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# Predictive Value of Myocardial Performance Index for Cardiac Events in Patients Hospitalized for First Myocardial Infarction

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**Abstract:** We sought to assess the ability of The Myocardial Performance Index (MPI), measured at entry, to predict in-hospital cardiac adverse events in a series of patients with first Acute Myocardial Infarction (AMI). A complete 2-dimential and Doppler echocardiographic examination was performed within 24 h of arrival at the coronary care department in 78 patients (61 men and 17 women; mean age 58±2 years) with first AMI. Patients were divided later into 2 groups according to their in-hospital course: group 1 comprised 46 patients with an uneventful course and group 2 comprised 32 patients with a complicated in-hospital course (death, heart failure, arrhythmias, post-AMI angina or Re MI). There were no significant differences between the 2 groups with regard to history of hypertension, diabetes mellitus, hypercholesterolemia, cardiac enzymes and response to thrombolytic, however patients with lateral MI more commonly had events (26 vs. 15%; p= 0.01) and those who received thrombolytic had less events (32 vs. 66%; p=0.01). Echocardiographic findings showed significant difference in Left Ventricle Ejection Fraction (LVEF) (40± 8% vs. 33±2%; p=0.005) between two groups; however, MPI showed no significant difference between two groups (0.50±0.14 vs. 0.47±0.16; p= 0.43) and we did not find any cut point with acceptable sensitivity and specificity for predicting in-hospital complications. E wave acceleration time at 91ms showed a sensitivity of 87 and specificity of 78 and in factor analysis the component comprising of LVEF, Left Ventricle End-Systolic Diameter (LVESD), ratio of early to late peak velocities (E/A), E-wave Deceleration Time (EDT), Isovolumic Relaxation Time (IVRT) showed sensitivity of 87 and specificity of 67%. Our findings suggest that in the acute phase of AMI, the MPI measured in admission cannot be a useful to predict which patients are at high risk for in-hospital cardiac events.

**Key words:** Myocardial performance index, LV ejection fraction, Regional Wall Motion Abnormality (RWMA), Left Ventricle Outflow Tract (LVOT)

## INTRODUCTION

The Myocardial Performance Index (MPI), combining systolic and diastolic time intervals as an expression of global myocardial performance, correlates with overall cardiac function (Düzenli *et al*., 2007; Morner *et al*., 2007; Haddad *et al*., 2007; Renner *et al*., 2007; Ozdemir *et al*., 2007 ). Two-dimensional and Doppler echocardiography facilitate the evaluation of different periods of the cardiac cycle, allowing the acquisition of a combined systolic and diastolic index of LV performance in a simple, reproducible and reliable manner. This index, which is independent of heart rate and BP, is correlate well with invasive measures of LV systolic and diastolic function such as changes in the maximum rate of rise of LV pressure (Düzenli *et al*., 2007; Morner *et al*., 2007; Haddad *et al*., 2007; Renner *et al*., 2007; Ozdemir *et al*., 2007; Mansouri and Lavine, 2007; Xu *et al*., 2007; Nada *et al*., 2007; Azzolin *et al*., 2006; Wichi *et al*., 2007; Parthenakis *et al*., 2002 ).

MPI measures the ratio of isovolumic time intervals to ventricular ejection time (Düzenli *et al*., 2007; Renner *et al*., 2007; Ozdemir *et al*., 2007; Mansouri and Lavine, 2007; Xu *et al*., 2007; Nada *et al*., 2007; Azzolin *et al*., 2006; Baysal *et al*., 2002). This index has been described as a non-invasive Doppler measurement of ventricular function. It is defined and calculated as the Doppler derived sum of the Isovolumetric Contraction Time (ICT) and the Isovolumetric Relaxation Time (IRT) divided by the Left Ventricular Ejection Time (LVET)

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(Ortiz and Lavine, 2006). In previous studies, the index has been found to be reproducible, easily obtainable and to correlate closely with invasive measures of both systolic and diastolic function, being independent of heart rate and left ventricular geometry.

In cardiac amyloidosis, idiopathic dilated cardiomyopathy, primary pulmonary hypertension, the index was shown to reflect disease severity and to have incremental prognostic value (Baysal *et al*., 2002). It has prognostic significance in patients with cardiomyopathy, congestive heart failure and following a myocardial infarction (Azzolin *et al*., 2006; Ortiz and Lavine, 2006). Also, the presence of coronary artery disease is related to MPI (Uzun, 2006).

We conducted this study to assess the ability of a the Myocardial Performance Index (MPI), measured in admission, to predict in-hospital cardiac adverse events in a series of patients with first Acute Myocardial Infarction (AMI).

## MATERIALS AND METHODS

The prospective cohort and observational-descriptive study was performed on 78 patients with myocardial infarction admitted in Tabriz Shahid Madani Heart Center from 2003 to 2004.

Inclusion criteria were having the first episode of MI without history of cardiac disease or with stable and unstable angina. The cases with right ventricle MI and non ST elevation MI were excluded from the study.

The patients with ST elevation MI admitted to Tabriz Shahid Madani Heart Center underwent bed-side or in echo lab Doppler and two-dimensional echocardiography. Also, demographic characteristics, cardiovascular risk factors, use or nonuse of thrombolytic therapy and its results, echocardiographic findings, ECG findings, cardiac enzymes (peak value of CTNI and CKMB), angiographic findings and medications were collected in a questionnaire.

All echocardiographic exams were performed by commercially available equipment (vivid 7, GE) and onsite portable machine. Echocardiographic study were including Left Ventricular Ejection Fraction (LVEF), regional WMA, mitral flow pattern including E/A, E Deceleration Time (EDT), LV end systolic and end diastolic diameter and (if possible) Regional Wall Motion Score Index (WMSI) (25 cases). LVEF was calculated usually by Biplane Simpson's rule and when using the systems lacking this setting or when the operator was no familiar or when we had time limitation because of patient unstability, we calculated it by ocular method. WMSI was considered in 16 segments and following grading,

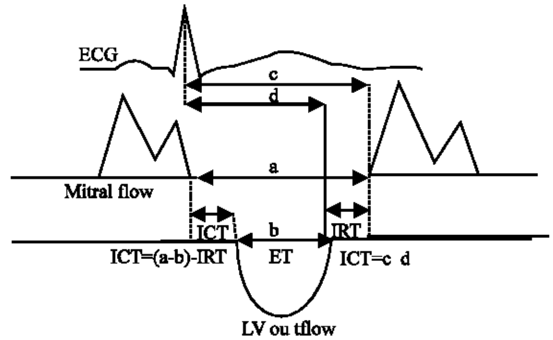


Fig. 1: Schema of doppler time intervals and myocardial performece index (Tie index) (ET, Ejection Time; ICT Isovolumic Contraction Time; IRT, Isovolumic Relaxation Time)

according the American society of echocardiographic guidelines: Normal (=1), Hypokinesia (=2), Akinesia (=3), Dyskinesia (=4), Aneurismal (=5).

Mitral flow Doppler was recorded with placement of pulse Doppler in the Tip of mitral valve leaflet and LV outlet flow was measured from the apical 5 chamber view using pulse Doppler. The mitral closure-to-opening interval (a) was the time from cessation to the onset of mitral inflow. Ejection Time (ET) was measured as the duration of LVOT flow (b). The Isovolumic Relaxation Time (IRT) was measured from the cessation of LVOT flow to the onset of LV inflow. The Isovolumic Contraction Time (ICT) was measured by subtracting IRT from (a-b). The myocardial performance index (Tie index): (ICT+IRT)/ET, was obtained by subtracting ET from the interval between cessation and onset of the mitral inflow velocity to give the sum of ICT and IRT (Fig. 1) (Tei *et al*., 1995; Yilmaz *et al*., 2007; Kang *et al*., 1998).

The patients received thrombolytic therapy by streptokinase in admission, if indicated. The patients included in the study within 24 of admission, were followed up regarding MI complications including heart failure (according Framingham criteria) (Zipes *et al*., 2005), post MI angina, arrhythmias, Repeat MI (ReMI) and death.

The collected data were analyzed with SPSS 11 statistical software using ROC and Kappa tests, factorial analysis and T test. The P values less than 0.05 were considered significant.

## RESULTS

We studied 78 cases of ST elevation MI with mean age of 58.3±2.1 years, of which 61 (78.2%) were male and 17 (21.8%) were female. MI was anterior in 48 (61.5%), lateral in 35(44.9%), inferior in 30(38.5%) and posterior in 23 (29.5%) cases.

Of 78 cases, 32 were complicated including post MI angina (12 cases), heart failure (10 cases), death (5 cases), ReMI (3 cases) and arrhythmias (ventricular tachycardia, atrial fibrillation) (2 cases). The complicated patients were named Group 2 and other patients were named Group 1. Group 2 were including 22 male and 10 female (p=0.088). The mean ages of patients in group 1 and group 2 were 61±3 years and 56±2 years, respectively (p=0.09). The prevalence of cardiovascular risk factors, hyperlipidemia, diabetes mellitus and family history of hypertension was not significantly different in two groups, but complications were seen less in smokers (Table 1). The medications were not significantly different in two groups and were not effective on MPI, except for dioxin, diuretics and inotropic agents that were used more in group 2.

The MI surface was not significantly related with complication rate. So, complication rate in patients having anterior and/or antero-posterior MI was not significantly different with that in patients having inferior and infero-posterior and/or infero-postero-lateral MI (Fig. 1). However, when there was lateral surface (e.g.) antero-lateral and infero-postero-lateral) involvement, the complication rate was more (p=0.01).

The mean MPI of group 1 and 2 in follow up period was 0.47±0.16 and 0.50±0.14, respectively, with no significant difference (p=0.4).

Evaluation of Receiver Operator Characteristic Curve (ROC Curve) with different cut points from 0.30-0.75 revealed no significant specificity and sensitivity. Also, the area under ROC Curve for MPI was not statistically significant. In evaluation of areas under ROC Curves, the largest area between echocardiographic indices was belong to EAT (E wave Acceleration Time) which was 0.84 and regarding cut point of 91ms it had the sensitivity and specificity of 87 and 78%, respectively. Although we achieved acceptable under-curve area for WMSI (wall motion score index) of 0.72 with sensitivity of 75 and specificity of 89%, regarding the high missing data of 75% in about 20% of patients, the statistical value of this index was not significant.

Because over mentioned indices separately had limited predictive value, for further evaluation of MPI beside other echocardiographic findings, we performed factorial analysis. This analysis revealed that all of echocardiographic findings constitute 3 components, of which in second component (including LVEF, LVESD, E/A, EDT and IVRT), acceptable under-curve area of 75% with sensitivity of 87.5 and specificity of 67% were predictive for in-hospital complications and surprisingly, this predictive value was independent for MPI. LV ejection fraction was s ignificantly higher in uncomplicated patients (Table 2), but other echocardiographic findings including LVESD, LVEDD, E/A, EDT, EAT and IVRT was not significantly different between two groups (Table 2).

Table 1: The clinical differences of complicated (group 2) and uncomplicated (group 1) patients with ST elevation MI

| | Group 1 | Group 2 | P value |
|---|---|---|---|
| Number | 46 | 32 | |
| Age (year) | 61±3 | 56±2 | 0.09 |
| Male | 38 | 22 | 0.08 |
| Hypertension | 12 (16%) | 13 (17%) | 0.2 |
| Diabetes mellitus | 9 (12%) | 9 (12%) | 0.4 |
| Smoking | 30 (39%) | 11 (14%) | 0.007 |
| Hyperlipidemia | 12 (16%) | 14 (18%) | 0.14 |
| Thrombolytic therapy | 39 | 19 | 0.01 |
| Response to Thrombolytic therapy | 22 | 11 | 0.4 |
| Peak CKMB | 196 | 211 | 0.6 |
| CTNI | 9.5 | 9.6 | 0.9 |

Table 2: Echocardiographic findings of complicated (group 2) and uncomplicated (group 1) patients with ST elevation MI

| | Group 1 | Group 2 | P value |
|---|---|---|---|
| LVEF | 0.40±0.08 | 0.33±0.10 | 0.005 |
| LVEDD | 4.6±0.6 | 4.7±0.5 | 0.4 |
| LVESD | 3.6±0.6 | 3.7±0.7 | 0.38 |
| RWMSI | 1.47±0.41 | 2±0.6 | 0.09 |
| E/A | 0.96±0.31 | 1.1±0.6 | 0.26 |
| EDT | 152±34 | 141±44 | 0.26 |
| EAT | 76±23 | 90±13 | 0.1 |
| MPI | 0.47±0.15 | 0.50±0.14 | 0.4 |
| IVRT | 85±19 | 83±16 | 0.6 |

LVEF: Left Ventricle Ejection Fraction; LVEDD: Left Ventricle End-Diastolic Diameter; LVESD: Left Ventricle End-Systolic Diameter; RWMSI: Regional Wall Motion Score Index; E/A: Ratio of Early to Late Peak Velocities; EDT: E-wave Deceleration Time; Eat: E Wave Acceleration Time; MPI: Myocardial Performance Index; IVRT: Isovolumic Relaxation Time

In other analyses, because MPI was not significant in all cases, the cases were classified according other variables and MPI were measured in subclasses.

The complication rate was not significantly different in patients <60 years and >60 years (35% in comparison with 48%; p=0.33). Although MPI was not significantly different in complicated and non-complicated patients in both age groups (46.7 in vs. 53.4% in <60 years and 47 vs. 48% in >60 years) (p=0.6).

In thrombolytic therapy and response to it and its effect on echocardiographic indices and MPI, we did not any difference between groups, except for LVEF which was significantly higher in responders to thrombolytic therapy (40±8 vs. 32±8% and 0.009). However, complication rate was not significantly different between responders and non-responders to thrombolytic therapy (27 vs. 41% and p=0.47). Also, those received thrombolytic therapy were complicated more than those did not undergo thrombolytic therapy.

Angiographic findings showed that the relation of the number of involved arteries with complication rate and echocardiographic findings was not significant. The comparison of LVEDP and cardiac enzymes in two groups is showed in Table 1. The complication rate was higher in patients with history of stable angina than those with history of unstable angina or without history of ischemic heart disease, but there was not significant difference in MPI between these groups (Fig. 2).

Because MPI was not significant in all complications, the complications were evaluated separately and in subclasses; so, first analysis was performed separately for death, congestive heart failure, Post MI angina, ReMI and arrhythmia (Fig. 3) and then because of the paucity of samples in some of these groups, the complications were classified in two groups (group A: death, congestive heart failure and arrhythmia; and Group B: Post MI angina, ReMI). Then the comparison of ROC curves and echocardiographic indices showed that MPI has not statistical predictive value as an independent variable.

## DISCUSSION

The data suggest that Doppler-derived MPI reflects severity of global left ventricular dysfunction in early phase of acute MI and may be a useful parameter in these patients (Sekuri *et al*., 2004). Xu *et al*. (2007) suggested that MPI is a more sensitive and useful quantitative parameter to assess the LV function than the EF and Fractional Area Change (FAC) measurements used routinely.

This study showed that Tie index or MPI is not valuable predictive of in-hospital events; this finding is compatible with the study of Schwammenthal \. who examined 417 consecutive patients with AMI within 24 h of hospital admission. They assessed Doppler echocardiographic measures of systolic, diastolic and global myocardial performance. The end points of the study at 30 days were death (4.7%), congestive heart failure (23%) and recurrent infarction (4.8%) and occurred in 109 patients. LVEF and EDT are powerful and independent echocardiographic predictors of poor outcome following AMI. MPI was not independently related to outcome in this model (OR, 1.09; 95% CI, 0.59 to 2.14). They suggested that one possible factor that may have confounded the diagnostic accuracy of the MPI is the phenomenon of pseudonormalization. With deteriorating myocardial function (indicated by a prolongation of isovolumic contraction time, a shortening of ejection time and the appearance of a restrictive filling pattern) an increase in MPI is prevented by a shortening of the isovolumic relaxation time. The shortened isovolumic relaxation time reflects, of course, an increase in left atrial pressure and not an improvement in relaxation. The lack of increase in MPI, not the shortening of the EDT, is therefore misleading. The behavior of MPI can be accurately termed pseudonormalization, since it has the same pathophysiologic basis as pseudonormalization of the LV filling pattern (Tei, 1995).

So, they defined another index for improvement of assessment of global myocardial performance by relating the sum of the isovolumic time intervals to the sum of the heterovolumic time intervals (ejection time and filling time). This isovolumic time/heterovolumic time ratio (I/H) index should express the time "wasted" by the myocardium to generate and decrease LV pressure without moving blood (*ie*, without performing external work). I/H was determined as (a-b)/(b + c), where c is the mitral filling period. Although this index was not significantly different in complicated and non-complicated groups, multivariate analysis did not identified it as independent predictors of adverse events; so, the authors suggested that the absence of predictive value of MPI not only is pathophysiologic reasons but also, other factors are effective (Tei, 1995).

In a study similar to ours, Ascione *et al*. (2003) examined 96 patients (81 men and 15 women; mean age 58±9 years) with first AMI by complete 2-dimensional and Doppler echocardiography within 24 hours of arrival at the coronary care department. The mean value of the MPI was significantly higher in patients with cardiac events than in those without events (0.65 +/-0.20 vs. 0.43 +/-0.16, p =.0001). A MPI >/= 0.47 showed a sensitivity of 90 and specificity of 68% for identifying patients with events. In a multivariable model, the MPI at admission remained independently predictive of in-hospital cardiac events (odds ratio 15.6, 95% confidence interval 2.4-99, p =.003). In their study, age, LVEF, WMSI and LVESV were other predictive factors and EDT, LVEDV, E velocity, A velocity, E/A and IVRT were not significantly different. They suggested that in the acute phase of AMI, the MPI measured at entry may be useful to predict which patients are at high risk for in-hospital cardiac events.

In addition to variables in Ascione *et al*. (2006) study, we studied variables including thrombolytic therapy and its effect, medications, angiographic findings and LVEDP, which can alter the in-admission indices, echocardiographic findings and the patients' prognosis. The entire over mentioned variables were not significantly different in complicated and uncomplicated patients and were not effective on echocardiographic findings including MPI; except for thrombolytic therapy, in which the responders had higher LVEF than non-responders (40 vs. 32%). Although the complication rate was lower in responders, because of the paucity of samples, this difference was not statistically significant. Azzolin *et al*. (2006) evaluated the predictive value of MPI for cardiovascular complications in patients at low risk during the postoperative period of CABG. No association was found between MPI and cardiovascular complications and longer hospital stay in this group of patients and this index was considered not adequate as an isolated predictive method.

Nada *et al.* (2007) showed that Tei index shows an age-related increase and concluded that the effect of aging must be considered in the clinical application of TEI index. Spencer *et al.* (1998) determined the Tei index in 141 subjects without cardiovascular disease (age 16-78 years). There were statistically significant variations in ejection time, isovolumic relaxation time and the Tei index with aging. There was a moderate linear correlation between isovolumic relaxation time and age ($r = 0.49$, $p < 0.001$) and the Tei index and age ($r = 0.33$, $p < 0.001$). They demonstrated that when assessing myocardial performance in patients using this index, age-normalized values should be used (Nada *et al.*, 2007). In our study, the complication rate and MPI were not significantly different in patients <60 and > 60 years ($p = 0.33$).

Studies showed the predictive value of MPI in CHF and dilated cardiomyopathy. Dujardin *et al.* (1998) measured MPI in 75 patients. The values of the Doppler index in patients with idiopathic-dilated cardiomyopathy ($0.85\pm0.32$) were significantly higher than values in controls ($0.37\pm0.08$). During follow-up of 5 years, 36 patients died. Univariate analysis demonstrated that the MPI was significant predictor of outcome. MPI reflects disease severity and has incremental prognostic value in dilated cardiomyopathy. Ease of use, nongeometric dependency, excellent separation of clinical groups and a strong relation to outcome enhance its appeal.

Hole and Skaerpe followed up 71 patients with acute MI without heart failure for 2 years. MPI did not contribute significantly to the prediction of any changes in the measures of diastolic or systolic function at 3 months or 2 years. Baseline MPI was significantly higher in patients who later developed heart failure ($0.55\pm0.16$) than in other patients ($0.43\pm0.13$), but had no independent predictive power for the development of heart failure or death relative to end-systolic volume index and deceleration time of early mitral filling wave (Hole and Skaerpe, 2003). Their study indicates the need for long-term follow-up of patients after MI, which was not considered in our study. It is possible that MI patient without in-hospital complication, to be affected by HF; this explain the cases with high MPI with normal in-hospital follow-up in our study. Also, some patients are in higher risk of ischemic events and HF in admission and have higher MPI because of systolic and diastolic dysfunction. However, using later invasive therapies such as PCI, which is performed extensively at first admission, prevents such complication in ischemic crises and remodeling, causing the false positive cases of MPI. Because this item was not considered in our study and previous studies, it is recommended to be evaluated in future surveys.

A surprising finding in our study was the definition of cut point of 91ms for E wave acceleration time which showed the predictive value of in-hospital events with acceptable specificity and sensitivity. Also, powerful statistical analysis of intrinsic relationship of variables showed that the factor including LVEF, LVESD, E/A, EDT and IVRT is predictive of in-hospital events with specificity and sensitivity of 87 and 67%, respectively this finding indicate that the echocardiographic finding should be considered in together, to increase the predictive value.

LVEF was in our study as a important predictive index for short-term and long-term complications after MI.

One of the limitation of our and the similar studies is the consideration of non-homogenous complications with the topic of post MI complication, because the pathophysiologic mechanism of ischemic complications (post MI angina, ReMI) is different from HF and death due to them. Although we analyzed these complications separately, the number of these complications was less and we did not separate them in the beginning of the study. This item has been considered in Lavine study, which studied 109 patients following their first MI with two-dimensional and Doppler within 24 h of MI. He divided patients into those who developed CHF within 15 days (43 patients) and without CHF (66 patients). Nineteen patients in the no CHF group developed late CHF. In this study, MPI in both early and late cases of post MI had predictive value of >0.6 (Lavine, 2003).

Barberato and Pecoits Filho (2006) showed that the Tei index was affected by hemodialysis-induced preload alterations, as well as other mitral inflow Doppler-derived parameters. The Tei index increased (from $0.57\pm0.07$ to $0.65\pm 0.09$) because of significant prolongations in isovolumetric relaxation time. Yilmaz *et al.* (2006) suggest that the shortened IRT in patients with restrictive filling pattern results in reduction of the MPI. These findings shoes that MPI is not preload-independent and alteration in loading status especially after MI in unstable patients can explain our findings. Another limitation of MPI studies is the absence of absolute definition of cut point and normal range in healthy individuals and patients. The cut point varies from 0.45 to 0.7 in different articles (Ascione *et al.*, 2003; Lavine, 2003, Cacciapuoti *et al.*, 2004). Also, the use of different echocardiography machine decreased the accuracy of measurements.

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