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R-Wave Modified Tissue Doppler Imaging Myocardial Performance Index for the Assessment of Cardiac Function in Children with Congestive Heart Failure: A Feasibility Study

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: The aim of this study was to evaluate the feasibility of an R-wave modified tissue Doppler imaging (TDI) myocardial performance index (MPI), or MPI TDI-R, for the assessment of cardiac function in children with congestive heart failure (CHF).

Material/Methods: Forty children with CHF and 40 normal children were evaluated using the modified pediatric Ross heart failure grading system. TDI recorded the spectrum of diastolic function at the mitral valve annulus to measure the MPI. Twelve-lead electrocardiogram (ECG) measured the R-wave in the QRS complex, resulting in the modified MPI TDI-R. Correlation between the MPI TDI-R, other echocardiographic indices, and the Ross heart failure grades were analyzed, with reproducibility analysis.

Results: Compared with normal children, the MPI TDI and MPI TDI-R were significantly increased in the pediatric CHF group (P<0.01). The MPI TDI-R was significantly correlated with other indices of cardiac function and Ross grading for CHF in children (r=0.769). The MPI TDI-R showed good correlation with the findings of the MPI TDI, calculated by traditional methods. Receiver-operating characteristic (ROC) curve analysis showed that the MPI TDI-R had a sensitivity of 67.5%, and a specificity of 97.5%. The reproducibility of the MPI TDI-R was confirmed to be superior when compared with the non-modified MPI TDI.

Conclusions: This feasibility study showed that the modified MPI TDI-R, formed by combining the MPI TDI with synchronous surface ECG measurements, was simple to perform, reproducible, and provided a specific index for the assessment of cardiac function in children with CHF.

MeSH Keywords: Child • Diagnosis • Echocardiography, Doppler • Electrocardiography • Heart Failure

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Background

The myocardial performance index (MPI), also known as the Tei index, is used in tissue Doppler imaging (TDI) of cardiac function and is usually combined with the use of the 12-lead electrocardiogram (ECG). The MPI TDI is a comprehensive indicator of global or combined systolic and diastolic myocardial function [1,2]. Traditionally, the MPI has been calculated from the pulsed-wave (PW) Doppler recordings of blood velocity waveforms across the mitral valve, and across the left ventricular outflow tract.

On the mitral valve flow spectrum, the time interval of the endpoint of the A-peak to the onset of the E-peak is measured and defined as the time interval, which includes the isovolumetric contraction time (ICT), the ejection time (ET), and the isovolumetric relaxation time (IRT). On imaging of the left ventricular outflow spectrum, the time interval is measured from the onset to the end of the S-peak and is defined as the B-time interval. The MPI can also be derived from imaging recordings of myocardial wall motion during a cardiac cycle using TDI. The cardiac imaging method of TDI has become the most widely used method of quantitative and qualitative evaluation of cardiac function in patients with heart failure, with high sensitivity, ease of performance, and high reproducibility [3,4].

However, in our experience, the application of TDI has shown that the endpoint of the peak late A-wave (peak late diastolic velocity) can be difficult to identify, and measurement of this late diastolic endpoint was subject to observer error between different examiners, which could affect the reporting accuracy of the peak late A-wave time interval, as well as the resulting MPI. Therefore, it is possible that the synchronous use of surface electrocardiography (ECG) examination could be a used to modify MPI TDI by substituting the endpoint of the late diastolic peak late A-wave in TDI by using the measurement of the R-wave in the QRS complex using surface ECG.

The R-wave modified MPI TDI, or MPI TDI-R, was evaluated for the first time in this feasibility study in the assessment of cardiac function in children with congestive heart failure (CHF).

Material and Methods

Children studied and clinical data

This feasibility study included 40 children with congestive heart failure (CHF), who were recruited to the study, between July 2015 to July 2017, in the Nanjing Children's Hospital, China. There were 40 healthy children who were recruited as the normal control group. This study was approved by the local Ethics Committee of the Nanjing Childrens Hospital, China. All participants included in the study has signed written informed consent to participate in the study, provided by their parents or guardians. All study participants underwent a detailed clinical history and physical examination, including an electrocardiogram (ECG), echocardiogram, and laboratory tests for levels of myocardial enzymes, cardiac troponin, and brain natriuretic peptide (BNP) [5].

The CHF group included 22 male and 18 female infants and children, aged from 2 months to 144 months (mean, 57.9±36.9 months); the mean weight was 18.0±8.8 kg; the mean heart rate was 90.1±9.6 beats/min. In the CHF group, ten children were diagnosed with dilated cardiomyopathy, two children were diagnosed with noncompaction of the ventricular myocardium, 11 children were diagnosed with congenital heart disease, ten children had a history of previous corrective surgery for congenital heart disease, and seven children had a previous history of myocarditis.

The healthy, or control, group included 25 male and 15 female infants and children, aged from 8 months to 130 months (mean, 55.6±20.8 months); the mean weight was 19.0±6.8 kg; the mean heart rate was 91.3±10.3 beats/min. There were no significant differences in terms of age, weight, gender, or heart rate between the normal group and the CHF group (P>0.05), which indicated that the two groups were comparable in this study (Table 1).

Table 1. Clinical data of all children in congestive heart failure (CHF) group and healthy group.

	CHF group (n=40)	Healthy group (n=40)	χ^2/t	*P*
Gender (n)				
Male	22	25	0.46	0.50
Female	18	15		
Age (months)	57.9±36.9	55.6±20.8	0.34	0.73
Weight (kg)	18.0±8.8	19.0±6.8	0.57	0.57
Heart rate (beats/min)	90.1±9.6	91.3±10.3	0.54	0.59

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The revised Ross classification for heart failure in children

The revised Ross classification for heart failure in children was used to grade cardiac function both study groups [6]. Children were divided into the normal (or non-CHF) group (grade 0–2, Class 0); the mild CHF group (grade 3–6, Class 1); the moderate CHF group (grade 7–9, Class 2); and the severe CHF group (grade 10–12, Class 3) [6]. The study included 40 cases of Ross Class 0; nine cases of Ross Class 1; 23 cases of Ross Class 2; and eight cases of Ross Class 3.

Doppler echocardiography and surface electrocardiogram (ECG)

Doppler echocardiography was performed using a Philips iE33 quantitative echocardiography system (Philips, Eindhoven, Netherlands) with an S5-1 or S8-3 transducer and a scanning speed of 100 mm/sec. Imaging was performed in the left lateral position according to children's age and acoustic conditions. All subjects were imaged in the supine position or the left lateral position in a quiet environment. Children who could not remain still during the procedure were given 5% chloral hydrate syrup (at a dose of 1 ml/kg) orally, or per rectum.

During imaging, synchronous body surface electrocardiography (ECG) was performed. Compact discs (CDs) were used to store the imaging data for analysis. After conventional echocardiography, cardiac imaging parameters were measured during three cardiac cycles, with the mean value recorded. The left ventricular ejection fraction (LVEF) and the left ventricular fractional shortening (LVFS) were investigated using M-mode echocardiography using the parasternal long axis view.

Measurement of the tissue Doppler imaging myocardial performance index (TDI MPI) and the R-wave modified tissue Doppler imaging myocardial performance index (MPI TDI-R)

Pulsed-wave tissue Doppler imaging (TDI) was performed from the cardiac apical four-chamber view by imaging the sample volume at the tip of the mitral valve leaflets to record the mitral inflow velocity pattern. The left ventricular outflow was measured using Doppler imaging with the sample volume positioned above the aortic valve.

The pulse wave (PW) myocardial performance index (MPI)=(a–b)/b according to standard Doppler quantitation principles.

Pulsed-wave TDI velocities were obtained in the apical four-chamber view with the sample volume measured at the lateral mitral valve annulus, on the left ventricular free wall. The Doppler beam was aligned as parallel as possible to the direction of the maximum annular motion, to obtain the optimum

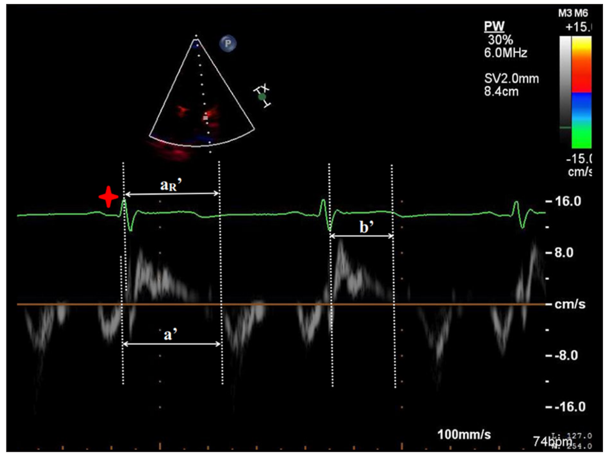

Figure 1. Doppler ultrasound mapping of the motion of the cardiac mitral valve annulus and the R-wave modified tissue Doppler imaging myocardial performance index (MPI TDI-R). The volume of the left ventricle (LV) free wall. The mitral valve flow spectrum includes the time interval of the endpoint of peak A to the onset of peak E, which is measured and defined as the time interval, which includes isovolumetric contraction time (ICT), ejection time (ET) and isovolumetric relaxation time (IRT). The myocardial performance index (MPI)=(ICT+IRT)/ET=(a–b)/b. The R-wave modified tissue Doppler imaging (TDI) myocardial performance index (MPI) or MPI TDI-R=(aR–b)/b. TDI – tissue Doppler imaging; MPI – myocardial performance index; LV – left ventricle; ICT – isovolumetric contraction time; ET – ejection time; MPI TDI – tissue Doppler imaging myocardial performance index; MPI TDI-R – R-wave modified tissue Doppler imaging myocardial performance index.

spectrum of TDI from the motion of the mitral valve annulus (Figure 1). The 'a' component was measured from the trailing edge of the A-wave to the leading edge of the subsequent E-wave. The 'b' component was measured from the leading edge to the trailing edge of the S-wave with the calculation of the MPI TDI=(a–b)/b.

The surface ECG changes were synchronously recorded. The time interval from the top of the R-wave was recorded, as the starting point of the isovolumetric contraction phase, to the subsequent onset of the E-wave, defined as the 'aR' component. The calculation of the R-wave modified MPI TDI-R=(aR–b)/b.

Reproducibility analysis

To analyze the reproducibility of the new index, MPI TDI-R, a total of 12 patients were randomly identified, and for each, the MPI TDI and MPI TDI-R were measured and compared. The mean percentage intra-observer and inter-observer error were calculated.

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Table 2. Comparison of cardiac function indexes between normal group and heart failure group.

	Groups		Average (n=80)	*P* values
	Normal group (n=40)	CHF group (n=40)		
EF	(67.8±2.9)%	(58.8±12.8)%	(63.3±10.3)%	P<0.01**
ICT	(51.6±15.1) ms	(64.2±19.5) ms	(57.9±18.5) ms	P<0.01**
IRT	(42.5±11.5) ms	(57.2±22.9) ms	(49.9±19.5) ms	P<0.01**
ET	(268.9±20.7) ms	(248.5±44.2) ms	(258.7±35.8) ms	P<0.01**
MPID	0.23±0.06	0.37±0.19	0.30±0.16	P<0.01**
MPI_{TDI}	0.35±0.07	0.53±0.21	0.44±0.18	P<0.01**
ICT_{TDI-R}	(38.7±12.5) ms	(53.9±21.3) ms	(46.3±19.0) ms	P<0.01**
MPI_{TDI-R}	0.30±0.06	0.48±0.19	0.39±0.17	P<0.01**

* *P*<0.05; ***P*<0.01.

Statistical analysis

The data were analyzed using SPSS version 19.0 software (SPSS, IBM, Chicago, IL, USA). All quantitative data were expressed as the mean ± standard deviation (SD). Comparison between groups was performed using one-way analysis of variance (ANOVA), followed by the least significant difference (LSD) post hoc test. Linear regression analysis was used to analyze the associations between cardiac function indicators. The relationship between MPI TDI-R and the grades used in the revised Ross classification for heart failure in children was assessed using Spearman's nonparametric correlation coefficient. P-values <0.05 were considered statistically significant.

Results

Comparison of the indices of cardiac function between the normal group and the group with congestive heart failure (CHF)

Compared with the normal group, the left ventricular ejection fraction (LVEF) and the left ventricular fractional shortening (LVFS) were decreased in the CHF group. The isovolumetric contraction time (ICT), the isovolumetric relaxation time (IRT), the myocardial performance index (MPI), the tissue Doppler imaging myocardial performance index (MPI TDI), and the R-wave modified tissue Doppler imaging myocardial performance index (MPI TDI-R) were all significantly increased in the CHD group (P<0.01) (Table 2).

Correlation between the the R-wave modified tissue Doppler imaging myocardial performance index (MPI TDI-R) with other indices of cardiac function

The findings using the MPI TDI-R correlated well with other cardiac function parameters, including the LVEF (r=–0.680), LVFS (r=–0.657), ICT (r=0.314), and IRT (r=0.677), respectively). The results from the MPI TDI-R were significantly correlated with the classic MPI (r=0.820), and the MPI TDI (r=0.844) (Figures 2, 3).

The modified parameters of the MPI TDI-R also correlated well with classic parameters. The modified isovolumetric contraction time (ICT) TDI-R was less than ICT (Table 3). There was also a positive correlation between the MPI TDI-R with Ross pediatric heart failure grades (r=0.769, P<0.01) (Figure 4). Demographic data of modified Ross cardiac function classification in all 80 study participants are shown in Table 4, which shows the differences in the modified index (MPI TDI-R) for children with different degrees of CHD. These results suggested that the MPI TDI-R could provide a more accurate assessment of cardiac function in children with CHF, compared with the parameters of LVEF, ICT, IRT, and MPI TDI, respectively.

Comparison of the receiver-operating characteristic (ROC) curve for MPI TDI and MPI TDI-R

The receiver-operating characteristic (ROC) curves were created for the findings of the MPI TDI and MPI TDI-R in the diagnosis of CHF. The area under the curve (AUC) for MPI TDI was 0.833 (95% CI, 0.745–0.921). The AUC for MPI TDI-R was 0.862 (95% CI, 0.778–0.946). When the cutoff value was 0.395 according to ROC curve analysis, the MPI TDI-R resulted in its highest sensitivity value (67.5%) and specificity (97.5%) (Figure 5).

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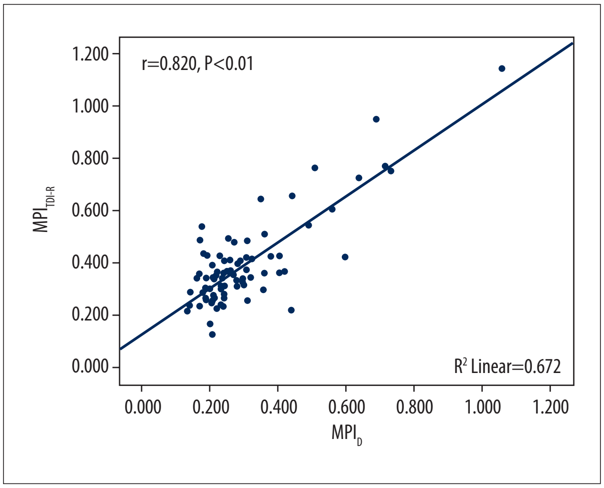

Figure 2. Comparison between the diameter as measured by the R-wave modified tissue Doppler imaging myocardial performance index (MPI TDI-R), with the classic or standard tissue Doppler imaging myocardial performance index (MPI TDI) diameter. TDI – tissue Doppler imaging; MPI – myocardial performance index; LV – left ventricle; ICT – isovolumetric contraction time; ET – ejection time; MPI TDI – tissue Doppler imaging myocardial performance index; MPI TDI-R – R-wave modified tissue Doppler imaging myocardial performance index.

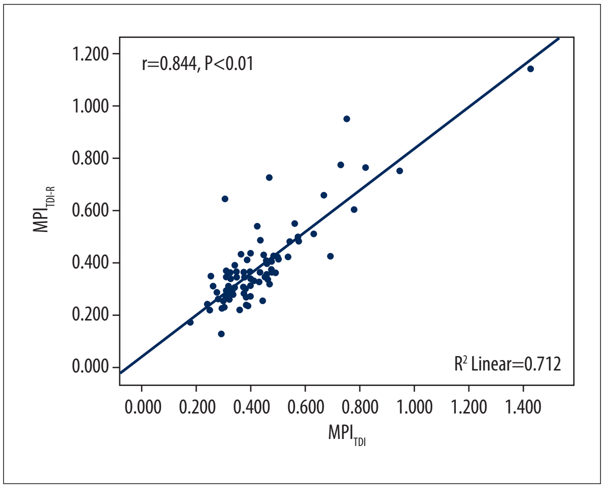

Figure 3. Comparison between the diameter as measured by the R-wave modified tissue Doppler imaging myocardial performance index (MPI TDI-R) with the classic or standard modified tissue Doppler imaging myocardial performance index (MPI TDI). TDI – tissue Doppler imaging; MPI – myocardial performance index; LV – left ventricle; ICT – isovolumetric contraction time; ET – ejection time; MPI TDI – tissue Doppler imaging myocardial performance index; MPI TDI-R – R-wave modified tissue Doppler imaging myocardial performance index.

Table 3. Correlation between MPI_{TDI-R} with other cardiac function indexes.

Cardiac function parameters	Percentage difference* (%)	Correlation coefficient (r)	*P* values
a & aR’	7.1±4.9	0.780	<0.01**
a’ & aR’	5.8±4.3	0.839	<0.01**
ICT & ICT_{TDI-R}	40.4±29.6	0.309	<0.01**
MPID & MP_{TDI-R}	18.6±16.5	0.890	<0.01**
MPITDI & MPI_{TDI-R}	20.3±15.3	0.844	<0.01**

* Percentage difference between cardiac function parameters before and after modified. Computational formula=Absolute value of the difference of the parameter before and after modified/Mean value of the parameter before and after modified.

Reproducibility analysis for MPI TDI and MPI TDI-R

The reproducibility of the new index, MPI TDI-R, was compared with the MPI TDI and analyzed in 12 children with CHF who underwent Doppler imaging. The intra-observer mean percentage error for the MPI TDI and MPI TDI-R were (3.3±2.3%) and (2.5±2.3%), respectively. The inter-observer mean percentage error for the MPI TDI and MPI TDI-R were (5.0±3.3%) and (3.5±1.8%), respectively, with significant differences between MPI TDI and MPI TDI-R in the intra-observer and inter-observer mean percentage errors, respectively (P<0.05).

Discussion

The R-wave modified tissue Doppler imaging myocardial performance index (MPI TDI-R) was evaluated for the first time in this feasibility study. The findings showed that the modified MPI TDI-R, formed by combining the standard MPI TDI with synchronous surface electrocardiogram (ECG) measurements, was simple to perform, reproducible, and provided a specific index for the assessment of cardiac function in children congestive heart failure (CHF).

The condition of CHF in children has a complex pathophysiology and is most commonly due to congenital heart disease. The appropriate evaluation of cardiac function is key to making

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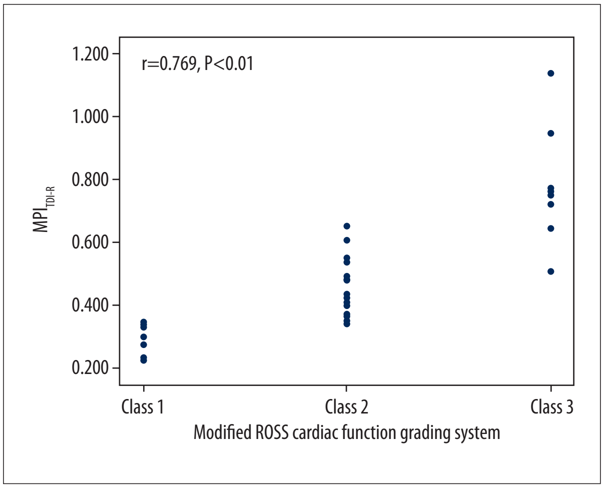

Figure 4. Scatter diagram to compare the findings of the R-wave modified tissue Doppler imaging myocardial performance index (MPI TDI-R) with the clinical Ross grades used to classify heart failure in children [6]. TDI – tissue Doppler imaging; MPI – myocardial performance index; LV – left ventricle; ICT – isovolumetric contraction time; ET – ejection time; MPI TDI – tissue Doppler imaging myocardial performance index; MPI TDI-R – R-wave modified tissue Doppler imaging myocardial performance index.

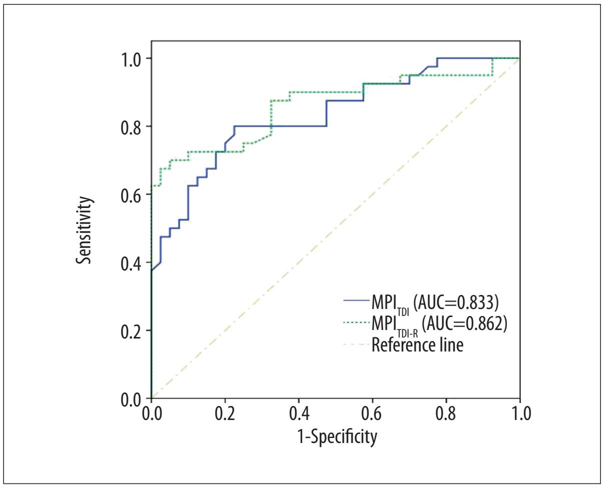

Figure 5. Comparison of receiver-operating characteristic (ROC) curve characteristics for the tissue Doppler imaging myocardial performance index (MPI TDI) with the R-wave modified tissue Doppler imaging myocardial performance index (MPI TDI-R). The area under the curve (AUC), for the receiver-operating characteristic (ROC) curves, are shown in parentheses. TDI – tissue Doppler imaging; MPI – myocardial performance index; LV – left ventricle; ICT – isovolumetric contraction time; ET – ejection time; ROC – receiver-operating characteristic; AUC – area under the curve; MPI TDI – tissue Doppler imaging myocardial performance index; MPI TDI-R – R-wave modified tissue Doppler imaging myocardial performance index.

Table 4. Comparison of MPI_{TDI} and MPI_{TDI-R} between different grades of heart failure by modified ROSS classification.

Modified ROSS classification	Cases	MPI_{TDI} (range)		MPI_{TDI-R} (range)	
Non-CHF (class 0)	40	0.35±0.07	(0.18~0.49)	0.30±0.06	(0.13~0.41)
Mild-CHF (class 1)	9	0.37±0.06	(0.30~0.46)	0.31±0.05	(0.22~0.35)
Moderate-CHF (class 2)	23	0.51±0.10	(0.35~0.78)**	0.45±0.08	(0.34~0.65)*
Severe-CHF (class 3)	8	0.76±0.34	(0.30~1.43)	0.78±0.19	(0.51~1.14)#

* P<0.01, compared with Mild-CHF (class 1) values; # P<0.01, compared with Moderate-CHF (class 2) values.

the best treatment decisions for children with CHD [7]. Cardiac catheterization is considered to be the gold standard diagnostic method in many cases of CHD, but this method is invasive [8,9]. The combined use of cardiac tissue Doppler imaging (TDI) and the myocardial performance index (MPI) is a diagnostic modality that can quantify the indices of both systolic and diastolic ventricular function, and is a simple and noninvasive measurement method, which has good correlations with other invasive and noninvasive methods of diagnosing cardiac function [10]. The use of the MPI with TDI has been used to evaluate a variety of cardiac diseases in children and adults [11,12]. Studies have shown that TDI is less influenced by the heart rate, cardiac preload, and vascular regurgitation when compared with the combined pressure wave (PW) and MPI [13], and correlated better with the findings from cardiac catheterization [10].

The present study evaluated the MPI TDI and compared the findings with the modified MPI TDI-R, formed by combining the MPI TDI with synchronous surface ECG measurements. In TDI, the start of the isovolumetric contraction time (ICT) in the imaging spectrum to the vertex of the R-wave crest of the QRS complex measured by synchronous surface ECG, also represented the start of isovolumetric contraction phase. It might be possible to speculate that the new or modified index, MPI TDI-R has the potential to be more accurate than MPI TDI because the R wave vertex is easier to recognize. In 2015, in a study by Besli et al., the MPI and the use of the pre-ejection period (PEP)-derived MPI, also combined MPI TDI with synchronous ECG monitoring, to evaluate patients in sinus rhythm with hypertensive heart disease, and showed that their modified method could be used in conjunction with, or instead of, the MPI TDI in these patients [14].

From the findings of the present study, children with CHF had reduced cardiac function parameters detected by TDI that included reduced left ventricular ejection fraction (LVEF), left ventricular fractional shortening (LVFS), and ejection time (ET), and increased MPI TDI and MPI TDI-R. The findings in children with CHF probably affected both ventricular systolic and diastolic dysfunction as has been previously shown [15]. In this study, receiver-operating characteristic (ROC) curve analysis showed that the MPI TDI-R had a sensitivity of 67.5%, and a specificity of 97.5%, which was better than for MPI TDI.

Currently, the clinical diagnostic criteria for pediatric heart failure are based on the revised Ross classification for heart failure in children, which was used in the present study [6]. Also, some laboratory tests can be useful diagnostic markers for heart failure, including plasma brain natriuretic peptide (BNP), but these plasma markers have a low diagnostic sensitivity. In the present study, the myocardial performance index (MPI) was combined with TDI and the use of the Ross classification for heart failure in children. The findings from the modified MPI TDI-R were significantly correlated with the modified Ross cardiac function grading (r=0.781), which was a greater association than for MPI TDI (r=0.587). For the more severe degrees of heart failure in three groups, the MPI TDI-R values showed a significant difference (P<0.01) indicating greater diagnostic ability, However, for children without heart failure and with mild heart failure, both MPI TDI-R and MPI TDI were similar. Harjai et al. found that the MPI >1.14 was a strong and independent indicator of heart failure due to any cause, and was also associated with an increased risk of mortality, which was a better predictor than LVEF or other commonly used indicators of cardiac function [16].

This study was a small feasibility study and had several limitations. The small number of patients studied, and the fact that the study was performed at a single center could have introduced study bias. Also, the relationship with laboratory indices of childhood CHF, including BNP, N terminal-pro BNP (NT-Pro BNP) and the use of other clinical diagnostic criteria or classification systems for grading heart failure requires further study.

Conclusions

The R-wave modified tissue Doppler imaging myocardial performance index, MPI TDI-R, was evaluated for the first time for the assessment of cardiac function in children with congestive heart failure (CHF) in this feasibility study. The findings showed that the MPI TDI-R was a simple technique to learn and use, had good reproducibility, and was more accurate when compared with traditional MPI TDI method. Further large-scale controlled studies are required to support these initial study findings.

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