Myocardial Doppler at rest for the identification of myocardial viability

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Background. **Echocardiography may permit the detection of a nonviable myocardium. The aim of this study was to test if resting pulsed wave-tissue Doppler imaging (PW-TDI) might yield additional markers.**

Methods. **Fifty patients (38 males, 12 females, mean age 63 ± 6 years) with left ventricular dysfunction (ejection fraction 35 ± 10%) underwent echocardiography. The posterior septum, anterior septum, lateral, inferior, anterior and posterior walls were sampled on the basal segments in the apical views at PW-TDI. The following variables and cardiac phases were tested: 1) the isovolumic contraction phase velocity, polarity or detectability, 2) the ejection phase velocity, a detectable interval between the ejection phase and aortic valve closure, or ejection phase shape, and 3) the isovolumic relaxation phase velocity or ejection velocity/post-systolic shortening ratio. From the tested PW-TDI variables, viable and nonviable patterns were assembled, taking rest-redistribution ^{201}thallium single-photon emission computed tomography as the independent reference for myocardial viability. Patients with significant loading alterations, mitral or aortic valve disease, and arrhythmias were excluded.**

Results. **Out of 219 dyssynergic segments, viability as identified according to conventional rest echocardiographic criteria appeared in 94 (47%), as identified at PW-TDI in 116 (53%), and as identified at nuclear imaging in 105 (48%). The resting PW-TDI variables consistent with absent myocardial viability were as follows: 1) an isovolumic contraction phase velocity equal to the ejection phase velocity ± 1 cm/s, or absent, 2) an ejection phase velocity ≤ 4 cm/s, usually with a gap between the ejection phase and aortic valve closure, or any shape of ejection but the typical single phase, and 3) an isovolumic relaxation phase velocity < 5 cm/s with an ejection phase velocity/isovolumic relaxation phase velocity ratio < 0.8. The accuracy for the identification of myocardial viability was: agreement 73%, kappa 0.44 for echocardiography, and agreement 75%, kappa 0.47 for PW-TDI.**

Conclusions. **PW-TDI nonviable patterns may be a helpful additional tool for the identification of patients without residual myocardial viability.**

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Introduction

The identification of a dyssynergic but viable myocardium is relevant for both functional improvement and for the formulation of a better prognosis after coronary revascularization in patients with ischemic cardiomyopathy and a depressed left ventricular function[1]. Rest echocardiography has been used for the identification of a nonviable myocardium in order to select patients who would not gain any benefit from revascularization procedures. The presence of either a left ventricular wall end-diastolic thickness < 6 mm and/or the replacement, at echocardiography, of a fine granular texture by highly reflective linear echoes, associated with the absence of systolic thickening in dyssynergic myocardium, have been identified as markers of an absent myocardial viability in rest studies[2,3]. Pulsed wave-tissue Doppler imaging (PW-TDI), in its longitudinal or long-axis application, quantifies the velocities of myocardial fibers during their contraction from the cardiac base to the cardiac apex, thus reflecting the overall performance of the respective wall and might be more sensitive than rest echo in identifying noncontracting, nonviable fibers. We tested the hypothesis that in patients with severe left ventricular dysfunction, PW-TDI parameters can rule out myocardial viability, as identified at rest-redistribution ^{201}thallium (^{201}Tl) single-photon emission computed tomography (SPECT), used as an independent reference technique.

Methods

Patient characteristics. Fifty patients (38 males, 12 females, mean age 63 ± 6 years), with ischemic left ventricular dysfunction (ejection fraction 35 ± 10%), underwent conventional echocardiography at rest, PW-TDI and rest-redistribution ^{201}Tl SPECT for the identification of viable myocardium. The inclusion criteria were: 1) a clinical history of stable ischemic heart disease (i.e. no recent myocardial infarction, unstable angina or overt heart failure), 2) a resting left ventricular ejection fraction < 45%, as assessed according to the Simpson's echocardiographic discs method, 3) the coexistence of segments suggestive of myocardial viability with others suggestive of myocardial nonviability, on the basis of the resting echocardiographic criteria, and 4) no primary cardiomyopathy.

Resting two-dimensional echocardiographic analysis. The parasternal long-axis, short-axis, apical 4-chamber, 2-chamber, and long-axis images were recorded on SVHS. Off-line visual assessment of the echocardiographic images was performed independently by two investigators. Each ventricular segment was scored on a four-point scale: 1 = normal, 2 = hypokinetic, 3 = akinetic, and 4 = dyskinetic. Criteria for myocardial nonviability in the left ventricular segments at rest were either the presence of a left ventricular wall end-diastolic thickness < 6 mm and/or the echocardiographic replacement of a fine granular texture by highly reflective linear echoes, associated with the absence of systolic thickening in dyssynergic myocardium.

In cases of poor thickness/texture detection, the corresponding segment was excluded from the two-dimensional analysis. The inter- and intraobserver agreement for wall motion assessment was 94 and 97% respectively. The ejection fraction was measured using the summation of discs method (Simpson's rule).

Nuclear study. Rest-redistribution ^{201}Tl SPECT was performed and used as the independent reference technique for myocardial viability. With the patient on the fasting state, 3 mCi (110 MBq) of ^{201}Tl were injected intravenously. The images were acquired after 10-15 min of walking, requested in order to achieve constriction of the splanchnic vasculature, and repeated 4 hours later. Rest and redistribution images were displayed side-by-side for comparison. A 16-segment model, similar to the echocardiographic one, was adopted for the interpretation of the SPECT images. Dyssynergic segments were considered viable in the presence of normal perfusion, of a moderate defect with ^{201}Tl > 50% of the maximal (100%) uptake or of a reversible defect at redistribution. Myocardial viability was deemed significant when present in at least two adjacent segments[4].

Pulsed-wave tissue Doppler imaging. An Acuson Sequoia (Mountain View, CA, USA) echocardiographic imaging system with a 3.5 MHz probe and a pulse repetition frequency of 4.5-6.0 KHz was used. A temporal resolution of 4-3 ms was achieved. The sample volume width was set at 3 mm. The Doppler velocity profiles and the electrocardiographic and phonocardiographic tracings were simultaneously recorded on videotape. All measurements were performed off-line. A mean of 5 beats was obtained in cases of significant (> 15%) beat-to-beat variability of the PW-TDI velocity profile.

The left ventricle was studied by using the 6-segment model: the posterior septum, anterior septum, lateral, inferior, anterior and posterior walls were sampled at PW-TDI on the basal segments in the apical views to assess the longitudinal myocardial contraction. The mitral and tricuspid annuli served as anatomical reference points in order to reproduce a comparable depth of sampling. A careful selection was made for the best quality of the velocity profile envelope.

Cases of a doubtful isovolumic contraction phase (IVCP) could be confirmed as the interval between the sound signal of mitral valve closure as evaluated at phonocardiography and the onset of the ejection phase (EP) motion as evaluated at PW-TDI. The two-dimensional echo image in split screen format was helpful in cases of an inadequate phonocardiographic signal. Similarly, the isovolumic relaxation phase (IVRP) could be confirmed as the interval between the sound signal of aortic valve closure as evaluated at phonocardiography and the onset of early diastolic motion as evaluated at PW-TDI. As a consequence, at phonocardiography EP could be defined as the interval between IVCP and IVRP. This last definition was helpful in the identification of cases in which the duration of EP as evaluated at phonocardiography exceeded the duration of EP as evaluated at PW-TDI, with a consequent eye-detectable interval between the two signals which was nonquantitatively assessed. Conversely, EP as evaluated at PW-TDI was deemed normal when characterized by a single, monophasic velocity profile directed towards the transducer and ending at the beginning of IVRP.

On the basis of the aforementioned descriptions, the following continuous and categorical PW-TDI variables were investigated: 1) the IVCP velocity, polarity, or detectability, 2) the EP velocity, an eye-detectable interval between the end of EP and aortic valve closure, or EP shape, and 3) the IVRP velocity or EP/IVRP velocity ratio. The right ventricular free wall was added for comparison.

Exclusion criteria. Patients with significant valvular heart diseases, significantly altered systemic or pulmonary pressures or with cardiac shunts were excluded since PW-TDI was reported to be partially load-dependent[5]. Further exclusion criteria were: significant left ventricular hypertrophy, left bundle branch block, cardiac cycles with extrasystolic or post-extrasystolic beats or any significant rhythm disorder potentially biasing any of the assessed PW-TDI variables.

Statistical analysis. Data are expressed as mean ± SD, percentages or dichotomous variables. For continuous variables, the cut-off values were obtained using receiver operating characteristic (ROC) curves. The diagnostic accuracy was expressed as sensitivity, specificity and agreement, on the basis of their standard definitions, and expressed together with the corresponding confidence intervals. The relative kappa value was calculated. Differences were deemed statistically significant for $p < 0.05$.

Results

The characteristics of the study population are summarized in table I.

Out of 219 (73%) dyssynergic segments, standard echocardiography optimally recognized the aforementioned thickness/texture criteria in 201 segments and identified a viable pattern in 94 (47%). PW-TDI identified viable patterns in 116 (53%) segments, and rest-redistribution ^{201}Tl SPECT in 105 (48%) (Table II). Pooled examples of viable and nonviable PW-TDI patterns with the corresponding isovolumic and EP variables are shown in figure 1.

Prediction of viability by pulsed-wave tissue Doppler imaging. In many cases, after an adequate learning curve, the recognition of the main cardiac phases by means of the PW-TDI velocity profile appeared feasible. Phonocardiographic and electrocardiographic tracings were used as reference in cases of difficult allocation of the cardiac phases.

On the basis of the aforementioned descriptions of the PW-TDI variables, analyzed for each cardiac phase (IVCP, EP and IVRP), the following optimal definitions of myocardial nonviability were found:

1) IVCP velocity: a) equal to EP velocity ± 1 cm/s or b) absent;

2) EP velocity: a) ≤ 4 cm/s, usually with an eye-detectable gap between the EP and aortic valve closure or b) any shape of ejection but the typical single monophasic motion phase, ending at the beginning of the IVRT;

3) IVRP velocity: a) < 5 cm/s until absent or b) with an EP/IVRP velocity ratio < 0.8.

The cut-off values and corresponding areas under the ROC curves are shown in table III.

No negative polarity of the IVCP velocity values was found.

We were able to classify the PW-TDI nonviable variables of each cardiac phase into four main nonviable patterns, in decreasing order of segmental prevalence (Table IV).

Conversely, PW-TDI patterns not complying with the pre-specified definition of nonviability were allocated as viable and appeared in 116 (53%) segments. False positive and false negative data for myocardial viability are shown in table V. The overall accuracy of PW-TDI viable patterns in predicting myocardial viability is shown in table VI. In our population right ventricular free wall PW-TDI exhibited only viable patterns. Eighteen dyssynergic segments (8%), in which the thickness/texture analysis appeared doubtful, were withdrawn from the two-dimensional echo analysis. Conversely, PW-TDI appeared feasible in all segments, confirming its superior accuracy versus two-dimensional echocardiography.

Discussion

The main result of our study is that resting PW-TDI patterns may accurately identify absent myocardial viability. In comparison to the conventional nonviable parameters derived from standard resting echocardiography, PW-TDI appears superior in case of suboptimal echocardiographic images. Moreover, PW-TDI has the potential of rendering quantitative and objective the subjective evaluation of echocardiographic myocardial viability.

Most studies so far addressed the diagnostic value of isolated variables. The task of assessing more variables appeared more challenging.

The assessment of myocardial viability is relevant in patients with ischemic left ventricular dysfunction, in whom coronary revascularization may improve both the functional status and survival[6].

Table I. Clinical data of patients.

Age (years)	63 ± 6
Male gender	38 (76%)
Previous infarction	39 (78%)
Angina pectoris	11 (22%)
Left ventricular ejection fraction (%)	35 ± 10
Beta-blocking agents	31 (62%)

Table II. Number of viable segments at resting echocardiography, pulsed-wave tissue Doppler imaging (PW-TDI) and rest-redistribution ^{201}thallium single-photon emission computed tomography.

	PS	L	I	A	P	AS	All walls
Echocardiography	14	21	14	18	17	14	94 (47%)
PW-TDI	18	23	16	22	20	17	116 (53%)
Nuclear imaging	17	21	14	18	19	16	105 (48%)

A = anterior wall; AS = anterior septum; I = inferior wall; L = lateral wall; P = posterior wall; PS = posterior septum.

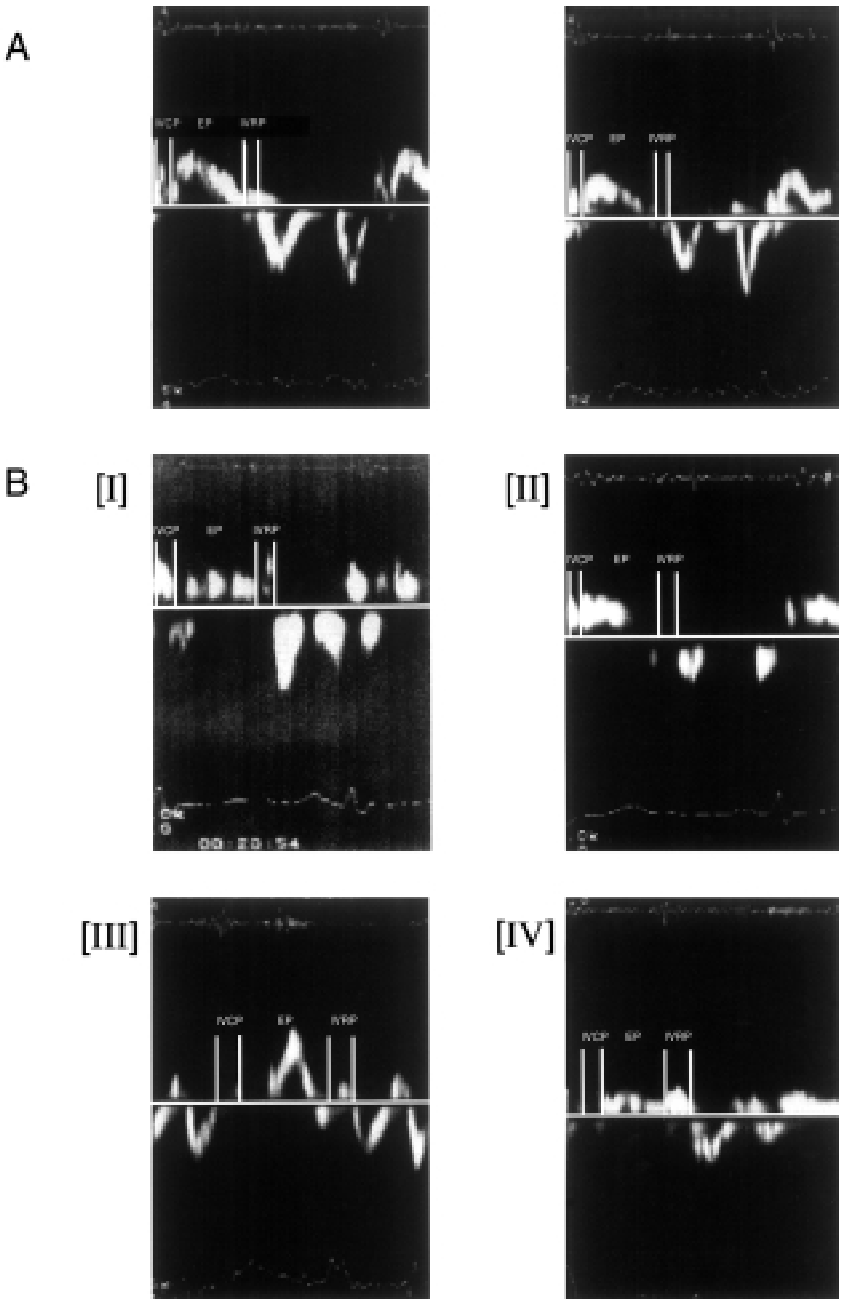

Figure 1. A: *examples of viable pulsed-wave tissue Doppler imaging patterns.* B: *examples of nonviable pulsed-wave tissue Doppler imaging patterns.* I: *isovolumic contraction phase (IVCP) velocity equal to ejection phase (EP) velocity ± 1 cm/s, EP velocity ≤ 4 cm/s and isovolumic relaxation phase (IVRP) velocity < 5 cm/s until zero.* II: *IVCP velocity equal to EP velocity ± 1 cm/s, EP velocity ≤ 4 cm/s with a detectable gap between the EP and aortic valve closure and IVRP velocity < 5 cm/s until zero, or EP/IVRP velocity ratio < 0.8.* III: *absent IVCP, atypical EP and IVRT motions.* IV: *absent IVCP, absent or negligible EP and IVRT motions.*

Table III. Cut-off values of quantitative parameters for the recognition of nonviable segments.

Parameters	Cut-off values	Area under ROC curves
IVCP velocity (cm/s)	EP velocity ± 1	0.57
EP velocity (cm/s)	≤ 4	0.56
IVRP velocity (cm/s)	< 5	0.63
EP/IVRP velocity ratio	< 0.8	0.68

EP = ejection phase; IVCP = isovolumic contraction phase; IVRP = isovolumic relaxation phase; ROC = receiver operating characteristic.

Either a left ventricular wall end-diastolic thickness < 6 mm and/or echocardiographic replacement of the fine granular texture by highly reflective linear echoes in dyssynergic myocardium, associated with the absence of systolic thickening in dyssynergic myocardium, are known resting markers of myocardial nonviability[2,3]. Rest echocardiography coupled with pharmacological stressors, e.g. dobutamine[7], has been widely used for the recognition of myocardial viability. Nevertheless, this approach is associated with significant interobserver/intraobserver variability[8] and is not totally devoid of com-

Table IV. Main pulsed-wave tissue Doppler imaging nonviable patterns and their segmental prevalence.

I. IVCP velocity equal to EP velocity ± 1 cm/s, EP velocity ≤ 4 cm/s and IVRP velocity < 5 cm/s until zero	43 segments
II. IVCP velocity equal to EP velocity ± 1 cm/s, EP velocity ≤ 4 cm/s with a detectable gap between the EP and aortic valve closure and IVRP velocity < 5 cm/s until zero, or EP/IVRP velocity ratio < 0.8	32 segments
III. Absent IVCP, atypical EP and IVRP motions	15 segments
IV. Absent IVCP, absent or negligible EP and IVRP motions	13 segments

EP = ejection phase; IVCP = isovolumic contraction phase; IVRP = isovolumic relaxation phase.

Table V. False positive and false negative viable myocardial segments.

	False positive	False negative
Echocardiography	27	28
PW-TDI	33	22
Pattern I	–	10
Pattern II	–	7
Pattern III	–	3
Pattern IV	–	2

PW-TDI = pulsed-wave tissue Doppler imaging.

plications[9]. In our study, rest PW-TDI was found to be significantly accurate in identifying myocardial viability as compared to a nuclear reference standard.

PW-TDI appears to be only minimally influenced by loading changes, at least within physiological ranges. Recently, interest has been focused on the evaluation of the isovolumic phases. The evaluation of the isovolumic phases was deemed accurate by the high temporal resolution of PW-TDI. Among the many parameters obtainable, we focused on the following cardiac phases: IVCP, EP and IVRP.

On the basis of evidence in the literature, it has been suggested that assessment of the IVCP may predict myocardial viability[10]. The IVCP velocity was previously used for the recognition of a viable myocardium[11,12]. In scarred segments IVCP velocity is only slightly lower than EP velocity[13]. In our experience, IVCP velocity, when combined with a small or quantitatively immeasurable EP, may be suggestive of a nonviable myocardium.

A significant reduction in the EP velocity and/or duration may also rule out myocardial viability[13]. An EP velocity reduction renders velocity measurement more difficult and less accurate. Conversely, the short duration of the EP renders the gap between EP and aortic valve closure eye-detectable. The premature decrease and disappearance of EP velocity, prior to aortic valve closure, may be related to both an inadequate contractile power and inertial factors[14].

In normally contracting myocardium, after aortic valve closure which starts the IVRP, a short-lasting motion of the cardiac base away from the cardiac apex usually terminating before mitral valve opening, may be detected at PW-TDI[15]. In dyssynergic segments, during the IVRP, an opposite motion of the cardiac base towards the cardiac apex may be appreciated. This motion may be considered the equivalent of tardokinesis, which is visually detectable as a prolonged myocardial shortening when it exceeds 90 ms[16]. PW-TDI, due to its high temporal resolution, largely overcomes this limitation. In experimental studies a significantly appreciable IVRP motion was reported as a marker of myocardial viability[17,18]. Similar findings are reported for PW-TDI in clinical settings, where both the EP and post-systolic shortening velocities predicted the presence of myocardial viability in dyssynergic segments[19,20]. Dyssynergic viable segments tend to exhibit both EP and post-systolic shortening, compared to nonviable segments in which the EP appears atypical or negligible. In this context of disorganized EP motions, the presence of an IVRP motion might be interpreted as a passive phenomenon.

Resting standard echocardiography confirmed a mildly accurate prediction of myocardial viability, without the need of stressors. The accuracy of PW-TDI without stressors in identifying myocardial viability did not appear significantly superior to standard echocardiographic resting criteria. A trend was apparent for a higher sensitivity of PW-TDI. In our opinion adding resting PW-TDI does not replace the incremental value of stressing techniques. However, we were able to add an objective combination of quantitative parameters to the subjective echocardiographic analysis. From this starting point, further refinements of single

Table VI. Diagnostic accuracy of resting echocardiography and pulsed-wave tissue Doppler imaging (PW-TDI) variables in the evaluation of myocardial viability. A trend towards a higher sensitivity of PW-TDI is detectable.

	Sensitivity (%)	Specificity (%)	Agreement (%)	Kappa
Echocardiography	71 (65-76)	75 (69-81)	73 (68-78)	0.44
PW-TDI	79 (74-84)	71 (64-75)	75 (70-81)	0.47

or combined variables may warrant exploration. Moreover, PW-TDI reaffirmed its superior feasibility when compared to standard echocardiographic images in cases of doubtful viability assessment, due to suboptimal thickness/texture detection.

As an alternative to TDI, strain and strain rate have been used to assess myocardial viability, mostly in stress settings. Preliminary findings suggest that strain and strain rate under inotropic stimulation may be more accurate than TDI. The strain rate represents velocity gradients between two points, thus measuring regional deformation, independently of cardiac translation and segmental tethering, both limitations of TDI. At present strain rate analysis requires specific softwares, not as widely available as TDI. The strain rate has been reported to be superior to two-dimensional echocardiography and TDI for the recognition of a viable myocardium during low-dose dobutamine[21]. Therefore, the strain rate appears to be a promising alternative to TDI still under investigation for clinical use and technical ameliorations (e.g. angle-dependency limitation).

Study limitations. The angle-dependency, still a major limitation of PW-TDI, seemed to be minimized by the longitudinal approach. In fact, the rationale for applying PW-TDI in the apical views at the basal segments is largely supported by prior studies[22-24]. Similarly, the limitation of heart translation and twisting could be minimized by the apical approach, in which the basal velocities are amplified and the cardiac apex is used as a fixed pivot for any other movement. Therefore, the only relevant bias could be the effect of segmental tethering. Tethering between dyssynergic and normal segments should be expected to be magnified by the inotropic stimulation usually utilized to assess viable myocardium. Our approach was limited to resting conditions, thus possibly reducing this bias.

Our approach did not address all the available parameters and especially the time intervals. We limited this latter assessment to the qualitative eye detection of a gap between EP by PW-TDI and the onset of IVRP.

Among extremes of PW-TDI viable patterns for normal (or hyperkinetic) myocardium and nonviable patterns for scarred myocardium, a "grey" zone remained, in which the allocation of PW-TDI patterns was difficult.

In conclusion, PW-TDI resting patterns may accurately rule out myocardial viability without the need of any stressor. PW-TDI confirmed its superiority to standard echocardiographic images in cases of suboptimal parietal imaging. Technical ameliorations and software developments could further enhance the utility of these indexes in ruling out myocardial viability, as a pre-stress screening of patients with ischemic cardiomyopathy, or as an alternative in cases of stress testing unfeasibility.

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