Regional Diastolic Function by Pulsed Doppler Myocardial Mapping for the Detection of Left Ventricular Ischemia During Pharmacologic Stress Testing
A Comparison With Stress Echocardiography and Perfusion Scintigraphy

Helene von Bibra, MD, Anja Tuchnitz, MD,* Annegret Klein, MD,* Jan Schneider-Eicke, MD,† Albert Schömig, MD,* Markus Schwaiger, MD†
Stockholm, Sweden and Munich, Germany

OBJECTIVES
We evaluated regional diastolic function by pulsed Doppler myocardial mapping for the detection of left ventricular ischemia during pharmacologic stress testing.

BACKGROUND
Evaluation and quantification of diastolic myocardial function remain a challenge for imaging techniques in stress tests.

METHODS
A prospective study compared the detection of coronary artery stenosis:
1) by pulsed Doppler myocardial mapping,
2) by two-dimensional echocardiographic dobutamine stress test, and
3) by perfusion scintigraphy in 64 patients using coronary angiography for reference.
An age matched subgroup of 10 patients with normal angiograms and two-dimensional echocardiographic stress test served as control group. Peak myocardial contraction velocity (VC) and lengthening rate during early diastolic left ventricular (LV) filling (VE) were measured in 12 LV segments from three apical views.

RESULTS
In controls, myocardial velocities increased during stress by $3.6 \text{ cm/s} (p < 0.001)$. In LV segments depending on a stenosed artery (n = 70), VE decreased by $1 \text{ cm/s}$ and, thus, was different from control segments (n = 112, p < 0.001) and from scar segments (n = 13, p < 0.01), whereas the change of VC was similar to that in scar segments. A stress induced 2 cm/s reduction of VE discerned the best diagnostic accuracy (sensitivity 84%, specificity 93%) in comparison with two-dimensional echocardiography (78% and 71%) and perfusion scintigraphy (61% and 86%). Using receiver operating curves at incremental levels of luminal narrowing, these relations persisted.

CONCLUSIONS
Quantification of diastolic myocardial function by pulsed Doppler myocardial mapping during dobutamine stress test was shown to be a feasible, accurate, reproducible, noninvasive technique that should be considered to be a sensitive alternative to the present echocardiographic and scintigraphic imaging techniques for stress tests. (J Am Coll Cardiol 2000;36: 444–52) © 2000 by the American College of Cardiology

Stress echocardiography has emerged as a sophisticated method for the noninvasive detection of coronary artery disease. The diagnostic accuracy, however, depends on the quality of images and interpreters (1) as stress echocardiography usually is not analyzed quantitatively.

Diastolic left ventricular (LV) abnormalities are sensitive early signs of myocardial ischemia (2–4) and have the additional advantage of persisting longer than systolic disturbances (5,6). So far, evaluation of diastolic wall motion has not been possible with semiquantitative stress echocardiography, due to its low frame rate with respect to the short duration of early diastolic events. The latest ultrasound development of Doppler myocardial imaging (7,8), however, has shown its potential for quantification of regional myocardial velocities at high time resolution in animal experiments (9) and could be similarly effective in human studies.

The purpose of this prospective study was: 1) to evaluate the feasibility of pulsed myocardial Doppler (PMD) as an imaging technique for dobutamine stress tests, 2) to define the quantitative diastolic myocardial response to dobutamine stress in normal, in ischemic and in scar segments of the LV, and 3) to compare the diagnostic value of quantitative diastolic function by PMD for the detection of coronary stenosis with the visual assessment of systolic wall motion by traditional stress echocardiography and the scintigraphic evaluation of stress induced perfusion inhomogeneities using coronary angiography as the standard of reference.

METHODS

Patient selection. Patients who had been admitted for a control coronary angiography six months after percutaneous transluminal coronary angioplasty and stent implantation (n = 51) or for diagnostic angiography (n = 13) were prospectively enrolled in this study. Patients with unstable
angina, malignant arrhythmias, significant valvular heart disease, hypertrophic cardiomyopathy or severe hypertension were excluded from participation. Sixty-four patients consented to undergo dobutamine stress testing before angiography and scintigraphy in a protocol approved by the Institutional Review Board of the Technische University, Munich. All patients (44 men, 20 women, mean age 59 ± 9 years) were in sinus rhythm, 27 had a history of myocardial infarction (anterior in 13, inferior in 11 and posterolateral in 3) and five had impaired LV function.

**Dobutamine infusion protocol.** Beta-adrenergic blocking agents were withdrawn for the preceding 24 h. Dobutamine was infused at doses of 5, 10, 20, 30 and 40 μg/kg/min for 5 min each. A 12-lead electrocardiogram, blood pressure and two-dimensional echocardiograms were taken at 2 min after the onset of each level of dobutamine infusion. The 10 μg/kg/min and peak dobutamine rate were maintained until the additional PMD traces had been acquired. The infusion of dobutamine was stopped if one of the following end points was reached: 1) angina (n = 9), 2) 2 mm ST segment depression of the electrocardiogram (n = 1), 3) new or worsened wall motion abnormalities (n = 2). A submaximal stress test with early discontinuation of the dobutamine infusion resulted due to: 1) significant rhythm disturbance (n = 2) and 2) intolerable side effects (n = 3). There were no significant adverse reactions like myocardial infarction, pulmonary edema or sustained ventricular tachycardia.

**Two-dimensional echocardiography.** The patient remained in stable left lateral decubitus position throughout the study. A commercial ultrasound system (Acuson 128 XP/10; Mountain View, California) with a 2.5 MHz transducer was used to obtain the standard views (10). Studies were recorded on a S-VHS video recorder and simultaneously downloaded into a digital analysis system (Tom Tec Imaging, Cine View Version 5.14, Munich, Germany) for display in a quad screen format.

Two independent observers who were unaware of the patient’s clinical data graded LV wall motion using the standard 16 segment model and scheme for the localization of the coronary stenosis (10) as: 0 = not analyzable due to poor image quality, 1 = normal, 2 = hypokinetic, 3 = akinetic or 4 = dyskinetic. Acute ischemia was defined as a stress induced reduction of systolic thickening or wall motion in ≥2 segments.

**Doppler myocardial imaging.** By applying modified filter settings in the conventional pulsed Doppler technique, Doppler myocardial imaging selectively detects low Doppler shifts in tissue signals and, thus, measures regional myocardial velocities. Pulsed Doppler myocardial mapping traces were recorded at rest, at 10 μg/kg/min and at peak dose dobutamine in three apical views at a 60° angle: four- and two-chamber view and apical long axis view. The LV image was carefully aligned to minimize the angle of incidence between myocardial walls and the Doppler tissue cursor. The sampling gate was fixed at a size of 10 mm, the gain minimized to its optimum and the Nyquist limits of spectral pulsed Doppler set at −20 and +20 cm/s. As experience has shown that spectral Doppler curves derived from the left ventricular apex are often nonanalyzable, only two sampling sites were used within each of the six myocardial walls, and the sampling gate consecutively moved to the clearest spectral trace: 1) in the basal third and 2) in the transition of the middle to the apical third of the wall. The resulting 12 LV segments were combined to reflect the territories of the coronary arteries: apical septum, anterior septal and anterior segments were ascribed to the left anterior descending coronary artery (LAD), basal septum and inferior segments to the right coronary artery (RCA) and lateral and posterior segments to the circumflex coronary artery (CX). A one-lead electrocardiogram and a phonocardiogram were recorded simultaneously. Pulsed Doppler myocardial mapping traces with on-line measurements of systolic and early diastolic peak velocities were printed with a 50 mm/s paper speed and recorded on S-VHS video.

The peak velocity was determined as the average from three consecutive beats each in the prejection phase (Vpre), during LV contraction in the ejection period (Vc), during early diastolic LV filling (Ve) as lengthening rate and during atrial contraction (Ve). According to the results from an earlier pilot study, Ve was used as a specific indicator for ischemic response during dobutamine stress; a stress induced decrease by ≥2 cm/s indicated acute ischemia and, thus, a positive test. Reproducibility of velocity measurements during peak stress was assessed for Vc and Ve in three consecutive cardiac cycles in all LV segments of five randomly selected patients and, furthermore, by determining intra- and interobserver variability for the same recordings.

For evaluating quantitative myocardial velocity response to dobutamine stress test in normal, ischemic and scar segments, LV segments were selected according to the following criteria:

1) Normal: all analyzable LV segments in the control group, which was defined using an exclusion of significant coronary stenosis in angiography in conjunction with a normal stress echo test (n = 112);
2) Ischemic: from the three to five LV segments that...
compose the territory of an anatomically stenosed coronary artery as defined by angiography (n = 70), the segment with the maximal stress induced decrease of $V_e$ was selected. This definition of a pathologic response was designed in analogy to stress echo reading, where one would not expect all LV segments supplied by a stenosed coronary artery to demonstrate stress induced wall motion abnormalities either;

3) scar: LV segments in the 12 segment model used in PMD that had a fixed perfusion defect assigned by perfusion scintigraphy (identical basal segments in PMD and perfusion scintigraphy [SPECT] or combined middle with apical segments in SPECT for mid-to-apical segment in PMD) in conjunction with akinesia in two-dimensional echocardiography at rest (n = 13).

**Myocardial SPECT.** A randomly distributed subgroup of 45 patients also underwent sequential dual-isotope SPECT imaging with intravenous Thallium (90-110 Mbq Thallium-201-chlorid) for the resting state and Technetium-99m-Sestamibi (800-1200 Mbq Technetium-99m-MIBI) for peak stress after treadmill exercise according to the Bruce protocol. Scintigraphic images were recorded in tomographic technique (SPECT, Siemens, Munich, Germany). Perfusion scintigraphy was interpreted by two experienced observers who were unaware of the patient’s clinical, sonographic and angiographic data. They used the same LV segmentation model as in stress echocardiography and a scoring system (1 = normal perfusion to 4 = severe perfusion abnormality) for tracer uptake. A reversible perfusion defect was assigned if the stress/ rest score was $\geq 1$ and a fixed perfusion defect if rest score $\leq 3$ was unchanged at stress.

**Coronary arteriography.** Biplane coronary angiograms were obtained by the Judkins technique with a standard cineangiographic system (Siemens) in multiple views. Two experienced observers who were unaware of the patient’s sonographic and scintigraphic data graded luminal diameter narrowing as 0, $<25$, 25, 50, 75, 90 and 100% in 15 arterial segments; in cases of persisting disagreement between observers, the average of both values was assigned. Intra- and interobserver variability was established after six months in 13 randomly selected patients. In this study, the definition of a significant anatomical stenosis implied a $\geq 50\%$ luminal narrowing localized in the first or middle segments of the coronary arterial tree.

**Statistical analysis.** Data are presented as mean $\pm$ standard deviation in text and tables or as box plots of the percentiles in the graphs. Pulsed Doppler myocardial mapping data during rest and peak stress were compared with Wilcoxon signed rank test and differences among the groups with Kruskal-Wallis analysis of variance by ranks with a multiple comparison procedure using a significance level at p $< 0.05$. Diagnostic accuracy of the noninvasive tests is described as sensitivity, specificity and positive and negative predictive value. The discriminatory power of $V_e$ for stress test was determined by receiver operating characteristic curves (11) for incremental diagnostic criteria. Receiver operating characteristic curves were also used for the comparison of the three noninvasive stress tests and the area under the curve calculated (12). Reproducibility of PMD measurements during peak stress was expressed as the maximal mean difference $\pm$ maximal standard deviation between each of three successive beats and as the coefficient of variation between two observers.

**RESULTS**

**Coronary angiography.** Significant coronary artery stenosis was excluded in 14 patients. From this entity, the ten patients with normal LV function and normal stress echocardiograms were taken as a control group (six men, four women, age 59 $\pm$ 8 years). One-vessel disease was present in 20 patients, and multivessel disease was present in 30. There were significant lesions of the LAD in 36 patients, of the RCA in 21 and of the CX in 13 patients. A diameter reduction by $\geq 75\%$ was observed in 37 patients and by $\geq 90\%$ in 20 arteries. When assessed for normality versus significant ($\geq 50\%$) stenosis, intraobserver and interobserver agreement both occurred in 97% of the 76 arterial segments. With respect to the individual seven grades of arterial diameter reduction, intraobserver (interobserver) agreement occurred in 85% (65%) of segments. Differences in the remaining segments did not exceed 1 grade.

**PMD.** Pulsed Doppler myocardial mapping could be performed in all patients. Mean duration of Doppler image acquisition including on-line analysis was 6 $\pm$ 1 min each at low dose and at peak dobutamine. During the stress test, heart rate increased from 65 $\pm$ 10 to 118 $\pm$ 23 beats per min, systolic blood pressure from 131 $\pm$ 20 to 152 $\pm$ 19 mm Hg, and diastolic blood pressure remained unchanged (82 $\pm$ 10 and 78 $\pm$ 11 mm Hg). Quality of Doppler tracings was sufficient for analysis in 94% of the LV segments. Nonanalyzable Doppler curves occurred mainly during peak stress in mid-to-apical regions with decreasing frequency at the following sites: anterior (3%), lateral (1%), inferior, septal and posterior wall. It is noteworthy, that the peak of $V_e$ remained discernible from $V_A$ even at higher heart rates up to 154 beats per min, when E and A waves were beginning to merge (Fig. 1, top).

Reproducibility during peak stress: the maximum of the mean differences between three successive beats was $=0.3 \pm 1.0$ cm/s for $V_c$ and $=0.2 \pm 1.0$ cm/s for $V_v$, and the coefficient of variation was $=4.5 \pm 9.1\%$ for intraobserver and $=5.1 \pm 16.4\%$ for interobserver variability.

**Control group.** The individual response of regional myocardial velocities to dobutamine stress is illustrated in Figure 1, top. The mean response of PMD data was evaluated in the control group for the comparison to ischemic and to scar segments. In controls the mean values for systolic and diastolic peak velocities increased significantly during dobutamine stress (Fig. 2). The ratio of early to late diastolic velocities remained unchanged. At the resting state, peak
velocities were faster in basal regions compared with the apical ones ($p < 0.01$) (Table 1), but their reaction to dobutamine stress remained uniform: a highly significant increase of velocities by $3.6\text{ cm/s}$. Myocardial velocity response in the groups of ischemic and scar segments. Figure 1, middle and bottom, demonstrates individual PMD traces in patients with significant stenosis of the LAD or the RCA with a stress induced decrease of peak lengthening rate $V_E$ by $2\text{ cm/s}$. The respective mean values are listed in Table 2. In ischemic segments ($n = 70$) stress induced mean decrease was $1.6\pm2\text{ cm/s}$ for $V_E$ and $0.47\pm0.35$ for the ratio $V_E/V_A$. These changes were significant compared with the control ($p < 0.001$) and with the scar segments ($p < 0.01$). Concomitantly, peak contraction velocity increased to a smaller extent than it did in the control segments ($p < 0.001$) but not differently from scar segments. Figure 3 demonstrates boxplots of the percentiles for each of these systolic and diastolic parameters illustrating the smallest overlap of the individual data in the differentiation between control and ischemic response to stress for change in $V_E$. There was a significant correlation between change in $V_E$ and $V_C$ in the control segments ($r = 0.7$, $p < 0.001$) but not in the ischemic segments ($r = 0.2$, NS).
V_e reduction as specific sign of stress induced ischemia. Receiver operating curves discriminated the best cut-off point in the level of V_e reduction at 2 cm/s (Fig. 4A) and, for incremental luminal narrowing (Fig. 4B), the most discriminatory power at ≥50% diameter reduction, which is consequently used for further analysis: sensitivity was 84%, specificity 93%, the positive predictive value was 98% and the negative predictive value 74%. In patients with one-vessel disease, sensitivity was 85%. Eight patients had false negative tests associated with submaximal stress test (n = 2), noisy spectral traces (n = 2), a 50% stenosis (n = 4) with negative results also in both other stress tests in two patients. The localization of the segments with a stress induced reduction of V_e by ≥2 cm/s allowed the correct identification of the stenosed vessel in 80% of patients both with one-vessel and with multivessel disease. These diastolic data are superior when compared with the systolic parameter change in V_c with a cut-off level of ≥2 cm/s stress induced increase for a positive test (sensitivity 78%, specificity 29%).

Conventional stress echocardiography. Conventional stress echocardiography was successfully performed in all patients and provided sufficient image quality for analyses (score ≥1) in 81% of the LV segments. Score 0 was assigned most often to the anterior wall in the two-chamber view (8%), to the posterior (3%) and lateral wall (2%). Sensitivity for the diagnosis of significant coronary stenosis was 78% and specificity 71% at ≥50% luminal narrowing. In patients with one-vessel disease, sensitivity was 75%. Eleven patients had false negative tests associated with submaximal stress test (n = 2), reduced image quality with score 0 in ≥6 segments (n = 3) and wall motion abnormalities in one LV segment only (n = 6). Localization of the stenosed artery

Table 1. Regional Contraction (V_c) and Lengthening Rate (V_e) in the Control Group

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th></th>
<th>Peak Stress</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>V_c</td>
<td>V_e</td>
<td>V_c</td>
</tr>
<tr>
<td>Septum b</td>
<td>8.1</td>
<td>-8.4</td>
<td>14.4</td>
</tr>
<tr>
<td>Septum a</td>
<td>7.0</td>
<td>-7.3</td>
<td>14.0</td>
</tr>
<tr>
<td>Anterior septum b</td>
<td>9.1</td>
<td>-8.0</td>
<td>15.2</td>
</tr>
<tr>
<td>Anterior septum a</td>
<td>7.1</td>
<td>-6.3</td>
<td>13.7</td>
</tr>
<tr>
<td>Anterior wall b</td>
<td>8.0</td>
<td>-9.7</td>
<td>11.4</td>
</tr>
<tr>
<td>Anterior wall a</td>
<td>6.4</td>
<td>-7.4</td>
<td>11.4</td>
</tr>
<tr>
<td>Lateral wall b</td>
<td>7.0</td>
<td>-9.3</td>
<td>15.3</td>
</tr>
<tr>
<td>Lateral wall a</td>
<td>6.1</td>
<td>-7.4</td>
<td>15.2</td>
</tr>
<tr>
<td>Posterior wall b</td>
<td>7.8</td>
<td>-8.3</td>
<td>14.6</td>
</tr>
<tr>
<td>Posterior wall a</td>
<td>6.5</td>
<td>-6.4</td>
<td>12.6</td>
</tr>
<tr>
<td>Inferior wall b</td>
<td>8.2</td>
<td>-8.4</td>
<td>15.5</td>
</tr>
<tr>
<td>Inferior wall a</td>
<td>7.0</td>
<td>-7.4</td>
<td>14.7</td>
</tr>
</tbody>
</table>

p < 0.001 for each regional velocity comparing rest to stress. b = basal; a = mid-to-apical.

V_c = peak contraction velocity during left ventricular ejection; V_e = peak velocity during early diastolic filling.

Table 2. Myocardial Velocities at Rest and During Dobutamine Challenge

<table>
<thead>
<tr>
<th>Control (n = 104)</th>
<th>Rest</th>
<th>p &lt;</th>
<th>Stress</th>
</tr>
</thead>
<tbody>
<tr>
<td>V_re (cm/s)</td>
<td>6.2</td>
<td>0.001</td>
<td>17.3 ± 7.2</td>
</tr>
<tr>
<td>V_c (cm/s)</td>
<td>7.2</td>
<td>0.001</td>
<td>14.1 ± 7.4</td>
</tr>
<tr>
<td>V_e (cm/s)</td>
<td>-7.5</td>
<td>0.001</td>
<td>-11.2 ± 3.8</td>
</tr>
<tr>
<td>V_A (cm/s)</td>
<td>-8.1</td>
<td>0.001</td>
<td>-12.2 ± 4.6</td>
</tr>
<tr>
<td>V_c/V_A</td>
<td>1.0</td>
<td>NS</td>
<td>0.9 ± 0.4</td>
</tr>
<tr>
<td>Ischemic (n = 84)</td>
<td>Rest</td>
<td>p &lt;</td>
<td>Stress</td>
</tr>
<tr>
<td>V_re (cm/s)</td>
<td>5.9</td>
<td>0.001</td>
<td>12.1 ± 5.5†</td>
</tr>
<tr>
<td>V_c (cm/s)</td>
<td>7.0</td>
<td>0.001</td>
<td>10.0 ± 3.7†</td>
</tr>
<tr>
<td>V_e (cm/s)</td>
<td>-8.3</td>
<td>0.001</td>
<td>-7.3 ± 2.3†</td>
</tr>
<tr>
<td>V_A (cm/s)</td>
<td>-7.7</td>
<td>0.001</td>
<td>-11.5 ± 3.4</td>
</tr>
<tr>
<td>V_c/V_A</td>
<td>1.13</td>
<td>0.001</td>
<td>0.67 ± 0.27‡</td>
</tr>
<tr>
<td>Scar (n = 13)</td>
<td>Rest</td>
<td>p &lt;</td>
<td>Stress</td>
</tr>
<tr>
<td>V_re (cm/s)</td>
<td>6.1</td>
<td>0.03</td>
<td>10.2 ± 5.5†</td>
</tr>
<tr>
<td>V_c (cm/s)</td>
<td>5.2</td>
<td>NS</td>
<td>9.7 ± 4.7</td>
</tr>
<tr>
<td>V_e (cm/s)</td>
<td>-5.8</td>
<td>NS</td>
<td>-5.9 ± 3.3†</td>
</tr>
<tr>
<td>V_A (cm/s)</td>
<td>-7.2</td>
<td>0.005</td>
<td>-10.5 ± 3.0</td>
</tr>
<tr>
<td>V_c/V_A</td>
<td>0.84</td>
<td>0.035</td>
<td>0.70 ± 0.15*</td>
</tr>
</tbody>
</table>

V = myocardial peak velocity; V_c = during atrial contraction; V_e = during LV contraction; V_A = during early diastolic LV filling; V_c/V_A = relation of early to late diastolic velocity; V_re = during the pre-ejection phase.

*p < 0.05; †p < 0.01; §p < 0.001 compared with control; §§p values comparing scar to ischemic segments.

Figure 3. Box plot of the percentiles (same setting and abbreviations as Fig. 3) of stress induced changes of myocardial velocities for the comparison of control segments with ischemic and scar segments. Individual data demonstrate least overlap for the ischemic versus the control data in ΔV_e. Ischemic ΔV_e is also significantly lower than ΔV_e in scar segments (p < 0.01). **p < 0.01 and ***p < 0.001 for the comparison with control segments; §§p < 0.01 for the comparison with ischemic segments.
was correct in 60% of patients with one-vessel and in 87% of the patients with multivessel disease.

**Localization of positive tests in PMD and twodimensional echocardiography.** Positive stress tests were diagnosed from different segmental involvement in patients with LAD disease: reduced VE was observed in a similar number of septal versus anterior segments (n = 12 versus 11) and stress induced wall motion abnormalities predominantly in septal (n = 19) versus anterior segments (n = 2). In patients with RCA disease, the positive results were localized similarly in both imaging modalities. With regard to a positive test in stress echocardiography due to apical wall motion abnormalities (n = 26), 10 patients had a pathologic reduction of lengthening rate in mid-to-apical segments, 10 patients in basal segments; two of these tests were false positive according to angiography and correctly identified as negative test by PMD, and four were missed by PMD contributing 50% in the total of eight false negative PMD tests.

**SPECT.** Tracer uptake was interpreted as normal in 12 patients, five of whom had no significant stenoses on angiography. There was a stress induced perfusion defect in 22 patients and a fixed large perfusion defect in 13 patients. Sensitivity for the diagnosis of significant coronary stenosis was 61% and specificity 86%. Fifteen patients had false negative tests associated with a submaximal stress test (n = 1), extensive collaterals (n = 2), severe three-vessel disease (n = 2) and a 50% luminal narrowing (n = 10). Two false negative results in spite of a ≥90% diameter reduction were associated with either one-vessel disease and collaterals or advanced three-vessel disease and reduced LV global function.

**Comparison of the three noninvasive imaging stress tests.** The receiver operating characteristic curves of Figure 4C illustrate the superior discriminatory power of the PMD stress test compared with stress echocardiography and SPECT.

**DISCUSSION**

To our knowledge, this is the first full report of a myocardial pulsed Doppler study for the evaluation of regional diastolic function during dobutamine stress test. This study demonstrates that PMD is feasible and yields a test with improved sensitivity compared with the traditional echocardiographic and perfusion imaging methods.

**Resolution of timing and velocities.** Due to the low time resolution inherent in the respective imaging methods, stress tests using two-dimensional echocardiography or scintigraphy have been limited to systolic indexes of LV function. The high diastolic peak velocities are of short duration, particularly with increasing heart rates; therefore, a Doppler technique with high temporal resolution is required. Spectral pulsed Doppler imaging offers two important advantages in accuracy compared with two-dimensional color Doppler:

1) its high repetition frequency of 250 versus 25 to 70 Hz in color Doppler and
2) fast Fourier analysis for the calculation of peak versus mean velocities derived by autocorrelation techniques with inherently lower peak velocities (1.6 ± 1.8 cm/s) (13). Therefore, the pulsed Doppler mode was used throughout this study, and peak E versus peak A waves could be discerned even at high heart rates (Fig. 1).

**Myocardial function in longitudinal axis in a 12 segment model of the LV.** In this study, myocardial function was studied in the LV longitudinal axis using an apical transducer position as this provides an acceptable range of insonation angle in all LV segments. Extent and timing of LV long axis function are integral parts of global myocardial function and demonstrate significant correlation to traditional systolic (14,15) and diastolic parameters of LV function (16,17). It is important to note that subendocardial fibers in particular are oriented along the long axis of the LV (18) and that subendocardial function is more affected by ischemia. Thus, shortening and lengthening velocities in the LV long axis may mirror subendocardial function and could be particularly sensitive parameters for acutely induced ischemia during stress tests.

The 12 segment model of the LV was based on three apical views at a 60° angle to optimize spatial resolution in...
the LV circumference. Two measuring sites along each LV wall (basal and mid-to-apical) were considered sufficient due to the following characteristics of PMD. The position of the apex is relatively fixed with reference to the imaging transducer resulting in two consequences:

1) a strictly apical position of the sample gate often renders nonanalyzable Doppler curves and  
2) the velocity of a more basal segment represents the sum of the longitudinal axial displacement of all myocardial fibers from this segment to the apex, thus also reflecting velocities of the more proximal myocardial region of this imaging plane.

**Response to dobutamine stress in controls.** The reproducibility data of PMD show clearly that the measured and stress induced changes of velocities are in a much higher range and, thus, are meaningful. There was a perfect age match between control and patients groups in this study, which is important for the evaluation of diastolic LV function (19). The range of peak velocities at rest and regional inhomogeneities as observed in this study have also been reported for myocardial long axis function by other investigators (17,19–21). The differences between regional velocities, however, are small (±2 cm/s) when compared with the increase of velocities during peak stress (6.8 ± 5.5 cm/s for systolic and 3.6 ± 3.3 cm/s for the diastolic velocities).

Whereas a stress induced increase of systolic velocities is considered to be a normal myocardial reaction (19–21), there are hardly any data available on the normal diastolic response to pharmacologic stress in myocardial Doppler technique, probably due to the limited time resolution of two-dimensional color Doppler. We have observed an identical increase of lengthening rate during dobutamine challenge comparing the control group of this study with a group of young normals (mean age 25 ± 4 years) (22) and, thus, consider this increase to be the normal functional response. The presented findings confirm that dobutamine stress induces a sufficiently uniform response in normal regional myocardial function, which is the prerequisite for stress tests.

**Diastolic response in patients with coronary artery stenosis.** The predominant observation in this study was the stress induced reduction of lengthening rate in LV segments associated with a stenosed artery. The mechanisms for this impairment of LV rapid filling are not addressed by this study design. However, in the total context of its occurrence in exercise induced ischemia, some of the most likely mechanisms appear to be delay and decrease in myocardial relaxation, which have been ascribed to the persistence of local myocardial tension and postsystolic constriction in earlier experimental (9,23–25) and human studies (7,26–28). In the intact LV, the “almost explosive character of rapid filling” (25) is based on the interaction of configuration restoring forces from elastic recoil and impedance with hemodynamic loading factors from wall stress and from the hydraulic effect of coronary circulation (23,25,29). This latter effect becomes suppressed on a beat-to-beat basis when the gradient for coronary inflow is diminished (25). It is conceivable that a stress-induced reduction of the coronary hydraulic effect contributes to the reduction of regional subendocardial lengthening rate, which was observed only in ischemic LV segments, as reduced VE was not seen in the presence of normal angiographic flow, irrespective of the state of myocardial function or absence of perfusion (Fig. 3). Furthermore, this decrease of VE did not correlate with the simultaneous changes of contraction velocity in the ischemic segments (r = 0.2) as opposed to the significant correlation of these parameters in the control segments (r = 0.7, p < 0.001).

**Systolic response in patients with coronary artery stenosis.** If compared with control segments, the stress induced increase of peak contraction velocity was 50% smaller in segments with acute ischemia (Fig. 3). This has been described as a diagnostic parameter for significant coronary artery stenosis in studies using color Doppler imaging with postprocessing and bicycle ergometry or dobutamine stress (20,30) but did not provide a clinically meaningful discrimination from control and scar segments in our patient population with complex ischemic heart disease. The effect of tethering from surrounding healthy tissue cannot be differentiated by assessing change in VE as demonstrated by the similar range of values in scar segments and ischemic segments (Fig. 3).

**Stress echocardiography.** Our data confirm the same range of sensitivity and specificity as previously reported for patients with a high incidence of myocardial infarction (31,32). The combination of higher sensitivity and lower specificity when compared with SPECT may be attributed to the excellent spatial resolution of two-dimensional echocardiography, which enables the visualization of subendocardial wall motion abnormalities. In patients with borderline image quality, the anterior wall often renders nonanalyzable images so that the localization of the diseased artery may not be as precise as desired (in one-vessel disease 60% compared with 80% by PMD). Thus, the standard 16 segment model for analysis did not prove superior to the 12 segment model for PMD. The apparent differences in the local display of systolic versus diastolic abnormalities by the respective ultrasound methods demonstrated in this study that the nonquantitative assessment of systolic wall motion abnormalities by two-dimensional echocardiography renders inferior results if compared with the measurement of regional lengthening rate by PMD (Fig. 4C).

**SPECT.** Our SPECT data confirm a range of sensitivity and specificity as previously reported for a patient selection with a high incidence of myocardial infarction (31,33). The maximal discriminatory power for scintigraphic perfusion imaging at a level of ≥75% diameter reduction and its inferior sensitivity (61%) if compared with the Doppler evaluation of diastolic function (84%) may be due to the lack of absolute data for regional perfusion. Furthermore,
SPECT cannot discern collateral from normal anterograde perfusion nor, due to its spatial resolution (10 mm to 15 mm), the degree of subendocardial from the degree of subepicardial perfusion (34).

**Diagnostic accuracy and image quality.** Supposedly, some of the inherent characteristics of PMD contribute to the superior diagnostic accuracy of PMD if compared with stress echocardiography and SPECT. The high sensitivity and accuracy for subendocardial disturbances of early diastolic function may be reflected by the optimal discriminatory power at ≥50% diameter reduction. Furthermore, the signal-to-noise ratio of pulsed Doppler allowed 94% of the LV segments to be analyzed compared with 81% in two-dimensional echocardiography. The reason for this superior image quality of the Doppler technique is its relative independence of chest wall attenuation (8). Thus, it is possible to obtain diagnostic quality PMD curves even from patients who are considered poorly echogenic on standard two-dimensional echocardiography. This advantage may help to make PMD useful and reproducible in the clinical setting for any normal quality echo laboratory.

**Study limitations.** The measurement of myocardial velocities is affected by the translation and rotation of the LV throughout the cardiac cycle. These effects are minimized due to the intraindividual comparison of resting and stress velocities and the high angle of incidence from the apical transducer position. Finally, there are very close relations between the vectors of all three dimensions within the myocardium (35). Thus, the integration of different myocardial regions or velocity vectors within one imaging plane has not prevented clinically useful assessment of LV function by any of the standard imaging modalities used for reference in cardiology which are, obviously, also subjected to the phenomena of translation and rotation. As heart rates ≥160 beats per min lead to a merging of E and A waves in regional myocardial velocity traces, the Doppler imaging modality appears more suitable for patients ≥36 years. A phonocardiogram may be required for the timely definition of early diastolic velocity in very asynchronous LV segments. The coronary angiograms had not been analyzed quantitatively. However, the reproducibility data were sufficiently good to accept the angiographic evaluation as the reference in cardiology which are, obviously, also subjected to the phenomena of translation and rotation. As heart rates ≥160 beats per min lead to a merging of E and A waves in regional myocardial velocity traces, the Doppler imaging modality appears more suitable for patients ≥36 years. A phonocardiogram may be required for the timely definition of early diastolic velocity in very asynchronous LV segments. The coronary angiograms had not been analyzed quantitatively. However, the reproducibility data were sufficiently good to accept the angiographic evaluation as the reference method throughout this comparative study.

As they represent the same pretest selection bias as the patients who are considered poorly echogenic on standard two-dimensional echocardiography. The reason for this superior image quality of the Doppler technique is its relative independence of chest wall attenuation (8). Thus, it is possible to obtain diagnostic quality PMD curves even from patients who are considered poorly echogenic on standard two-dimensional echocardiography. This advantage may help to make PMD useful and reproducible in the clinical setting for any normal quality echo laboratory.

**Potential clinical implications.** Facing the current lack of a reliable technique to accurately quantify regional myocardial diastolic function in humans, PMD may have a major clinical implication in this respect. In this study it has proven to be an accurate, reproducible, noninvasive and quantitative technique that should be considered a promising alternative to the present echocardiographic and scintigraphic imaging techniques for stress tests. Image acquisition including on-line analysis was not more time consuming than in standard echocardiographic stress tests with off-line quad screen analysis. The quantifiable nature of this new technique combined with the improved signal-to-noise ratio should make it an appropriate tool for the evaluation of viability (36) as well as the prognostic value of diastolic myocardial dysfunction.

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