Original Article
Application of the Tei index in neonates with perinatal asphyxia

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Abstract: The aim of this study was to assess myocardial performance by using tissue Doppler imaging (TDI) and to correlate the Tei index with cardiac enzymatic change in infants with perinatal asphyxia. Twenty moderate asphyxiated, twenty severe asphyxiated, and thirty nonasphyxiated term infants were investigated. Serum cardiac troponin I (cTnI) and creatine kinase-myocardial band (CK-MB) levels were measured between 12 and 48 h of life. Conventional two-dimensional Doppler echocardiography and TDI were done during the first week of life. Serum CK-MB levels were significant differences (P<0.05), but serum cTnI levels were not (P>0.05) between the asphyxiated neonates and controls. Right ventricular (RV) and left ventricular (LV) Tei indexes were significantly higher in asphyxiated neonates and the levels of serum CK-MB were significantly higher in asphyxiated neonates. In the ROC, The LV Tei index and RV Tei index were higher in asphyxiated infants than the control group. In the existence of serum cTnI, the CK-MB correlated positively with the RV Tei index (r = 0.66, P<0.001) and the LV Tei index (r = 0.61, P<0.001). On the other hand, FS did not correlate with serum cTnT concentrations (r = -0.29, P = 0.07). This indicates a high sensitivity of TDI correlate with cardiac enzymatic in detecting myocardial damage inasphyxiated infants.

Keywords: Tissue Doppler imaging, Tei index, neonates, perinatal asphyxia

Introduction

Perinatal asphyxia (PA) or neonatal hypoxia-ischemia is one of the main reasons of morbidity and mortality in newborn infants. Hypoxia causes acidosis and ischemia leading to irreversible organ damage, especially myocardial function [1, 2]. Thus, detecting myocardial injury is a useful tool to predict the mortality and morbidity in infants with perinatal asphyxia [3]. However, the current clinical assessment alone is inadequate to guide management or predict outcome.

In recent years, some studies have shown the significance of cardiac enzymes to assess myocardial injury, such as serum creatine kinase-myocardial band (CK-MB) and cardiac troponin I (cTnI) [4]. Cardiac troponin I (cTnI) is a protein component of the tropomyosin complex involved in regulating cardiac muscle contractility [5]. Creatine kinase-myocardial band (CK-MB) is another cardiac biomarker that has been reported to increase with exercise or chest pain in humans [6]. They have been reported as prognostic factors to determine the level of cardiac damage frequently [7]. Tissue Doppler imaging (TDI) is a relatively new echocardiographic technique that provides quantitative information for the assessment of myocardial function. TDI gives direct information about ventricular systolic and diastolic functions [8, 9]. Moreover, the Tei index may be a more effective for analysis of global cardiac dysfunction than systolic or diastolic measures alone. The Tei index, a Doppler-derived time interval index that combines both systolic and diastolic cardiac performances, is easily derived using Doppler mitral valve inflow and aortic outflow velocities [10]. Moreover, left ventricle Tei index and right ventricle Tei index are parameters of evaluating systolic and diastolic functions of ventricles, respectively. With TDI, the Tei index can be determined from myocardial velocities despite limited two-dimensional (2D) acoustic windows and may be more accurate in pediatric patients because it is less altered by heart rate

Table 1. LV systolic and diastolic parameters in patients and controls

	Group I (n = 20)	Group II (n = 20)	Group III (n = 30)	P_1	P_2
EF (%)	69.8 ± 3.9	72.6 ± 3.2	74.7 ± 2.5	<0.01	<0.05
FS (%)	34.8 ± 4.1	38.2 ± 3.3	41.8 ± 2.5	<0.05	<0.05
Mitral E/A	1.05 ± 0.2	1.23 ± 0.24	1.35 ± 0.25	>0.05	>0.05
DT (ms)	87.3 ± 17.5	91.9 ± 18.6	110.5 ± 11.2	>0.05	<0.01

Note: P_1 comparison between groups 1 & 2; P_2 comparison between groups 2 & 3. EF: ejection fraction, FS: Fractional shortening, E/A: The ratio of early to late peak velocities, DT: Deceleration time.

variability [11]. However, little information is available on the value of TDI in diagnosing myocardial dysfunction in neonates with perinatal asphyxia.

Therefore, the aim of the study is to investigate the myocardial function by using tissue Doppler imaging and to correlate the Tei index with cardiac enzymatic change in infants with perinatal asphyxia.

Methods

Study design

This prospective study was carried out from Jan 2013 to December 2013 and was approved by the Ethics Committee of the Zhengzhou city maternal and child health care. A total of 70 term newborns (gestational age between 32 and 36 weeks) were consecutively enrolled. All the babies were born in the tertiary Obstetrics Clinic of Zhengzhou city maternal and child health care, and the parents gave written informed consent for their children's participation in the study. Seventy newborns were classified into three groups: Group I: Twenty neonates with mean gestational (10 males and 10 females); Group II: Twenty neonates with severe asphyxia (10 males and 10 females); Group III (control group): Thirty healthy neonates without asphyxia (16 males and 14 females).

Blood gas analysis, serum cTnI and serum CK-MB were evaluated at first week in patients and in controls. To measure cTnI and CK-MB in serum, STAT Immunoassay (Siemens Diagnostics, Germany), ECLIA Immunoassay (Boehringer Mannheim, Canada), Konelab autoanalysis (Konelab, Finland) and Triage Test (Biosite, USA) were used, and the cutoff values for the

diagnosis of myocardial damage were 0.4 ng/mL and 4.3 ng/mL respectively.

Echocardiography together with TDI was performed at first week in patients and in controls. Echocardiographic studies were performed on 'Vivid i' (GE) ultrasound system, using 3-7 MHz transducers. Tissue Doppler measurements were performed according to previously defined parameters, on basal segments of interventricular septum, left ventricular (LV) lateral wall and right ventricular (RV) basal free wall, by setting the TDI mode [9, 12-14].

Left ventricular measurements were obtained at end-systole and end diastole according to the recommendation of the American society of echocardiography. Left ventricular end-systolic and end-diastolic diameters and volumes (LVESD, LVESV, LVEDD, and LVEDV) were computed using the Simpson rule. Left ventricular ejection fraction was calculated as: % EF = (EDV-ESV)/EDV. Left ventricular fractional shortening was calculated as: % FS = (EDD-BSD)/EDD. Peak velocities of early (E) and late (A) filling were derived from atrioventricular valve inflow velocity profiles. The ratio of early to late peak velocities (E/A) was calculated. Deceleration time (DT) was measured as the time from peak b velocity to the intercept of the deceleration of flow with the baseline.

Measurement of myocardial Tei index

Doppler time intervals were measured from the atrioventricular valve inflow and ventricular outflow tracings [15]. The intervals (a) between the end of the late diastolic annular velocity and the onset of the early diastolic annular velocity were equal to the sum of the isovolumetric contraction time (ICT), isovolumetric relaxation time (IRT), and ejection time (ET). The ET (b) was measured as the duration of the systolic annular velocity. The sum of the ICT and IRT was obtained by subtracting b from a. Then the LV Tei and RV Tei indexes were calculated as (a-b)/b. The IRT was measured from the pulsed-wave Doppler tissue recordings as the time interval from the end of the systolic annular velocity to the onset of the early diastolic annu-

Table 2. Serum cardiac enzymes levels in the studied group

	Group I (n = 20)	Group II (n = 20)	Group III (n = 30)	P_1	P_2	P_3
cTnI (ng/mL)	0.26 ± 0.2	0.18± 0.13	0.1 ± 0.11	>0.05	>0.05	<0.01
CK-MB (ng/mL)	86.8 ± 58.9	22.8 ± 9.3	12.9 ± 18.5	<0.05	<0.01	<0.01

Note: P_1 comparison between groups 1 & 2; P_2 comparison between groups 2 & 3; P_3 comparison between groups 1 & 3. cTnI: cardiac troponin I, CK-MB: Creatine kinase-myocardial band.

Table 3. Myocardial time intervals (ms) in patients and controls

	Group I (n = 20)	Group II (n = 20)	Group III (n = 30)	P_1	P_2	P_3
LV ICT	50.2 ± 12.6	45.6 ± 6.3	44.1 ± 5.6	>0.05	>0.05	>0.05
RV ICT	50.5 ± 9.3	46.8 ± 10	44.5 ± 4.9	>0.05	>0.05	>0.05
LV IRT	51.6 ± 10.4	42.5 ± 6.1	42.2 ± 3.3	<0.01	<0.05	<0.01
RV IRT	47.2 ± 6.3	41.6 ± 5.8	40.5 ± 3.4	<0.01	>0.05	<0.01
LV ET	152.4 ± 20.7	156.72 ± 15.1	187.9 ± 15.1	>0.05	<0.01	<0.05
RV ET	156.8 ± 21.9	152.9 ± 21.5	179.8 ± 13.8	>0.05	<0.05	<0.05
LV Tei index	0.68 ± 0.2	0.56 ± 0.11	0.46 ± 0.04	>0.05	<0.05	<0.01
RV Tei index	0.64 ± 0.17	0.6 ± 0.22	0.46 ± 0.06	>0.05	<0.05	<0.01

Note: P_1 comparison between groups 1 & 2; P_2 comparison between groups 2 & 3; P_3 comparison between groups 1 & 3. LV ICT: Left ventricular isovolumetric contraction time, RV ICT: Right ventricular isovolumetric contraction time, LV IRT: Left ventricular isovolumetric relaxation time, RV IRT: Right ventricular isovolumetric relaxation time, LV ET: Left ventricular ejection time, RV ET: Right ventricular ejection time.

Table 4. Diagnostic value of different markers of myocardial dysfunction

	Cutoff value	Sensitivity (%)	Specificity (%)	AUC
cTnI	0.08	85	95	0.982
CK-MB	0.06	90	85	0.984
LV Tei index	0.46	95	95	0.991
RV Tei index	0.34	100	90	0.989

Note: AUC means Area under the ROC curve. cTnI: cardiac troponin I, CK-MB: Creatine kinase-myocardial band, LV ET: Left ventricular ejection time, RV ET: Right ventricular ejection time.

lar velocity and the ICT was obtained by subtracting the IRT from (a-b).

Statistical analysis

Continuous unrelated variables were compared by t-tests, One-Way Analysis-Of-Variance (ANOVA) tests with Fisher's Least Significant Difference (LSD) for post-hoc pair-wise comparisons and independent samples Kruskal-Wallis tests with pair-wise post-hoc tests. Categorical data were compared by Chi-square tests. Variance analyses, paired sample t-tests and

Fridman test for repeated measurements were used for related variables. The diagnostic utility and cutoff values of different markers of myocardial dysfunction were determined using receiver operating characteristic (ROC) curves.

Results

LV systolic and diastolic parameters in patients and controls are presented in **Table 1**. There were significant differences between the group I and II (69.8% vs. 72.6% and 34.8% vs. 38.2% with P<0.01 and P<0.05, respectively) in the terms of LV EF and FS. In addition, LV EF, FS and DT were significantly different between the group II and III (72.6% vs. 74.7%, 38.2% vs. 41.8% and 91.9 ms vs. 110.5 ms with P<0.05, P<0.05 and P<0.01, respectively).

In the Blood gas analysis, the result was shown in **Table 2**. Serum cTnI levels and serum CK-MB levels were normal (0.1 ng/mL and 12.9 ng/mL) in the group III. Serum cTnI level of group I and II was high (0.26 ng/mL and 0.18 ng/mL, respectively) according to manufacturer's cutoff values, and the differences of serum cTnI levels were not significant (P>0.05) between group I and II. However, serum CK-MB levels were still high (86.8 and 22.8 ng/mL, respectively) in the group I and II, and they were significant differences (P<0.05) between group I and II.

Myocardial time intervals in patients and controls were presented in **Table 3**. IRT at all segments together with ICT were the highest in the group I and group II. ET values were significantly the lowest and Tei indexes were significantly highest at all segments in the group I and group II at first week in patients than in controls.

Table 4 shows the cutoff values, sensitivity, specificity, and area under ROC curves for dif-
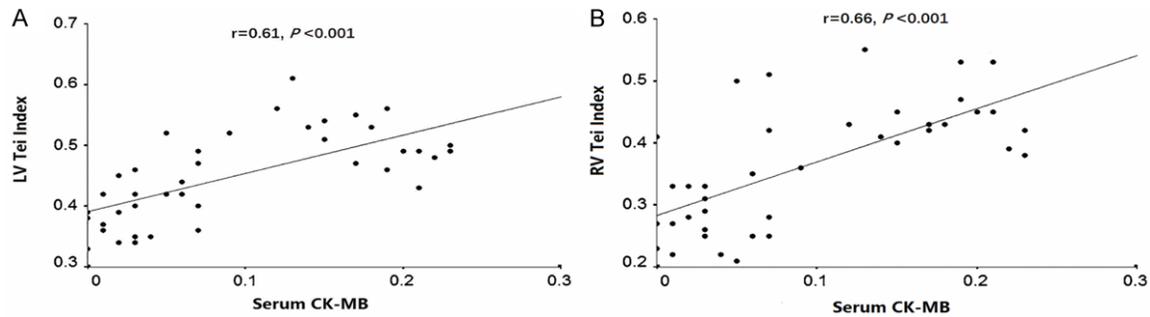
Figure 1. Correlations between Tei indexes findings and serum CK-MB in the existence of serum cTnI using Spearman's correlation coefficient.

ferent markers of myocardial dysfunction. The LV and RV MPI had the highest diagnostic value compared to cTnI and CK-MB.

The LV Tei index and RV Tei index were higher in asphyxiated infants than the control group as described in **Figure 1**. In the existence of serum cTnI, the CK-MB correlated positively with the RV Tei index (r = 0.66, P<0.001) and the LV Tei index (r = 0.61, P<0.001). On the other hand, FS did not correlate with serum cTnT concentrations (r = -0.29, P = 0.07).

Discussion

The cardiac involvement in perinatal hypoxia is closely related with the fate of the infant. For this reason, it is important to know whether the myocard is effected or not in an infant with perinatal hypoxia [16]. Recognition of neonatal hypoxic myocardial injury based on clinical findings, electrocardiographic changes and conventional echocardiography is often inconclusive. This study is one of the studies investigating the use TDI in assessing global and regional myocardial performance in asphyxiated infants and in assessing the relationship between these measurements and cardiac enzymatic change, highly sensitive and specific markers of myocardial injury.

To determine the level of cardiac damage, echocardiography recording were performed and cardiac enzymes were determined. These data were related to clinical presentation and patients' outcome [17]. However, Conventional echocardiographic changes suggestive of myocardial damage are present only when the damage is severe, which is far from being a valuable tool to demonstrate the myocardial damage in perinatal hypoxia [18]. Our results underline

that CK-MB is an early marker of severity of PA and mortality. The number of studies demonstrating increased sensitivity and specificity of CK-MB in perinatal hypoxia is increasing day by day. It is also stated that the sensitivity of CK-MB is higher than cTnI in infant with perinatal hypoxia. The presence of significant differences between the group I and II for LV EF and FS, and lower group II values of LV EF, FS and DT in patients have demonstrated time-dependent changes of myocardium in these infants.

To our knowledge, only one recent study [19] has evaluated the use of TDI in infants with asphyxia. The study assessed only the LV systolic function; our study, on the other hand, evaluated both systolic and diastolic functions of both ventricles. We evaluated the LV and RV Tei indexes, which are sensitive markers for global myocardial function. The LV and RV Tei indexes of global myocardial function were significantly higher in our asphyxiated infants than in controls, indicating both LV and RV dysfunction in these infants; moreover, they were more sensitive than other markers of myocardial dysfunction in identifying the asphyxiated newborns. The Tei index has been reported to be useful for the assessment of global function of each ventricle, independent of geometric assumptions, changes in preload or afterload, heart rate, and blood pressure [18, 20]. It has been used to analyze systolic and diastolic global ventricular function in various congenital and acquired cardiac abnormalities in children. To our knowledge, there is no study evaluating time-dependent changes in perinatal hypoxia by using both myocardial enzymes and TDI. We have also demonstrated that the RV and LV Tei indexes correlated with serum CK-MB in the existence of serum cTnI. The result demonstrat-

ed that mitral peak systolic velocity correlates positively with CK-MB and indicates a high sensitivity of TDI in detecting myocardial damage inasphyxiated infants.

Measurement of serum cTnI is accepted as the "gold standard" test for diagnosis and management of adult acute coronary syndromes, largely replacing the CK-MB isoform according to the good specificity of serum cTnI in perinatal hypoxia [21]. However, the sensitivity of cTnI was lower than that of serum CK-MB in our findings. We have also investigated that the RV and LV Tei indexes correlated with serum CK-MB in perinatal hypoxia. The result demonstrated that the Tei indexes of right and left ventricular correlates positively with CK-MB in the existence of serum cTnI and indicates a high sensitivity of TDI in detecting myocardial damage inasphyxiated infants.

Conclusions

Our findings show that serum CK-MB and serum cTnI could be used as sensitive parameters to detect myocardial damage due to perinatal hypoxia. The TDI technique appears more sensitive than conventional echocardiography and Doppler techniques to the subtle changes in cardiac performance that occur after perinatal asphyxia. Moreover, the RV and LV Tei indexes correlated positively with CK-MB in the existence of serum cTnI, which indicates a high sensitivity of TDI in detecting myocardial damage in asphyxiated infants.

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Disclosure of conflict of interest

None.

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