was defined as an ejection fraction of 50% or less.

In the same context**, Eidem *et al.*** [4], the E/E ratios at the lateral and septal mitral annuli did not change significantly with increasing LV preload, demonstrating preload independence in their study of children with VSD.

Despite the above evidence suggesting that E/E' is independent of preload and is instead directly related to LV filling pressures, we found that the lateral and medial (septal) mitral E/E′ values were significantly higher in diseased (either before or after dialysis) as compared to

control subjects (P 0.001). As a result, the preload dependence of this ratio was reflected in the considerable decreases in both lateral and medial mitral E/E′ after dialysis (P= 0.001 and P= 0.01 respectively).

In agreement, with **Fijalkowski** [15] and **Su *et al.*** [9], standard echocardiographic parameters and mitral annulus tissue Doppler were assessed in ESRD patients before and after HD. In contrast to mitral inflow parameters (E) and mitral E/E′, which were shown to be considerably impacted by load changes, TDI estimates of mitral annulus velocities (E′) were found to be less load-dependent indicators of diastolic function.

In accordance with our results, **Jacques *et al.*** [16], showed that E/E' is inversely proportional to LVEDP (rather than directly proportional).

The finding that E/E' has an inverse relationship to LV filling pressure in constrictive pericardial illness further substantiates the idea that E/E' is not necessarily predictive of LV filling pressure [17].

Also a significant increase of both septal & lateral Tricuspid E/E′ of diseased than control (P <0.001) re Longitudinal basal, mid, and apical septal segments strain values were significantly lower in patients with ESRD compared to control (16.1±1.5, 17.2±1.4, 19.3±1.7 vs 27.3±2.4, 28.2±3.0, 31.4±2.8 respectively P= <0.001), while these values increase after HD significantly (16.1±1.5, 17.2±1.4, 19.3±1.7 vs 17.6±1.5, 19.1±1.5, 21.2±1.7 respectively, p= <0.001) but not reach a normal value of control group.

Strain rate imaging has previously demonstrated that persons with end-stage renal disease (ESRD) have lower longitudinal heart tissue velocities and myocardial deformation [18].

Moreover, the longitudinal strain showed a significant increase in values of the septal wall from base to apex (27.3±2.4, 28.2±3.0, 31.4±2.8) respectively, this is in concordance with a previous study that showed a significant increase of strain after dialysis and also increases strain values of the septal wall from base to apex [19].

CONCLUSION

The high rates of cardiovascular death in children with CRF are likely attributable to the common occurrence of serious cardiac abnormalities in these kids., TDI is a superior diagnostic method than conventional echocardiography in the diagnosis of systolic dysfunction as in our cases that appeared normal by conventional echocardiography. Also, TDI is less load-dependent in septal mitral & tricuspid E′&E′/A ′ Also strain and SR are load dependent so hydration status should be taken into consideration.

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