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Clinical value of TEI index in the diagnosis of myocardial dysfunction of the left ventricle in patients with connective tissue dysplasia.

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ABSTRACT

The Tei index has been successfully used for the integrated assessment of systolic and diastolic myocardial function of the left ventricle (LV). However, in the scientific literature there is no mention of the use of this indicator in the study of central hemodynamics in persons with connective tissue dysplasia (CTD) with the localization of lesions of the intracardiac structures in a form of minor heart anomalies (MHA), some of which may acquire independent clinical value, contributing to the development of cardiovascular disease or becoming a risk factor for cardiac disease. to determine the diagnostic significance of Tei index in the evaluation of myocardium performance of the left ventricle in patients with connective tissue dysplasia and to choose an optimal method for its measurement. We examined 33 people with one MHA (1st group) and 45 persons with two or more MHA (2nd group) aged from 20 to 40 years, and 29 almost healthy individuals were included in the control group. Index Tei was measured in three ways: according to the Doppler transmitral flow (D-Echo) and in the mode of pulsed-wave tissue Doppler imaging (PTD) of the lateral (index Tei_{MFRM}) and medial part (index Tei_{MFRM}) of the mitral fibrous ring (modified index). Tei index according to the results of D-Echo in the 1 and 2 groups was 0.48±0,05 conventional units (c.u.) and 0,53±0,07 c.u., that is higher than in healthy individuals (0,40±0,04 c.u., p<0.001). At calculating the modified index were shown similar dynamics. In persons with multiple MHA Tei_{MFRL} index and Tei_{MFRM} index were the highest, and amounted to 0,51±0,09 c.u. and 0,52±0,08 c.u. respectively. That was significantly higher than in the 1st and control groups. Comparative analysis of methods of measurement has shown that the greatest diagnostic value had a method of calculating the index Tei in the PTD mode of the medial part of the fibrous ring of mitral valve (MFR). The increase of Tei_{MFRM} index of more than 0.50 c.u. is an early marker of diastolic LV dysfunction in individuals with CTD with a sensitivity of 66.7% and a specificity of 64.1%.
Keywords: Tei index, connective tissue dysplasia, small anomalies of the heart, diastolic dysfunction of the left ventricle and pulsed-wave tissue Doppler of the fibrosus mitral annulus.

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INTRODUCTION

In the medical literature in recent years, the Tei index is referred to be the echocardiographic index of quantitative assessment of systolic and diastolic function of the left and right ventricle. It is characterized as a non-invasive, sensitive indicator of overall cardiac dysfunction and is the ratio of the amount of isovolumic relaxation time and a contraction of the myocardium to the time of the expulsion of blood. The name of index includes the name of the author, who proposed for the first time in 1995 to calculate it by the Doppler spectrum of transmitral and transaortic flows (Vasiuk, 2012). This figure is known as the “index of performance of the ventricles of the heart”, “myocardial index of total dysfunction of the heart”, “index of myocardial performance”, “Doppler echocardiographic index”, “Doppler index”, “myocardial work index” (Rybakov, Alekhin, Mitkov, 2008).

In the diagnosis of myocardial dysfunction of the left ventricle (LV) index Tei can be calculated in two modes: according to the pulsed-wave Doppler echocardiography (D-Echo) and according to the pulsed-wave tissue Doppler imaging (PTD). In the latter case it is called as a modified Tei index.

1. Tei index in D-Echo mode is measured according to the schedule of Doppler spectrum of mitral diastolic and systolic flows by the formula: IVC + IVR / PEB, where IVC and IVR – time of isovolumic contraction and isovolumic relaxation of the left ventricle, the PEB – period of ejection of blood into the aorta. The indicator is calculated as the result of averaging values over several cardiac cycles (to eliminate the influence of heart rate) (Abramian et al., 2011).

2. Tei index in PTD mode is calculated according to the maximum speed of movement of fibrous rings (FR) of atriventricular valves as the ratio of the difference of the time interval between the beginning of a positive wave IVC before the beginning of E´ (a) and a time of a systolic S´ wave (b) according to the formula: (a-b)/(b), where E´ is the maximum velocity of an early diastolic motion of FR, S´ is the maximum systolic speed of FR. The measurement of time intervals according to the PTD is more useful, because the analysis of one cardiac cycle is conducted. To calculate the Tei index were studied both - the lateral and medial part of the FR of the mitral valve (Zemtsovskiy, 2000).

The theoretical meaning of the Tei index is to estimate the ratio of potential and kinetic energies of myocardium of the LV, therefore, it characterizes the global (by the motion of the fibrous rings of the atrioventricular valves) or segmental (by the motion of a particular segment of the wall of the ventricles) myocardial function of LV (Alyokhin et al, 2007).

The change in the Tei index is associated with impaired systolic and diastolic function of the myocardium. Tei index is considered as an early marker of the occurrence of myocardial hypertrophy of the left ventricle in hypertensive disease, is characterizes the global contractility of the left ventricle in such diseases as hypertension, dilated cardiomyopathy, amyloidosis of the heart (Szwast et al., 2014). Tei index is recognized as an independent predictor of the outcome in chronic heart failure (CHF) in both adults and children (Potolova, Kopylova, 2013). PTD is the preferred method in pediatric practice because it is less sensitive to heart rate variability. According to Sanchez Mejia et al. Tei index, which is calculated in the PTD mode of the interventricular septum, reflects the severity of a heart failure in children, and is more accurate than the ejection fraction of the left ventricle. An optimal value of sensitivity (100%) and specificity (60%) assessment of the severity of chronic heart failure with an index value Tei were obtained at index > 0,51 c.u. (Tkachenko, Beresten`, 2006).

More recent publications indicate new diagnostic opportunities of Tei index and thus enhance its application in practice. Ozturk S et al. revealed the relationship between Tei index, measured in PTD mode and LV systolic asynchronism in patients with ectasia of the coronary arteries, verified according to the coronary angiography. A study of intraventricular systolic asynchronism during a post-processing of image of the cardiac tissue synchronization (TSI, Tissue Synchronization Imaging) showed that in patients with ectasia of the coronary arteries there is a systolic asynchrony, and Tei index was significantly higher in them than in the control group (0,63 ± 0,12 c.u. and 0,52 ± 0,12 c.u. respectively, p <0.001). According to the study a high level of Tei index was recognized as an independent risk factor for the development of systolic asynchronism in persons with this pathology (Martynov, 1995).

Bruch C. et al. determined the diagnostic significance of Tei index in patients with severe mitral insufficiency of different genesis according to D-Echo. With this purpose were examined 12 patients with primary mitral regurgitation (first group), including those with a prolapse or myxomatosis mitral valve, rupture of chordae and the formation of the so-called "hammering of the leaflet" of the mitral valve. 25 patients constituted a group with a secondary mitral regurgitation (second group), developed on the background of ischemic or dilated cardiomyopathy, 16 people were included in the control group. In the second group there was a significant decrease in LVEF (29±13%, p <0.001) compared with the control and the first group. Tei index in the opposite was the highest, and amounted to 0.87±0,3 c.u., 0,42±0,07 c.u. and 0,38±0,05 c.u., respectively (p<0.001). In addition, in patients with a secondary mitral regurgitation was detected a significant correlation of this index with the end-systolic volume of the LV. The value of Tei index > 0.51 c.u. with a sensitivity of 92% and a specificity of 88% allows differentiating the secondary mitral regurgitation from the primary. Thus, this ratio is a sensitive indicator of a systolic dysfunction in patients with severe mitral valve insufficiency and can be used as a marker of secondary mitral regurgitation (Onishchenko, 2005).

Tei index is informative not only in the evaluation of systolic, but also in the evaluation of diastolic function of the LV. Was described the diagnostic significance of Tei index in identifying of diastolic dysfunction in the work of Baykan M. et al. in patients with Itsenko-Cushing`s syndrome. Tei index (that was calculated according to the PTD of the lateral portion of the mitral fibrosus annulus) in patients with this pathology was significantly higher than in the control group and was positively correlated with cortisol levels in blood serum (Alekhin, 2002). According to Vasyuk A. Y. et al. the decrease in Tei index in persons who receive antihypertensive therapy is recognized as the earliest marker for improving of diastolic function of the myocardium of the left and right ventricle in the D-Echo and PTD modes (Vasiuk, 2012).

It should be taken into account the limited sensitivity of Tei index in combination of ischemic heart disease with valve defects and arterial hypertension. The presence of significant atrioventricular regurgitations is the main limitation for the use of this indicator. The disadvantages of Tei-index are the impossibility of identifying the leading mechanisms of myocardial dysfunction: reduced contractility, impaired and incomplete relaxation, changes of preload and postload (Bart, 2005).

According to earlier studies, the use of this index is limited with right ventricular dysfunction in patients with pulmonary pathology and diseases related to the load on the right heart, and pulmonary hypertension (Alyokhin et al, 2007). However, Hilde J. M. et al. demonstrated the successful use of Tei index for the assessment of right ventricular function in patients with chronic obstructive pulmonary disease (COPD) without evidence of pulmonary hypertension. Was found a significant correlation between the magnitude of systolic pressure in the pulmonary artery, the wall thickness of right ventricle and Tei index measured according to PTD of the basal part of the lateral wall of the right ventricle. This study shows that Tei index correlating with the index of systolic pressure in the lung artery (SPLA) is an early indicator of right ventricular dysfunction and is a marker of subclinical stage of COPD in patients without signs of pulmonary hypertension (Malev et al., 2012).

Successful use of Tei index in various diseases of the cardiovascular system does not cause doubts about its relevance. However, in the scientific literature there is no mentioning of the use of this indicator in the study of central hemodynamics in persons with connective tissue dysplasia (CTD) with the localization of lesions in intracardiac structures in a form of minor heart anomalies (MHA). Currently were described of more than 30 types of MHA, some of which may acquire an independent clinical value, contributing to the development of cardiovascular disease or becoming a risk factor for cardiac disease.

So, false chords and anomalous trabecula can cause reducing of diastolic function of the left ventricle that occurs because of the opposition to the relaxation in their high location (Galindo, 2013; Alyokhin et al, 2007; Malev and others, 2013). In asymptomatic patients with mitral valve prolapse was revealed the deterioration of diastolic myocardial deformation, which is due to the increased activity of the profibrotic cytokine TGF-β and myocardial fibrosis (Puerto, Gratacós, 2006; Komarova, Ivanova, 2013). Heart rhythm disorders and conductivity are very typical for a dysplastic heart. The extrasystoly is associated with the mitral valve prolapse. It is caused by direct mechanical effects of an excess valve to the endocardium of the LV. So, false chords and anomalous trabecular can cause a development of arrhythmias. They often have elements of muscle and the conduction systems, which in turn, creates conditions for the development of arrhythmias with a re-entry mechanism. Often such complications of MHA as the separation of the chords of the mitral valve, rupture of the aneurysm of interatrial septum, paradoxical embolism with an open oval window, as well as an acute bacterial endocarditis can cause a sudden cardiac death in young adults (Uresti, 2012; Sal'nikov et al., 2012). Taking this fact into the consideration we believe it is important to search for an informative indicator of the presence or absence of myocardial dysfunction of the LV.

The aim of the study was to determine the diagnostic significance of Tei index in the assessment in the performance of the LV myocardium in patients with connective tissue dysplasia and to choose the optimal method for its measurement.

MATERIALS AND METHODS

There were examined 78 people with MHA in the age from 20 to 40 years and 29 practically healthy persons, that have formed the control group, in which according to Echocardiography did not have any signs of the syndrome of connective tissue dysplasia of the heart. In the 1st group were included 33 people with a single MHA, the vast majority of them were men (of 87.9%). In the 2nd group were included 45 people with two or more MHA, among them men were also prevailed – 34. All patients did not have any specific cardiac or “vascular” complaints and were primarily headed by clinicians in a case of a “functional noise of heart” during auscultation and/or in the identification of “nonspecific changes on ECG. Part of them was at the dispensary about the previously identified MHA.

All patients were performed: a supine ECG in 12-leads and transthoracic echocardiography in B-mode, Doppler, M-mode on the ultrasound machine Vivid E9 (GE Healthcare, matrix sector phased sensor with a frequency of 3.5 MHz). In doubtful cases for verification of detected MHA was conducted a transesophageal Echocardiography using 4D transducer in real-time. Measurement of sizes and volumes of heart chambers, ejection fraction and myocardial mass, as well as the evaluation of the diastolic function of the left ventricle were carried out according to the recommendations of the European Association and American society of specialists in Echocardiography (EAE/ASE) with the use of Doppler mode imaging tissue (Zemtsovskiy, Lobanov, Davtyan, 2009).

Tei index was measured in three ways: according to the traditional D-Echocardiography (according to the Doppler range of the transmitral flow frequencies offset) and in the PTD mode, on the Doppler recording of the motion of the lateral and medial parts of the fibrous ring of the mitral valve (modified index). In calculation was used the following formula: LIMP = (MSO-AVET) / AVET, where LIMP (left index of myocardial performance – the Tei index.

MCO (mitral valve closure to opening) - an interval from the closing to opening of the mitral leaflets, i.e., the period of the closed mitral valves.

AVET (aortic valve ejection time) is the period of ejection of blood from LV.

Calculation of Tei index by the first method in D-mode of Echocardiography was performed in the apical five-chamber position, while the control volume was located in the output tract of the left ventricle closer to the front leaflet of the mitral valve (figure 1). This registration of a flow often allows recording the clicks of the aortic and mitral valves closing, which simplifies the measurement of time intervals. At the same time to eliminate the influence of a heart rate was taken an average value over the several cardiac cycles.

A modified Tei index was calculated in the PTD mode in the apical 4-chamber sections of the heart with simultaneous recording of ECG monitoring with a patient`s breath holding according to the chart of a maximum velocity of lateral and medial parts of the mitral fibrous ring (Tei_{MFRL} index and Tei_{MFRM} index respectively). The start point of counting down the time phases was considered the R-wave of the ECG (figure 2). The period of a mitral valve closing to opening (MCO) is measured as the interval between the start of the positive wave of the isovolumic contraction and the beginning of a maximum velocity of an early diastolic motion of MFR (E´). The period of expulsion of blood into aorta AVET corresponds to the time of the systolic wave S´. Were also calculated isometric phases of cardiac cycle: time of isovolumic relaxation and contraction.

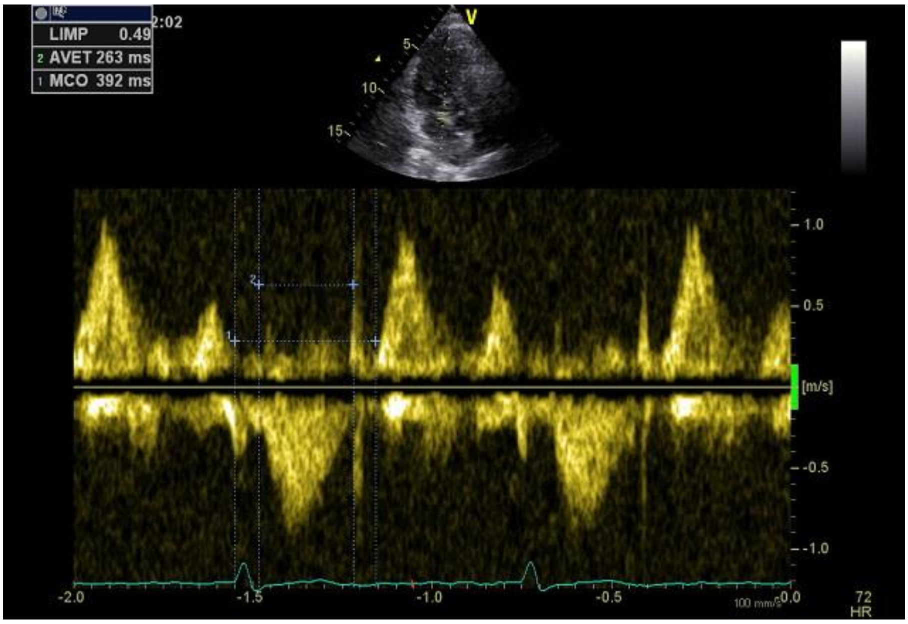

Figure 1. The calculation of Tei index in D-mode of Echocardiography of mitral flow

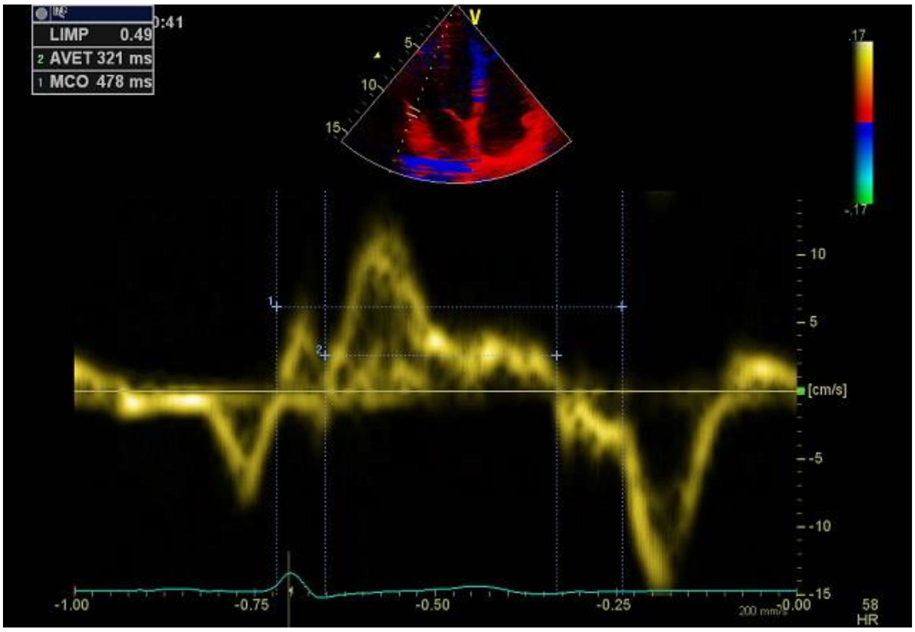

Figure 2. Calculation of Tei index in the PTD-mode of the lateral portion of the fibrose annulus of the mitral valve. Symbols are in the text.

The obtained data were subjected to a mathematical processing using the software package "Statistica 8". For larger number of factors was used an analysis of variance or criterion of Kruskal-Wallis. The difference in the mean and median for two independent sample distributions were determined in accordance with T-student test or U-criterion of Mann-Whitney.

THE RESULTS OF THE STUDY

The examined groups were comparable on most demographic and anthropometric data. Standard echocardiographic hemodynamic parameters such as end systolic and diastolic dimensions and volumes, stroke and minute volume and ejection fraction, and myocardial mass of LV were also higher in the group with many MHA, but did not differ significantly. When comparing the size of the heart chambers was found that individuals with MHA, both in the first and second groups, had larger left atrium than in the control group (34,4±2.1 mm 36,0±2,3 mm 34,0±1.3 mm, respectively, $p<0.05$). In their correlation to the body surface area, a similar trend is preserved, but the obtained values differed significantly only in persons with multiple MHA (18.6±1.6 mm/m^2, $p<0.01$).

Traditional assessment of LV diastolic function according to D-Echocardiography of a transmitral flow through such indicators as the ratio of the velocity of early and late diastolic LV filling (E/A) and a deceleration time of transmitral flow in the phase of early filling did not reveal diastolic dysfunction in the studied groups. However, it was noted the slowdown of relaxation of the LV myocardium in the form of a significant decrease of the peak E in persons with two or more MHA compare with the control group (83,2±13.3 cm/s and 92.4±12.3 cm/s, respectively, $p<0.01$) and elongation of IVR time, which amounted to 66.5±8,9 ms and 55.8±6,6 ms, respectively ($p<0.001$).

Analysis of the diastolic function of the LV in PTD mode showed similar results. Persons of the 1st group showed a slight decrease in the maximum velocity of early diastolic motion of the lateral (Tei_{MFRL}´), and medial (Tei_{MFRM}´) part of MFR (16,9±2.3 cm/s and 13.7±2.2 cm/s, respectively), with minimum values in the 2nd group (15.7±3.4 cm/s and 13.5±2.5 cm/s, respectively, $p<0.05$) that were significantly lower than in the control group. Thus, a more greater decrease in the E´ peak in persons with multiple MHA may be due to a more greater development of fibrosis of the LV. Tei_{MFRL} time (according to PTD of the lateral part of MFR), as in the 1st and 2nd groups were significantly increased compared with the control group and amounted to 59.6±11,1 ms ($p<0.05$) and 64.4±12,9 ms ($p<0.001$), respectively. Tei_{MFRM} time in the 1st group tended to increase (69,0±11,8 ms), in the group with multiple MHA was significantly higher compared with the control group (72,1±11,7 ms, $p<0.05$).

A significant elongation of the IVR time with the lateral and medial part of the MFR along with the reduction of Tei_{MFRL}´ and Tei_{MFRM}´ peaks in patients with MHA indicates the violation of the processes of relaxation of the myocardium of the left ventricle. For a more detailed assessment of diastolic function, we turned to the calculation of Tei index.

Tei index, the period of closed mitral valves, time of ejection into the aorta with measuring in a standard mode of D-Echocardiography of transmitral flow in healthy individuals were 0.40±0,04 c.u., 411,6±23,8 ms and 293,5±19,2 ms, respectively. The 1st and 2nd groups showed lengthening of the MCO time (423,9±25,8 ms and 435,0±29,2 ms, respectively) along with the slight reduction of ejection time into the aorta AVET (286,4±18,9 ms and 285,1±22,4 ms), in this connection Tei index was found to be significantly higher compared to the control group (0,48±0,05 c.u. and 0,53±0,07 c.u., $p<0,001$).

Phases of isometry, both contraction and relaxation were lengthening with an achievement of significant differences in individuals with multiple MHA. Thus, the increase in the index was mainly due to the reliable extension of the period of the closed mitral valves on the background of a slight shortening of ejection time into the aorta, in other words by increasing the duration of the isometric phase of cardiac cycle, mainly IVR. Its maximum value in the1st group was 0,58 c.u., in the 2nd group - 0.68 c.u.

When calculating the modified Tei index in PTD mode of the lateral and medial part of MFR (index Tei_{MFRL} and index Tei_{MFRM}) compared with the previous method were shown similar dynamics. In individuals with MHA there was a significant value increase compared to health with achieving its peak values in the group with multiple anomalies. When analyzing data of PTD of MFR in healthy individuals from the control group Tei_{MFRL} index, and Tei_{MFRM} index amounted to 0,37±0,05 c.u. and 0,41±0,05 c.u. respectively. In individuals with one MHA was discovered a little bit longer time of Tei_{MFRL} and Tei_{MFRM} (419,7±26,5 ms and 418,2±26,5 ms, respectively), in this regard, the were significantly higher Tei_{MFRL} and Tei_{MFRM} indexes (0,44±0,05 c.u., $p<0.001$ and 0.49±0,06 c.u., $p<0.0001$). The period of expulsion of blood into aorta ($AVET_{MFRL}$ and $AVET_{MFRM}$) was tended to decrease, but did not really differ from the control group (292,2±18,0 ms and 281,4±15,7 ms). In the isometric phases of the cardiac cycle there was a slight lengthening of time of IVC_{MFRL} and IVC_{MFRM} (73,1±12.0 ms and 70.2±12,6 ms) on a background of a predominant elongation of time of IVR_{MFRL} and IVR_{MFRM} (59,6±11,1 ms and 69,0±11,8 ms, $p<0.05$).

Changes among the individuals in the 2nd group were the similar and more significant: Tei_{MFRL} index and Tei_{MFRM} index were the highest and amounted to 0,51±0,09 c.u. and 0,52±0,08 c.u., that is significantly higher compared to the control group (p<0.0001) and the 1st group (p<0.05). The increase of indexes were mainly due to the lengthening of time of MCO_{MFRL} and MCO_{MFRM} (429,8±33 ms and 430,5±28,2 ms, p<0.001), mostly by the increasing of the isovolumic contraction phase (82,4±16,6 ms, p<0.001) and 70.4±9,8 ms, p<0.05), relaxation of the LV myocardium (64,4±12,9 ms, p<0.001, and 72.1±11,7 ms, p<0.05 respectively), while the AVET time did not change significantly (284±18,7 ms and of 279.5±34,6 ms).

The increasing of Tei index was identified according to the D-Echocardiography of a transmitral flow, as well as according to PTD both of the lateral and medial part of the MFR, along with the extension of an IVR phase evidence of the violation of LV diastolic function in individuals with syndrome of connective tissue dysplasia of heart.

A comparative analysis of three methods of Tei index measurement by means of ROC analysis presented in figure 3, where a visual assessment of the location of 3 curves relative to each other indicates their comparative effectiveness. LIMP1 curve corresponds to the Tei index that is calculated in D-mode of Echocardiography of the transmitral flow. Curves LIMP2 and LIMP3 correspond to the modified Tei index that was calculated in the PTD mode of lateral and medial part of the MFR (Tei_{MFRL} index and Tei_{MFRM} index, respectively). Curve LIMP3 is located above and to the left of the diagonal connecting the lower left and upper right corners of the chart “sensitivity/specificity”, as well as the curves of LIMP1 and LIMP2, which indicates a greater predictive ability of the model of the three. This is more clearly confirmed by the value of the area under the characteristic curves, under the curve LIMP3 it was the highest and amounted to 0,734±0,067 (95% confidence interval 0,603-0,865).

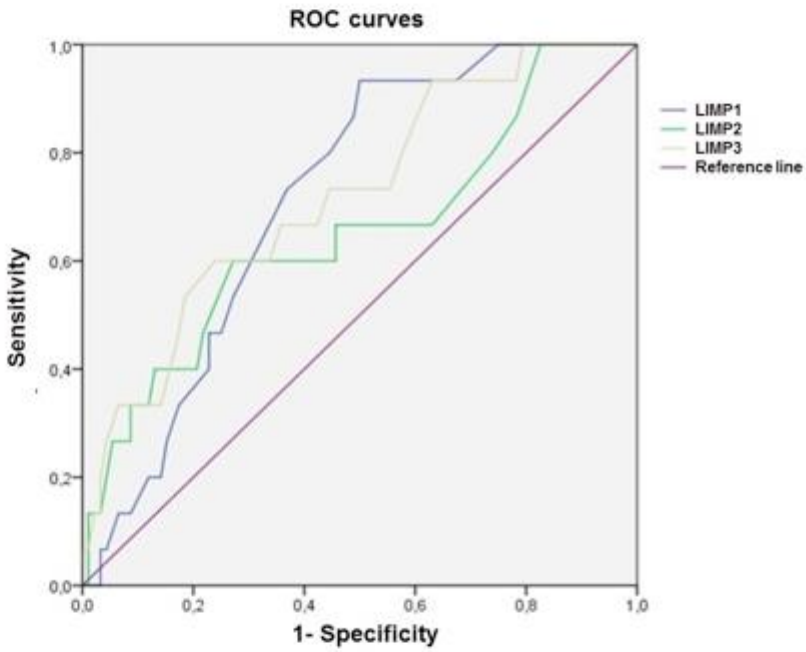

Figure 3. The characteristic curve of Tei index for the diagnosis of diastolic dysfunction of LV in individuals with MHA.

Analysis of ROC curves showed that among the three methods of measurement of Tei index the preference should be given to the PTD method of the medial part of MFR. While the predictive ability of the model can be described as good (interval AUC of 0.7-0.8). In addition, in this mode in all the studied groups an indicator was significantly higher (p<0.01): in the control group it amounted to 0,41±0,05 c.u., in the 1st group 0,49±0,06 c.u., in the 2nd 0,52±0,08 c.u. This may indicate an earlier violation of the relaxation process in the interventricular septum compared with the lateral wall of the LV. The value of the index Tei_{MFRM} ≥ 0,50 c.u. allows detecting a diastolic dysfunction of the LV in those with MHA with sensitivity of 66.7% and specificity of 64.1%.

DISCUSSION

Increasing of Tei index that was measured in three ways, in a conjunction with the elongation of isovolumic relaxation phase, increase in size of the left atrium and a make a reduction of peaks E, $Tei_{MFRL}{}'$ and

Tei_{MFRM}´ compared with the control group. This constitutes a violation of a diastolic LV function in patients with connective tissue dysplasia. At the same time in the group with multiple MHA Tei index was the highest with calculation both in the traditional mode of D-Echocardiography of a transmitral flow (0,53±0,07 c.u.), and in the PTD mode of the lateral and medial part of MFR (0,51±0,09 c.u. and 0,52±0,08 c.u. respectively). Increasing in Tei index occurred mainly because of the reliable lengthening of the period of the closed mitral valves (MCO) on the background of a slight shortening of time of ejection into the aorta (AVET), in other words, by increasing the duration of the isometric phase of the cardiac cycle. Thus, the quality of the myocardium in individuals with MHA differs mainly by the changing of the potential energy, while a kinetic component does not change significantly.

CONCLUSIONS

1. Comparative analysis of methods of measurement have shown that the greatest diagnostic value has a method of Tei index calculating in the mode of pulsed-wave tissue Doppler of a medal part of the fibrous ring of the mitral valve IFC.
2. Increasing of Tei index of more than 0.50 c.u. is an early marker of myocardial dysfunction of the left ventricle in patients with connective tissue dysplasia and minor heart anomalies with a sensitivity of 66.7% and a specificity of 64.1%.

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