Predictive value of tissue Doppler imaging for left ventricular ejection fraction, remodelling, and infarct size after percutaneous coronary intervention for acute myocardial infarction

Joost P. van Melle1*, Pieter A. van der Vleuten1, Yoran M. Hummel1, Robin Nijveldt2, Rene A. Tio1, Adriaan A. Voors1, and Felix Zijlstra1

1Thoraxcenter, Department of Cardiology, University Medical Center Groningen, University of Groningen, PO Box 30.001, Groningen 9700 RB, The Netherlands; and 2Department of Cardiology, VU University Medical Center, Amsterdam, The Netherlands

Received 7 August 2009; accepted after revision 9 February 2010; online publish-ahead-of-print 7 March 2010

Aims
To investigate in ST-elevation myocardial infarction (STEMI) patients the value of tissue Doppler imaging (TDI) for an early estimation of the extent of myocardial salvage, left ventricular (LV) remodelling, and residual LV ejection fraction (LVEF).

Methods and results
In 50 STEMI patients hospitalized for primary percutaneous coronary intervention (PCI), we investigated whether TDI can predict LVEF, infarct size, and LV remodelling as measured by magnetic resonance imaging (MRI) at 4 months post-MI. TDI was assessed within 24 h after MI with colour-coded TDI. Systolic and diastolic velocities from the six basal myocardial segments derived from three standard apical windows were averaged as a measure of global longitudinal velocity (i.e. Sm-6 and Em-6/Am-6, respectively). Sm-6 was shown to be a significant predictor of LVEF at 4 months. In addition, Sm-6 was a significant predictor of infarct size. No significant correlations were found between Sm-6 and LV remodelling. In addition, Sm-6 appeared to be a valuable clinical tool for identification of patients with LVEF < 40% or LVEF > 40% with acceptable positive predictive values.

Conclusion
Sm-6 is a significant predictor of post-MI LVEF and infarct size as measured by MRI. In contrast, TDI-derived velocities do not predict LV remodelling.

Keywords
STEMI • Tissue Doppler imaging • LV function

Introduction
The main goal in the management of acute myocardial infarction (MI) is an early restoration of coronary artery flow in order to preserve viable myocardium. Primary percutaneous coronary intervention (PCI) has proven to be superior to other reperfusion strategies in terms of mortality reduction and preservation of left ventricular (LV) function.1 Despite improvements in the treatment of MI, 30% of patients show LV remodelling post-MI.2 Moreover, it is expected that almost 30% will have an LV ejection fraction (LVEF) below 40% at 6 months post-MI.3 Both decreased LVEF and LV remodelling are associated with adverse prognosis.4 Therefore, early identification of high-risk patients is crucial in order to optimize medical treatment [e.g. medication, identification of candidates for cardiac rehabilitation programmes or internal cardiac defibrillator (ICD)].

In recent years, tissue Doppler imaging (TDI) has proven to be a valuable clinical echocardiographic tool to measure tissue velocities. It has been studied in a wide variety of cardiac pathology (e.g. LV dysynchrony, ischaemia, cardiomyopathies).5 Data on the use of TDI in the context of acute MI to predict post-MI LV function are sparse. Therefore, we investigated whether TDI may be a valuable tool in the prediction of residual LVEF and/or LV remodelling, which we assessed 4 months post-MI using magnetic

* Corresponding author. Tel: +31 50 361 2355; fax: +31 50 361 4391; Email: j.p.van.melle@thorax.umcg.nl
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resonance imaging (MRI). In addition, we investigated the relationship between TDI measures and MRI-derived delayed contrast enhancement (DCE) as a measure of infarct size.

**Methods**

**Patients**

We prospectively studied patients with an acute (onset of symptoms <12 h), large (peak creatinine kinase > 1000 U/L) ST-elevation myocardial infarction (STEMI) referred to our catheterization laboratory for primary PCI of one of the proximal coronary artery segments (segment 1, 2, 3, 6, 7, 11, 12, or 13 according to the CASS classification). Exclusion criteria were the occurrence of an additional PCI in a vessel other than the culprit vessel, contraindication(s) for MRI, poor acoustic window preventing adequate echocardiography, concomitant disease with a life expectancy <1 year, and history of MI, coronary artery bypass grafting, heart failure, moderate to severe valvular disease, cardiomyopathy, or congenital heart disease. In short, all patients had undergone primary PCI for STEMI, and it was not expected that percutaneous or surgical coronary intervention would follow in the aftermath of the index MI. Myocardial blush grades were assigned as previously described by van ’t Hof et al., 0, no myocardial blush; 1, minimal myocardial blush or contrast density; 2, moderate myocardial blush or contrast density but less than that obtained during angiography of a contralateral or ipsilateral non-infarct-related coronary artery; and 3, normal myocardial blush or contrast density, similar to that obtained during angiography of a contralateral or ipsilateral non-infarct-related coronary artery. Persistent myocardial blush suggests leakage of contrast medium into the extravascular space and is given a grade of 0.

The institutional review board approved the study protocol and all patients provided written informed consent.

**Echocardiographic protocol**

In the present study, we related the data of two imaging modalities (i.e., tissue Doppler echocardiography at baseline and MRI). Therefore, to allow the assessment of a cross-modality relationship, we used the standardized 17-segment model as recommended by the American Heart Association.

Patients referred for primary PCI underwent an echocardiographic examination within 24 h after admission (and after PCI) using a commercially available echocardiograph (GE Healthcare, Vivid 7, Horten, Norway) with a 3.5 MHz probe. The independent echocardiographers (J. P. M., P. A. V.) were blinded from all MRI data. All participants were in sinus rhythm. TDI data were recorded digitally at a high frame rate, as recommended previously, and analysed post hoc (GE EchoPAC version 71.2). For each measurement, the mean value of two different cardiac cycles was obtained.

In order to assess longitudinal myocardial regional function, segmental myocardial velocities were derived from colour-coded TDI in the apical views (two-, three-, and four-chamber). The sample volumes were placed in the middle of each myocardial segment, which resulted in the recording of peak systolic velocities (Sm), early (Em), and late (Am) diastolic velocities. Velocities of each myocardial segment were recorded. Analogous to publications in the field of cardiac resynchronization therapy, we calculated the average of six basal segment velocities (Sm-6, Em-6, and Am-6) to obtain a global measure of longitudinal velocity. We chose to investigate the predictive value of these particular variables, because these measures combine velocities from all three standard apical views, representing all major areas of the LV myocardium. Besides TDI measurements, also baseline wall motion score index was assessed according to the recommendations of the European Association of Echocardiography.

**Magnetic resonance imaging protocol**

MRI examination was performed on a 1.5-T clinical scanner (Sonata, Siemens, Erlangen, Germany) using a phased array cardiac receiver coil, within 2 days after primary PCI and at 4 months. Electrocardiogram-gated images were acquired during repeated breath-holds of ~10 s. LV function was determined with cine imaging, using a segmented steady state free precession pulse sequence in multiple short-axis views every 10 mm covering the entire left ventricle. Typical in plane resolution was 1.6 × 1.9 mm², with slice thickness of 6.0 mm (repetition time/echo time = 3.2/1.6 ms, flip angle 60°, matrix 256 × 156, temporal resolution 35–50 ms). DCE images were acquired to determine infarct size, using a gadolinium-based contrast agent (Dotarem, Guerbet, Roissy, France). A 2D segmented inversion recovery gradient-echo pulse sequence was used, 15 min after contrast administration (0.2 mmol/kg), with slice locations identical to the cine images. Typical in plane resolution was 1.4 × 1.8 mm², with slice thickness of 6.0 mm (repetition time/echo time = 9.6/4.4 ms, flip angle 25°, matrix 256 × 166, triggering to every other heart beat). The inversion time was set to null the signal of viable myocardium, and typically ranged from 260 to 350 ms.

**Data analysis and definitions**

All MRI data were analysed on a separate workstation using dedicated software (Mass version 2006beta, Medis, Leiden, The Netherlands). Cine and DCE images were acquired during the same imaging session, and therefore matched by using slice position. On all short-axis cine slices, the endocardial and epicardial borders were outlined manually on end-diastolic and end-systolic images. LV volumes and LVEF were calculated. LV remodelling at 4 months of follow-up was derived from the two MRI studies and defined as an increase in LV end-systolic volume (LVEDV) ≥15% between baseline and 4 months. Segment location was defined on cine and DCE images according to the 17-segment model. Total infarct size was calculated by the summation of all slice volumes of hyperenhancement, using a standardized and predefined definition (signal intensity > 5 standard deviation (SD) above the mean signal intensity of remote myocardium), and expressed as percentage of LV mass.

For analysis of segmental function, the two most basal and two most distal slices were excluded, because segmental evaluation at these levels is not considered reliable due to the LV outflow tract and partial volume effect, respectively. All MRI images were analysed by two observers who were blinded to patient data and clinical status.

**Statistical analysis**

Continuous data are expressed as mean ± SD and categorical data are presented as absolute values and percentages. Comparison between continuous data was performed using paired and unpaired t-tests, where appropriate. Categorical data were compared by χ² test. Correlations were assessed by the Pearson correlation coefficient. Clinical, echocardiographic and Doppler variables (either as a continuous or as a categorical variable) were compared for their ability to predict LVEF and LV remodelling by the Cox regression model. A P-value of ≤0.05 was considered statistically significant. Statistical analyses were performed with SPSS 14.0 for Windows. Intra- and inter-observer variability was assessed by reviewing the recordings of 15 random patients and expressed as percentage ± SD.
Results

The study population comprised 50 patients. All patients were treated with aspirin, heparin, abiciximab, and clopidogrel, according to Dutch practice guidelines. Other concomitant medication at discharge included beta-blockers (98%), ACE-inhibitors/angiotensin II receptor blockers (92%), statins (100%).

Baseline clinical and angiographic characteristics are presented in Table 1. Forty-three patients (86%) were males. Mean age was 55.1 (± SD 9.2). Fifty-two percent of the patients had an LAD-related infarction. In 98% of the patients, a post-procedural TIMI 3 flow was documented. During the hospitalization for index MI, LVEF (MRI) was 42% (± SD 9).

Velocities were obtained from recordings with a mean frame rate of 163 ± 24 frames/s. Intra-observer variability was 2.8% (SD 3.8), whereas the inter-observer variability was 7.6% (SD 7.6). In general, mean velocities from lateral myocardial LV segments were significantly higher than those of the septal myocardial LV segments (P < 0.02 for peak systolic velocity and P < 0.001 for diastolic velocities). Mean values for Sm-6, Em-6, and Am-6 were 5.0 (± SD 0.9), 5.7 (± SD 0.9), and 5.4 (± SD 1.6), respectively.

Follow-up at 4 months: left ventricular ejection fraction, left ventricular remodelling, and infarct size

Four months after MI, mean LVEF had increased (when compared with baseline) to 47% (± SD 10) (absolute increase in LVEF of 6%). Eleven patients (22%) had an LVEF below 40%. In 4 months, mean LVESV decreased 4.1% (± SD 22.0). However, nine patients (18%) could be identified as having ≥15% increase in LVESV when compared with baseline, indicating clinically relevant remodelling. The change in LVESV was inversely correlated with the change in LVEF (Figure 1; r = −0.79; P < 0.001). DCE MRI at 4 months post-MI revealed that the mean infarct size was 12.6% of the left ventricle (± SD 6.6). Corrected for body surface area, this is equivalent to 6.3 g/m² (± SD 3.1).

Tissue Doppler imaging for the prediction of left ventricular ejection fraction, left ventricular remodelling, and infarct size at 4 months

LVEF at baseline was a significant predictor of LVEF at 4 months (β = 0.72; P < 0.001). Using univariate linear regression, Sm-6 was shown to be a significant predictor of LVEF at 4 months (β = 0.50; P = 0.001) (Figure 2). Sm-6 remained significantly related to LVEF at 4 months, even after adjustment for age and sex (β = 0.57; P = 0.001). Neither Em-6 nor Am-6 were related to LVEF (P = 0.22 and P = 0.07, respectively).

A value of Sm-6 < 3.0 cm/s predicted an LVEF < 40% with a sensitivity of 33% and a specificity of 100%. An Sm-6 < 3.0 cm/s has a positive predictive value (PPV) of 100% to predict an LVEF < 40% (measured with MRI at 4 months).

A value of Sm-6 > 5.0 cm/s predicted an LVEF > 40% with a sensitivity of 62% and a specificity of 78%. An Sm-6 > 5.0 cm/s has a PPV of 92% to predict an LVEF > 40% (measured with MRI at 4 months).

Table 1  Baseline characteristics (n = 50)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) (SD)</td>
<td>55.1 (9.2)</td>
</tr>
<tr>
<td>Male (%)</td>
<td>43 (86)</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>28 (56)</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>8 (16)</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Hyperlipidaemia (%)</td>
<td>9 (18)</td>
</tr>
<tr>
<td>Body mass index (kg/m²) (SD)</td>
<td>25.7 (3.4)</td>
</tr>
<tr>
<td>TIMI 3 flow after PCI (%)</td>
<td>49 (98)</td>
</tr>
<tr>
<td>Myocardial blush grade</td>
<td></td>
</tr>
<tr>
<td>No or minimal</td>
<td>9 (18)</td>
</tr>
<tr>
<td>Moderate</td>
<td>21 (42)</td>
</tr>
<tr>
<td>Normal</td>
<td>20 (40)</td>
</tr>
<tr>
<td>Peak CK (U/L) (SD)</td>
<td>3293 (1974)</td>
</tr>
<tr>
<td>Infarct related artery</td>
<td></td>
</tr>
<tr>
<td>LAD (%)</td>
<td>26 (52)</td>
</tr>
<tr>
<td>RCX (%)</td>
<td>6 (12)</td>
</tr>
<tr>
<td>RCA (%)</td>
<td>18 (36)</td>
</tr>
<tr>
<td>Wall motion score index (SD)</td>
<td>1.48 (0.34)</td>
</tr>
</tbody>
</table>

Values are expressed as number (%) or mean (standard deviation, SD). SD, standard deviation; TIMI, thrombolysis in myocardial infarction; PCI, percutaneous coronary intervention; CK, creatinine kinase; LAD, left anterior descending coronary artery; RCX, ramus circumflexus, RCA, right coronary artery.

Figure 1  Relationship between remodelling and change in LVEF.

In total, 54% of the patients in the study cohort had either an Sm-6-value of < 3 cm/s or ≥ 5 cm/s at baseline. Of these patients, and using these cut-off values, 96% was correctly classified at baseline.

LVEF at baseline was a significant predictor of infarct size at 4 months as a percentage of LV volume (β = −0.63; P < 0.001). Sm-6 predicted also infarct size (Figure 3). (β = −0.50; P = 0.001). After adjustment for age and sex, Sm-6 was still significantly related to infarct size (β = −0.42; P = 0.01).
No significant correlations were found between the TDI parameters (nor LVEF at baseline) and LV remodelling.

**Discussion**

The primary finding of this study was that colour-coded TDI may serve as a robust and reproducible echocardiographic tool to predict LVEF and infarct size at 4 months post-MI. Using a TDI-derived global measure (i.e. Sm-6), 54% of the MI patients are unequivocally classifiable into two categories with respect to their LVEF at 4 months as measured with MRI (i.e. LVEF < 40% or LVEF > 40%) with 96% accuracy. However, TDI was not able to predict LV remodelling at 4 months.

Our data showed that LVEF and LV geometry changes in the months after primary PCI. Whereas most patients showed improvement in LVEF (mean absolute increase in LVEF of 6%), most likely due to reconvalescence of stunned myocardium, other patients showed no change, or even a decrease, over time. The absence of an increase in LVEF has been related to the process of LV remodelling as illustrated previously by Bolognese et al.² We confirmed this finding showing an inverse relationship between remodelling and the change in LVEF during the first 4 months post-MI. Owing to this dynamic process in the early post-MI period, early measurements of LVEF may be misleading, despite successful restoration of coronary flow. Nevertheless, an early estimation of the extent of myocardial salvage and residual LVEF, preferably during hospitalization for index MI, is desirable. For example, during daily practice, it is important to identify, at an early stage, MI patients who will be ICD candidates.

In a cross-sectional setting, positive correlations have been found between systolic myocardial velocities and LVEF.¹⁴–¹⁷ For example, Gulati et al.¹⁴ showed in a population with various underlying cardiac diseases that pulsed wave derived peak systolic velocity, measured as an average from six sites at the level of the mitral annulus correlated well ($r = 0.85$) with LVEF. However, no studies have investigated whether myocardial and/or annular velocities are related to LVEF at a time point when LVEF is generally accepted to have stabilized (i.e. 4 months).¹⁸

In our study, the best predictor of LVEF at 4 months was the average of six basal myocardial segments (i.e. Sm-6). This relationship remained significant after adjustment for age and sex. We used the screening abilities of Sm-6 to identify patients with LVEF greater or <40% (area under the curve 0.79; $P = 0.009$; Figure 4). Although numbers were low for patients with poor LVEF, Sm-6 < 3.0 cm/s...
appeared to be an excellent predictor to identify post-MI patients with LVEF < 40% (PPV 100%). Sm-6 can also be used to identify patients with LVEF > 40%. In that case, we used a cut-off value for Sm-6 > 5 cm/s. The sensitivity of an Sm-6 > 5.0 cm/s to identify post-MI patients with LVEF > 40% was 62%, whereas the specificity was 78%. Yet, the strength of this cut off lies in the high PPV of 92%. In other words, 92% of the patients identified by our model as having an Sm-6 > 5.0 cm/s will have an LVEF > 40% at 4 months after MI. Therefore, the finding of an Sm-6 < 3.0 cm/s or an Sm-6 > 5.0 cm/s appears to be a useful clinical tool to differentiate patients with an LVEF < 40% from patients with an LVEF > 40%. In our cohort, 54% of patients could be convincingly classified at baseline (accuracy 96%). For the remainder of patients, those with an Sm-6 between 3 and 5 cm/s, we recommend a repeated measurement of LVEF at 4 months.

**Left ventricular remodelling**

To the best of our knowledge, only one study by Park et al.19 investigated whether myocardial velocities had predictive power in terms of LV remodelling. In this study, 46% of the patients showed remodelling, in contrast to 18% of the patients in our study. This difference can be explained by the difference in percentage of anterior infarctions included (100 vs. 52%, respectively). In the study by Park et al.,19 no relationship was found between peak systolic velocities and LV remodelling. We confirmed the absence of an association between myocardial velocities (either systolic or diastolic) and the process of LV remodelling. In addition, we extended their finding because (i) we included not only patients with anterior infarction, (ii) we used MRI for volume assessments, and (iii) the average time to follow-up echocardiography was 14.7 ± 8.4 months in the study by Park et al.,19 whereas the time to follow-up MRI in our study was 4 months. Several variables have been previously identified to predict an increase in LV volume, such as infarct size19,20 and patency of infarct-related artery.21 More recently, LV dysynchrony immediately after MI12 and longitudinal strain18 have been suggested to predict LV remodelling.

**Infarct size**

Mean infarct size was 12.6% of the volume of the left ventricle. Infarct size on contrast-enhanced MRI may be superior to LVEF and LV volumes for predicting long-term mortality in patients with MI.22 We established a firm inverse relationship between Sm-6 and the extent of myocardial necrosis at 4 months, even after adjustment for age and sex.

**Limitations**

Several limitations of the present study need to be addressed. We included only patients with STEMI and therefore our findings need to be confirmed in other MI populations. In addition, we used colour-coded TDI and not pulsed wave derived tissue velocities. We assessed only longitudinal velocities and not circumferential or radial velocities. Finally, tissue velocities may not accurately reflect regional function due to tethering caused by contraction of adjacent segments. Among the strengths of our study are the well-described population using ‘gold standard’ measurements of LVEF and remodelling with MRI. Second, because we included patients with single vessel disease LV function assessments are not confounded by the possibility of hibernating myocardium.

**Conclusions**

An early estimation of the extent of myocardial salvage is desirable during hospitalization for MI. The average peak systolic velocities of the six basal myocardial segments (Sm-6) may serve as a clinical tool for the identification of STEMI patients with LVEF > 40% and those with LVEF < 40% at 4 months follow-up. In addition, Sm-6 is a significant predictor of infarct size. In contrast, TDI-derived velocities do not predict LV remodelling.

**Conflict of interests**: none declared.

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