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Long-Term Prognostic Value of an Index of Myocardial Performance in Patients with Myocardial Infarction

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Summary

Background: The Tei index of myocardial performance (IMP), which combines parameters of both systolic and diastolic ventricular function, is a useful prognostic factor in many clinical settings.

Hypothesis: This study assessed the long-term prognostic value of IMP in patients discharged from hospital after acute myocardial infarction (AMI).

Methods: Doppler/echocardiographic studies were recorded in 90 consecutive patients on Day 14 ± 2 following an AMI. The IMP was calculated from the Doppler recordings, as a sum of isovolumetric contraction time and isovolumetric relaxation time, divided by the ejection time.

Results: The patients were followed for an average (SD) of 57.8 (16.1) months. During this period there were 22 (24%) cardiac events, defined as cardiac deaths (10) or nonfatal recurrent myocardial infarctions (12). After multivariate Cox analysis, Tei index > 0.55 (relative risk [RR] 4.45; 95% confidence interval [CI] 1.28–15.45; p = 0.019), LV end-systolic volume > 65 ml (RR 3.23; 95% CI 1.34–7.79; p = 0.009), and mitral E wave deceleration time ≤ 0.145 s (RR 2.94; 95% CI 1.24–6.92; p = 0.014) were the only independent predictors of cardiac events during the follow-up period. In a subgroup of patients with preserved LV systolic function (ejection fraction > 0.40), IMP was the only predictor of cardiac events (RR 6.37; 95% CI 1.32–30.77, p = 0.02).

Conclusions: The Tei index of myocardial performance, which is simple and easy to calculate, is a useful tool for risk assessment in patients following myocardial infarction, and in a subgroup of patients with normal or only mildly impaired systolic function.

Key words: myocardial infarction, prognosis, Doppler echocardiography, index of myocardial performance

Introduction

Indices of left ventricular (LV) systolic dysfunction are important predictors of outcome following myocardial infarction (MI).[1, 2] The prognostic significance of diastolic indices, such as elevated pulmonary wedge pressure and restrictive LV filling, has also been demonstrated.[3, 4] Systolic and diastolic function are tightly coupled: (1) at a cellular level, since adenosine triphosphate (ATP) is essential both for active contraction and relaxation;[5] (2) at a myocardial level, because regional systolic asynchrony influences global diastolic function;[6] and (3) at a hemodynamic level, because systolic function influences LV filling.[7] The duration of diastole is an important determinant of myocardial perfusion,[8] and the ratio of the diastolic to the systolic pressure–time index is used to assess a relationship between subendocardial oxygen supply and demand.[9] For these reasons, the recently described Tei index of myocardial performance,[10] which combines parameters of both systolic and diastolic ventricular function, could be a suitable tool for assessing the prognosis of patients following MI. The clinical value of the index has been examined in normal individuals[11] and in patients with dilated cardiomyopathy,[11, 12] amyloidosis,[13] anthracycline cardiomyopathy,[14] and essential hypertension.[15] Other studies have compared the index of myocardial performance with hemodynamic indices in ischemic and dilated cardiomyopathy.[16, 17] These reports concluded that the index is a sensitive adjunctive parameter for the assessment of cardiac function.[18] Recently, a paper on the value of the Tei index in the early phase of MI was published.[19] In the present study, we analyzed the long-term prognostic value of the index of myocardial performance in patients who survived the acute phase of MI.

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Methods

Patients

The study group comprised 90 consecutive hospital survivors of acute MI. For admission to the study, the patients needed to satisfy two of three diagnostic criteria: (1) a history of typical chest pain, and/or (2) evolutionary ST-T changes in at least two contiguous electrocardiographic (ECG) leads diagnostic for MI; and/or (3) a transient rise of creatinine kinase in excess of twice the upper normal limit. Exclusion criteria were (1) persistent atrial fibrillation, (2) sinus tachycardia > 100 beats/min, (3) significant mitral and/or aortic regurgitation/stenosis, and (4) Doppler and/or two-dimensional (2-D) echocardiographic recordings that were technically inadequate for quantitative analysis. All patients agreed to participate and the Ethics Committee of our Institution approved the study.

Follow-Up

Follow-up data were obtained prospectively for each patient from the outpatients' clinic and hospital records, written correspondence, and telephone and personal communication. Cardiac events were defined as cardiac deaths or nonfatal recurrent MI. The cause of death was determined from hospital documentation, information from attending physicians, and death certificates. The diagnosis of recurrent nonfatal MI was made on the basis of hospital admission records.

Two-Dimensional and Doppler Echocardiographic Examination

Two-dimensional echocardiographic and Doppler studies were performed on Day 14 ± 2 after an acute MI, using a commercially available ultrasound machine (Acuson 128 XP Computed Sonography; Acuson Inc., Mountain View, Calif., USA) with a 2.5 or 3.5 MHz transducer. These investigations were recorded on super VHS videotape for subsequent offline analysis. The wall motion score index was calculated according to the recommendations of the American Society of Echocardiography.[20] Left ventricular end-diastolic and endsystolic volumes and ejection fraction were measured from standard apical two- and four-chamber views, according to the Simpson's biplane disc method.[20]

Pulsed Doppler recordings of mitral inflow velocities were obtained by placing the 1.5–2.5 mm sample volume at the tips of mitral leaflets during diastole in the apical four-chamber view. The LV outflow tract velocity pattern was recorded with the sample volume positioned immediately below the aortic valve.

Echocardiographic/Doppler Measurements

All 2-D and Doppler measurements were carried out offline by two observers (P.S. and J.R.) using a commercially available digitizing system (Prism-Lite Windows, Prism-Lite Imaging, Inc., Louisville, Colo., USA). All measurements were performed blindly, without the knowledge of the patients' clinical status. Three to five consecutive beats were measured and averaged for all Doppler measurements. The following transmitral parameters were analyzed: early (E) and late (A) peak filling velocities, the E/A ratio, the E wave deceleration time and the interval between cessation and onset of mitral inflow (a). Left ventricular ejection time (ET) (b) was measured from the LV outflow velocity profile. The sum of the isovolumetric contraction time and the isovolumetric relaxation time (Σ IVC + IVR) was calculated by subtracting (b) from (a). The index of myocardial performance was calculated as a sum of isovolumetric contraction time and isovolumetric relaxation time divided by ejection time [(Σ IVC + IVR)/ET] or [(a − b)/b], following the approach described by Tei.[10]

Statistical Analysis

Descriptive Statistics

All continuous variables are described using the standard parameters: mean value (standard deviation [SD]), median value, and range. Categoric data are expressed as absolute numbers and percentages.

Survival Analysis

Survival free of cardiac death and recurrent nonfatal MI were estimated using the Kaplan-Meier method. Univariate and multivariate Cox proportional hazards models were used to investigate the ability of selected clinical, echocardiographic, and Doppler variables to predict cardiac event-free survival in a total population and in a subgroup of patients with preserved LV systolic function (ejection fraction > 0.40). The following variables were included in the univariate Cox model: age (> 60 years), gender, heart failure history, history of MI, non-Q MI, maximal creatine kinase level (> 1500 U/l), fibrinolytic therapy, beta-blocker therapy, angiotensin-converting enzyme inhibitor administration, wall motion score index > 1.3, ejection fraction ≤ 0.40, LV end-systolic volume > 65 ml, ejection time ≤ 0.240 s, deceleration time ≤ 0.145 s, and index of myocardial performance > 0.55. Variables that were statistically significant at a level of $p < 0.05$ in this analysis were included in a multivariate analysis. A backward selection method was used to identify the variables that were statistically significant ($p < 0.05$). Cardiac event-free survival curves were then computed for these variables using the Kaplan-Meier method. All statistical calculations were performed with Statistical Package for Social Sciences for Windows 6.0 (SPSS Inc., Chicago, Ill., USA).

Correlations

Statistical relationships between the Doppler measurements, heart rate, and blood pressure, the index of myocardial performance, and other echocardiographic indices of systolic and diastolic function, were assessed by simple linear correlations and were considered significant when $p < 0.05$.

TABLE I Baseline clinical characteristics (90 patients, age ± standard deviation, 58 ± 12 years)

	N (%)
Sex (male	71 (79)
Smoking	59 (66)
Hypertension	42 (47)
Diabetes	11 (12)
History of heart failure	28 (31)
History of MI	18 (20)
Fibrinolytic treatment	34 (38)
ACE inhibitors	43 (48)
Beta blockers	51 (57)
Infarction site	
Inferior/posterior	43 (48)
Anterior/lateral	47 (52)
Q-wave MI	56 (62)

Abbreviations: MI = myocardial infarction, ACE = angiotensin-converting enzyme.

Results

The characteristics of the patients included in the study are described in Table I. Echocardiographic/Doppler measurements are presented in Table II. For the whole group studied, the average index of myocardial performance was mean (SD) 0.57 (0.19); 43 patients had an index of myocardial performance of ≤ 0.55: mean (SD) 0.42 (0.09), and 47 patients had an index of > 0.55: mean (SD) 0.71 (0.14).

Compared with patients with an index of myocardial performance ≤ 0.55, those with an index of myocardial performance > 0.55 were more likely to have a history of heart failure (23 vs. 38%); a history of previous myocardial infarction (12 vs. 28%); were less likely to have received fibrinolytic therapy (44 vs. 32%) and beta blockers (65 vs. 49%). Patients with a higher index of myocardial performance had greater LV end-systolic volume (62 vs. 55 ml), smaller ejection fraction (42 vs. 48%), shorter deceleration time (0.159 vs. 0.178 s), and ejection time (0.250 vs. 0.280 s).

TABLE II Echocardiographic/Doppler findings

	Mean ± SD
LVEDV (ml)	110 ± 19
LVESV (ml)	59 ± 17
EF	0.47 ± 0.09
WMSI	1.5 ± 0.4
E/A	1.08 ± 0.53
DT (s)	0.167 ± 0.041
ET (s)	0.27 ± 0.03
IMP	0.57 ± 0.19
HR (beats/min)	71 ± 10

Abbreviations: SD = standard deviation, DT = mitral E wave deceleration time, E/A = mitral E wave to A wave velocity ratio, EF = ejection fraction, ET = ejection time, HR = heart rate, IMP = index of myocardial performance, LVEDV = left ventricular end-diastolic volume, LVESV = left ventricular end-systolic volume, WMSI = wall motion score index.

Clinical Outcomes

The patients were followed up on for an average (SD) of 57.8 (16.1) months (range 0.4–74.2). During this period, there were 22 (24%) cardiac events (10 cardiac deaths and 12 nonfatal MIs). Patients with or without cardiac events during follow-up did not differ with respect to their demographic and clinical characteristics, with the exception of a history of congestive heart failure, which was present in half of those with subsequent events (11/22), but only in one-fourth of the event-free survivors (17/68). Three patients (3%) died from noncardiac causes (two carcinomas, one stroke).

In the group with an index of myocardial performance > 0.55, 9 deaths and 10 nonfatal subsequent MIs (and the two deaths from carcinomas) were observed. In the group with an index of myocardial performance ≤ 0.55, there were three cardiac events (one death and two nonfatal MIs) and one death from stroke. Event-free Kaplan-Meier survival curves of patients with an index of myocardial performance below/equal and over 0.55 are shown in Figure 1.

Of the 62 patients (48%) with an ejection fraction > 0.40, 30 had an index of myocardial performance > 0.55. Cardiac events occurred in 2 of 32 patients (6%) with an index of myocardial performance ≤ 0.55 and 8 of 30 (27%) patients with an index of myocardial performance > 0.55.

Analysis Using Cox Proportional Hazards Models

In the univariate Cox analysis, a history of heart failure, decreased ejection fraction, increased LV end-systolic volume, prolonged ejection time, shortened deceleration time, and a higher index of myocardial performance were all predictive of cardiac events at the $p < 0.05$ level. These results are presented

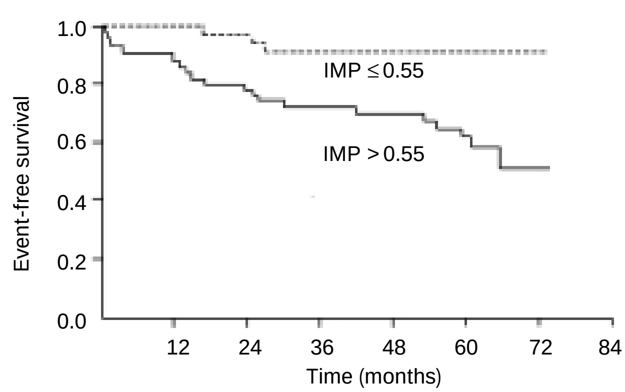

FIG. 1 Kaplan-Meyer event-free survival curves for the subgroups of patients with myocardial infarction and an index of myocardial performance (IMP) ≤ 0.55 and > 0.55.

TABLE III Univariate Cox model of clinical, echocardiographic, and Doppler variables predicting cardiac events

	RR	95% CI	p Value
Age > 60 years	1.03	0.44–2.40	0.93
Male gender	1.13	0.48–3.58	0.60
Heart failure	2.54	1.10–5.87	0.03
History of MI	2.19	0.89–5.38	0.09
Non-Q MI	0.51	0.19–1.41	0.20
Fibrinolytic therapy	1.52	0.65–3.54	0.33
ACE inhibitors	0.64	0.33–1.19	0.09
Beta blockers	0.56	0.24–1.31	0.18
CK max > 1500 U/l	1.94	0.84–4.53	0.12
WMSI > 1.3	2.10	0.76–5.75	0.15
EF ≤ 0.40	3.00	1.28–7.03	0.01
LVESV > 65 ml	3.79	1.62–8.90	0.002
ET ≤ 0.240 s	3.40	1.47–7.89	0.004
DT ≤ 0.145 s	2.84	1.21–6.67	0.02
IMP > 0.55	7.14	2.11–24.17	0.001

Abbreviations: RR = relative risk, CI = confidence interval, CK = creatine kinase, ACE = angiotensin-converting enzyme, MI = myocardial infarction. Other abbreviations as in Table II.

in Table III. All of these variables were included in the multivariate model. The results are reported in Table IV. Only the index of myocardial performance, LV end-systolic volume, and deceleration time (in descending order of importance) were significant predictors of cardiac events. In a subgroup of patients with preserved LV systolic function, an index of myocardial performance was the only predictor of cardiac events (RR 6.37, 95% CI 1.32–30.77, p = 0.02).

Correlations of the Index of Myocardial Performance with Heart Rate, Blood Pressure, and Echocardiographic/ Doppler Variables

Table V reports linear Pearson correlation coefficients between heart rate and selected Doppler variables. The index of myocardial performance correlated weakly (R = 0.21) with the heart rate. There was also a weak correlation (R = −0.48) between heart rate and aortic ejection time. Other variables did not correlate significantly.

The index of myocardial performance correlated significantly with systolic and diastolic function variables: E wave deceleration time (R = −0.21; p = 0.04), LV end-systolic volume (R = 0.30; p = 0.005), ejection fraction (R = −0.26; p = 0.01), and wall motion score index (R = 0.29; p = 0.005). The index of myocardial performance did not correlate significantly with systolic or diastolic blood pressure.

TABLE IV Multivariate Cox model analysis

	RR	95% CI	p Value
IMP > 0.55	4.45	1.28–15.45	0.019
LVESV > 65 ml	3.23	1.34–7.79	0.009
DT ≤ 0.145 s	2.94	1.24–6.92	0.014

Abbreviations as in Tables II and III.

Discussion

Long-term survival after MI depends on a number of factors. One of the most important is LV systolic function, and echocardiography has been used extensively to assess patients' future risks.[2] Invasive measures of LV filling and restrictive filling patterns that can be described with Doppler echocardiography can also provide prognostic information when managing patients with MI.[3, 4, 21] Measurements of systolic and diastolic function can provide complementary information.[22] For these reasons, Tei's description of the index of myocardial performance,[10] which combines both systolic and diastolic parameters of ventricular function, may be a suitable tool for assessing the prognosis of patients with MI.

Comparison with Previous Studies

Poulsen *et al.* followed up a group of 60 patients with MI and 30 controls for approximately 20 months, and demonstrated that an index of myocardial performance ≥ 0.60 reflects severity of LV dysfunction and has incremental prognostic value in patients with MI.[23] In a very recent study of a group of 60 patients, they also demonstrated that an index detected and graded LV dysfunction and identified patients at risk for the development of congestive heart failure.[19]

In the present study, we have demonstrated that an index of myocardial performance > 0.55, measured in the late phase of an acute MI, is a useful, independent long-term predictor of cardiovascular events. The index of myocardial performance scores in this study ranged from 0.2 to 1.0 and was very similar to the range reported in a similar earlier study of patients with ischemic heart disease (0.29–0.90).[16] The "cut-off" value of an index in our study was very similar to the one in the studies of Poulsen *et al.*[19, 23] Of importance is the fact that we have demonstrated that the Tei index retains its prognostic value in a subgroup of patients with preserved LV systolic function. This is in agreement with the results of the study by Kouris *et al.*, who observed abnormal values of the Tei index in patients

TABLE V Correlation of Doppler variables with the heart rate

	R (Pearson)	p Value
IMP	0.211	0.05
ET	−0.482	0.0001
DT	−0.252	NS
A	−0.076	NS
E/A	0.198	NS

Abbreviation: NS = not significant. Other abbreviations as in Table II.

with coronary artery disease and apparently normal systolic and diastolic function.[24] In contrast to the earlier study,[15] we observed a weak correlation between the index and heart rate; however, as very little of the variability of the heart rate explains the variability of an index, the correlation seems of little, if any, clinical importance.

Another index, which included only systolic time intervals—pre-ejection period and ejection time—has been studied extensively in the past, and its long-term prognostic value in patients with MI was demonstrated.[25] Left ventricular systolic dysfunction, regardless of its cause, lengthens pre-ejection period and shortens ejection time, so that the pre-ejection period/ejection time ratio increases.[26] Isovolumetric contraction time is included in the numerator of the Tei formula and is an important component of pre-ejection period, correlating inversely with +dP/dT.[27] Isovolumetric relaxation time, another component of the Tei formula included in the numerator, corresponds to the time constant of LV relaxation (tau),[28] which is significantly longer in patients with previous MI.[29] The value of tau increases through all stages of diastolic dysfunction,[30] so that isovolumetric relaxation time becomes prolonged with abnormal relaxation in most patients with coronary artery disease. As left atrial pressure increases, however, the mitral valve tends to open earlier, shortening isovolumetric relaxation time.[31, 32] In patients with elevated LV filling pressures, this phenomenon is "compensated" by the shortening of ejection time, with an earlier closure of the aortic valve, and by the shortening of the total duration of late mitral inflow, with premature mitral valve closure and prolongation of isovolumetric contraction time.[33, 34] As a result of the interplay between measures of systolic and diastolic function, the index of myocardial performance increases, thus providing functional and prognostic information.

Study Limitations

Neither isovolumetric contraction time nor isovolumetric relaxation time have been calculated separately from the Doppler recordings. For this reason, we have not been able to determine the relative importance of all components of the equation, although we have demonstrated (confirming the findings of earlier studies) that ejection time was a significant prognostic factor (at the univariate analysis).

We were not able to control load in a clinical setting; however, as in the Tei report,[11] no correlation with arterial blood pressure values was observed. The correlation between the Tei index score and heart rate was very weak, but caution should be used in extrapolating these results to patients with a heart rate exceeding 100 beats/min. Exclusion of patients with a heart rate > 100 beats/min could cause selection bias toward exclusion of patients with more severe LV impairment, but ejection fraction ranging from 0.24 to 0.69, wall motion score index from 1 to 2.5, E to A ratio from 0.42 up to 3.68, and deceleration time from 0.112 to 0.290 s indicate that patients with preserved as well as those with severely impaired systolic and diastolic function were included in the study.

Conclusion

The Tei index of myocardial performance, which combines systolic and diastolic time intervals, is simple and easy to calculate. It appears to be useful in clinical practice for assessing the future risks of patients with myocardial infarction, and in a subgroup of patients with preserved left ventricular systolic function.

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