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ECHOCARDIOGRAPHIC ASSESSMENT OF LEFT AND RIGHT VENTRICULAR DIASTOLIC FUNCTIONS IN CHILDREN WITH DILATED CARDIOMYOPATHY*

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SUMMARY: Alehan F, Özkutlu S, Alehan D, Saraçlar M. (Cardiology Unit, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Echocardiographic assessment of left and right ventricular diastolic functions in children with dilated cardiomyopathy. Turk J Pediatr 1998; 40: 337-346.

We evaluated left and right ventricular diastolic functions by pulsed Doppler echocardiography in 16 children with dilated cardiomyopathy and in 20 healthy age-matched control subjects. The cardiomyopathy group demonstrated an abnormal relaxation pattern of the left ventricle. In the cardiomyopathy group compared to normal subjects, peak early filling velocities (43.3 ± 11 cm/s versus 60.4 ± 11 cms/s, p < 0.01), the corresponding velocity-time integrals (3.3 ± 1.4 cm versus 4.6 ± 1.2 cm, p < 0.01) and the ratio of peak early filling velocity to late filling velocity (1.22 ± 0.47 versus 1.49 ± 0.23, p < 0.05) were significantly lower whereas isovolumic relaxation time was significantly longer (58.9 ± 19.8 ms versus 49.7 ± 8.9 ms, p < 0.05). In addition, right ventricular diastolic filling was also impaired in children with dilated cardiomyopathy. Peak early filling velocities (41 ± 7.9 cm/s versus 47.5 ± 8.8 cm/s, p < 0.05) and the corresponding velocity time integrals (3.0 ± 1.0 cm versus 3.87 ± 1.1 cm, p < 0.05) were significantly decreased, while isovolumic relaxation time was significantly increased (60.6 ± 16.3 ms versus 52.2 ± 12.8 ms, p < 0.05) in the cardiomyopathy group. The study suggests that abnormalities of both right and left ventricular diastolic function may occur, and should be searched for, in pediatric patients with dilated cardiomyopathy.

Key words: dilated cardiomyopathy, diastolic function, Doppler echocardiography, children.

Impaired systolic function and reduced cardiac output are the hallmarks of dilated cardiomyopathy. However, an increasing number of patients with signs and symptoms of congestive heart failure, in the absence of overtly abnormal systolic performance, are now being recognized[1, 2]. This has emphasized the importance of diastolic filling and has shifted the interest from systolic functions to diastolic functions. Consequently, the possible role of impaired diastolic function in dilated cardiomyopathy was only recently appreciated.

Several studies have shown the utility of Doppler echocardiography in assessing left ventricular filling and have demonstrated diastolic abnormalities in adult patients with dilated cardiomyopathy[3-5]. However, there are only a few reports assessing diastolic function in pediatric patients with dilated cardiomyopathy, particularly in terms of right ventricular function.

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The purpose of this study was to evaluate left and right ventricular diastolic functions in children with dilated cardiomyopathy using Doppler echocardiographic indices.

Material and Methods

Patient group consisted of 16 patients with clinical and echocardiographic diagnosis of dilated cardiomyopathy in the absence of clinical evidence of myocarditis and primary valvular disorder (mean age 6.55 years, range 2 months-15.5 years). All patients had cardiomegaly as determined from chest x-ray (cardiothoracic ratio > 0.5). M-mode echocardiographic study demonstrated left venticular enlargement (end-diastolic dimension greater than 25% above the normal value as predicted from the age and body surface area)[6], decreased fractional shortening (< 25%) and a marked increase of E point-septal separation[7]. Mean ejection fraction measured in the study group was also reduced (41.6 ± 11.2%). Two dimensional echocardiography revealed a dilated nonhypertrophic left ventricle with diffuse hypokinesia or akinesia of left ventricular wall motion in all patients. None of the cases had significant arrhythmia, atrioventricular block or pacemaker implants at the time of the study. Presumed etiology of dilated cardiomyopathy was idiopathic in 15 patients and adriamycin-induced in one. Each patient was clinically stable during the time of examination. None of the patients was receiving parenteral inotropic or ventilatory support at the time of the study. Digoxin was being administered to all but one patient. Three patients were receiving a diuretic, five captopril, and three both, in addition to digoxin. One patient was treated with captopril alone.

Control group consisted of 20 healthy children with a similar age distribution (mean age. 6.6 ± 2.5 years).

Echocardiographic Examination

Complete two-dimensional and Doppler echocardiographic examinations were performed on each subject by one investigatior using a Toshiba Sonolayer SSH 160 A echocardiographer with 2.5, 3.75, and 5 MHz transducers. Examinations were recorded on a standard VHS videotape and measurements were made from the replay. Continuous wave and color Doppler echocardiography were applied to each patient with standard methods to rule out valvular abnormalities that are not infrequent in patients with dilated cardiomyopathy[8].

Each subject underwent pulsed Doppler echocardiographic examination of mitral and tricuspid valves from an apical four-chamber view. The Doppler cursor was placed at the tips of the valve leaflets, in the left and right ventricular inflows, almost parallel to the direction of flow. We simultaneously recorded the subjects' electrocardiogram, phonocardiogram and respiration (using a pressure transducer placed over the subphrenic region) (Fig. 1). Care was taken to keep the positions of the body and the transducer unchanged during the recording.

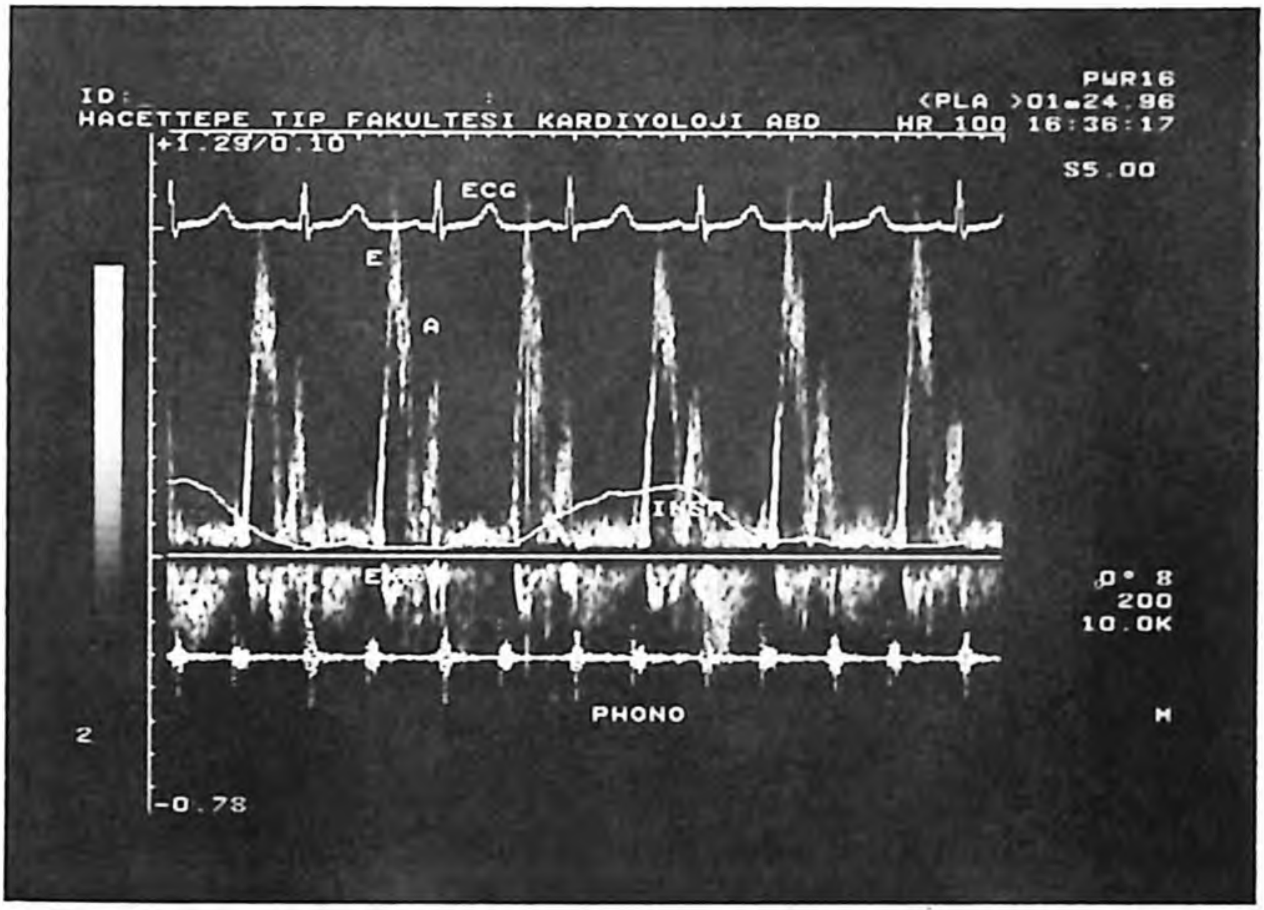

Fig. 1: Pulsed Doppler transmitral spectral tracing with simultaneous respiratory recordings. The electrocardiogram (ECG), phonocardiogram (PHONO), inspiration (INSP), and expiration (EXP) are labeled. E: peak early filling velocity (peak E); A: peak late filling velocity (peak A).

Doppler Analysis

The pulsed Doppler recordings were analyzed using an off-line computer system. For the determination of ventricular filling dynamics, the cardiac cycles with the most clearly defined flow velocity waveform and with the maximum early diastolic filling velocity were chosen and measurements were made from the end expiratory cardiac cycles. The following parameters were obtained from the spectral display: peak early filling velocity (peak E) (in centimeters per second) and peak late (atrial) filling velocity (peak A) (in centimeters per second), from which the ratio of early to late peak filling velocity (peak E/A ratio) was derived; early diastolic velocity-time integral (E integral) (in cm) and late diastolic velocity-time integral (A integral) (in cm), from which E/A integral was derived; total diastolic filling period (TDF), defined as the interval between the onset and termination of diastolic filling velocity; the acceleration time (AT), defined as the interval between the onset of diastolic flow and peak E; deceleration time (DT), defined as the interval between peak E and the termination of early diastolic filling; early acceleration slope (OE slope); early deceleration slope (EF slope);

and isovolumic relaxation time (IVRT), defined as the interval between closure of the aortic or pulmonary valve (in respect to the ventricle being studied), determined from phonocardiogram, and onset of diastolic flow.

Data Analysis

All Doppler measurements reported are the average of three cardiac cycles at end-expiration. All values are reported as mean ± 1 SD. A two-tailed unpaired t-test was used for statistical analysis; $p < 0.05$ indicated a significant difference between the groups.

Intraobserver Variability

All echocardiographic studies and measurements were performed by the same cardiologist (S.Ö). Intraobserver variability was calculated as described previously[9] and was low for most of the Doppler indices for Doppler velocity measurements $r = 0.99$, for all time interval measurements $r = 0.99$, for velocity-time integral measurements $r = 0.98$, and for acceleration and deceleration slope $r = 0.97$.

Results

The cardiomyopathy group consisted of 11 female and five male patients. There were no significant differences in age, heart rate (104 ± 23 beats/min versus 99 ± 13 beats/min) or systolic blood pressure (95 ± 16 mmHg versus 104 ± 18 mmHg) between the cardiomyopathy group and the control group, respectively. Clinical data of the patients are illustrated in Table I.

Comparison of left ventricular filling in patients with cardiomyopathy and normal children showed significant differences in various parameters. Peak early filling velocities (Peak E) and the corresponding velocity-time integrals (E integral) were significantly lower (43.3 ± 11.4 cm/s versus 60.4 ± 11.4 cm/s, $p < 0.01$; and 3.3 ± 1.4 cm versus 4.6 ± 1.2 cm, $p < 0.01$) in the cardiomyopathy group (Fig. 2). In addition, the ratio of peak early filling velocity to late filling velocity was significantly lower, whereas isovolumic relaxation time was significantly longer, in patients with cardiomyopathy (Table II).

Significant differences were also obtained in some indices of right ventricular filling. Peak early filling velocities (41 ± 7.9 cm/s versus 47.5 ± 8.8 cm/s, $p < 0.05$) and the corresponding velocity-time integrals (3.0 ± 1.0 cm versus 3.87 ± 1.1 cm, $p < 0.05$) were significantly decreased, while isovolumic relaxation time was significantly increased ($p < 0.05$), in the cardiomyopathy group compared to normal children (Fig. 3). Right ventricular filling parameters are given in Table III.

The demonstrated abnormalities of left and right ventricular diastolic filling were compatible with the impaired relaxation pattern of both ventricles.

Table I: Clinical Data of the Patients

Patient	Sex	Age (mo)	Weight (kg)	Heart Rate (bpm)	Drug Therapy
1	F	70	17	83	Dig
2	M	135	29	75	Dig+cap
3	F	48	12	115	Dig+cap
4	F	188	49.5	100	Dig
5	F	43	15	125	Dig+diur+cap
6	F	48	14.5	78	Dig+diur
7	M	90	17	113	Dig+cap
8	F	12	10.5	132	Dig+diur
9	F	152	40	99	Dig
10	M	156	34	114	Dig+diur
11	F	149	45	63	Dig
12	M	96	23	84	Cap
13	F	12	9.5	96	Dig+diur+cap
14	F	39	12.5	115	Dig+diur+cap
15	M	2	4.4	148	Dig+cap
16	F	18	7.9	130	Dig+cap

bpm : beats per minute cap : captopril dig : digoxin
diur : diuretic F : female M : male mo : month

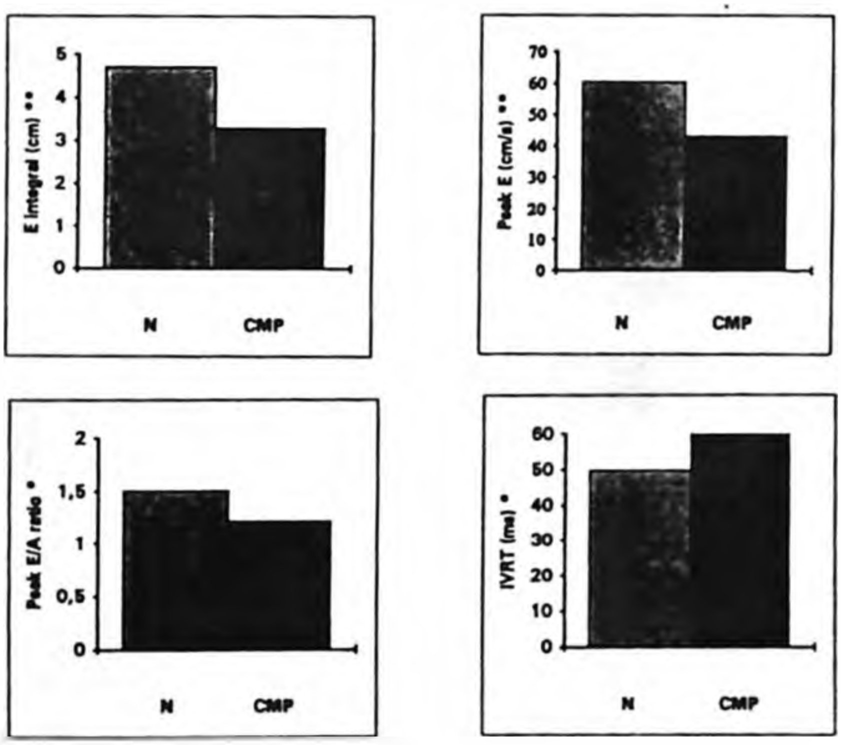

Fig. 2: Left ventricular echocardiographic parameters of normal subjects (N) and patients with cardiomyopathy (CMP). In the cardiomyopathy group, peak early filling velocity (Peak E), ratio of early to late filling velocity (Peak E/A ratio), and early diastolic velocity-time integral (E integral) were significantly decreased, while isovolumic relaxation time (IVRT) was significantly increased when compared with normal subjects (*$p < 0.05$; **$p < 0.01$).

Table II: Left Ventricular Diastolic Parameters in Normal Subjects and in Patients with Cardiomyopathy

	Cardiomyopathy	Normal	p Value
Peak E (cm/s)	43.3 ± 11.4	60.4 ± 11.4	< 0.01
Peak A (cm/s)	37.6 ± 10	40.5 ± 6.8	NS
Peak E/A ratio	1.22 ± 0.47	1.49 ± 0.23	< 0.05
E integral (cm)	3.31 ± 1.4	4.69 ± 1.2	< 0.01
A integral (cm)	1.85 ± 0.6	2.19 ± 0.6	NS
E/A integral	1.85 ± 0.7	2.14 ± 0.5	NS
AT (ms)	66.3 ± 15	70.3 ± 12.2	NS
DT (ms)	82.1 ± 25.7	89.2 ± 16.4	NS
TDF (ms)	281 ± 67	294.5 ± 40	NS
EF Slope (cm/s^2)	5.7 ± 1.9	5.44 ± 1.5	NS
OE Slope (cm/s^2)	8.83 ± 3.7	9.48 ± 2.1	NS
IVRT (ms)	58.9 ± 19.8	49.7 ± 8.9	< 0.05

AT: acceleration time; A area: late (atrial diastolic velocity-time integral. DT: deceleration time; EF slope: early deceleration slope. E area: early diastolic velocity-time integral. IVRT: isovolumic relaxation time. NS: non-significant. OE slope: early acceleration slope. Peak A: peak late filling velocity. Peak E: peak early filling velocity. TDF: total diastolic filling period. For definitions see the methods section.

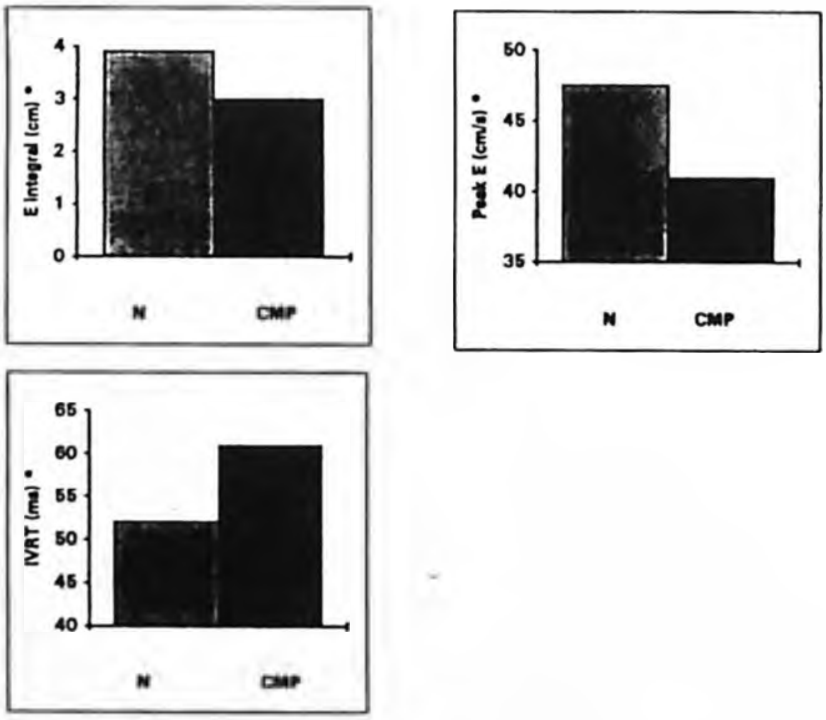

Fig. 3: Right ventricular echocardiographic parameters of control subjects (N) and cardiomyopathy (CMP) group. In the cardiomyopathy group, peak early filling velocity (Peak E) and early diastolic velocity-time integral (E integral) were significantly decreased, while isovolumic relaxation time (IVRT) was significantly increased, when compared with normal subjects. * $p < 0.05$.

Table III: Right Ventricular Diastolic Parameters in Normal Subjects and in Patients with Cardiomyopathy

	Cardiomyopathy	Normal	p Value
Peak E (cm/s)	41 ± 7.9	47.5 ± 8.8	< 0.05
Peak A (cm/s)	35.9 ± 6.8	37.9 ± 7.1	NS
Peak E/A ratio	1.16 ± 0.27	1.25 ± 0.22	NS
E integral (cm)	3.0 ± 1.0	3.87 ± 1.1	< 0.05
A integral (cm)	2.17 ± 0.72	2.23 ± 0.51	NS
E/A integral	1.46 ± 0.46	1.67 ± 0.71	NS
AT (ms)	73.6 ± 16.8	71.2 ± 13.7	NS
DT (ms)	81.8 ± 27.7	92.9 ± 20.8	NS
TDF (ms)	272.6 ± 89.1	296.9 ± 52.4	NS
EF Slope (cm/s^2)	5.0 ± 2.0	4.17 ± 0.86	NS
OE Slope (cm/s^2)	7.15 ± 2.2	7.71 ± 2.55	NS
IVRT (ms)	60.6 ± 16.3	52.2 ± 12.8	< 0.05

Abbreviations as in Table II and methods section.

Discussion

The use of transmitral Doppler recordings in assessing left ventricular diastolic function has received increased attention in clinical cardiology. Hence, several studies in adult patients with dilated cardiomyopathy recently demonstrated diastolic abnormalities as being responsible for symptoms during periods of clinical deterioration[10-13]. Three distinct filling patterns have been described. The first, characterized by a prolonged isovolumic relaxation time, slow deceleration of early filling velocity and a decrease in E/A ratio, is associated with "impaired relaxation". The second type, called the "restrictive" pattern, is characterized by a short isovolumic relaxation time, rapid filling in early diastole (high E velocity), reduced atrial filling velocity (a velocity) and an increase in E/A ratio. The third pattern is called a "normalized" or "pseudonormal" pattern[14]. The restrictive pattern is usually seen in patients with an advanced form of disease, while the impaired relaxation is usually associated with a mild form of the disease[14, 15].

In this study in the cardiomyopathy group we detected significant reductions in left ventricular early filling velocity, early velocity-time integral and in E/A ratio, whereas a significant increase was detected in isovolumic relaxation time. These changes were in accord with impaired relaxation of left ventricle. All our patients were clinically stable during the study period; therefore; an abnormal relaxation pattern was compatible with the clinical status of our patients. Our findings are also in agreement with previous studies, demonstrating abnormal relaxation patterns in adults with a mild or moderate form of dilated cardiomyopathy. However, in the only other study performed in six children with dilated cardiomyopathy, Riggs[16] reported an increased rather than decreased early to late peak filling velocity (peak E/A) ratio in the cardiomyopathy group. The finding of a higher peak E/A ratio was supposedly related to the increased left atrial pressure due to mitral insufficiency present in most of their patients.

Unlike the case with left ventricular filling, right ventricular diastolic filling has not been studied extensively in either adults or in children with dilated cardiomyopathy. In one study assessing right ventricular diastolic function in patients with dilated cardiomyopathy by cinemagnetic resonance, Suziki et al.[17] demonstrated impairment of diastolic function of the right ventricle. Their findings were consistent with the notion of the existence of impaired early diastolic filling of the right ventricle in patients with dilated cardiomyopathy. In the only other study performed in children by Doppler echocardiography[16], the E/A integral, peak early velocity and peak E/A ratio were each lower in the cardiomyopathy group, while the peak A velocity was higher. Isovolumic relaxation time was not evaluated in this investigation. In the present study, peak E velocity and the corresponding velocity-time integral were significantly lower, and the isovolumic relaxation time significantly higher, in the cardiomyopathy group. Our findings are in favor of impaired relaxation of the right ventricle and suggest that the cardiomyopathic process is a diffuse process associated with impairment of both right and left ventricular diastolic filling.

Study Limitations

The most important limitation of the study lies in the complexity of the physiology that is evaluated. Diastole represents a complex interplay of multiple factors, including ventricular and atrial systolic and diastolic properties and loading conditions, and the pattern of filling may not reflect all diastolic properties. Heart rate, respiration, age, and valvular regurgitation are some of the factors that could also alter diastolic filling[16, 18-22]. In the current study, end expiratory values of diastolic indices were used in order to minimize the effects of respiration, and patients with valvular regurgitation were not included in the study. Also, there were no significant differences in age, heart rate, or systolic blood pressure between the control group and the group with dilated cardiomyopathy. Therefore, we think that these variables were unlikely to have had significant effects on our results.

Lack of an invasive hemodynamic assessment of the patients could be considered as a limitation. However, the purpose of the study was to evaluate diastolic filling by Doppler echocardiography, which is a noninvasive method. Furthermore, previous studies with simultaneous Doppler echocardiographic and hemodynamic measurements have demonstrated that the findings were closely correlated with each other[14, 23].

In conclusion, this study shows that in addition to left ventricular diastolic dysfunctilon, abnormalities of right ventricular diastolic filling may also occur in children with dilated cardiomyopathy. In light of these findings, we recommend Doppler echocardiographic assessment of left and right ventricular diastolic filling in every patient with dilated cardiomyopathy.

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