International Journal of Science and Research (IJSR)
ISSN: 2319-7064
ResearchGate Impact Factor (2018): 0.28 | SJIF (2019): 7.583

Echocardiographic Evaluation of Diastolic Function via Tissue Doppler Index, TDI, in Children with Heart Failure

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Abstract: ***Background and Aims: The diastolic function was previously less understood and rarely evaluated in children. But, in order to fully assess the function of the left ventricle, the diastolicfunction must be evaluated, as the increased filling pressures of the left ventricle is the final common pathway in all cases of heart failure. TDI has been proved to be an independent and accurate index in the evaluation of the left ventricle diastolic function in all studies that have been done in pediatrics. In this study, we are trying to understand the changes in diastolic function (via TDI) starting from the early stages of heart failure regardless of the EF value. Methods: This prospective study has two major groups, the first group included 206 normal children who have a complete normal clinical and echocardiographical study of the heart. The second group (205 children) contains two subgroups: Those with the first stage of HF according to ROSS classification, and the other subgroup with the II or III stage of HF. After dividing each group (the normal and the pathological groups) into five age-groups : 1 month-1 year , 1-3 years , 3-6 years , 6-9 years , 9-13 years , we measured the transmitral flow velocities E/A , and the TDI parameters at the level of the mitral annules. And then we compared the results in each age group between the normal children and the patients. Results: The E / A ratio did not show any statistical value since P value was always greater than 0.05 in all stages of heart failure and in all age groups. Whereas, TDI have shown a great value as a predictor index in heart failure in children. In the first HF stage , septal E/e' ratio , lateral E/e' ratio, and the average E/e' ratio,have shown a significant statistical value as the P value was less than 0.05 in all age groups except in the age group (3-6 years ,with no obvious reason). On the other hand , all measurements of TDI including (septal e' , lateral e' , septal E/e' , lateral E/e', average E/e') have shown significant changes in all age groups in the stages II and III of HF in pediatric patients , despite the EF was normal in all patient except in 5 of them with the III stage of HF. Conclusion: TDI is an independent and accurate index of the filling LV pressures. In this study we proved that TDI shows significant changes from the first stages of heart failure in pediatric patient, regardless of the value of EF.***

Keywords: Heart Failure, Tissue Doppler Index, Diastolic Function, Echocardiography, ROSS Classification

1. Introduction

Heart failure in children is a clinical and pathophysiological syndrome that results from ventricular dysfunction, volume or pressure overload, either alone or in combination [1] .The International Society for Heart and Lung Transplantation (ISHLT) stratified pediatric HF into four stages (Stages A–D) as in Table 1 [1], which is useful to identify those at risk for HF and who are currently asymptomatic (Stage A) versus those on the other end of the spectrum (Stage D),who have advanced HF and, thus, would require therapeutic interventions for maintenance of end-organ function[2].The reported incidence of HF in children is 0.97 to 7.4 per 100,000[3]. Congenital heart disease confirms 25-75% of all cases of heart failure in pediatrics [4].

Stage (Class)	Description
A	Patients with increased risk of developing HF but with normal cardiac function andchamber size. Examples: univentricular heart, previous exposure to anthracycline, Duchenne muscular dystrophy, congenitally corrected transposition of the greatarteries, h/o familial dilated cardiomyopathy.
B	Patients with abnormal cardiac morphology or function with no past or currentsymptoms of HF. Examples: asymptomatic dilated LV, isolated LV noncompaction.
C	Patients with past or current HF symptoms and structural or functional heart disease.
D	Patients with end-stage HF requiring continuous infusion of inotropic agents, mechanical circulatory support, cardiac transplantation, or hospice care.

Table 1.Heart failure staging in children.

The well-known New York Heart Association (NYHA) HF classification does not apply to youngchildren on a practical level and is thought to lack the sensitivity needed to assess and capture theprogression of HF severity in children. For this reason, the modified Ross HF classification[5] is usedfor the assessment of children younger than six years with HF. A comparison of two classifications is shown in Table 2.

The term diastolic dysfunction is used to describe abnormal mechanical(diastolic) properties of the ventricle and includes decreased LV distensibility, delayed relaxation, and abnormal filling, regardless ofwhether the EF is normal or reduced and whether the patient issymptomatic or asymptomatic. In contrast, the term diastolic HF isused to describe patients with the symptoms and signs of HF anda normal EF and diastolic dysfunction[6].

Table 2: NYHA and modified Ross classification of heart failure in children

Modified Ross Classification of HF in Children < 6 year	NYHA Classification of HF in Children > 6 year
Class I: Asymptomatic	Class I: Asymptomatic.
Class II: Mild tachypnea or diaphoresis with feeding in infants; dyspnea on exertion in older children.	Class II: Slight or moderate limitations of physical activity.
Class III: Marked tachypnea or diaphoresis with feeding ininfants. Prolonged feeding times with growth failure; Marked dyspnea on exertion in older children.	Class III: Marked limitation of physical activity.

Class IV: Symptoms such as tachypnea, retractions, grunting, or diaphoresis at rest.	Class IV: Symptoms at rest.

Diastolic heart failure should always be considered when LVEF is normal on two-dimensional echocardiography in patients with clinical evidence of heart failure. The diagnosis can be confirmed if Doppler echocardiography and myocardial tissue imaging provide evidence for impaired myocardial relaxation. Early identification of diastolic dysfunction in asymptomatic patients by the use of echocardiography may provide an opportunity to manage the underlying etiology to prevent progression to diastolic heart failure[7]

2. Diastolic Performance

For the left ventricle to function effectively as a pump, it must beable not only to eject but also to fill, which is its diastolic function.Diastolic function conventionally has been assessed on the basisof the LV end diastolic pressure-volume (P-V) relation[8] .A shift of the curve upward and to the left has beenconsidered to be the hallmark of diastolic dysfunction.
Two-dimensional and Doppler echocardiography is an easy and non-invasive way to assess the diastolic function[9].

Mitral valve inflow[10]
Peak E-Wave Velocity (cm/sec): Early diastole (after T-wave on EKG)
Peak A-Wave Velocity (cm/sec): Late diastole (after P-wave on EKG)
All flow velocities across the mitral valve are affected by preload and post-convection, as well as heart rate and age. Usually E is greater than A. Diastolic Dysfunctin has four main grades:
Grade 1: Impaired relaxation, decreased suction of the LV, E <A.
Grade 2: Psuedonormalization , increased stiffness of LV, and elevated left atrial pressure (LAP) , E>A.
Grade 3: (reversible): Restrictive filling, high LAP, noncompliant LV. E>>A.May be reversible with reduction of preload.
Grade 4: (irreversible): Same as grade 3, but can not be reversible with reduction of preload.

The following figure (figure 1) shows the stages of diastolic dysfunction according to transmitral velocities.

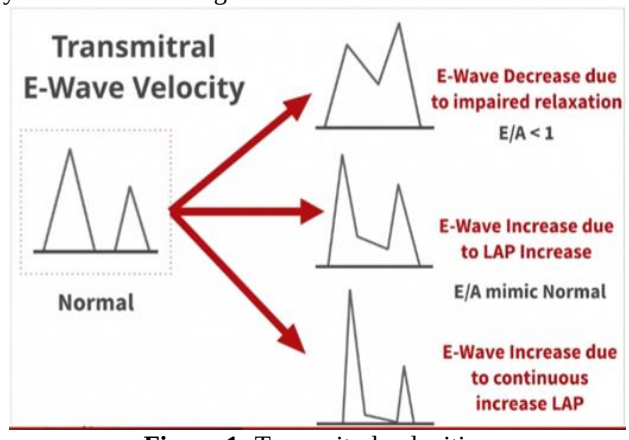

Figure 1: Transmitral velocities

Tissue Doppler Index TDI
Diastolicventricular function is determined by the evaluationof the longitudinal movement at the level of themitral, tricuspid and septal annulus, with thecalculation of early and late diastolic velocities(2 negative waves: Ea or E'; Aa or A' respectively)[11]. Tissue Doppler imaging (TDI) for echocardiographic evaluation of myocardial function was first described in 1989[12].

The difficulties come when attempting to measure the relaxation of the myocardium while negating any effect of pre- or afterload[13].Eidem BW et al,studied the impact of LV preload and after load on TDI in congenital heart defects , they found that LV preload do not significantly affect the majority of TDI velocities in children with ventricular septal defects. In addition, significantly increased chronic LV afterload in children with aortic valve stenosis is associated with decreased TDI velocities in the absence of other identifiable abnormalities of LV function[14]

In a study performed by Butnario A et al , to measure the systolic and diastolic function in congestive heart failure in pediatric patients, they found that while some conventional parameters of the diastolicfunction were maintained within normal or pseudonormal values in patients with heart failure,the diastolic dysfunction being confirmed in thesecases by TDI measurements and their correlation[15] .Nagueh et al, were the first to show that E/e′ ratio (ratio of transmitral E velocity and TDI mitral annular e′ velocity) corresponded to PCWP . In 125 patients classified by systolic and diastolic function and symptoms, PCWP correlated strongly with E/e′ ratio r = 0.87[16].

3. Aim of our study

There is an increased interest in studying the value of TDI in children, especially as an independent and accurate index in determining the function of the heart. Despite the studies on it are still few, most of these studies in pediatrics have proved its important and significant value. On the other hand, the diastolic function is still not well understood in pediatrics and there are no guidelines for it till now.

In this study we are trying to understand the changes in the diastolic function via TDi from the first stages of heart failure regardless of the value of EF.

4. Results

Our study is a prospective cohort study conducted at Damascus University Children Hospital between 2018 and 2019 .The baseline characteristics of the study groups are presented in table 3.

Table 3: (M: males, F: female)

	Normal		ROSS I		ROSS II – III	
	M	F	M	F	M	F
1month-1 year	21	17	6	3	16	21
1year -3 years	20	17	9	7	7	7
3-6 years	22	22	22	10	5	6
6-9 years	25	20	18	6	6	10
9-13 years	28	14	15	9	12	10
Sum	116	90	70	35	46	54

Table 4 shows the mean value (with the standard deviation) for every measurement in each age group in normal children. We did not find an important impact of the growth on the TDI values, as there were no significant changes between the age groups. This dose not correlate with the study of Eidem et al which was done on 325 normal children and concluded that Age was alsosignificantly correlated with most TDI velocities[14].

Table 4: Results of the echocardiographic parameters measured in normal children in each age group

Age Group	1month-1 year	1 year-3years	3 -6 years	6-9 years	9-13 years
Number	38	37	44	45	42
E/e'	1.17 ±0.12	1.4 ±0.41	1.56 ±0.36	1.58±0.29	1.58 ±0.36
Septal e'	11.7 ±2.6	12.7 ±3.07	12.8 ±2.3	12.2 ±1.7	12.09 ±1.8
Septal E/e'	7.8 ±1.5	8.19 ±1.5	8.2 ±1.3	8.12 ±1.2	7.68 ±1.5
Lateral e'	13.3±2.8	15.5±3.03	16±2.8	14.7 ±3.3	14.2 ±3.2
Lateral E/e'	7.2 ±1.5	6.8 ±1.3	6.2 ±1.2	6.8 ±1.3	6.8 ±1.7
Average E/e'	7.5 ±1.3	7.4 ±1.2	7.48 ±1.06	7.47 ±1.15	7.2 ±1.3

Transmitral flow velocities: E/A ratio:
This ratio did not show any important change between the normal children and those with heart failure, P value was always much bigger than 0.05 in all age groups (table 5).

Table 5

	Normal	ROSS I	P value	ROSS II - III	P value
1month – 1 year	1.17±0.12	1.1±0.27	0.39	1.2±0.34	0.37
1 – 3 years	1.4±0.41	1.4 ±0.29	0.97	1.5 ± 0.49	0.80
3-6 years	1.56±0.36	1.6 ±0.42	0.44	1.68 ± 0.54	0.39
6-9 years	1.58±0.29	1.58±0.25	0.84	1.6 ± 0.44	0.99
9-13 years	1.58±0.36	1.49±0.38	0.33	1.46 ± 0.44	0.24

Important Notice: The EF was normal (> 55%) in all the pediatric patients except 5 of the stage III patients, in the age groups (2 patient - 6-9 years-) (3 patient -9-13 Years).

Septal e':
When comparing Septal mitral e' velocity between the Normal and ROSS I group, there was an important change in two of the age-groups (1 month – 1 year , 6-9 years) where P value was less than 0.05. While it shows no statistical significant changes in the other age- groups , where P value was more than 0.05 . On the other hand those with the second and third stage of HF have shown significant changes in all age groups. (table 6)

Table 6

	Normal	ROSS I	P value	ROSS II -III	P value
1 month-1 year	11.7±2.6	9.8±1.2	0.000	8.03 ± 3.3	0.009
1 -3 years	12.7±3.07	11±2.47	0.055	10.7 ± 2.17	0.032
3-6 years	12.8±2.3	12.5±2.4	0.607	10.07 ± 2.6	0.002
6-9 years	12.2±1.7	11.07±2.1	0.017	9.58 ± 2.08	0.000
9 -13 years	12.09±1.8	11.17±1.9	0.062	9.16 ± 3.1	0.000

Septal E/e':
Analysis of the measurements of this ratio has shown very significant changes in both the groups of HF (the I , II and III stage HF) , and for all the age groups ,with one exception in the children between 3-6 years with the first HF stage . Table (7) .

Table 7

	Normal	ROSS I	P value	ROSS II - III	P value
1 month-1 year	7.8±1.4	12.6±3.8	0.000	13.9 ± 4.9	0.000
1-3 years	8.19±1.5	10.35±2.3	0.000	12.1 ± 3.2	0.000
3-6 years	8.2±1.3	8.63±2.05	0.314	10.07 ± 2.6	0.002
6-9 years	8.14±1.2	9.5±2.4	0.002	14.3 ± 2.7	0.000
9-13 years	7.68±1.5	9.08±2.5	0.000	12.6 ± 4.1	0.000

Lateral e':
When comparing Lateral mitral e' velocity between the Normal and ROSS I group, there was an important change in three of the age-groups (1 month – 1 year, 1-3 years , and 9-13 years)where P value was less than 0.05 . While it shows no statistical significant changes in the other age- groups (P value was more than 0.05). On the other hand those with the second and third stage of HF have shown significant changes in all age groups. Table (8).

Table 8

	Normal	ROSS I	P value	ROSS II - III	P value
1 month-1year	13.3±2.8	11.08±1.3	0.010	10.25±2.9	0.003
1-3 years	15.5±3.03	13.21±4.64	0.036	12.10±3.19	0.001
3- 6 years	16±2.8	14.9±3.4	0.141	13±3	0.003
6 -9 years	14.7±3.2	13.5±3.4	0.137	12±2.5	0.003
9 -13 years	14.23±3.2	12.5±2.7	0.030	11.03±3.9	0.001

Lateral E/e':
This ratio has shown the same changes as the Septal E/e' ratio. Table (9).

Table 9

	Normal	ROSS I	P value	ROSS II-III	P value
1 month–1 year	7.5±1.5	9.9±2.9	0.000	12.16±3.8	0.000
1-3 years	6.8±1.3	9.2±2.4	0.000	10.9±3.7	0.000
3-6 years	6.2±1.2	7.2±1.9	0.191	9.3±2.4	0.000
6-9 years	6.8±1.3	8.15±2.3	0.004	11.3±1.8	0.000
9-13 years	6.8±1.7	8.2±2.2	0.006	10.7±3.7	0.000

Average E/e':
As in tha Lateral and Septal E/e' ratios , there were significant changes in this ratio in all the stages of HF and for all the age groups, except those from 3-6 years with HF stage I .

Table 10

	Normal	ROSS I	P value	ROSS II-III	P value
1 month–1 year	7.49±1.3	11.17±3.1	0.000	13.03±1.3	0.000
1 -3 years	7.4±1.2	9.74±2.2	0.000	11.6±3.2	0.000
3 -6 years	7.48±1.06	7.9±1.7	0.169	10.79±2.7	0.000
6 -9 years	7.47±1.15	8.8±2.2	0.001	12.8±2.1	0.000
9 -13 years	7.2±1.3	8.6±2.2	0.001	11.6±3.8	0.000

5. Discussion

Classification of HF in pediatrics depends on clinical signs and symptoms. Declining of EF usually correlates with the

advanced stages. In this study, usefulness of Tissue Doppler Index as an early, accurate and independent index of diastolic dysfunction was emphasized. We find an important value to study TDI in HF pediatric patients from the first stages.

Transmitral flow velocities (one of the conventional diastolic function measurements) did not have a value in determining the LV filling pressure. This corresponds to the fact that it is affected by pre and after load changes, heart rate, mitral regurgitation and other physiological and pathological situations.

All measurements of diastolic function via TDI including: mitral septal e', mitral lateral e', mitral septal, lateral and average E/e', have shown significant and important changes in children patients even with mild symptoms of HF on exertion (stage II) regardless of EF. Where, in our study, EF was normal in all patient with stage II HF have a normal EF ratio. And was low (40 – 50%) in only 5 patients with heart failure stage III.

Despite , measurements of septal and lateral e' have not proved to be useful in stage I heart failure patients (the changes were not significant for all age groups) , correcting these values by calculating E/e'(Septal , Lateral and the average) ratios presented an important clue of LV filling pressure increased.

The last result has one exception in the patients aged 3-6 years. We could not explain this clearly .This group was relatively the largest one , most of the patients in this group have been classified under the first stage of heart failure due to their exposure to anthracycline (about 75%) , in the other age groups (1 month – 1 year , 1 -3 years , 6-9 years , 9 -13 years) the percentage of anthracycline exposure was respectively (33.3 % , 68.75 % , 66.6% , 54%) .

6. Conclusion

Traditional measurement of diastolic function starting eith E/A ratio has no value in pediatrics in all age groups of this study. This corresponds with all previous studies which confirm the inaccuracy and the lack of independence of this ratio in children. TDI presents an important information about the diastolic function and the filling pressure of LV from the first stage of HF in pediatrics. This can be helpful in the monitoring and treatment plan. More studies should be done in order to better understanding of the diastolic function in pediatrics ; especially in the first stage of heart failure , where usefulness of TDI could not be confirmed in all age groups in this study .

References

[1] Kirk, R.; Dipchand, A.I.; Rosenthal, D.N.; Addonizio, L.; Burch, M.; Chrisant, M.; Dubin, A.; Everitt, M.; Gajarski, R.; Mertens, L.; et al. The international Society of Heart and Lung Transplantation Guidelines for the management of pediatric heart failure: Executive summary. J. Heart Lung Transpl. 2014, 33, 888–909.
[2] Bibhuti B. Das . Current State of Pediatric Heart Failure . Joe DiMaggio Children's Heart Institute, Memorial Health Care System, Hollywood, FL 33021,USA; 28 June 2018 .
[3] Rossano, J.W.; Kim, J.J.; Decker, J.A.; Price, J.F.; Zafar, F.; Graves, D.E.; Morales, D.L.; Heinle, J.S.; Bozkurt, B.; Towbin, J.A.; et al. Prevalence, morbidity, and mortality of heart failure-related hospitalization in the United States: A population based study. J. Card. Fail. 2012, 18, 459–470.
[4] Rosenthal, D.; Chrisant, M.; Edens, E.; Mahony, L.; Canter, C.; Colan, S.; Dubin, A.; Lamour, J.; Ross, R.; Shaddy, R.; et al. International Society of Heart and Lung Transplantation: Practice guidelines for management of heart failure in children. J. Heart. Lung Transpl. 2004, 23, 1313–1333.
[5] Ross, R.D. The Ross classification for heart failure in children after 25 years: A review and an age-stratified revision. Pediatr.Cardiol. 2012, 33, 295–300.
[6] Allan L.KleinMD,MarioJ.Garsia MD . Diastology , clinical approach to diastolic heart failure . Saunders Elsevier 2008 . Chapter 6 . Page 64 .
[7] Oh JK, Hatle L, Tajik AJ, et al: Diastolic heart failure can be diagnosed by comprehensive two-dimensional and Doppler echocardiography. J Am CollCardiol 2006;47:500–506.
[8] Little WC: Diastolic dysfunction beyond distensibility: Adverse eff ects of ventricular dilatation. Circulation 2005; 112:2888–2890.
[9] OH JK, APPLETON CP, HATLE LK, et al. The non-invasive assessment of left ventricular diastolic function with twodimensional and Doppler echocardiography. J Am SocEchocardiog. 1997; 10:246-70.
[10] Lester S, Tajik AJ, Nishimura RA, Oh JK, Khandheria BK, Seward JB, et al. Unlocking the mysteries of diastolic function. J Am CollCardiol (2008) 51(7):679–89. doi:10.1016/j.jacc.2007.09.061.
[11] WILLENHEIMER R, CLINE C, ERHARDT L, ISRAELSSON B. Left ventricular atrioventricular plane displacement: an echocardiographic technique for rapid assessment of prognosis in heart failure. Heart.1997; 78:230-6.
[12] Isaaz K, Thompson A, Ethevenot G, Cloez JL, Brembilla B, Pernot C. Doppler echocardiographic measurement of low velocity motion of the left ventricular posterior wall. The American Journal of Cardiology 1989;64:66–75.
[13] Panesar , D.K .; Burch , M . Assessment of Diastolic Function in Congenital Heart Disease .Pediatric Cardiology. Front. Cardiovasc. Med., 15 February 2017.
[14] EIDEM BW, MCMAHON CJ, AYRES NA. Impact of chronic left ventricular preload and afterload on Doppler tissue imaging velocities; a study in congenital heart disease. J Am SocEchocardiog. 2005; 18:830-8.
[15] Butnariu A, Zamfir C, Iancu M, Iacob D, Samasca G, Lupan I. Systolic and Diastolic Function in Congestive Heart Failure Pediatric Patients. Rom J Intern Med. 2016 Jan-Mar;54(1):37-46.
[16] Nagueh SF, Middleton KJ, Kopelen HA, Zoghbi WA, Quiñones MA. Doppler tissue imaging: a noninvasive technique for evaluation of left ventricular relaxation and estimation of filling pressures. J Am CollCardiol (1997) 30(6):1527–33. doi:10.1016/S0735-1097(97)00344-6 .