

Clinical Research

Tei Index as a Method of Evaluating Left Ventricular Diastolic Dysfunction in Acute Myocardial Infarction

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Introduction: The Doppler index of overall left ventricular (LV) myocardial performance –the Tei index– has been shown to be a reliable indicator of all changes in LV systolic dysfunction, retaining an inverse relationship with the ejection fraction. The aim of this study was to examine the corresponding behaviour in relation to LV diastolic dysfunction in patients with acute myocardial infarction (AMI), a relationship that has not been studied previously.

Methods: The study included 105 patients (77 men) with first AMI who were classified into four groups according to the severity of LV diastolic dysfunction: a) 25 patients with normal diastolic function (NDF), b) 36 with decreased peak filling rate pattern (DFR), c) 33 with impaired relaxation (IR) and d) 11 with pseudonormal or restrictive physiology (PN/RP). A complete echocardiographic study, including all conventional systolic and diastolic echo/Doppler parameters as well as measurement of the Tei index, was performed on the eighth post-infarction day (mean 8.07 ± 0.96 days) in all patients.

Results: In the patients with IR (0.77 ± 0.05) the index was significantly greater than in those of the NDF (0.55 ± 0.03 , $p < 0.01$) or DFR (0.65 ± 0.02 , $p < 0.01$) groups. The index in the DFR group was greater than in the NDF group, though not significantly so. In contrast, the index in the PN/RP patients (0.59 ± 0.05) was significantly lower than in the patients with IR ($p < 0.01$), whereas it did not differ from that of the patients in the NDF or DFR groups ("pseudonormalisation" of the index).

Conclusions: The Tei index detects with reliability milder types of diastolic dysfunction. However, because of its "pseudonormalisation" in patients with PN/RP, the Tei index cannot be considered a reliable indicator of more severe patterns of LV diastolic dysfunction in AMI patients.

During its short lifespan to date the well-known Doppler index of overall myocardial performance –the Tei index– has been shown to demonstrate: a) powerful prognostic value in significant heart diseases such as dilated cardiomyopathy,^{1,2} cardiac amyloidosis,³ idiopathic pulmonary hypertension,⁴ and, recently, myocardial infarction;⁵⁻⁸ b) superiority over conventional systolic and diastolic Doppler parameters in the identification and evaluation of patients with a large va-

riety of diseases;^{1,3,4,9,10} and c) various other advantages compared to classical diastolic Doppler parameters, such as not being influenced by changes in blood pressure^{3,11} or heart rate,^{3,11,12} being independent of age and sex,¹³ while not appearing to be affected significantly by loading conditions.^{14,15}

However, the left ventricular (LV) index, while having been found to reflect faithfully the severity of systolic dysfunction,^{1,3,16} retaining an inverse relationship

with the ejection fraction,¹⁶ does not appear to be so successful as far as the severity of LV diastolic dysfunction¹⁷ is concerned. In a recent study¹⁷ we found for the first time a “pseudonormalisation” of the LV index in a subgroup of patients with acute myocardial infarction (AMI) and diastolic dysfunction of restrictive physiology. Recently, Bruch et al¹⁸ found the same limitation of the index in patients with coronary artery disease and congestive heart failure from predominant LV diastolic dysfunction. In contrast to the early phase, the above limitation seems to disappear in the hyper-acute⁵ and chronic^{6,19} phases of myocardial infarction. In any case, the behaviour of the index in relation to the standard forms of LV dysfunction has not been studied systematically so far.

In light of the above, the aims of this study were as follows: 1) to detect changes in the Tei index and its clinical value in relation to the type of LV diastolic dysfunction in patients with a first AMI, something that has not been investigated before, and 2) to interpret the “pseudonormalisation” of the index.

Material and methods

The study population included 105 patients (77 men), mean age 60 ± 10 years, with first AMI, 60 (57%) with an inferior and 45 (43%) with an anterior infarction. The criteria for AMI were typical precordial pain with accompanying electrocardiographic changes suggestive of AMI and a concomitant increase in cardiac enzyme levels. The patients were classified into four groups according to the severity of their LV dysfunction:^{20,21} a) 25 patients (21 men), mean age 52 ± 2 years, with preserved normal diastolic function (NDF);^{20,21} b) 36 patients (27 men), mean age 61 ± 1 years, with decreased peak filling rate pattern (DFR); c) 33 patients (21

men), mean age 64 ± 1 years, with impaired relaxation (IR); and d) 11 patients (8 men), mean age 64 ± 2 years, with pseudonormal or restrictive physiology (PN/RP). The classification of the patients was based on the transmitral and pulmonary venous flow velocity patterns, obtained with transthoracic pulsed Doppler echocardiography (Table 1). To distinguish the patients of the IR group from those in the DFR group the criteria E/A ratio <0.7 and E wave deceleration time >250 ms were used.²⁰ Patients in the PN/RP group were distinguished from those in the NDF group by the criteria ratio of systolic to diastolic peak pulmonary venous flow velocity <0.5 and peak velocity of the atrial systolic pulmonary venous reversal wave >0.35 m/s.^{20,21}

A complete echocardiographic study including all the conventional systolic and diastolic echo/Doppler parameters, as well as measurement of the Tei index at rest, was performed on about the eighth post-infarction day (mean 8.07 ± 0.96 days) in all patients during the morning and with the patients in a fasted state. Thrombolytic treatment was given in 58 patients (55%), renin-angiotensin system inhibitors in 63 (60%). Systemic hypertension was found in 48 patients (46%). Patients with any of the following characteristics were excluded: previous history of infarction, atrial fibrillation, artificial pacemaker, left bundle branch block, high degree atrioventricular block, previous history of angioplasty or coronary bypass surgery, the presence of any valvular disease of greater than mild degree, age over 75 years.

The echocardiographic examination (one- and two-dimensional, Doppler) was performed using an ATL-UM9 device (Advanced Technology Laboratories) and a 2.5 MHz phased array transducer. With the patient reclining on the left side, and using a parasternal long-axis view at the level of the LV, we measured its end-diastolic diameter, while the left

Table 1. Classification of left ventricular diastolic dysfunction based on characteristics of transmitral flow and pulmonary venous flow obtained using transthoracic pulsed Doppler echocardiography.

Groups	E/A	E _{DT} (ms)	S/D	A _{PV} (m/s)
Normal diastolic function	1-2	150-200	≥ 1	<0.35
Decreased peak filling rate pattern	0.7-1	200-250	≥ 1	<0.35
Impaired relaxation	<0.7	>250	≥ 1	<0.35
Pseudonormal/restrictive physiology	>2	<150	<0.5	≥ 0.35

A - peak transmitral flow velocity at atrial systole, A_{PV} - peak diastolic pulmonary venous reversal flow velocity at atrial systole, D - peak diastolic pulmonary venous flow velocity, E - peak transmitral flow velocity during early diastole, E_{DT} - E deceleration time of early diastole, S - peak pulmonary venous systolic flow velocity.

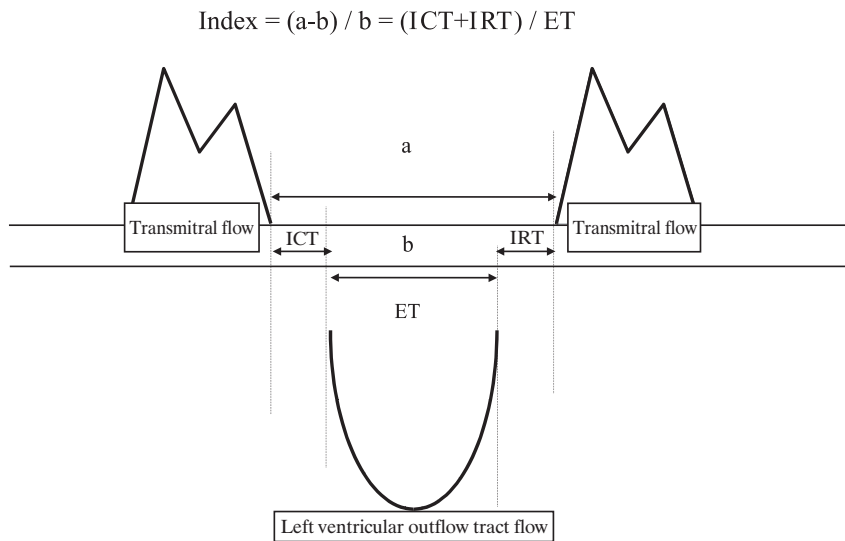


Figure 1. Schematic representation of the measurement of the Tei index. The index is defined as the ratio $(a-b)/b$, where a is the interval between cessation and onset of the mitral inflow and b is the left ventricular ejection time (also denoted by ET). The isovolumic relaxation time (IRT) is the interval between the aortic valve closure and the onset of mitral valve flow, while the isovolumic contraction time (ICT) is the interval between the cessation of mitral inflow and the onset of aortic valve flow.

atrial dimension was assessed at the level of the aorta by M-mode. The ejection fraction was measured using the Bullet method. Evaluation of the LV filling pattern was made from the apical four-chamber view with the pulsed Doppler sample at the tip of the mitral valve leaflets during diastole,²⁰ when the following parameters were recorded: a) peak flow velocity early at diastole (E wave); b) peak flow velocity during atrial systole (A wave); c) the E/A ratio; and d) the deceleration time of early diastolic filling (the time interval from the peak of the E wave to the point of intersection of the downsloping initial filling velocity with the baseline). From the apical five-chamber view with the pulsed Doppler sample in the LV outflow tract, in such a way as to record mitral valve and aortic flow simultaneously, we calculated the isovolumic relaxation time (IRT), namely the time from the closing of the aortic valve until the opening of the mitral valve.^{20,22} This method of studying LV diastolic function is well-established in the international literature and has been correlated with both radioisotope and angiographic methods for evaluating diastolic function.^{22,23}

Also from the apical five-chamber view, with the pulsed Doppler sample volume placed first in the LV outflow tract and then just below the aortic valve, we calculated, respectively, the systolic parameters isovolumic contraction time (ICT, the time from the closing of the mitral valve to the opening of the aortic valve) and ejection time (ET, the time between the opening and the closing of the aortic valve). From the apical four-chamber view, with the pulsed Doppler sample volume at the origin of the right pulmonary

vein and with the aid of colour Doppler, we recorded the pulmonary venous flow²⁴ and calculated the systolic/diastolic peak velocity ratio and the peak velocity of the atrial systolic pulmonary venous reversal flow. Finally, we calculated the Tei index, which combines systolic and diastolic LV time intervals, using the formula $(a-b)/b$, where a is the interval between the closing and the opening of the mitral valve and b is equal to the LVET. These intervals are derived from the time intervals of transmitral flow velocities and the flow in the LV outflow tract, as obtained separately by pulsed Doppler echocardiography (Figure 1). The a interval includes the ICT, ET and IRT, which are established indexes of systolic and diastolic LV function. Thus, if the b interval –i.e. the ET– is subtracted from a what remains is the sum ICT+IRT, so the index may also be expressed by the formula ICT+IRT/ET (Figure 1).

Each of the above parameters was measured at the end of exhalation and the mean value of five successive measurements was used for the calculations.

All patients gave their informed consent to the study procedure, which conformed to the established ethical principles for medical research in Greece and to the Helsinki Declaration as revised in 2000.

Statistical analysis

All quantitative data are expressed as mean value \pm standard deviation or standard error of the mean. The t-test was used to compare quantitative parameters and the χ^2 test for qualitative data. A p value <0.05 was the criterion for statistical significance.

Table 2. Clinical characteristics and general echocardiographic findings.

	NDF (n=25)	DFR (n=36)	IR (n=33)	PN/RP (n=11)
Age (years)	52 ± 2	61 ± 1 ¹⁺⁺	64 ± 1 ¹⁺⁺	64 ± 2 ¹⁺⁺
Men/Women	21/4	27/9	21/12	8/3
Heart rate (beats/min)	67 ± 2	70 ± 2	77 ± 2 ¹⁺⁺	88 ± 2 ¹⁺⁺
Systolic BP (mmHg)	112 ± 25	117 ± 25	117 ± 29	104 ± 31 ^{2+,3+}
Diastolic BP (mmHg)	73 ± 20	74 ± 16	74 ± 16	71 ± 21
Thrombolytic treatment	20 (80%)	17 (47%) ¹⁺	19 (58%)	3 (27%) ¹⁺⁺
RAS-inhibitors	19 (76%)	21 (58%)	19 (58%)	4 (36%)
Systemic hypertension	9 (36%)	18 (50%)	18 (55%)	3 (27%)
LVEDD (cm)	5.0 ± 0.1	5.0 ± 0.1	4.7 ± 0.1 ^{1+,2+}	5.6 ± 0.1 ^{1+,2+,3++}
Left atrium (cm)	3.9 ± 0.1	4.0 ± 0.1	3.9 ± 0.1	4.2 ± 0.1
Ejection fraction (%)	59 ± 2.0	54 ± 1.9	48 ± 2.1 ¹⁺⁺	40 ± 4.2 ¹⁺⁺

BP - blood pressure, DFR - decreased peak filling rate pattern, IR - impaired relaxation, LVEDD - left ventricular end-diastolic diameter, NDF - normal diastolic function, PN/RP - pseudonormal/restrictive physiology, RAS - renin-angiotensin system.

⁺p<0.05; ⁺⁺p<0.001; ¹p comparison of NDF group with each of the other groups; ²p comparison of DFR group with each of the other groups; ³p IR vs. PN/RP.

Results

Patient characteristics

The clinical and general echocardiographic characteristics of the patients in the study groups are shown in table 2. The patients in the study groups were comparable as regards sex, diastolic blood pressure, systemic hypertension, treatment with renin-angiotensin system inhibitors and left atrial size. Patients in the NDF group were significantly younger than those in the other groups. Patients in the PN/RP group had significantly lower systolic blood pressure than those in the DFR and IR groups, no different from those in the NDF group. The heart rate and end-diastolic LV diameter in the PN/RP group were significantly greater than in the other groups. Thrombolytic treatment was more common in the NDF and IR groups.

Doppler parameters

A comparison of the Doppler parameters in the study groups is shown in table 3. Patients in the PN/RP group had a significantly greater E wave and a smaller A wave than those in the other groups, resulting in a significantly greater E/A ratio for those patients. As would be expected, the opposite was true for patients with IR. The E wave deceleration time was significantly shorter in the PN/RP group and significantly longer in the IR group compared to the other groups.

The isovolumic relaxation time in the IR group was significantly prolonged and the ejection time significantly shorter than in the NDF and DFR groups, resulting in a significantly higher Tei index in the IR group than in the latter two groups (Figure 2). The isovolumic relaxation time in the DFR group was significantly longer than in the NDF group, although those groups did not differ as regards ejection time and isovolumic contraction time. As a result, the index in the DFR group was greater than that in the NDF group, though not to a statistically significant degree (Figure 2). The ejection time in the PN/RP group was significantly shorter and the isovolumic contraction time longer than in the NDF and DFR groups, but not sufficiently to compensate for the significant shortening in isovolumic relaxation time in the PN/RP group. This resulted in a Tei index for the PN/RP group that did not differ significantly from that of the NDF and DFR groups (“pseudonormalisation” of the index – figure 2). The isovolumic relaxation time of the patients in the IR group was significantly greater than in the PN/RP group, whereas the ejection time and isovolumic contraction time did not differ significantly, leading to a significantly greater Tei index in the IR group than in the PN/RP group (Figure 2). The reversal pulmonary venous A wave in the PN/RP patients was significantly greater and the ratio of the systolic to the diastolic pulmonary venous wave was significantly smaller than in the other three groups.

Table 3. Doppler measurements.

	NDF (n=25)	DFR (n=36)	IR (n=33)	PN/RP (n=11)
E (m/s)	0.78 ± 0.03	0.62 ± 0.02 ¹⁺⁺	0.47 ± 0.02 ^{1++,2++}	0.96 ± 0.06 ^{1++,2++,3++}
A (m/s)	0.60 ± 0.02	0.80 ± 0.03 ¹⁺⁺	0.88 ± 0.03 ¹⁺⁺	0.44 ± 0.03 ^{1++,2++,3++}
E/A ratio	1.32 ± 0.04	0.83 ± 0.05 ¹⁺⁺	0.53 ± 0.01 ^{1++,2++}	2.29 ± 0.16 ^{1++,2++,3++}
E _{DT} (ms)	191 ± 4	224 ± 6 ¹⁺⁺	285 ± 8 ^{1++,2++}	128 ± 6 ^{1++,2++,3++}
IRT (ms)	110 ± 4	132 ± 4 ¹⁺	148 ± 6 ^{1++,2+}	89 ± 7 ^{1++,2++,3++}
ICT (ms)	56 ± 2	61 ± 2	60 ± 3	67 ± 4 ¹⁺
ET (ms)	281 ± 6	270 ± 5	247 ± 6 ^{1++,2+}	242 ± 10 ^{1++,2+}
Tei index	0.55 ± 0.03	0.65 ± 0.02	0.77 ± 0.05 ^{1++,2+}	0.59 ± 0.05 ³⁺
A _{PV}	0.28 ± 0.005	0.30 ± 0.004 ¹⁺	0.33 ± 0.006 ^{1++,2++}	0.36 ± 0.004 ^{1++,2++,3+}
S/D ratio	1.46 ± 0.004	1.49 ± 0.003	1.75 ± 0.02 ¹⁺⁺	0.41 ± 0.02 ^{1++,2++,3++}

ET - ejection time, ICT - isovolumic contraction time, IRT - isovolumic relaxation time. Other abbreviations as in previous tables.

⁺p<0.05; ⁺⁺p<0.001; ¹p comparison of NDF group with each of the other groups; ²p comparison of DFR group with each of the other groups; ³p IR vs. PN/RP.

Discussion

This study was designed to detect changes in the Tei index in relation to the type of diastolic LV function in patients with AMI. The main finding was that the index undergoes “pseudonormalisation” in patients with a pseudonormal or restrictive physiology, a fact that significantly reduces the value of the method in the assessment of LV diastolic dysfunction.

We found that the index in patients with impaired relaxation was significantly higher than in patients with normal diastolic function or decreased peak filling rate pattern. Additionally, in the latter group the

index was greater than in the patients with normal diastolic function, although the difference did not reach statistical significance. In contrast, the Tei index in patients with pseudonormal/restrictive physiology was significantly lower than in those with impaired relaxation, whereas it did not differ from that of patients with normal diastolic function or decreased peak filling rate pattern, implying a serious limitation of the index (“pseudonormalisation” of the Tei index). It thus seems that during the early phase of myocardial infarction, although the Tei index reflects the severity of LV diastolic dysfunction in patients with decreased peak filling rate pattern or with impaired relaxation,

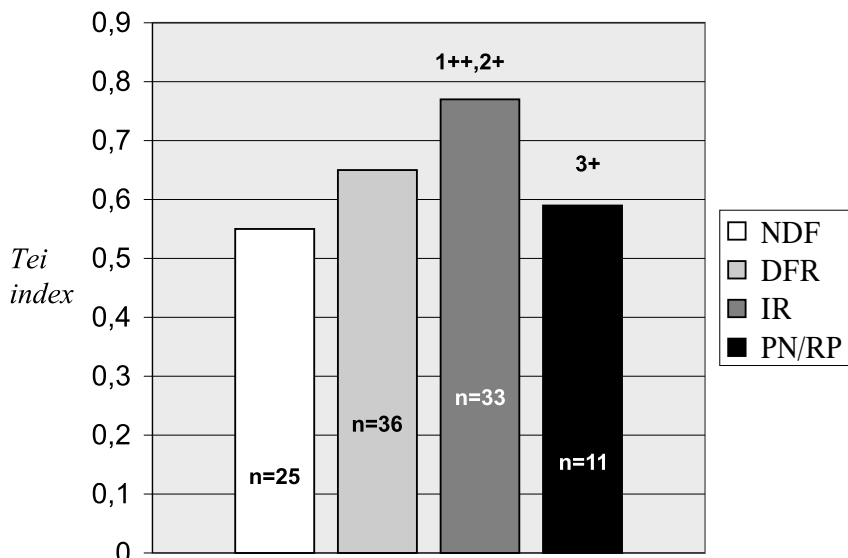


Figure 2. “Pseudonormalisation” of the Tei index in patients in the early phase of a first myocardial infarction. In those with a pseudonormal or restrictive physiology (PN/RP) the index was significantly smaller than in patients with impaired relaxation (IR), but did not differ from that in patients with normal diastolic function (NDF) and those with decreased peak filling rate pattern (DFR).

⁺p<0.05; ⁺⁺p<0.001; ¹p comparison of NDF group with each of the other groups; ²p comparison of DFR group with each of the other groups; ³p IR vs. PN/RP.

because of this “pseudonormalisation” it fails to do so in patients with pseudonormal or restrictive physiology. This weakness arises from the sole diastolic component of the index, isovolumic relaxation time, which as a pure relaxation parameter can detect disturbances related to the relaxation process but not those that develop in the most severe forms of LV diastolic dysfunction.²⁵⁻²⁷ If we consider that these latter types of diastolic dysfunction usually concern patients with advanced heart disease of various causes,^{25,28-30} it is easy to see that this limitation seriously reduces the clinical usefulness of the index as an LV diastolic parameter.

The above finding stands in contradiction to other studies that measured the index in the hyper-acute⁵ and chronic^{6,19} phases of myocardial infarction and showed that the limitation did not apply. An interpretation of this different behaviour of the index follows, along with an explanation of its “pseudonormalisation” during the early phase of myocardial infarction.

Interpretation of the “pseudonormalisation” of the Tei index

In a study by Poulsen et al,⁵ the index was measured during the hyper-acute phase of myocardial infarction, one hour after the patients’ arrival in the coronary care unit. This is a time when, because of the acute ischaemia and the start of necrosis, there is known to be a severe degree of LV systolic dysfunction.^{31,32} This disturbance, as detected by the systolic parameters of the Tei index, causes a degree of deterioration in those parameters that is sufficient, not only to balance out the shortening of the isovolumic relaxation time that is seen in patients with pseudonormal/restrictive physiology, but also to cause a significant increase in the value of the index.⁵ In contrast, during the early phase of myocardial infarction (8th. post-infarction day, when our patients were examined) the compensatory hypertrophy of the healthy myocardium that has already developed,^{31,32} and which in this phase is useful and makes up for the lost myocardium, causes a significant improvement in the LV systolic dysfunction and hence in the systolic parameters of the Tei index. As a result, these factors no longer balance out the short isovolumic relaxation time, leading to “pseudonormalisation” of the index. Finally, during the chronic phase of myocardial infarction the LV dilatation that has developed as a result of remodelling,^{31,32} in combination with the scarring of the infarct area, causes a new deterioration in

the systolic parameters of the index that, as in the hyper-acute phase, eliminates its “pseudonormalisation.”^{6,19} The above explanation illustrates why the systolic Doppler parameters –as opposed to the isovolumic relaxation time– are able to detect every change in systolic function and shows why the index is a reliable LV systolic parameter.

The phenomenon of “pseudonormalisation” of the index, resulting from the fact that the LV systolic function is better during the early phase of myocardial infarction than it is in either the hyper-acute or the chronic phase, is also supported by other studies. One is the original study by Tei et al³³ of patients with dilated cardiomyopathy and severe LV systolic dysfunction, which in accordance with the above argument prevented the “pseudonormalisation” of the index. Another is a recent study by Bruch et al¹⁸ involving patients with coronary artery disease and congestive heart failure. Although the latter authors found significantly high values of the index in patients who had mixed ventricular dysfunction, they found significantly low values in those who had predominantly diastolic LV dysfunction.

Zhang et al,³⁴ in a recent study, demonstrated the ability of the index to discriminate between normal and falsely normalised/restrictive transmitral flow. Those investigators, using the criterion E/A ratio ≥ 1 combined with LV mid-diastolic pressure ≥ 12 mmHg, created a group of patients the same size as our own. However, a careful comparison of Zhang’s patients with the present study (E/A 1.7 ± 0.8 vs. 2.29 ± 0.16 and E wave deceleration time 170 ± 30 vs. 128 ± 6 ms) clearly shows that the two groups represent different degrees of severity as far as a restrictive physiology is concerned. Of course, in our patients we had no haemodynamic evaluation of filling pressure, but the significantly high E/A ratio and E wave,³⁵⁻³⁸ the significantly short E wave deceleration time,³⁵⁻³⁸ the confirmation of these findings from the pulmonary venous flow³⁹⁻⁴¹ in combination with the systolic LV dysfunction,^{35,38} are all strong indications of increased filling pressure. It is thus clear that in the milder forms of pseudonormal/restrictive physiology the index can withstand “pseudonormalisation” (probably because there is a lesser degree of shortening of the isovolumic relaxation time), whereas it fails in the presence of more severe patterns.

Limitations of the study

Satisfactory recording of pulmonary venous flow was achieved in 71 of our 105 patients (68%). In the re-

mainder, the classification was made based mainly on the findings for transmitral flow, in combination with the clinical picture and the ejection fraction.^{35,38} The determination of patients with normal diastolic function was based on the findings for transmitral and pulmonary venous flow velocity patterns.^{20,21} Tissue Doppler echocardiography or the one-dimensional colour Doppler technique, methods that have been shown to be relatively independent of conventional diastolic Doppler parameters,⁴²⁻⁴⁵ could probably have improved the detection of further diastolic functional abnormalities in these patients. Those methods, though, were not chosen as part of a routine examination in the present study.

A large number of studies, of both healthy individuals¹⁵ and patients,^{15,18,46} together with a recent experimental study,¹⁶ have shown a partial correlation between the Tei index and preload. This limitation does not appear to apply to reclining patients with myocardial infarction¹⁵ and so is unlikely to have had a material effect on our results.

There was some inhomogeneity among the study groups, as regards age, heart rate and systolic blood pressure. Considering that the Tei index is independent of changes in those parameters,³⁻¹¹⁻¹³ this disparity should not have affected the behaviour of the index in our groups. Also, the subgroups were not comparable with respect to the taking of thrombolytic treatment, but there is no evidence showing that thrombolysis affects the values of the index. In the case of renin-angiotensin system inhibitors, which have been shown to improve the index significantly,¹⁰ our study groups were comparable.

Conclusions

Although the Tei index can successfully detect the severity of the milder forms of LV diastolic dysfunction (which concern the relaxation process) in patients with AMI, it fails in more severe forms (pseudonormal or restrictive physiology) as a result of "pseudonormalisation" of the index in the subgroup of patients with a restriction. This drawback significantly reduces the clinical value of the index as a method of evaluating LV diastolic dysfunction in patients with AMI.

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