Review Article

The Tei Index of Myocardial Performance: Applications in Cardiology

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here are many limitations to the use of classical echocardiographic indexes for the estimation of systolic and diastolic left ventricular (LV) function. The ejection fraction (EF, an index of systolic function) and LV volumes are subject to large errors when the ellipsoid shape of the heart becomes spherical. Age, rhythm and conduction disturbances, and changes in loading all affect the Doppler signal of transmitral flow, which is the most commonly used method for studying diastolic function. Tei Chuwa devised and published in 1995 an index of myocardial performance (the Tei index) that evaluates the LV systolic and diastolic function in combination.1 The Tei index has proved to be a reliable method for the evaluation of LV systolic and diastolic performance, with clear advantages over older established indexes and prognostic value in many kinds of heart disease.

Calculation of the Tei index

The Tei index is a pure number and is calculated from the ratio of time intervals (a-b/b) derived with the aid of pulsed Doppler echocardiography (Figure 1). Locating the sample volume at the tips of the mitral valve leaflets, in the apical 4-chamber view, enables the measurement of a, which is the time interval between the end and the start

of transmitral flow. The sample volume is then located in the LV outflow tract, just below the aortic valve (apical 5-chamber view) for the measurement of b, the LV ejection time. The interval a includes the isovolumic contraction time (IVCT), the ejection time (ET) and the isovolumic relaxation time (IVRT), and the Tei index may also be expressed by the formula IVCT+IVRT/ET. For the evaluation of the right ventricular (RV) Tei index the a interval, from the end to the start of trans-tricuspid flow (the interval from the end of the A wave to the start of the E wave), is obtained from the apical 4-chamber view with the Doppler sample volume located between the tips of the tricuspid valve leaflets. The b interval (RVET) is measured from the parasternal long-axis view, with the sample volume located just below the pulmonary valve.

Tei index and age

A study of 161 children with no cardiovascular disease, aged from 30 days to 18 years, determined the range of normal values for the Tei index and the effect of age.² Tei was affected by age during the first 3 years of life, showing a progressive reduction until the age of 3, but then it showed no further changes. The Tei index for children aged <3 years was significantly greater (0.40 \pm 0.09) than for those aged

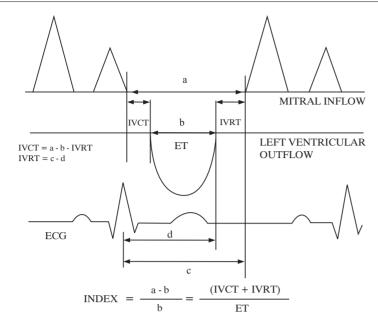


Figure 1. Schematic representation of the measurement of the Tei index. a: time interval from the end to the start of transmitral flow, b: left ventricular ejection time (also denoted by ET), c: time interval from the peak of the R wave on the ECG to the start of transmitral flow, d: time interval from the peak of the R wave on the ECG to the end of ejection time, ET: (b) left ventricular ejection time, IVCT: isovolumic contraction time, IVRT: isovolumic relaxation time.

between 3 and 18 (0.33 \pm 0.02). Furthermore, in 5 children with dilated cardiomyopathy, aged 12 to 17 years, the Tei index was significantly greater (0.78 \pm 0.28) than in healthy children. The age-dependent changes in the index may reflect changes during the maturation of the myocardial characteristics of the LV in neonates and children. During development, the relation between total collagen and total protein reaches normal levels in 5 months and the relation between type I collagen (which mainly provides rigidity) to type III collagen (which provides elasticity) stabilises after 3 years.

The RV Tei index in 150 healthy children, mean age 5.1 ± 5.5 years, was 0.24 ± 0.04 , irrespective of age.³

Tei index and preload

The effect of preload changes on the Tei index was investigated in 50 healthy volunteers and 25 patients with a previous infarction. Three procedures were performed successively, the Valsalva manoeuvre (preload reduction), passive raising of the lower limb (preload increase) and administration of sublingual nitroglycerine (preload reduction). In the controls the index increased significantly during the Valsalva manoeuvre (mainly as a result of a reduction in ET), after passive raising of the lower limb (primarily as a consequence of an increase in IVCT) and after nitroglycerine administration (as a result of a reduction in ET and a prolongation of IVCT). In contrast, no sig-

nificant changes were seen in the index in the infarction patients during the above preload variations. Briefly, in those patients when the preload decreased the IVCT/ET ratio showed a reduction while the IVRT/ET ratio increased, leaving the index unchanged. Although these result show a change in the Tei index under different preload conditions, the extent of the changes was small (<10%), a fact that explains the preservation of the prognostic value of the Tei index despite variations in preload.

Tei index and haemodynamic indexes

In a prospective study⁵ 17 patients with idiopathic dilated cardiomyopathy (EF: $24\% \pm 11\%$) and 19 patients with ischaemic heart disease (EF: $49\% \pm 13\%$) underwent catheterisation and a Doppler echo examination. In all cases simultaneous recordings were made of LV pressures and Doppler velocity curves and the following were calculated: maximum rate of pressure increase during isovolumic systole (peak +dP/dt), maximum rate of pressure decrease (peak dP/dt) and the time constant of pressure reduction during isovolumic relaxation (tau). The Tei index was found to be significantly correlated with all three variables, providing confirmation that it is a reliable measure of total LV function. The index was also found to be more sensitive in the evaluation of diastolic relaxation than parameters such as the deceleration time of the E wave (DE) and the E/A ratio, which showed a weaker correlation with peak -dP/dt and tau.

Tei index and heart failure (systolic and diastolic)

In patients with dilated cardiomyopathy the index was found to reflect the severity of LV dysfunction and was proved to be an independent prognostic factor for mortality, similar to the EF.⁶ The higher values of the Tei index in patients than in healthy individuals $(0.85 \pm 0.32 \text{ versus } 0.37 \pm 0.05)$ were attributable to prolongation of the isovolumic intervals and a shortening of ET. The Tei index was significantly correlated with NYHA class, EF and ventricular volumes, while values >0.77 were associated with higher 1-, 3- and 5-year mortality.

The usefulness of the index was studied in the detection of patients with mild to moderate heart failure. The Tei index was significantly greater in 43 patients with heart failure than in 38 controls and was correlated with LV end-diastolic pressures. Values >0.47 identified heart failure patients with a sensitivity of 86% and a specificity of 82%.

Harjai et al⁸ investigated the prognostic value of the Tei index in 60 patients with severe, symptomatic heart failure (EF <30%) of ischaemic aetiology or not. The endpoints were death from any cause and heart transplantation. During a follow up of 24 ± 19 months, 28 patients died (49%) and 2 (3.5%) underwent heart transplantation. A strong correlation was found between a high Tei index (>1.14) and the long term outcome, independently of other clinical and echo indexes that have been proved to have prognostic value, such as age, sex, EF, coronary artery disease, NYHA class, mitral regurgitation, RV systolic dysfunction and the deceleration time of early diastolic filling (DT). A Tei index >1.4 was an independent prognostic factor for death or emergency heart transplant during two years' follow up and had more predictive power than EF or NYHA class.

In another study⁹ the Tei index was evaluated at rest and after the administration of a low dose of dobutamine in 42 patients with idiopathic or ischaemic dilated cardiomyopathy and was correlated with parameters from cardiopulmonary exercise testing. An advanced NYHA class and a restrictive filling pattern were associated with higher values of the index, while a negative correlation was found between the Tei index and systolic indexes (stroke volume, cardiac output), diastolic indexes (E/A, A) and cardiopulmonary exercise testing parameters (peak oxygen consumption, anaerobic threshold). Dobutamine administration caused a shortening of IVRT and IVCT, prolongation of ET and improvement (reduction) of the Tei index. Multivariate

analysis revealed that the index was an independent prognostic factor for exercise tolerance.

In patients with isolated diastolic dysfunction, assessed in terms of the E/A ratio of transmitral flow or the S/D relation of the pulmonary veins, the index was found to be significantly elevated (0.69 \pm 0.11), mainly as a result of a prolongation of IVRT (Tei index in controls 0.46 \pm 0.08).¹⁰

Tei index and heart transplantation

In recent years much effort has been devoted to discovering a non-invasive technique to replace endomy-ocardial biopsy in heart transplant patients. Since systolic and diastolic dysfunction are often both present during episodes of cardiac rejection, the Tei index was investigated as a possible harbinger of acute rejection. In a small sample of post-transplant patients (5 boys and 3 girls, age 3-19 years) the values of the index ranged from 0.2 to 0.45 during periods of non-rejection and from 0.2 to 0.8 during periods of rejection, a difference that approached statistical significance (p=0.06). It seems that the Tei index might be a useful prognostic factor for cardiac rejection in post-transplant paediatric patients.

Similarly, in 13 post-transplant men a Doppler study was performed and the index was calculated during the same 24-hour period in which a myocardial biopsy was taken. ¹² The isovolumic systole and isovolumic relaxation times showed statistically insignificant prolongation and the ET shortened significantly with progressively increasing biopsy scores (stage I, II and III), while the increase in the Tei index was more significant. Multivariate stepwise regression analysis showed that the Tei index was the sole independent factor to be correlated with the biopsy score of the transplanted heart.

Tei index and coronary artery disease

In patients with acute myocardial infarction the Tei index was found to be significantly more pathological (greater) than in healthy controls $(0.705 \pm 0.026 \text{ versus } 0.455 \pm 0.023, \text{ p: } 0.000).^{13}$ Of the terms involved in the index, IVCT and IVRT were prolonged and ET was significantly shorter in the patients with acute myocardial infarction. The Tei index also showed predictive value in relation to the severity of coronary artery disease. It was more pathological in the group of infarction patients who had severe coronary artery

disease than in those with 1- or 2-vessel disease, for both anterior and inferior infarctions.

In 21 patients who had a complicated course after a first myocardial infarction (death, heart failure, arrhythmias, post-infarction angina) the mean value of the Tei index was significantly higher than in 75 patients with an uncomplicated course $(0.65 \pm 0.20 \text{ versus } 0.43 \pm 0.16, \text{ p: } 0.0001)$. The higher value of the Tei index was due to prolongation of the IVCT (72 ± 37 versus 44 ± 27 ms, p: 0.001) and shortening of the ET (245 ± 35 versus 265 ± 26 ms, p: 0.01). Tei index values ≥ 0.47 showed 90% sensitivity and 68% specificity in identifying patients with events, while in a multivariate model the index on admission continued to be an independent prognostic factor for in-hospital cardiac events.

Ling et al performed dobutamine stress echo testing in 27 individuals. The Tei index was significantly higher at peak dobutamine stress in the group with ischaemia (13 patients) than in the 14 subjects who had a negative test. More generally, the Tei index in the ischaemic subgroup showed an increase at peak stress, while in the remaining subjects the index showed no significant change as the test progressed. At the onset of ischaemia IVCT and IVRT were prolonged and the ET shortened, resulting in an increased, pathological Tei index. The index appears to be useful in the recognition of myocardial ischaemia and the development of LV dysfunction during a stress echo examination.

Tei Index and valvular disease

Haque et al¹⁶ investigated the effect of valve dysfunction on the Tei index, calculating the index in 76 patients with aortic or mitral valve disease before and after surgical valve replacement or repair. The authors found that the index may underestimate the presence of aortic stenosis, aortic regurgitation and mitral stenosis, while it may overestimate the presence of mitral regurgitation. The values of the Tei index increased postoperatively, to a statistically significant degree, in patients with aortic stenosis, aortic regurgitation and mitral stenosis, whereas it decreased in mitral regurgitation, though not significantly. The differences were most evident in aortic stenosis and were positively correlated with the preoperative values of peak aortic flow velocity.

In patients with severe aortic stenosis, symptoms of heart failure can be attributed to systolic, diastolic or combined LV dysfunction. In 10 symptomatic patients¹⁷ with severe aortic stenosis (orifice 0.6 ± 0.2

cm²), compromised systolic function (EF \leq 45%) and increased LV end-diastolic pressure determined invasively (32 \pm 8 mmHg), the IVCT was prolonged and the ET shortened, resulting in a significantly elevated Tei index compared to healthy controls. In 22 patients with severe, symptomatic aortic stenosis (orifice 0.7 ± 0.2 cm²), physiological systolic function and increased filling pressures (22 ± 7 mmHg), there was a shortening of IVRT and IVCT, a prolongation of ET and a consequent decrease in the value of the Tei index. Thus, the index was able to discriminate between those patients with severe aortic stenosis who had depressed systolic function and those whose systolic function was preserved. The index was significantly higher when there was combined systolic and diastolic dysfunction and significantly lower in the case of primarily diastolic dysfunction.

Tei index and pulmonary hypertension

The RV Tei index was found to be the most powerful Doppler parameter for distinguishing 26 patients with primary pulmonary hypertension from 37 healthy individuals $(0.93 \pm 0.34 \text{ versus } 0.28 \pm 0.04, \text{ p} < 0.001)$. ¹⁸ Furthermore, there was a significant correlation between the index and the patients' functional condition (symptoms) as well as with total survival. An increase in the index by 0.1 increased the risk of death by 1.3 times. The index was found to be independent of heart rate or loading conditions (RV systolic and diastolic pressure or diastolic pulmonary pressure or presence and severity of tricuspid regurgitation). The IVCT was prolonged in the patients, probably because of an earlier start of isovolumic systole due to increased RV end-diastolic pressures and an earlier intersection of the right atrial and RV pressure curves. The finding of a significant prolongation of IVRT showed the coexistence of RV diastolic dysfunction, while the shortened ET was attributed to an increase in pulmonary vascular resistance, to a reduction in RV filling with the reduction in stroke volume and to the presence of tricuspid regurgitation.

In a second study the index of RV dysfunction was also found to be a useful prognostic factor for an unfavourable outcome (cardiac death, lung transplant) in patients with primary pulmonary hypertension. ¹⁹ In comparison with published normal values, 53 patients with primary pulmonary hypertension were characterised by a shorter ET and prolongation of the IVCT and IVRT of the RV, resulting in higher values of the Tei index $(0.84 \pm 0.2 \text{ versus } 0.28 \pm 0.04)$.

In a follow up of mean duration 2.9 years, 30 patients died and 4 underwent lung transplantation. An increase in the index by 0.1 increased the undesirable events by 1.3 times, while patients with values <0.83 had a more favourable course.

Tei index and amyloidosis

In amyloidosis the cause of death is most commonly related with cardiac participation in the disease, which is manifested by disturbances of relaxation in the early stages and concomitant systolic dysfunction in the advanced stages. The Tei index was calculated in 45 patients with amyloidosis confirmed by biopsy and typical echocardiographic features showing myocardial involvement.²⁰ At the time of examination 23 patients had congestive heart failure and 20 were in NYHA functional class III or IV. The IVCT and IVRT were significantly longer and the ET shorter in patients with cardiac amyloidosis compared to matched healthy controls. These differences resulted in a significantly greater Tei index, especially evident when the combination of a low EF (<50%) and a short DT (≤150 ms) was present. During a follow up lasting more than 3 years, 29 of the 45 patients died (cardiac cause in 23, non-cardiac in 4 and unknown in 2). A multivariate analysis showed that the NYHA class and the Tei index were the only independent prognostic factors for clinical outcome. Patients with a Tei index >0.77 had a worse prognosis.

In another study,²¹ the RV Tei index allowed the non-invasive diagnosis of frequently occurring RV dysfunction in patients with cardiac amyloidosis. The RV Tei index was significantly greater in 30 patients with diffuse disease compared with 50 controls (0.54 \pm 0.16 versus 0.28 ± 0.05 , p<0.001). The patients showed prolongation of the IVCT and IVRT and shortening of the ET, resulting in a significant increase in the RV Tei index. The frequency of RV dysfunction expressed by IVCT prolongation was 63%, by ET shortening 43%, by IVRT prolongation 73% and by the RV Tei index 83% for all the patients with cardiac amyloidosis. The incidence of RV dysfunction found by the Tei index was similar to that previously reported and confirmed the clinical usefulness of the index in the identification of RV dysfunction in patients with diffuse disease.

Tei index and congenital heart disease

Eiden et al²² attempted to determine normal values of the RV and LV Tei indexes in healthy children and to evaluate the usefulness of the index in Ebstein's anomaly. Ebstein's anomaly was chosen as a model of congenital heart disease because of the frequent coexistence of left and right ventricular dysfunction, pathological wall movement and disturbed ventricular geometry. In 152 healthy children, mean age 9.3 ± 2.6 years, the RV Tei index was 0.32 ± 0.03 and the LV Tei index was 0.35 ± 0.03 . In 45 patients with Ebstein's anomaly, mean age 18 ± 14.8 years, both the RV and LV Tei indexes had significantly higher values than those found in age-matched volunteers. The IVRT and IVCT components of the index were significantly prolonged and the ET significantly shorter in the patients. An increase in RV dysfunction was associated with a progressive pathological increase in the RV Tei index. The index therefore appears to be a useful quantitative measure of ventricular function in patients with Ebstein's anomaly.

In another study the RV Tei index was evaluated as a method for assessing RV function in patients with congenital heart disease and the effect of ventricular volume and pressure overload on the index was also investigated.²³ The patients studied included those with an atrial septal defect (RV volume overload), pulmonary stenosis (RV pressure overload), corrected congenital transposition of the great vessels with moderate or severe left atrioventricular valvular regurgitation (pressure and volume overload), as well as patients with Ebstein's anomaly and severe RV dilatation and dysfunction. Patients with atrial septal defect or pulmonary stenosis and physiological RV function had normal values of the RV Tei index. Adults with atrial septal defect and physiological RV function had a statistically significant elevation of the RV Tei index, which was attributed to mild, subclinical RV dysfunction due to the chronic RV volume overload (more evident negative reaction in terms of diastolic performance with prolongation of the IVRT). The RV Tei index did not differ between patients with isolated pulmonary stenosis and healthy children, while it was significantly higher in those with Ebstein's anomaly or corrected congenital transposition of the great vessels with moderate or severe left atrioventricular valvular regurgitation (the increase was due to prolongation of the IVCT and IVRT and shortening of the ET). No significant change in the RV Tei index was seen in groups of postoperative patients, despite the relief from volume or pressure overload (the index appeared to be relatively independent of changes in preload or afterload).

Tei index and cardiotoxicity from chemotherapy

The value of the Tei index in determining subclinical cardiotoxicity was investigated in patients undergoing chemotherapy with anthracyclines.²⁴ It has been shown that the risk of cardiotoxicity is dose-related in various forms of chemotherapy. There are few publications concerning the effects of moderate doses of anthracyclines on ventricular myocardial performance in clinically asymptomatic children under treatment for malignant neoplasms. A significant difference in the Tei index was seen between 30 patients taking moderate to high doses of anthracyclines $(\geq 200 \text{ mg/m}^2)$ and 81 matched controls (0.45 ± 0.06) versus 0.33 ± 0.02 , p<0.05) and the levels were also higher than in 35 patients treated with lower (<200 mg/m²) anthracycline doses (0.45 \pm 0.06 versus 0.34 \pm 0.09, p<0.05). Prolongation of the IVRT and IVCT and significant shortening of the ET caused a significant increase in the index in those receiving moderate doses of anthracyclines. During the administration of a moderate dose of anthracyclines (≥200 and <400 mg/m²) 83% of the treated patients had a pathological index but normal fractional shortening, while during the administration of high doses ($\geq 400 \text{ mg/m}^2$) all patients had a pathological index while only 41% had pathological fractional shortening. The Tei index appears to be a sensitive, precise and easy method for the early identification of myocardial disturbances in patients treated with moderate doses of anthracyclines.

Conclusions

Measurement of the Tei index is non-invasive and easily obtained, it does not require the presence of an echocardiographer with great experience and it does not materially prolong the time required for the examination. The calculation of the index is not based on a geometric model or on volume measurements, it is first and foremost a ratio of time intervals, independent of ventricular geometry. It is also independent of blood pressure, heart rate and age and it appears to be of great prognostic value in many different clinical settings.

Of course, the Tei index has its disadvantages and its use may present difficulties. For example, its precise measurement is infeasible in patients with atrial fibrillation, frequent ventricular ectopic stimuli, disturbances of intraventricular or atrioventricular conduction, a permanent pacemaker, or when Doppler

images of sufficient quality cannot be acquired. Furthermore, it is affected to some degree by loading conditions.

The Tei index is not a gold standard method for the diagnostic approach to various heart diseases. However, it appears to be reliable for the evaluation of the severity of myocardial dysfunction in an appreciable number of diseases and can help determine which patients need early intervention, assuming that future studies confirm its prognostic power. Once its role has been further clarified, its ease of use and reproducibility could bring it into everyday clinical practice.

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