Doppler Tissue Imaging positive preejection velocity wave is a sign of non-transmural necrosis: Comparison with delayed-enhancement cardiac magnetic resonance

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Myocardial infarction; Myocardial viability; Tissue Doppler Imaging; Cardiac magnetic resonance

Abstract
Aims: Our purpose was to test the hypothesis that Tissue Doppler Imaging (TDI)-derived positive preejection velocity (PPV) is associated with transmural extent of necrosis in delayed-enhancement cardio-magnetic resonance (DE-CMR) in patients with reperfused myocardial infarction (MI).

Methods and results: Longitudinal myocardial velocities were recorded by TDI in 24 patients with MI reperfused with primary angioplasty, using an Acuson-Sequoia® equipment. The same day a CMR study was performed, including cine images in short axis and long axis views and DE images in the same views using a 3D-T1-Turbo-field-echo sequence, 15 min after administration of gadodiamide. Transmural extent of hyperenhancement in each segment was compared to presence or absence of PPV wave. A total of 384 segments were evaluated. Normo-hypokinetic segments (100%) showed a PPV wave, whereas it was only present in 53% of akinetic–dyskinetic segments ($p = 0.0005$). One hundred percent of the segments with absent-mild DE showed a PPV wave; this percentage was lower in segments with intermediate and transmural DE (63 and 10%, $p = 0.001$). The presence of PPV wave in an akinetic segment ruled out transmural necrosis with 97% sensitivity and 90% specificity.

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In the normal myocardial velocity pattern in Tissue Doppler Imaging (TDI), a positive wave often followed by a small negative wave can be seen during the preejection period (i.e. between the onset of ventricular activation and aortic valve opening). This wave is due to the myocardial thickening that takes place during the isovolumic contraction time and its peak approximately corresponds to the closure of the mitral valve.¹

The positive preejection velocity wave (PPV) is a very useful myocardial function index during ischemia.² Its potential usefulness as a predictor of myocardial viability has also been emphasized. In experimental models, preejection myocardial velocities after ischemia-reperfusion in dysfunctional segments highly correlated with the transmural extent of necrosis at pathology.³ However, this association has not been confirmed in clinical studies.

Delayed-enhancement cardiac magnetic resonance (DE-CMR) is an excellent non-invasive technique for reliable and accurate assessment of myocardial scar burden. Several experimental and clinical studies support that hyperenhanced regions have sustained irreversible ischemic injury.⁴,⁵ In this study, our aim was to test the hypothesis that TDI-derived positive preejection velocity was associated with transmural extent of necrosis in DE-CMR in patients with reperfused myocardial infarction.

**Methods**

**Patients**

Twenty-four patients were selected prospectively using the following inclusion criteria: (1) documented first episode of ST-segment elevation myocardial infarction (chest pain, ECG changes and laboratory markers); (2) primary angioplasty performed less than 12 h after symptoms onset and reestablishment of infarct-related artery patency (final TIMI flow grade 2–3); (3) one-vessel disease in coronary angiography; and (4) more than six months’ follow-up without adverse events. Exclusion criteria were: contraindication for CMR (pacemaker, implantable defibrillator, and claustrophobia), preference of the patient not to be included in the study, atrial fibrillation, and extremely poor image quality at echocardiography.

Informed consent was obtained from all subjects prior to entry into the study, which was approved by the Institutional Review Board of our institution. Clinical characteristics of the patients included in the study are described in Table 1. Mean time between primary PTCA and CMR was 10.5 ± 1.5 months.

**TDI echocardiography**

Pulsed-wave TDI echocardiography was performed using an ultrasound system with TDI capabilities (Acuson-Siemens Sequoia C512, Mountain View, California, USA). The preejection period or isovolumic contraction time was defined as the time interval between QRS complex onset and the beginning of the aortic flow curve recorded in the left ventricular outflow tract with pulsed-wave Doppler (Fig. 1). Longitudinal myocardial

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**Table 1** Clinical characteristics of the study group 
(n = 24)

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<tr>
<td><strong>Demographics</strong></td>
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<tr>
<td>Age (years)</td>
<td>62 ± 12</td>
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<tr>
<td>Male sex</td>
<td>17 (79.2%)</td>
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<tr>
<td><strong>Cardiovascular risk factors</strong></td>
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<tr>
<td>Active smoker</td>
<td>12 (50%)</td>
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<tr>
<td>Systemic hypertension</td>
<td>11 (45.8%)</td>
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<tr>
<td>Diabetes mellitus</td>
<td>3 (12.5%)</td>
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<tr>
<td>Dislipidemia</td>
<td>15 (62.5%)</td>
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<tr>
<td><strong>MI characteristics</strong></td>
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<tr>
<td>Peak CK-MB (mass)</td>
<td>201 ± 10</td>
</tr>
<tr>
<td>ECG evidence of anterior MI</td>
<td>17 (70.8%)</td>
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<tr>
<td>Killip class &gt; 1</td>
<td>3 (11.5%)</td>
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<tr>
<td>LVEF acute phase (%)</td>
<td>37 ± 6</td>
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<tr>
<td><strong>Angiographic data</strong></td>
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<tr>
<td>Infarct-related artery</td>
<td></td>
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<tr>
<td>LAD</td>
<td>17 (70.8%)</td>
</tr>
<tr>
<td>RCA</td>
<td>7 (29.2%)</td>
</tr>
<tr>
<td>Post-PTCA TIMI flow grade 3</td>
<td>21 (87.5%)</td>
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<tr>
<td><strong>Medical treatment during hospitalization</strong></td>
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<tr>
<td>Aspirin</td>
<td>23 (95.8%)</td>
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<tr>
<td>Clopidogrel</td>
<td>24 (100%)</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>21 (87.5%)</td>
</tr>
<tr>
<td>Statins</td>
<td>23 (95.8%)</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>15 (62.5%)</td>
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velocities were recorded from 16 segments corresponding to apical four-chamber, two-chamber and three-chamber views, following the segmentation model recommended by the American Society of Echocardiography. Gain was adjusted to obtain an optimal tissue signal and sweep speed was set at 150 mm/s. A sample volume of 5 mm was placed in the middle zone of each segment, at end expiration. All recorded studies were digitally stored and analyzed off-line by two experienced observers in TDI. In each segment, presence or absence of a PPV wave was determined. Differences in criterion between both observers were solved by consensus.

Cardio-magnetic resonance

A CMR study was performed in a Philips Gyroscan Intera 9.1 1.5 T scanner the same day as TDI in all patients. A five-element phased-array cardiac coil was used. Wall motion was assessed for two-, four- and three-chamber long axis views and short axis views by steady-state free precession imaging (echo time, 1.3 ms; repetition time, 2.6 ms; flip angle, 60°; field of view, 350 mm; spatial resolution, $2 \times 2 \times 8$ mm; and 30 phases per cardiac cycle).

Scar was evaluated 15 min after a 0.2 mmol/kg injection of gadodiamide (Omniscan, Amersham Health). A Medrad Spectris Solaris MR injection
system was used. A 3D inversion-recovery turbo field echo sequence with prepulse delay optimized for maximal myocardial tissue suppression (echo time/repetition time/flip angle, 3.6/8/15) was used for evaluation of scar. Images were obtained in short axis and long axis views. Angulation was kept constant for wall motion and scar imaging to match both types of images.

An investigator blinded to TDI data analyzed wall motion and DE-CMR images. Wall motion was graded as normokinesia, hypokinesia, akinesia and dyskinesia in the 16-segment model. Quantification of transmural extent of delayed enhancement was assessed on a five-grade scale in which a score of 0 indicated no hyperenhancement, a score of 1 hyperenhancement of 1–25% of the tissue, a score of 2 hyperenhancement of 26–50%, a score of 3 hyperenhancement of 51–75% and a score of 4 hyperenhancement of 76–100%.

Feasibility and reproducibility

The quality of TDI images was graded as "good" or "poor" by consensus of two investigators experienced in TDI. To study interobserver variability, the presence or absence of PPV wave was reassessed in 48 segments from 24 patients (two per patient) by a second observer trained in TDI. To study intraobserver variability, the presence or absence of PPV wave was reassessed in the same segments by the first observer three months later.

Statistical analysis

Continuous variables are expressed as mean ± SD and categorical variables are expressed as number (%). Comparisons between categorical variables were performed with chi-square test for trends. Predictive models to rule out transmural myocardial hyperenhancement were performed by receiver operating characteristics-area under curve statistics. p Values of less than 0.05 were considered of statistical significance. Statistical analysis was performed with SPSS 11.0.

Results

Feasibility and reproducibility

Assessment of 384 segments from 24 patients was performed both with TDI echocardiography and CMR. TDI echocardiographic image quality was graded as poor in 39 segments (10%), all of them apical segments. Interobserver agreement in detection of PPV wave was 89.6% (43/48). Intraobserver agreement was 100% (48/48).

Relation between wall motion and PPV wave

Among the 345 segments with good quality recordings, 315 showed a PPV wave (91%). The percentage of segments with PPV wave in the different groups defined according to wall motion was the following: 289 out of 289 normo-hypokinetic segments (100%) showed a PPV wave; this proportion was lower in akinetic segments (30 out of 52 segments, 58%) and in dyskinetic segments (0 out of 4, 0%); chi-square test for trends: \( p = 0.0005 \).

The presence of PPV wave showed high sensitivity to identify relevant myocardial systolic contraction defined as hypokinesia or normokinesia (100%), but specificity remained low (41%).

Relation between transmural extent of DE and PPV wave

In our series, the presence of PPV wave significantly diminished with increasing transmural extent of DE (Fig. 2). Among 308 segments with DE involving <50% of the myocardial wall, 100% showed a PPV wave, whereas it was only present in 14 segments out of 22 with DE involving 51–75% of the myocardial wall (63%) and in two segments out of 20 with DE involving >75% of tissue (10%).

Among the segments analyzed, 52 were akinetic or dyskinetic; all of them showed DE in more than 25% of myocardial wall. A separate analysis of akinetic–dyskinetic segments was performed, and PPV wave was significantly less frequent with increasing transmural extent of DE; 24 out of 32 segments with DE <75% of myocardial tissue showed a PPV wave, whereas only two segments out of 20 segments with DE involving >75% of myocardial tissue showed it \( (p = 0.0005) \).

ROC curve statistics were used for the prediction of absence of transmural myocardial necrosis based on the presence of a PPV wave. When a PPV wave was present, transmural myocardial necrosis could be ruled out with 97% sensitivity and 90% specificity (area under curve: 0.92). No significant differences were observed in measurements between segments from the LAD region compared to RCA or LCx regions:

Discussion

Quantitative analysis of contractile myocardial function based on Doppler Tissue Imaging has traditionally been based on evaluation of peak...
systolic myocardial velocities. However, several authors have recently recommended the assessment of myocardial velocities during isovolumic contraction and relaxation to increase diagnostic performance of Doppler Tissue Imaging. Edvardsen et al. have demonstrated that preejective systolic velocity is very sensitive to reductions in myocardial blood flow. This TDI component can be more reliable than ejective systolic velocities during severe ischemia, because it is less dependent on hemodynamic conditions and passive movements of the heart, such as translation and tethering.

Our study investigated whether the presence of TDI-derived positive myocardial preejection velocity is related to the content of non-necrotic myocardium in the region, using for the first time DE-CMR for that purpose. Several studies have focused on the potential of PPV to assess myocardial viability. In an ischemia-reperfusion experimental model developed by Pislaru et al., the PPV wave was related to the viable myocardial transmural extent remaining after reperfusion as evaluated in the anatomic study. More recently, Penicka et al. have demonstrated that the presence of a PPV wave in dysfunctional segments during the acute phase of myocardial infarction is useful for the prediction of contractile function recovery during follow-up, though the authors did not describe any mechanism relating the presence of a PPV wave to myocardial viability.

Using DE-CMR, we have demonstrated for the first time that PPV wave in TDI is strongly associated with non-transmural necrosis in patients with reperfused myocardial infarction, and this can be a mechanism explaining that in previous studies segments with PPV in the acute phase of myocardial

Figure 2  DE-CMR and TDI tracings from akinetic anterior segments in two patients with anterior myocardial infarction. In the first patient (A–B), extensive transmural necrosis in anterior wall was associated with absence of positive preejection velocity wave (PPV) in mid-anterior segment, whereas in the second patient (C–D), substantial subepicardial viability existed and was associated with persistence of PPV in mid-anterior segment.

TDI positive preejection velocity wave is a sign of non-transmural necrosis
infarction are more prone to recover during follow-up. As Kim and others have demonstrated, probability of myocardial contraction recovery during follow-up in patients with myocardial infarction is inversely proportional to the transmural extent of DE in CMR.\(^9\) We suggest that the presence of PPV reflects the integrity of a critical number of myocytes in a given segment (i.e. no scar or non-transmural scar), which is enough to generate a relevant shortening force during the very onset of the isovolumetric contraction time. In contrast, segments with a transmural scar are not able to generate motion during the ejection period and remain dysfunctional during the whole systole.

In our study, an important percentage of akinetic segments showed a PPV wave in spite of not being able to generate relevant systolic contraction. This finding supports the hypothesis that segments with residual viability, not enough to achieve significant functional systolic recovery, could be able to generate segment shortening during isovolumic contraction but not to overcome afterload during the ejective phase. Thus, these segments would remain dysfunctional during ejection in spite of epicardial residual viability. These data are in agreement with Penicka et al., who underlined that the PPV wave could overestimate prediction of myocardial recovery.

This question brings to focus the difference between the correct definition of viability (the presence of living myocytes) and the often-used clinical definition (improvement in contractile function). Our results suggest that best endpoint for PPV wave analysis may not be wall motion recovery, but transmurality of necrosis. Differentiation between transmural and non-transmural necrosis is of undeniable prognostic importance. It has been suggested that myocardial residual subepicardial viability, though not enough to improve myocardial contraction, may improve clinical outcomes by means of prevention of adverse ventricular remodeling, prevention of arrhythmias and prevention of new ischemic events.\(^5,10\)

In conclusion, we have provided a mechanism linking pre-ejectional myocardial velocities to myocardial viability. We have also shown that PPV wave analysis is a quick, easy and reproducible non-invasive method for assessment of myocardial viability in patients with MI and could provide additional information to contractile reserve assessment.

**Limitations**

The size of TDI velocities, including PPV wave, is larger in basal segments than in apical segments. This is partly due to technical factors (angulation between myocardial wall and ultrasound beam, as any other Doppler technique) but also reflects a physiological phenomenon.\(^{11}\) For this reason, we have not analyzed the relation between transmural extent of the necrosis and the absolute size of PPV wave. Only the presence or absence of PPV wave was taken into account for this comparison.

Patients referred for primary PTCA in our institution are generally with high-risk acute MI. However, in selected cases with final small infarcts, we cannot exclude that some degree of tethering may contribute to persistence of PPV. In any case, PPV does not seem to be so prone to tethering as TDI peak systolic velocities.\(^5\)

Our study is a transversal study, focused on patients with chronic myocardial infarction. Further studies aiming to analyse the acute MI setting are warranted.

**Conclusions**

The presence of a TDI positive preejective velocity is inversely related to the transmural extent of myocardial necrosis, as demonstrated with DE-CMR. In patients with myocardial infarction, a PPV wave accurately rules out transmural necrosis and thus can easily provide information regarding residual epicardial viability, which may increase the likelihood of a good clinical outcome.

**References**


