Prognostic Value of Cardiac Time Intervals by Tissue Doppler Imaging M-Mode in Patients With Acute ST-Segment–Elevation Myocardial Infarction Treated With Primary Percutaneous Coronary Intervention

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Background—Color tissue Doppler imaging M-mode through the mitral leaflet is an easy and precise method to estimate all cardiac time intervals from 1 cardiac cycle and thereby obtain the myocardial performance index (MPI). However, the prognostic value of the cardiac time intervals and the MPI assessed by color tissue Doppler imaging M-mode through the mitral leaflet in patients with ST-segment–elevation myocardial infarction (MI) is unknown.

Methods and Results—In total, 391 patients were admitted with an ST-segment–elevation MI, treated with primary percutaneous coronary intervention, and examined by echocardiography a median of 2 days after the ST-segment–elevation MI. Outcome was assessed according to death (n=33), hospitalization with heart failure (n=53), or new MI (n=25). Follow-up time was a median of 25 months. The population was stratified according to tertiles of the MPI. The risk of new MI, being admitted with congestive heart failure or death, increased with increasing tertile of MPI, being ≈3 times as high for the third tertile compared with the first tertile (hazard ratio, 2.8; 95% confidence interval, 1.7–4.7; P<0.001). MPI provided independent prognostic information in a multivariable Cox regression model adjusted for age, sex, previous MI, peak troponin, and systolic and diastolic echocardiographic parameters, with a hazard ratio of 1.24 (P=0.005) for the combined end point per each 0.1 increase in MPI.

Conclusions—MPI assessed by tissue Doppler imaging M-mode is a simple and reproducible measure that provides independent prognostic information, regardless of rhythm, incremental to conventional and novel echocardiographic parameters of systolic and diastolic function in patients with ST-segment–elevation MI treated with primary percutaneous coronary intervention. (Circ Cardiovasc Imaging. 2013;6:457-465.)

Key Words: cardiac time intervals ▪ myocardial performance index ▪ outcome ▪ STEMI ▪ TDI echocardiography

Prognostic value of cardiac time intervals is closely associated with normal cardiac biochemistry, mechanics, and physiology. Therefore, cardiac time intervals have been a target of investigation as markers of cardiac dysfunction for decades. The main concern has been how to obtain these cardiac time intervals in a fast, easy, noninvasive, and reproducible manner. To overcome this problem, Tei et al proposed obtaining the intervals from pulsed-wave Doppler echocardiography of the left ventricular (LV) outflow tract and mitral valve (MV) inflow and thereby calculating the index of combined systolic and diastolic performance, the myocardial performance index (MPI). Tissue Doppler imaging (TDI) is an alternative noninvasive approach to obtain the cardiac time intervals and thereby the MPI. With this method, the time intervals can be obtained from 1 projection and 1 cardiac cycle. In contrast, with the conventional method described by Tei et al, the time intervals are obtained from 2 projections and at least 2 cardiac cycles and may therefore be prone to errors caused by heart rate variability, which is not a concern with TDI. However, the time intervals obtained from TDI velocity curves are prone to regional differences in myocardial biochemistry, mechanics, and physiology, which will display regional differences in the cardiac time intervals. This can be overcome by analyzing the global time intervals through evaluating the MV movement by a simple color TDI M-mode analysis instead of the regional velocity curves. Thus, using color TDI M-mode through the mitral leaflet to estimate the cardiac time intervals is an improved method reflecting global cardiac time intervals and eliminating beat-to-beat variation. The advantage and validity of this method have previously been demonstrated. 

Clinical Perspective on p 465

Efforts to improve risk stratification, clarify pathophysiological mechanisms, and identify targets for therapeutic
intervention are of the utmost importance in patients with ST-segment–elevation myocardial infarction (STEMI). Echocardiography after an acute MI (AMI) is a routine procedure for risk stratification. The systole and the diastole are interdependent and coherent; therefore, improved risk stratification by combining the systolic and diastolic performance in 1 index may be possible. The aim of this study was to evaluate the prognostic value of the cardiac time intervals and the combined index of systolic and diastolic performance, the MPI, obtained by TDI M-mode method in patients with STEMI treated with primary percutaneous coronary intervention (pPCI).

Methods

Study Population
From September 2006 to December 2008, a total of 391 patients were admitted with STEMI, treated with pPCI, and underwent a detailed echocardiographic examination at Gentofte Hospital, University of Copenhagen, Copenhagen, Denmark. Five patients were excluded because of inadequate quality of the echocardiographic examination with regard to obtaining the cardiac time intervals.

The definition of an STEMI was presence of chest pain for >30 minutes and <12 hours, persistent ST-segment elevation ≥2 mm in at least 2 contiguous precordial ECG leads or ≥1 mm in at least 2 contiguous limb ECG leads (or a newly developed left bundle-branch block), combined with a troponin I increase >0.5 μg/L.

Baseline data were collected prospectively. Hypertension was defined as use of blood pressure–lowering drugs at admission. Diabetes mellitus was defined as fasting plasma glucose concentration ≥7 mmol/L, nonfasting plasma glucose concentration ≥11.1 mmol/L, or use of glucose-lowering drugs at admission. Troponin I was measured immediately on admission and after 6 and 12 hours.

Echocardiography

Echocardiography was performed using Vivid 7 ultrasound systems (GE Healthcare, Horten, Norway) with a 3.5-MHz transducer by experienced sonographers. At our institution, echocardiography is performed during the initial 5 days of admission (median, 2 days; interquartile range, 1–3 days). All participants were examined with conventional 2-dimensional echocardiography and pulsed-wave and color TDI according to standardized protocols. All echocardiograms were stored digitally and analyzed offline (EchoPac, GE Healthcare, Horten, Norway) by a single investigator who was blinded to all other patient data.

Conventional Echocardiography
From the parasternal long-axis view, the LV diameters and wall thickness were measured. From the apical position, peak velocity of early and atrial diastolic filling and deceleration time of the E wave were measured using pulsed-wave Doppler to record the mitral inflow. LV ejection fraction (LVEF) was obtained using the modified biplane Simpson method. Left atrial volume was estimated by the area-length method, and the left atrial volume index was calculated. The LV mass index was calculated by the formula using LV linear dimensions.

Two-Dimensional Strain Echocardiography
Two-dimensional strain analysis was performed from the apical 4-chamber, 2-chamber, and apical long-axis views (mean, 86 frames per second; SD, 23 frames per second). Peak longitudinal systolic strain was measured in all 3 apical projections and was averaged to provide global estimates.

Tissue Doppler Imaging
Pulsed-wave TDI tracings were obtained with the range gate placed at the septal and lateral mitral annular segments in the 4-chamber view. The peak longitudinal early diastolic (e') velocity was measured, and the average was calculated from the lateral and septal velocities and used to obtain the E/e'.

Color TDI loops were obtained in the apical 4-chamber view at the highest possible frame rate (mean, 169 frames per second; SD, 33 frames per second). The cardiac time intervals were obtained by placing a 2- to 4-cm straight M-mode line through the septal half of the mitral leaflet in the color TDI 4-chamber view, and the time intervals were measured directly from the color diagram (Figure 1). The isovolumic contraction time (IVCT) was defined as the time interval from the MV closure, determined by the color shift from blue/turquoise to red at end diastole, to the aortic valve opening, determined by the color shift from blue to red (Figure 1). The ejection time (ET) was defined as the time interval from the aortic valve opening to the aortic valve closing, determined by the color shift from red to blue at end systole (Figure 1). The isovolumic relaxation time (IVRT) was defined as the time interval from the aortic valve opening to the MV opening, determined by the color shift from red-orange to yellow (Figure 1). The method has previously been validated. Both isovolumic time intervals were divided by ET creating IVRT/ET and IV/IVCT/ET, respectively, and MPI was calculated as the sum of the 2 ([IVRT+IVCT]/ET).

Figure 1. The cardiac time intervals assessed by a color tissue Doppler imaging (TDI) M-mode line through the mitral leaflet. Left, Four-chamber gray-scale (bottom) and color TDI (top) views in end systole displaying the position of the M-mode line used for measuring the cardiac time intervals. Right, Color diagram of the TDI M-mode line through the mitral leaflet. AVO, aortic valve opening; MVC, mitral valve closing; and MVO, mitral valve opening.
Diastolic function was assessed using mitral inflow velocity profiles and pulsed-wave TDI tracings from the septal and lateral mitral annulus, according to the present guidelines. Patients with atrial fibrillation were defined as having diastolic dysfunction and were graded as 1, 2, or 3 according to the value of E/e'.

pPCI Procedure
pPCI was performed according to contemporary interventional guidelines using pretreatment with 300 mg acetylsalicylic acid, 600 mg clopidogrel, and 10 000 IU unfractionated heparin. Glycoprotein IIb/IIIa inhibitors were used at the discretion of the operator. Multivessel disease was defined as 2- or 3-vessel disease and complex lesions as type C lesions. Subsequent medical treatment included anti-ischemic, lipid-lowering, and antithrombotic drugs.

Follow-up and End Points
The primary end point was the combined end point of all-cause mortality, a new MI (re-MI), or admission with congestive heart failure (CHF). Secondary end points were all of the above analyzed separately. Follow-up was 100%. Follow-up data on re-MI and admission with CHF were obtained from the Danish National Board of Health’s National Patient Registry using International Classification of Diseases, 10th Revision (ICD-10) codes and thoroughly validated using hospital source data. Follow-up data on mortality were collected from the National Person Identification Registry.

Statistics
In Tables 1 and 2, proportions were compared using the χ² test, continuous gaussian-distributed variables with the Student t test, and non–gaussian-distributed variables with the Mann–Whitney test. Association with MPI was tested for LVEF and e' by multivariable regression analyses, including the prespecified baseline variables age and sex. Cumulative survival curves were established by the Kaplan-Meier method and compared by the log-rank test. Hazard ratios (HRs) were calculated by Cox proportional hazards regression analyses. The assumptions of linearity and proportional hazards in the models were tested. First-order interactions between all cardiac time intervals, including the combined indexes, and atrial fibrillation for the combined end point were tested.

Intraobserver and interobserver variabilities were determined by Bland-Altman plots and coefficients of variation (CVs) of repeated measurements of diastolic and systolic function, e' and graphic parameters of diastolic and systolic function, e' and E/e'.

Receiver-operator characteristic curves were constructed for IVCT/ET, IVRT/ET, and MPI in effort to find the optimal cutoff value to stratify patients according to major adverse outcome. Discriminating power was expressed as area under the receiver-operator characteristic curve.

Receiver-operator characteristic curves were constructed for IVCT/ET, IVRT/ET, and MPI in effort to find the optimal cutoff value for predicting the risk of re-MI, CHF, and mortality. The association between MPI and the established echocardiographic indexes of diastolic function was assessed using the χ² test.

Results
During follow-up (median, 25 months; interquartile range, 19–32 months), 25 patients (6.5%) were admitted with CHF, and 33 patients (8.5%) died. The combined end point was reached by 96 patients (24.9%). Baseline characteristics are displayed in Tables 1 and 2.

MPI and Conventional Echocardiography
The association between MPI and the established echocardiographic parameters of diastolic and systolic function, e' and LVEF, was tested (Figure 2). MPI increased independently with decreasing values of e' (P<0.001) and LVEF (P<0.001), after adjustment for age and sex.

Cardiac Time Intervals and Prognosis
The risk of a subsequent re-MI, being admitted with CHF or death, increased with increasing tertile of the IVCT (Figure 3A), being 2 times as high in the third tertile compared with the first tertile (HR, 2.0; 95% confidence interval [CI], 1.2–3.3; P=0.007). When interpreting the Kaplan-Meier curves, neither the IVRT nor the ET seems to provide easily comprehensible prognostic information because the risk of...
the combined end point did not increase incrementally with increasing or decreasing tertile, respectively (Figure 3B and 3C). We found no interactions between cardiac time intervals (including the combined indexes) and atrial fibrillation for the combined end point.

### MPI and Prognosis

All the indexes obtained by combining the cardiac time intervals IVRT/ET, IVCT/ET, and MPI were associated with an increased risk of reaching the combined end point with increasing tertile (Figure 4). The risk of a re-MI, being admitted with CHF or death, increased with increasing tertile of the combined indexes (Figure 4), being ≈2 times as high for the IVRT/ET and ≈3 times as high for the IVCT/ET and MPI in the third tertile compared with the first tertile (IVRT/ET: HR, 1.9; 95% CI, 1.2–3.2; \( P = 0.010 \); IVCT/ET: HR, 2.8; 95% CI, 1.6–4.7; \( P < 0.001 \); MPI: HR, 2.8; 95% CI, 1.7–4.7; \( P < 0.001 \)). Consequently, all the combined indexes were tested as predictors of an adverse outcome using Cox regression models (Table 3). Only the IVRT/ET and the MPI remained independent predictors of the combined outcome after adjustment for age, sex, peak troponin I, previous AMI, LVEF, peak global longitudinal systolic strain, diastolic function grade, LV internal diameter in diastole/body surface area, and LV mass index (Table 3). The optimal cutoff for predicting the combined end point was determined from the receiver-operating characteristic curves and was 0.14 for IVCT/ET, 0.42 for IVRT/ET, and 0.52 for MPI.

### MPI in Atrial Fibrillation and Outcome

Even in patients with atrial fibrillation, the MPI was significantly higher in patients with an adverse outcome (0.45 [95% CI, 0.34–0.55] versus 0.67 [95% CI, 0.58–0.76]; \( P = 0.005 \); Figure 5). Even after adjustment for age, sex, and LVEF, the MPI remained significantly higher in the group with an adverse outcome (0.44 [95% CI, 0.29–0.58] versus 0.67 [95% CI, 0.56–0.79]; \( P = 0.026 \)).

### Intraobserver and Interobserver Variability Analysis

Bland-Altman plots of intraobserver and interobserver differences of MPI are shown in Figure 6. The intraobserver

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**Table 2. Baseline Echocardiographic Characteristics in Patients With ST-Segment–Elevation Myocardial Infarction Treated by Primary Percutaneous Coronary Intervention Stratified According to Major Adverse Outcome**

<table>
<thead>
<tr>
<th></th>
<th>No Major Adverse Outcome (n=290)</th>
<th>Major Adverse Outcome (n=96)</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF, %*</td>
<td>47±8</td>
<td>41±9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GLS, %*</td>
<td>−12.8±3.7</td>
<td>−10.4±3.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVIdd/BSA, cm/m²*†</td>
<td>2.4 (2.3–2.7)</td>
<td>2.6 (2.4–2.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEDV/BSA, mL/m²†</td>
<td>48 (40–58)</td>
<td>50 (42–57)</td>
<td>0.23</td>
</tr>
<tr>
<td>LVESV/BSA, mL/m²†</td>
<td>25 (21–31)</td>
<td>29 (22–37)</td>
<td>0.001</td>
</tr>
<tr>
<td>LVMI, g/m²†</td>
<td>88 (73–106)</td>
<td>102 (84–118)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LAI, mL/m²*</td>
<td>25±7</td>
<td>25±7</td>
<td>0.81</td>
</tr>
<tr>
<td>E, m/s*</td>
<td>0.77±0.18</td>
<td>0.77±0.24</td>
<td>0.83</td>
</tr>
<tr>
<td>A, m/s*</td>
<td>0.74±0.19</td>
<td>0.75±0.23</td>
<td>0.68</td>
</tr>
<tr>
<td>E/A ratio*</td>
<td>1.09±0.37</td>
<td>1.09±0.37</td>
<td>0.95</td>
</tr>
<tr>
<td>DT, ms*</td>
<td>199±59</td>
<td>201±75</td>
<td>0.80</td>
</tr>
<tr>
<td>e’*</td>
<td>7.6±2.2</td>
<td>6.7±1.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>E/e’†</td>
<td>10.3 (8.1–12.4)</td>
<td>11.4 (9.1–14.4)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

A indicates peak transmitral late diastolic inflow velocity; BSA, body surface area; DT, deceleration time of early diastolic inflow; E, peak transmitral early diastolic inflow velocity; e’, average peak early diastolic longitudinal mitral annular velocity determined by pulsed-wave TDI; ET, ejection time; GLS, peak global longitudinal systolic strain; IVCT, isovolumic contraction time; IVRT, isovolumic relaxation time; LAI, left atrial volume index; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; LVIdd, left ventricular internal diameter in diastole; LVMI, left ventricular mass index; and MPI, myocardial performance index.

*Mean ±SD.
†Median (interquartile range).
variability analysis showed a mean±SD difference of $−0.004±0.029$ (CV, 6%) for patients with sinus rhythm and $0.031±0.055$ (CV, 9%) for patients with atrial fibrillation (Figure 6A). The interobserver variability analysis showed a mean±SD difference of $−0.022±0.084$ (CV, 16%) for patients with sinus rhythm and $0.017±0.096$ (CV, 16%) for patients with atrial fibrillation (Figure 6B).

**Discussion**

This prospective study of STEMI patients illustrates the prognostic information that can be obtained from cardiac time intervals and emphasizes the importance of combining the evaluation of the systolic and diastolic performance. Our study is the first to demonstrate that the cardiac time intervals can be valuable in risk stratification of patients with atrial fibrillation.
We found that MPI was associated with established echocardiographic parameters of both diastolic and systolic function. MPI increased with decreasing systolic function, determined by LVEF, and with increasing diastolic function, determined by e′ (Figure 2). Furthermore, prolongation of the systolic time interval, IVCT, and higher values of all the combined indexes, IVCT/ET, IVRT/ET, and MPI, were associated with an adverse outcome (Table 3 and Figures 3 and 4). In addition, the combined indexes of systolic and diastolic performance, the IVRT/ET, and the MPI provided independent prognostic information incremental to conventional and novel echocardiographic parameters of systolic and diastolic function and all other strong predictors in our population (Table 3).

**MPI and Conventional Echocardiography**

Invasive measures of systolic and diastolic performance, the LVEF and LV relaxation constant (τ), have previously been illustrated to be independent predictors of MPI obtained from TDI velocity curves. We found LVEF and e′ to be independent predictors of MPI determined by color TDI M-mode through the mitral leaflet. This illustrates that an ailing systolic or diastolic performance can be detected by an increasing value of the MPI when assessed by TDI. These results are interesting when we consider the potential advantages of obtaining the cardiac time intervals by color TDI M-mode through the mitral leaflet compared with the conventional method.

Besides obtaining all the cardiac time intervals from 1 cardiac cycle, the MPI obtained by TDI M-mode is less influenced by physical parameters compared with the conventional method. Hence, MPI based on simple cardiac mechanisms, that is, the passively opening and closing of the MV, is less confounded than MPI based on calculations from versatile blood flow patterns through the mitral and aorta valves. Furthermore, the precision and reproducibility of the cardiac time intervals and MPI are improved when they are obtained by the TDI M-mode method compared with the conventional method. In addition, the time intervals achieved by clear color shifts marking minimal changes in direction in the MV by the color TDI M-mode method are very easy to identify (Figure 1). In contrast, the time intervals obtained by the conventional method are assessed from velocity curves in which the signals may be scattered, making...

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**Table 3. Unadjusted and Adjusted Cox Proportional Hazards Regression Models Depicting the Combined Indexes of the Cardiac Time Intervals as Predictors of Outcome**

<table>
<thead>
<tr>
<th>Combined End Point (96 Events)</th>
<th>CHF (53 Events)</th>
<th>re-MI (25 Events)</th>
<th>Mortality (33 Events)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hazard Ratio (95% CI)</strong></td>
<td><strong>P Value</strong></td>
<td><strong>Hazard Ratio (95% CI)</strong></td>
<td><strong>P Value</strong></td>
</tr>
<tr>
<td>Unadjusted model</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IVRT/ET per 0.1 increase</td>
<td>1.34 (1.14–1.57)</td>
<td>&lt;0.001</td>
<td>1.28 (1.03–1.59)</td>
</tr>
<tr>
<td>IVCT/ET per 0.1 increase</td>
<td>1.53 (1.26–1.86)</td>
<td>&lt;0.001</td>
<td>1.68 (1.34–2.11)</td>
</tr>
<tr>
<td>MPI per 0.1 increase</td>
<td>1.30 (1.16–1.46)</td>
<td>&lt;0.001</td>
<td>1.32 (1.14–1.54)</td>
</tr>
<tr>
<td>Multivariable model adjusted for age, sex, peak Tnl, pre-MI, LVEF, diastolic function grade, LVMI, and LVIDd/BSA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IVRT/ET per 0.1 increase</td>
<td>1.29 (1.08–1.54)</td>
<td>0.005</td>
<td>1.21 (0.94–1.56)</td>
</tr>
<tr>
<td>IVCT/ET per 0.1 increase</td>
<td>1.42 (1.00–2.02)</td>
<td>0.053</td>
<td>1.43 (0.90–2.26)</td>
</tr>
<tr>
<td>MPI per 0.1 increase</td>
<td>1.26 (1.09–1.46)</td>
<td>0.002</td>
<td>1.22 (0.99–1.50)</td>
</tr>
<tr>
<td>Multivariable model adjusted for age, sex, peak Tnl, pre-MI, GLS, diastolic function grade, LVMI, and LVIDd/BSA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IVRT/ET per 0.1 increase</td>
<td>1.30 (1.09–1.56)</td>
<td>0.005</td>
<td>1.22 (0.94–1.58)</td>
</tr>
<tr>
<td>IVCT/ET per 0.1 increase</td>
<td>1.43 (0.98–2.08)</td>
<td>0.06</td>
<td>1.53 (0.93–2.49)</td>
</tr>
<tr>
<td>MPI per 0.1 increase</td>
<td>1.27 (1.09–1.48)</td>
<td>0.002</td>
<td>1.25 (1.00–1.55)</td>
</tr>
<tr>
<td>Multivariable model adjusted for age, sex, peak Tnl, pre-MI, LVEF, GLS, diastolic function grade, LVMI, and LVIDd/BSA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IVRT/ET per 0.1 increase</td>
<td>1.28 (1.07–1.53)</td>
<td>0.008</td>
<td>1.22 (0.94–1.57)</td>
</tr>
<tr>
<td>IVCT/ET per 0.1 increase</td>
<td>1.30 (0.89–1.90)</td>
<td>0.18</td>
<td>1.36 (0.83–2.24)</td>
</tr>
<tr>
<td>MPI per 0.1 increase</td>
<td>1.24 (1.07–1.45)</td>
<td>0.005</td>
<td>1.22 (0.98–1.51)</td>
</tr>
</tbody>
</table>

BSA indicates body surface area; CHF, congestive heart failure; CI, confidence interval; ET, ejection time; GLS, peak global longitudinal systolic strain; IVCT, isovolumic contraction time; IVRT, isovolumic relaxation time; LVEF, left ventricular ejection fraction; LVMI, left ventricular mass index; MI, myocardial infarction; MPI, myocardial performance index; peak Tnl, peak troponin I; and pre-MI, previous acute myocardial infarction.

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![Figure 5. Myocardial performance index (MPI) in patients with atrial fibrillation stratified according to outcome. Circles indicate absolute values; dotted lines indicate means.](http://circimaging.ahajournals.org/Downloaded from)
Cardiac Time Interval, MPI, and Prognosis

The MPI obtained by the conventional method can provide prognostic information in patients with various cardiac conditions, including AMI. Our study is the first to evaluate the prognostic value of the MPI assessed by TDI M-mode through the mitral leaflet in an STEMI population treated by pPCI. Previous studies on the predictive power of the MPI in patients with AMI have included patients with both non-STEMI and STEMI treated with either thrombolytic therapy or PCI. Our population is more homogeneous and less confounded by difference in therapy. We found that the cardiac time intervals when evaluated separately provided ambiguous and not easily comprehensible prognostic information (Figure 3). Only the IVCT seemed to provide prognostic information when interpreting the Kaplan-Meier curves, depicting the proportion of patients staying event free for patients stratified into tertiles of the cardiac time intervals (Figure 3A). For the IVRT and ET, the risk of the combined end point did not increase incrementally with increasing or decreasing tertile, respectively (Figure 3B and 3C). However, when we corrected the IVCT and the IVRT for heart rate by dividing it by ET, both combined indexes provided incremental prognostic information with increasing tertile (Figure 4A and 4B). This result is interesting because neither the IVRT nor the ET provided incremental prognostic information when evaluating them separately (Figure 3B and 3C), but when the information about the systolic and the diastolic performance is combined in 1 index (and thereby also indirectly adjusted for heart rate), the prognostic information becomes evident (Figure 4A and 4B). Only the combined indexes, including information on both the systolic and diastolic performance (the MPI and the IVRT/ET), were strong prognosticators after multivariable adjustment for the conventional and novel echocardiographic parameters of systolic and diastolic function (Table 3). The index including information only on the systolic performance, the IVCT/ET, did not provide prognostic information independent of other echocardiographic parameters (Table 3). Furthermore, we propose using a cutoff of 0.42 for IVRT/ET and 0.52 for MPI when these indexes are used for risk stratification in STEMI patients.

Figure 6. Intraobserver and interobserver variability analysis. Bland-Altman plots of intraobserver (A) and interobserver (B) differences of myocardial performance index assessed by color tissue Doppler imaging M-mode through the mitral leaflet for patients with sinus rhythm (n=25) and for patients with atrial fibrillation (n=14) showing the mean difference (solid lines) and 95% limits of agreement (dotted lines).
The MPI has previously been demonstrated to be a superior predictor of cardiovascular mortality and CHF compared with conventional echocardiographic measures of systolic and diastolic performance in a population of elderly men.\textsuperscript{17,18} In addition, this superiority of the predictive capacity of the MPI compared with conventional echocardiographic measures has been demonstrated in an AMI population.\textsuperscript{22} These and our results emphasize the prognostic information gained by combining the interdependent and coherent relations of systolic and diastolic function in a simple and feasible index. In addition, in accordance with our results, we have previously demonstrated that MPI obtained by the M-mode method was an independent predictor of all-cause mortality in the general population, providing prognostic information incremental to known confounders such as age, sex, body mass index, heart rate, blood pressure, and ischemic heart disease. In contrast, the MPI obtained by the conventional method was not an independent predictor when adjusted for the same confounders.\textsuperscript{10} The discrepancy in the predictive capacity of the MPI when obtained by the 2 different methods is probably attributable to the fact that the method by Tei et al\textsuperscript{4,5} seems to be influenced by more physical parameters than the M-mode method.\textsuperscript{10} This makes the MPI obtained by TDI M-mode less complex to interpret in a clinical setting.

**MPI in Atrial Fibrillation and Outcome**

In addition, it is not possible to obtain cardiac time intervals from velocity curves in patients with atrial fibrillation, regardless of whether they are obtained by the conventional method\textsuperscript{4-6} or by the newer TDI method.\textsuperscript{7} This is attributable to the absence of the A and a’ velocity curves in patients with atrial fibrillation, which are needed to obtain the time intervals by both methods. In contrast, all cardiac time intervals can be obtained by the color TDI M-mode method, regardless of the presence of atrial fibrillation. Thus, in patients with atrial fibrillation, color M-mode MPI can differentiate between high- and low-risk patients (Figure 5), even after adjustment for age, sex, and LVEF. However, the reproducibility seems lower in patients with atrial fibrillation than in patients with sinus rhythm (Figure 6). Nevertheless, the intraobserver and interobserver variability for TDI M-mode MPI in patients with atrial fibrillation seems superior to the variability found for the conventional method described by Tei et al\textsuperscript{4} in patients with sinus rhythm,\textsuperscript{10} which provides more optimism for this new method.

**Limitations**

The risk of residual confounders always exists in a nonrandomized study. Furthermore, we did not investigate the cause of death. However, we assume that individuals with cardiac dysfunction determined by echocardiography after STEMI are more likely to die of cardiovascular causes and that, if we were able to limit our analysis to cardiovascular deaths, the prognostic impact of MPI would be even greater. The investigator was not blinded for other echocardiographic parameters, which theoretically could have a potential for bias. Nevertheless, the combined indexes provide independent prognostic information after adjustment for all other systolic and diastolic parameters in our population, which would not be the case if the combined indexes contained only prognostic information gained from other echocardiographic parameters.

Echocardiography was performed a median of 2 days after pPCI, which is the typical time span for echocardiographic risk assessment in east Denmark, where various degrees of myocardial stunning might be present and may impact the cardiac time intervals. However, myocardial function can be affected for as long as 2 weeks after the intervention,\textsuperscript{20} at which point the myocardial function could be influenced by long-term compensatory mechanisms and the effects of additional therapeutic interventions, so the optimal time for risk assessment after pPCI is still to be investigated.

**Conclusions**

MPI assessed by TDI M-mode is a simple and reproducible measure that provides independent prognostic information, regardless of rhythm, incremental to conventional and novel echocardiographic parameters of systolic and diastolic function in patients with STEMI treated with pPCI.

**Sources of Funding**

This study was financially supported by the Faculty of Health Sciences, University of Copenhagen, Denmark. The sponsor had no role in the study design, data collection, data analysis, data interpretation, or writing of the article.

**Disclosures**

None.

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**CLINICAL PERSPECTIVE**

Changes in cardiac time intervals are sensitive markers of an ailing myocardium. As left ventricular (LV) systolic function deteriorates, the time it takes for myocardial myocytes to achieve an LV pressure equal to that of aorta increases, thereby resulting in a prolongation of isovolumetric contraction time. Furthermore, the ability of myocardial myocytes to maintain this high LV pressure decreases, resulting in the reduction in ejection time. As LV diastolic function declines further, early diastolic relaxation proceeds more slowly, explaining the prolongation of isovolumic relaxation time. Consequently, the myocardial performance index, defined as (isovolumic relaxation time+isovolumic contraction time)/ejection time, will increase, regardless of whether the LV is suffering from impaired systolic or diastolic function. Myocardial performance index has been demonstrated to increase even in patients with severe diastolic dysfunction, in whom a short isovolumic relaxation time is seen. This is attributable to the increase in isovolumic contraction time or decrease in ejection time. The new tissue Doppler imaging M-mode method of obtaining cardiac time intervals is easy, has a high reproducibility, and obtains all of the time intervals from the same cardiac cycle. The present study demonstrates that in patients with STEMI treated with primary percutaneous coronary intervention, the combined indexes of systolic and diastolic function (isovolumic relaxation time/ejection time and myocardial performance index) provide independent prognostic information, regardless of rhythm, incremental to conventional and novel echocardiographic parameters of systolic and diastolic function.
Prognostic Value of Cardiac Time Intervals by Tissue Doppler Imaging M-Mode in Patients With Acute ST-Segment–Elevation Myocardial Infarction Treated With Primary Percutaneous Coronary Intervention

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Circ Cardiovasc Imaging. 2013;6:457-465; originally published online March 27, 2013; doi: 10.1161/CIRCIMAGING.112.000230

Circulation: Cardiovascular Imaging is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-9651. Online ISSN: 1942-0080

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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