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Evaluation of Tissue Doppler Echocardiographic Imaging findings in children with pulmonary hypertension

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Tissue Doppler Imaging has become an important prognostic marker that can be used in follow-up and determination of the prognosis in pulmonary hypertension patients. We compared the Tissue Doppler imaging parameters of 34 patients with pulmonary hypertension and 43 healthy controls. In addition, Brain-Natriuretic Peptide levels, pulmonary artery systolic pressures measured with echocardiography, 6-minute walking tests and New York Heart Association functional classification were compared.

Among patients with Eisenmenger syndrome and idiopathic pulmonary hypertension, Tissue Doppler imaging parameters were mostly similar. In patients with New York Heart Association functional class 3, mitral septal annulus E/Ea (p=0.050) and mitral lateral annulus myocardial performance index (p=0.009) were higher than class 2 patients. In patients with higher Brain Natriuretic Peptide level, mitral lateral annulus and tricuspid septal annulus Ea/Aa values were lower (p=0.046 and <0.001 respectively); tricuspid septal annulus E/Ea and interventricular septum myocardial performance index values were higher than in patients with normal Brain-Natriuretic Peptide level (p=0.006).

In conclusion tissue Doppler imaging findings were significantly impaired in children with pulmonary hypertension compared to the control group. Findings were similar in patients with idiopathic pulmonary hypertension and Eisenmenger syndrome. Mitral lateral annulus myocardial performance index value may have a prognostic importance due its significant association with poor functional class. Due to the significant associations between mitral lateral annulus, tricuspid septal annulus Ea/Aa, tricuspid septal annulus Ea and E/Aa, interventricular septum-myocardial performance index values and brain natriuretic peptide levels, these parameters may be used in evaluating response to therapy.

Key words: pulmonary hypertension, tissue Doppler imaging, echocardiography.

Pulmonary hypertension is defined as mean pulmonary artery pressure over 25 mmHg measured via cardiac catheterization[1]. Research has been directed towards early diagnosis and identifying possible prognostic factors of this disease because these patients suffer from high morbidity and mortality rates, because the treatment regimens are usually expensive, and their possibility of having lung transplantation is very low in some areas like Turkey.

Echocardiography is a non-invasive, easily performed modality routinly used in the diagnosis and follow up of pulmonary hypertension. In the last few years, some studies have shown Tissue Doppler imaging parameters are as sensitive in determining the prognosis as some invasive modalities and laboratory tests.

Despite the clear evidence regarding the importance of Tissue Doppler imaging findings in pulmonary hypertension, most studies were performed on the adult patient group. In this study, we aim to compare the Tissue Doppler imaging findings in pulmonary hypertension patients with other parameters used in the follow up of this disease.

Materials and Methods

Patients

Thirty-four patients with irreversible pulmonary hypertension (idiopathic pulmonary hypertension and Eisenmenger syndrome) followed up at our pediatric cardiology unit were included in this study. The research was reviewed and approved by Hacettepe University Clinical Researches Ethics Boards (16.02.2012 - FON 12/02-29), and participation involved informed consent. The diagnosis of all patients was confirmed by right heart catheterization (classification of pulmonary hypertension was made according to Fifth World Symposium held in 2013 in Nice)[2]. The functional capacity of the patients was determined according to New York Heart Association (NYHA) functional classification. The 6 minute walking tests (6MWT) were only conducted by the 24 patients over the age of 6 years. The diagnoses were idiopathic PH in 6 and Eisenmenger syndrome in the remaining 18 patients. NYHA functional class, 6MWT and Brain natriuretic peptide (BNP) values (pg/ml) were recorded on the same day Tissue Doppler imaging was performed. Subsequently, transthoracic two-dimensional, M-Mode, colored Doppler echocardiography and Tissue Doppler imaging were performed.

A healthy control group consisting of 43 children, homogeneous in terms of age, body weight and gender was chosen. These children had no other symptoms or systemic diseases. Their physical examination was normal. Their transthoracic echocardiography showed no pathologic findings and they took no medication. The same pediatric cardiologist performed the two-dimensional, M-mode, colored Doppler echocardiography and Tissue Doppler imaging on both control and patient groups.

Echocardiographic Evaluation

General Electric Vingmed System five Performance® (Vingmed Sound, Horten, Norway) device was used in the echocardiographic investigation. Transducers of 3.5 or 2.5 MHz were used. Two-dimensional and colored Doppler echocardiographic work up were performed at the apical 4 chamber, parasternal long axis, parasternal short axis, subcostal and at the suprasternal positions. M-Mode sample was measured by putting the tricuspid annular plane systolic excursion at the junction between the septal cusp of the tricuspid valve and the lateral wall of the right ventricule. In the 4 chamber window, when both the mitral and tricuspid valves were completely open, the pulse wave Doppler recording was taken at the tip of the mitral and the tricuspid valves. To measure the tissue Doppler, after switching to the automatically chosen Tissue Doppler imaging in the echocardiography device, the pulse wave sample was placed on the mitral lateral, mitral septal, tricuspid lateral and at the junction of the septal cusp of the tricuspid valve with the ventricule. And for the interventricular septum, the pulse wave sample was positioned parallel to the septum and it was put at its upper 1/3 part. Measurements of mitral and tricuspid flow velocity (m/sec) of the early rapid filling wave (E), peak velocity of the late filling wave due to atrial contraction (A) and myocardial performance index (MPI) were taken. Using the Tissue Doppler imaging, late diastolic velocity (Aa, cm/sec), early diastolic velocity (Ea, cm/sec), systolic velocity (Sa, cm/sec), myocardial performance index, acceleration time (AT, msec), deceleration time (DT, msec), isovolumic contraction time (IVCT, msec), isovolumic relaxation time (IVRT, msec), ejection time (ET, msec) of the mitral valve, tricuspid valve and the interventricular septum were measured. Myocardial performance indexwas calculated by the following formula: (IVRT + IVCT)/ET.

Statistical Analysis

Data was transferred to, and analyzed using SPSS 18 PASW statistics program. The normal distribution of the groups was evaluated. Variables showing normal distribution were mainly tested using the difference between 2 means (T-test). Mann-Whitney U test was used for data that did not show normal distribution. Parameters where T-test was used were written as mean ± standard deviation and where Mann-Whitney U test was used, it was written as

Table I. Comparison of the Tissue Doppler Imaging Parameters of Patient and Control Group.

	Patient group (n 34) [mean (SD) or median (range)]	Control group (n 43) [mean (SD) or median (range)]	p
Male/female	15/19	23/20	0.414
Age. years*	13 (1.1-32)	9 (2.1-18)	0.191
Weight. kg*	35.5 (6-66)	31 (11-65)	0.576
TAPSE (mm)*	15 (7-32)	25 (19-35)	<0.001
Mitral E velocity*	0.79 (0-1.57)	0.45 (0.33-0.78)	<0.001
Mitral A velocity	0.65 (±0.42)	0.99 (±1.52)	0.165
Mitral E/A	1.42 (±0.52)	1.66 (±0.23)	0.017
Mitral MPI*	0.97 (0.42-1.25)	0.8 (0.6-1.4)	0.104
Tricuspid E velocity	0.68 (±0.21)	0.42 (±0.1)	<0.001
Tricuspid A velocity*	0.51 (0.32-0.90)	0.60 (0.44-0.95)	0.006
Tricuspid E/A	1.37 (±0.36)	1.54 (±0.21)	0.017
Tricuspid MPI*	0.88 (0.33-2.3)	0.76 (0.57-1.11)	0.053
Mitral lateral			
Sa	7.25 (±3.13)	7.68 (1.84)	0.481
Ea	10.38 (±3.96)	11.7 (±2.56)	0.100
Aa*	7.4 (3.9-20.36)	6.7 (3.8-11.2)	0.108
Ea/Aa*	1.4 (0.27-2.8)	1.7 (1.37-2.8)	0.021
E/Ea*	0.09 (0.03-0.24)	0.07 (0.03-0.84)	0.024
MPI*	0.73 (0.27-2.41)	0.51 (0.3-0.94)	0.001
Mitral septal			
Sa	6.55 (±2.0)	7.26 (±1.23)	0.074
Ea	7.51 (±2.59)	11.12 (±1.49)	<0.001
Aa*	6.52 (3.55-19.75)	7 (3.5-11)	0.469
Ea/Aa	1.14 (±0.529	1.61 (±0.25)	<0.001
E/Ea*	0.12 (0.05-0.28)	0.7 (0.04-0.84)	<0.001
MPI*	0.66 (0.35-1.51)	0.53 (0.33-1.22)	<0.001
Tricuspid lateral			
Sa	10.36 (±3.63)	12.37 (±2.17)	0.006
Ea	10.29 (±3.77)	14.80 (±2.37)	<0.001
Aa	11.27 (±5.30)	9.78 (±1.95)	0.128
Ea/Aa	1.37 (±0.36)	1.54 (±0.21)	<0.001
E/Ea*	0.72 (0.4-6.0)	0.42 (0.03-0.08)	<0.001
MPI*	0.79 (±0.27)	0.59 (±0.13)	<0.001
Tricuspid septal			
Sa*	6.32 (3.2-18.3)	8.1 (5.2-9.05)	<0.001
Ea	7.75 (±2.34)	11.66 (±1.70)	<0.001
Aa	6.555 (±2.52)	7.08 (±1.47)	0.283
Ea/Aa	1.28 (±0.45)	1.67 (±0.25)	<0.001
E/Ea*	0.09 (0.05-0.34)	0.06 (0.04-0.07)	<0.001
MPI*	0.76 (±0.24)	0.54 (±0.15)	<0.001
Interventricular septum			
Sa	5.70 (±2.58)	6.40 (±0.959	0.140
Ea	7.05 (±3.03)	9.79 (±2.32)	<0.001
Aa*	4.73 (2.68-20.6)	5.5 (0.86-7.2)	0.001
Ea/Aa*	1.39 (0.37-3.38)	1.88 (1.35-2.70)	<0.001
MPI*	0.71 (0.33-1.33)	0.5 (0.25-0.85)	0.003

Data are given as mean±SD
*Data are given as median (range)
MPI: myocardial performance index; TAPSE: tricuspid annular plane systolic excursion

Table II. Comparison of the Other Statistically Significant Tissue Doppler Imaging Parameters of Patient and Control Group.

	Patient group (n 34) [mean (SD) or median (range)]	Control group (n 43) [mean (SD) or median (range)]	p
Mitral septal			
ET	231.4 (±49.5)	252.7 (±27.1)	0.029
Mitral lateral			
IVRT	84.8 (±33.5)	69.6 (±24.6)	0.032
ET	218.4 (±52.7)	252.8 (±32.0)	0.002
Tricuspid septal			
IVCT	85.0 (±33.2)	70.9 (±22.2)	0.029
IVRT	81.8 (±31.0)	63.7 (±19.4)	0.005
ET*	226.5 (128-336)	253 (188-311)	0.004
Tricuspid lateral			
AT	55.9 (±22.3)	72.7 (±18.2)	0.001
IVRT	96.1 (±38.3)	69.0 (±18.4)	<0.001
IVCT*	76 (45-173)	74 (32-119)	0.030
IVS			
DT	69.6 (±23.3)	59.0 (±17.3)	0.024
IVRT	85.2 (±44.2)	65.0 (±19.0)	0.017
ET	223.5 (±54.1)	255.4 (±30.6)	0.003

Data are given as mean±SD
*Data are given as median (range)
DT: decelaration time; ET: ejection time; IVCT; isovolumic contraction time; IVRT; isovolumic relaxation time; IVS; interventricular septum

median (minimum-maximum). Pearson test was used to compare numerical data. Chi-Square test was used for categorical data. To control for age and body weight, partial correlation coefficient was used.

Results

The study included 34 patients with irreversible pulmonary hypertension and 43 childen in control group. The patient and control groups were homogeneous in terms of age, gender and body weight and no statistically significant difference was found between them. The Tissue Doppler imaging and other parameters of the patient and control group along with their statistical relationship are shown in Table I and II.

Ten patients in the patient group were diagnosed with idiopathic pulmonary hypertension. Twenty-four patients had Eisenmenger syndrome. Causes of Eisenmenger syndrome were as follows: large or multiple ventricular septal defect (11 patients), large secundum atrial septal defect (1 patient), high venosum atrial septal defect (2 patients), patent ductus arteriosus (4 patients), large ventricular septal defect + atrial septal defect + pulmonary artery anomaly (1 patient), patent ductus arteriosus + atrial septal defect (1 patient), patent ductus arteriosus + partial abnormal pulmonary venous return anomaly (1 patient). Table III shows the statistically significant parameters between the idiopathic pulmonary hypertension and Eisenmenger syndrome groups. The other parameters did not show a statistically significant difference.

Patients included in the study were in class 2 or 3 of the NYHA classification and there were no patients in class 1 or 4. The mean age for NYHA class 2 patients were 12.9 (±7.4) years and 11.8 (±17.1) for class 3 patients. No significance difference was found between two groups in terms of age. Both idiopathic pulmonary hypertension and Eisenmenger syndrome groups had a mean of 2.4 in the NYHA functional class ($p>0.05$). Patients with NYHA class 2 had a mean of 495 meters in 6MWT compared to a mean of 403 meters in class 3 patients, but the difference was not

Table III. Comparison of the Parameters of Patients with Idiopathic Pulmonary Hypertension and Eisenmenger Syndrome Groups.

	Idiopathic PH (n:10) [mean (SD) or median (range)]	Eisenmenger syndrome (n:21) [mean (SD) or median (range)]	p
Male/Female	6/4	11/10	1.000
Age, years	5 (1.1-20)	13 (3-21)	0.087
Weight, kg*	15.5 (±6-57)	36 (±10-65)	0.114
NYHA functional class	2.5 (2-3)	2.5 (2-3)	1.000
BNP (pg/ml)	30 (11-620)	48 (10-660)	0.756
6MWT (meter)	450 (335-540)	467 (285-655)	0.780
TAPSE (mm)	13 (10-17)	16 (7-32)	0.494
Tricuspid A velocity	0.46 (0.32-0.67)	0.64 (0.34-0.90)	0.031
Tricuspid E/A	1.57 (1.13-2.31)	1.24 (0.74-2.08)	0.028
Mitral lateral annulus			
Sa	5.43 (4-7.64)	7.46 (4-20.9)	0.010
Interventricular septum			
Aa	6.1 (2.68-20.6)	4.2 (2.8-9.43)	0.019
Mitral septal AT	41 (25.6-64.1)	51.3 (29-105)	0.043
Mitral septal IVCT	54.7 (38.4-105)	77.1 (51.3-336)	0.013
Mitral septal ET	206.2 (121.8-286)	256 (173-317)	0.013
Mitral lateral ET	179 (110-270)	237 (141-339)	0.048
Tricuspid septal ET	190.5 (128-282)	230 (192-336)	0.004
Tricuspid lateral IVCT	60 (45-100)	86 (65-173)	0.001
Tricuspid lateral ET	201.5 (120-305)	252 (176-355)	0.048
IVS ET	195 (99-262)	250 (76-307)	0.003

Data are given as median (range)
*Data are given as mean±SD
6MWT: 6 minute walking tests; AT: Accelaration time; BNP: Brain natriuretic peptide; DT: decelaration time; ET: ejection time; IVCT; isovolumic contraction time; NYHA: New York Heart Association; TAPSE: tricuspid annular plane systolic excursion;

statistically significant (p=0.210). Tricuspid annular plane systolic excursion of class 2 patients was 16.8 mm, whereas class 3 patients had 13.5 mm, no significant difference was present (p=0.287). The Tissue Doppler imaging parameters showing significant difference between NYHA class 2 and 3 are shown in Table IV.

Patients were divided in two groups according to their BNP levels. Group I included patients with ≤100 pg/ml levels and group II >100 pg/ml levels. The mean age was 10.8 (±5.9) years for group I and 12.6 (±7.2) years for group II. There were no significant difference between two groups in terms of age. Parameters that were significantly different are shown in Table V along with their p values.

The patients were divided into 2 groups according to 6MWT results, below and above 500 meters. The mean age of two groups were 13.8 (±3.6) and 15.8 (±5.2) years, respectively. There was no significant difference between

Table IV. The Tissue Doppler Imaging Parameters Showing Significant Difference Between NYHA Functional Class II and III.

Tissue Doppler imaging parameters	NYHA functional class		p
	II	III	
Mitral septal E/Ea	0.11 (0.05-0.28)	0.14 (0.08-0.25)	0.050
Mitral lateral MPI	0.65 (0.27-1.51)	0.83 (0.51-2.41)	0.009
Tricuspid septal ET	229 (178-336)	205 (128-301)	0.039
IVS Ea	7.9 (3.37-18.5)	5.28 (3.4-9.22)	0.032
IVS Ea/Aa	1.6 (0.56-3.38)	1.16 (0.37-2.14)	0.042
IVS IVCT	58 (28-105)	83 (32-147)	0.039

Data are given as median (range)
ET: ejection time; IVCT; isovolumic contraction time; IVS; interventricular septum; MPI: myocardial performance index

two groups in terms of age. Parameters that were significantly different are shown in Table VI along with their p values.

We could not compare the data of the Tissue Doppler imaging with the right heart catheterization because the time period between performing and Tissue Doppler imaging was not short enough and because the patients were already started on various medications. However, we compared the Tissue Doppler imaging measurements with the simultaneously performed echocardiographic studies which measured the systolic pulmonary artery pressure from the of the jet of tricuspid valve insufficiency. Parameters showing correlation with the echocardiographically measured systolic pulmonary artery pressure and their correlation coefficient are listed in Table VII. Patients were divided into 2 groups according to the echocardiographically measured systolic pulmonary artery pressure, less (group 1) and more (group 2) than 70 mmHg. Mitral flow-IVRT and interventricular septum-IVRT were significantly higher in group 2 ($p=0.036$ and 0.030, respectively). Tricuspid septal AT was significantly less ($p=0.015$).

Discussion

Many studies regarding the importance of Tissue Doppler imaging in children diagnosed with pulmonary hypertension were recently published. In this study, we identified statistically significant associations in some Tissue Doppler imaging parameters used in the diagnosis and follow up of pulmonary hypertension patients. We think these parameters may be used in the future for diagnosis and follow up of these patients.

The effects of pulmonary hypertension etiology on Tissue Doppler imaging

In our study, most Tissue Doppler imaging parameters did not show significant difference between the idiopathic pulmonary hypertension and Eisenmenger syndrome groups. This shows that, even though the original etiology of pulmonary hypertension may be different, similar mechanisms affect the Tissue Doppler imaging parameters after developing pulmonary hypertension[3,4]. One study reported that Tissue Doppler imaging findings in ventricular septal defect or patent ductus arteriosus secondary to left ventricular volume expansion showed minimal differences from normal children[5]. Thus, we think that the abnormal Tissue Doppler imaging findings in Eisenmenger syndrome patients, seen in our study, are caused by the increased pulmonary pressure and changes secondary to it. The abnormalities in Tissue Doppler imaging parameters seen in Eisenmenger syndrome and idiopathic pulmonary hypertension may be explained by the following: the increased right ventricular pressure pushes the interventricular septum towards the left ventricule which leads to disorders in the early filling of the left ventricle. Another factor is the delay in opening the mitral valve, and thus delay in filling. Moreover, the decrease in right ventricle output leads to decreased left ventricle preload and thus, decreases left ventricle filling. However, as shown in Table III, patients with Eisenmenger syndrome had a high tricuspid A flow and a low E/A flow. This shows that the tricuspid flow measurements using the pulse wave are affected more in these patients than the primary pulmonary hypertension patients.

Table V. The Tissue Doppler Imaging Parameters Showing Significant Difference Between Two Groups According to Brain Natriuretic Peptide Levels.

Tissue Doppler imaging parameters	BNP levels		p
	≤ 100 pg/ml	>100 pg/ml	
Mitral lateral Ea/Aa	1.58 (0.51-2.8)	0.86 (0.27-2.16)	0.046
Tricuspid septal Ea	8.84 (4.7-11)	5.24 (3.05-11.2)	0.002
Tricuspid septal Ea/Aa	1.43 (0.52-2.22)	0.91 (0.3-1.26)	0.000
Tricuspid septal DT	79.8 (32-114)	51.2 (23-105)	0.020
Tricuspid septal E/Ea	0.08 (0.05-0.13)	0.15 (0.06-0.34)	0.006
Interventricular septum MPI	0.61 (0.34-1.0)	0.97 (0.55-1.3)	0.006

Data are given as median (range)
BNP: Brain natriuretic peptide; DT: decelaration time; MPI: myocardial performance index

Table VI. The Tissue Doppler Imaging Parameters Showing Significant Difference Between 2 Groups According to 6 Minute Walking Test Distance (meter).

Tissue Doppler imaging parameters	6MWT distance		p
	< 500 m	≥500 m	
Mitral lateral Ea	7.3 (5.24-15)	12.19 (5.6-17.4)	0.048
Mitral lateral DT	57(32-88)	77.9 (35-102)	0.006
Tricuspid septal E/Ea	0.105 (0.05-0.34)	0.06 (0.05-0.15)	0.016
Tricuspid lateral E/Ea	0.08 (0.05-0.35)	0.05 (0.04-0.12)	0.023
Interventricular septum Sa	4.36 (2.9-12.6)	5.35 (4.47-14.07)	0.036

Data are given as median (range)
6MWT: 6 minute walking tests

Idiopathic pulmonary hypertension patients had a higher interventricular septum Aa because the elastic recoil is higher in this patient group or because the increase in myocardial stiffness affects the interventricular septum more than in Eisenmenger syndrome.

The association between Tissue Doppler imaging and the systolic pulmonary artery pressure measured using tricuspid regurgitation velocity

The pulmonary artery pressure measured using Doppler echocardiography correlated with the pressure measured directly via invasive methods[6]. In our study, we found associations between some Tissue Doppler imaging parameters and the systolic pulmonary artery pressure calculated from the tricuspid regurgitation velocity using the echocardiography (sensitivity of 79-100% and a specificity of 60-98%). When significant correlations were investigated, the parameter with the strongest correlation with high systolic pulmonary artery pressure was the mitral septal annulus Aa. Even though, the use of these parameters to estimate the systolic pulmonary artery pressure measured by invasive methods are currently contraversial, we want to remark that high mitral septal annulus Aa levels could point to high pulmonary artery pressure. We think this parameter may be especially useful in patients who have got no tricuspid regurgitation, and thus cannot have their systolic pulmonary artery pressure measured by echo.

The association between Tissue Doppler imaging and NYHA functional class

In our study, we did not compare Tissue Doppler imaging parameters with mortality and hospital admission. Mitral lateral annulus MPI value, which reflects the left ventricle systolic and diastolic dysfunction, was significantly higher in NYHA functional class 3 compared to class II. No similar association was found in the literature. This finding is more significant than the association between the mitral lateral annulus MPI value in pulmonary hypertension patients and NYHA functional class, and thus it may be more valuable in predicting the

Table VII. The Tissue Doppler Imaging Parameters Showing Correlation with the Echocardiographically Measured Systolic Pulmonary Artery Pressure and their Correlation Coefficient.

Tissue Doppler imaging parameters	K	p
Mitral A velocity	-0.632	0.050
Mitral E velocity	0.700	0.024
Tricuspid AT	-0.726	0.017
Mitral septal Aa	0.843	0.002
Mitral septal IVRT	-0.632	0.050
Mitral septal ET	0.787	0.007
Tricuspid septal Sa	0.650	0.042
Tricuspid septal ET	0.699	0.024
Tricuspid lateral AT	-0.734	0.016
Tricuspid lateral IVCT	0.720	0.019

prognosis of pulmonary hypertension patients. In our study, mitral septal annulus E/Ea value was significantly higher in NYHA functional class III compared to class II. As in lateral mitral annulus MPI, increased septal mitral annulus E/Ea is also associated with bad prognosis.

The association between Tissue Doppler imaging and 6 minute walking tests

Some studies reported that a 6MWT result less than 250 m, 332 m or 300 m is associated with bad prognosis[7-9]. Whereas, 6MWT results above 500 m indicate that the clinical condition of the patient is stable[1]. Takatsuki et al.[10] reported that mitral Sa is associated with 6MWT in children with primary pulmonary arterial hypertension. However, they stated that there was no association between 6MWT and tricuspid and interventricular septum Sa values. In our study, comparing the 6MWT above and below 500 m we found that tricuspid septal and lateral E/Ea were higher in the 6MWT <500 m group. These findings show that E/Ea measured at the septal and lateral tricuspid annulus had the strongest correlation with exercise capacity estimated by 6MWT.

The association between Tissue Doppler imaging and brain natriuretic peptide

One study, conducted on adult pulmonary hypertension of various etiologies compared the Tissue Doppler imaging findings with serum BNP values, and it reported that E/Ea values measured at the tricuspid and mitral valves correlated with high NT-proBNP values and they reported that these values strongly reflect cardiac remodeling[11]. Takatsuki et al.[10] reported that there is a significant correlation between tricuspid Ea and E/Ea and BNP levels in pediatric patients with idiopathic pulmonary arterial hypertension. However, mitral annulus and septum Ea values showed no correlation with the Sa values obtained at all three regions or with BNP levels. In our study, we found that the Tissue Doppler imaging parameters are affected more in patients with BNP values >100 pg/ml compared to those ≤100 pg/ml. The fact that these parameters are associated with the ventricular filling pressure and the wall tension explains the association with the brain natriuretic peptide value, which is also associated with the ventricular filling pressure. Just like brain natriuretic peptide, the statistically significant parameters in high BNP levels group (tricuspid septal Ea, Ea/Aa, E/Ea and IVS MPI) may be used in follow up treatment in patients with ventricular failure.

One study comparing BNP levels and MPI values reported that patients having MPI levels >0.45 had significantly higher levels of brain natriuretic peptide than patients whose MPI <0.45, independent of the presence or the absence of left ventricle systolic dysfunction[12]. In our study, patients having BNP >100 pg/ml and those with BNP ≤100 pg/ml had similar tricuspid and mitral annulus MPI values. However, interventricular septum MPI values were significantly higher in patients with BNP >100 pg/ml (p=0.006). Moreover, in patients with higher BNP levels (>100 pg/ml), interventricular septum MPI was ≥0.55. Even though, evaluation of the interventricular septum MPI value is diffucult because it is affected by age and body weight, in patients with high BNP levels, interventricular septum MPI is more significant than mitral and tricuspid MPI values. Therefore, interventricular septum MPI can be used to evaluate the response to treatment. However, more studies are needed to support these data.

Myocardial performance index (MPI)

One study on pulmonary hypertension patients showed that left ventricle and right ventricle MPI values were high due to an increase in left ventricle-IVRT and right ventricle-IVRT[13]. One study found that MPI was more valuable than tricuspid annulus Aa/Ea in evaluating right ventricle dysfunction[14,15]. In our study, MPI values from all sites (tricuspid lateral and septal annulus, mitral lateral and septal annulus and interventricular septum) in the patient groups were significantly high. In the literature, there are different data about the relationship between MPI and age and other variables. Ishii et al.[16] showed that in healthy children right ventricle MPI does not change with age, whereas another study reported that MPI decreases during the first three years of life and later does not change[17]. Our study found that mitral and tricuspid annulus MPI values are not affected by age, weight and gender, whereas interventricular septum MPI value showed a positive correlation with age and weight. We state that mitral and tricuspid annulus MPI measurements are more practical in determining prognosis and in follow up of pulmonary hypertension patients.

Tissue Doppler imaging findings were significantly impaired in children with pulmonary hypertension than in the control group; Tissue Doppler imaging findings in patients with idiopathic pulmonary hypertension or Eisenmenger syndrome were similar; mitral lateral annulus MPI, mitral septal annulus E/Ea, interventricular septum Ea and interventricular septum Ea/Aa values may have a prognostic importance due to their significant associations with poor functional class. In addition, we would like to mention that due to the significant associations between mitral lateral annulus and tricuspid septal annulus Ea/Aa, tricuspid septal annulus E/Aa, interventricular septum MPI values and brain natriuretic peptide levels, these parameters may be used in the evaluation of the response to therapy. Tricuspid septal and lateral annulus E/Ea show better correlation with 6MWT and thus, with excercise capacity. We want to remark that high mitral septal annulus Aa levels could point to high pulmonary artery pressure. More studies regarding the importance of Tissue Doppler imaging need to be conducted on children with pulmonary hypertension.

REFERENCES

1. Galie N, Hoeper MM, Humbert M, et al. Guidelines for the diagnosis and treatment of pulmonary hypertension: the Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS), endorsed by the International Society of Heart and Lung Transplantation (ISHLT). Eur Heart J 2009; 30: 2493-2537.
2. Simonneau G, Gatzoulis MA, Adatia I, et al. Updated clinical classification of pulmonary hypertension. J Am Coll Cardiol 2013; 62: 34-41.
3. Yu CM, Sanderson JE, Chan S, Yeung L, Hung YT, Woo KS. Right ventricular diastolic dysfunction in heart failure. Circulation 1996; 93: 1509-1514.
4. Ozer N, Tokgozoglu L, Coplu L, Kes S. Echocardiographic evaluation of left and right ventricular diastolic function in patients with chronic obstructive pulmonary disease. J Am Soc Echocardiogr 2001; 14: 557-561.
5. Krowka MJ. Pulmonary hypertension: diagnostics and therapeutics. Mayo Clin Proc 2000; 75: 625-630.
6. McGoon M, Gutterman D, Steen V, et al. Screening, early detection, and diagnosis of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. Chest 2004; 126: 14S-34S.
7. Sitbon O, Humbert M, Nunes H, et al. Long-term intravenous epoprostenol infusion in primary pulmonary hypertension: prognostic factors and survival. J Am Coll Cardiol 2002; 40: 780-788.
8. Miyamoto S, Nagaya N, Satoh T, et al. Clinical correlates and prognostic significance of six-minute walk test in patients with primary pulmonary hypertension. Comparison with cardiopulmonary exercise testing. Am J Respir Crit Care Med 2000; 161: 487-492.
9. Paciocco G, Martinez FJ, Bossone E, Pielsticker E, Gillespie B, Rubenfire M. Oxygen desaturation on the six-minute walk test and mortality in untreated primary pulmonary hypertension. Eur Respir J 2001; 17: 647-652.
10. Takatsuki S, Nakayama T, Jone PN, et al. Tissue Doppler imaging predicts adverse outcome in children with idiopathic pulmonary arterial hypertension. J Pediatr 2012; 161: 1126-1131.
11. Andeeva Iu A, Saidova MA, Martyniuk TV, Masenko VP, Chazova IE. [Tissue myocardial Doppler echocardiographic evaluation of right ventricle function and the level of natriuretic peptides in patients with pulmonary hypertension of various etiologies]. Ter Arkh 2010; 82: 27-34.

12. Ono M, Tanabe K, Asanuma T, et al. Doppler echocardiography-derived index of myocardial performance (TEI index): comparison with brain natriuretic peptide levels in various heart disease. Jpn Circ J 2001; 65: 637-642.
13. Chang SM, Lin CC, Hsiao SH, et al. Pulmonary hypertension and left heart function: insights from tissue Doppler imaging and myocardial performance index. Echocardiography 2007; 24: 366-373.
14. Miyahara Y, Ikeda S, Yoshinaga T, et al. Echocardiographic evaluation of right cardiac function in patients with chronic pulmonary diseases. Jpn Heart J 2001; 42: 483-493.
15. Yamaguchi K, Miyahara Y, Yakabe K, et al. Right ventricular impairment in patients with chronic respiratory failure on home oxygen therapy--non-invasive assessment using a new Doppler index. J Int Med Res 1998; 26: 239-247.
16. Ishii M, Eto G, Tei C, et al. Quantitation of the global right ventricular function in children with normal heart and congenital heart disease: a right ventricular myocardial performance index. Pediatr Cardiol 2000; 21: 416-421.
17. Eto G, Ishii M, Tei C, Tsutsumi T, Akagi T, Kato H. Assessment of global left ventricular function in normal children and in children with dilated cardiomyopathy. J Am Soc Echocardiogr 1999; 12: 1058-1064.