Transthoracic, harmonic mode, contrast enhanced color Doppler echocardiography in detection of restenosis after percutaneous coronary interventions. Prospective evaluation verified by coronary angiography

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Abstract  Aims To test the feasibility and accuracy of transthoracic, harmonic mode, contrast enhanced Doppler echocardiographic assessment of lesion severity after PCI treatment in native coronary arteries—the LAD, Cx and RCA.

Methods and results Prospective evaluation of 59 patients (66 arteries). Restenosis was diagnosed whenever maximal flow velocity at least doubled in comparison to the segment immediately proximal to the PCI site or when local velocity was at least 2 m/s. At 9 months of follow-up final comparison of Doppler echocardiography and coronary angiography was performed with regard to 44 arteries in 40 patients. Of LAD segments assessed, 15 were proximal and 15 middle. The figures for Cx segments were: 4 proximal and 2 mid, and for RCA 2 proximal, 5 middle and 1 distal (i.e. the posterior descending coronary artery).

On final coronary angiography there were 8 restenoses—all correctly diagnosed by echocardiography. There were 2 false-positive diagnoses of restenosis. Specificity for restenosis detection was 94% and sensitivity 100%.

Conclusion Transthoracic echocardiography allowed for accurate stenosis assessment of principal coronary arteries after successful PTCA. Feasibility of lesion site

Keywords
Doppler echocardiography; coronary artery; ultrasound contrast agent; restenosis; PCI.
Introduction

Percutaneous coronary intervention (PCI), especially when combined with stent implantation is a highly efficacious and minimally invasive procedure. However, restenosis at the angioplasty site is a fairly frequent phenomenon, which takes place in 10–50% of cases after bare metal stent implantations. Although numerous tests have been developed to assist in the detection of restenosis, they have many shortcomings. The traditional noninvasive methods (exercise test, stress scintigraphy) are not sufficiently sensitive to detect restenosis, are time consuming, or involve exposure to radiation. The gold standard for the identification of significant coronary artery disease—the coronary angiography—is costly and invasive. It seems, therefore, warranted to assess a noninvasive screening test which could be of use in the detection of restenosis.

Recently, the range of transthoracic echocardiographic applications has been greatly improved due to the development of harmonic imaging and ultrasound contrast agents. By using transthoracic echocardiography and fundamental mode color Doppler without the aid of ultrasound contrast agents we were able to assess directly significant portions of native coronary arteries: the left anterior descending (LAD), circumflex (Cx) and right coronary artery (RCA) in a substantial number of patients scheduled for coronary angiography; we were able to correctly diagnose stenoses not only of the LAD, but also of the Cx and RCA1 (Figs. 1 and 2). Hozumi et al.2 and Saraste et al.3 proved

Figure 1  An example of middle RCA stenosis found in a patient not included in present study. Left upper: color Doppler echocardiographic view of the prestenotic site. Right upper: velocity spectrum recorded within this site—maximal flow velocity is 0.4 m/s. Left lower: color Doppler echocardiographic view of the stenotic site. Right lower: velocity spectrum recorded within the stenosis—maximal flow velocity is 1.52 m/s. The velocity ratio (maximal velocity at the stenosis divided by maximal velocity proximal to stenosis) is 3.8. On coronary angiography, which was subsequently performed, an 80% of middle RCA stenosis was found.
that transthoracic Doppler echocardiography is useful in the noninvasive diagnosis of restenosis after percutaneous transluminal coronary angioplasty (PTCA) of the left anterior descending coronary artery. We assessed the value of transthoracic, contrast enhanced, harmonic mode Doppler echocardiography in the detection of restenosis in native coronary arteries—the LAD, Cx and RCA after the PTCA, with or without stent implantation.

Aims of the study

The primary goal of the study was to test the feasibility and accuracy of assessment of restenosis at the angioplasty site in native coronary arteries by means of transthoracic, harmonic mode, contrast enhanced echocardiography.

The secondary aim of the study was to test the influence of ultrasonic contrast agent enhancement on assessment of coronary artery restenosis.

Methods

Study design

We carried out a prospective observation of consecutive, unselected patients who underwent percutaneous transluminal coronary angioplasty (PTCA) of left anterior descending coronary artery (LAD), left circumflex coronary artery (Cx) or right coronary artery (RCA), with or without stent implantation. The decision regarding stent placement was at the operator’s discretion. It was not recommended by the protocol of the study to stent a lesion if the result after balloon angioplasty was optimal (residual diameter stenosis < 35%, no dissection compromising the vessel lumen). The study was conducted at the Jagiellonian University School of Medicine Hospital and was approved by the Ethics Committee of the University. Written informed consent was obtained from all participants.
The study patients were free to withdraw their consent any time they wished to do so.

Patients

Fifty-nine consecutive, unselected patients were enrolled (48 men; mean age 59 ± 8 years, range 44–73 years). The revascularisation procedure was performed in 4 patients due to unstable angina, the rest had stable angina. Forty patients had myocardial infarction in the past, and 8 had concomitant peripheral or extracranial arterial occlusive disease. Obesity was diagnosed in 30 patients (body mass index > 27; median 27.4, range 19.5–38.7), 42 had elevated total cholesterol levels (>5.2 mmol/l) and/or triglyceride levels (TG > 2.2 mmol/l), and 11 had diagnosed diabetes or elevated fasting glucose levels. Mild left ventricular hypertrophy (interventricular septum and/or posterior wall thickness of 1.2–1.4 cm) was detected in 9 patients.

The PCI was performed in 66 coronary arteries—in 7 due to chronic total occlusion and in 59 due to a stenosis (mean diameter stenosis 81.8 ± 10.8%, range 60–99%). In 36 arteries, bare metal stents were implanted, and the rest underwent balloon dilatation alone. In the left coronary artery, there were 20 interventions on proximal LAD, 16 on middle LAD, and 1 on distal LAD segments. In the Cx, there were 5 interventions on proximal, and 3 on middle segments. In the RCA, there were 4 interventions on proximal segment, 15 on middle segment and 2 on distal segment of the artery (see division of coronary arteries into segments used in present study below).

Examinations and tests

The patients underwent 2 sets of examinations: (1) clinical evaluation including history, physical examination and treadmill exercise stress test and (2) transthoracic, harmonic mode Doppler echocardiographic evaluation of the dilated segment of a coronary artery. The same set of examinations was repeated at 1, 3, 6 and 9 months of follow-up and whenever, for various clinical reasons (i.e. exacerbation of angina or positive exercise stress test), another coronary angiography was to be performed.

The follow-up assessment was carried out independently by 2 teams of investigators. One team was in charge of clinical examination, exercise stress test, coronary angiography and decisions concerning treatment, including repetitive coronary angiography and PCI. The other team was responsible for performing transthoracic, harmonic mode Doppler echocardiographic evaluation of a dilated segment of a coronary artery. Results obtained during follow-up by one team were not known to the other until the study was completed. Only cases in which control coronary angiography was performed within 4 weeks after the last echocardiographic examination were included in final analysis.

Control coronary angiography was performed at the completion of the study—at 9 months of follow-up or when it was clinically indicated.

Division of coronary arteries into segments

Each coronary artery was divided into 3 segments. The anterior wall of the left ventricle—from the aortic root towards the apex—was separated into 3 sections of approximately the same length. Segments of LAD within respective sections of the anterior wall were regarded proximal, middle and distal LAD. As the origin of the circumflex coronary artery could not always be localized, the left main coronary artery and the proximal part of the left anterior descending artery formed a common segment (Figs. 3 and 4). It was assumed that the circumflex coronary artery leaves the coronary sulcus at its lowermost point (as can be seen on parasternal short axis view). The left part of the sulcus between the aorta and its lowermost point was divided into 2 sections of approximately the same length, and segments of the circumflex artery within respective sections of the sulcus were considered proximal and middle Cx (Fig. 4). Part of the right coronary artery seen on parasternal short axis view was regarded as proximal RCA, while the part seen within the coronary sulcus in subcostal view was regarded as middle RCA. The distal part of the right coronary artery seen at the diaphragmatic surface of the heart within the posterior interventricular groove—the posterior descending coronary artery—was regarded as distal RCA (Fig. 5). Segments of coronary arteries visualized on coronary angiography were divided accordingly, so that valid comparisons could be carried out.

Transthoracic, harmonic Doppler evaluation of the dilated vessels

Echocardiography was performed with an Acuson Sequoia 512 ultrasound instrument (Acuson Corp., Mountainview, CA). Either a 5.0 or a 3.5 MHz narrow-band transducer in second harmonic mode
was used for B-mode examination. Both color Doppler coronary artery mapping and spectral Doppler coronary flow velocity assessment were performed at 2.5 or 2 MHz by 2 experienced echocardiographers.

The methodology of Doppler coronary artery examination was described in detail previously.1 In short, parasternal windows (both high and low, longitudinal and transverse sections), subcostal and apical windows (modified 5 chamber and 2-chamber views) were used (Figs. 3–5).

The coronary sulcus to the left and right of the aorta was searched for proximal- and mid-circumflex (Cx) and proximal right coronary artery (RCA), respectively, using high parasternal window, transverse and longitudinal sections and modified apical 5-chamber view. Middle RCA was examined using subcostal window, while distal RCA (posterior descending coronary artery) was visualized in modified apical 4-chamber or 2-chamber views. Segments of LAD were examined using parasternal high, parasternal low and apical windows, transverse and longitudinal sections. The best possible Doppler tracings (obtained with highest possible signal to noise ratio and lowest Doppler angle) were taken for analysis.

Echocardiographic evaluation of a dilated segment was performed in 2 stages: first, it was attempted to assess the vessel using conventional Doppler without the use of a contrast agent; then, it was repeated during intravenous infusion of Levovist (Schering AG) using harmonic Doppler. The agent, which was kindly provided by the manufacturer, was used according to a methodology described by Caiati et al.,4 i.e. in a constant intravenous infusion at a concentration of 300 mg/min and a rate of 1 ml/min which could be increased maximally to 3 ml/min or decreased to 0.5 ml/min according to the quality of Doppler signal enhancement achieved. A 3-grade scoring system4 was used in assessment of the quality of color Doppler and spectral Doppler recording before

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**Figure 3** Coronary angiography of left coronary artery. Division of LAD into segments: proximal (p), middle (m) and distal (d); and color Doppler echocardiography of middle and distal LAD in parasternal and apical views.
and during the contrast agent infusion, in which "1" was given, when no signal could be detected, "2" when the signal was suboptimal and "3" when it was excellent. The investigators performing transthoracic echocardiographic examinations were also asked to state on each occasion whether the infusion of contrast agent provided better or worse images in comparison to contrast unenhanced examinations.

Each time before starting an echocardiographic examination, an S-VHS-recording of the initial coronary angiography was reviewed. It was used to guide the echocardiographic examination—served as an aid to localize the PCI site. The dilated segment was carefully assessed and local aliasing on color Doppler mapping (representing local flow turbulence) or stents implanted during the PCI were sought, which indicated the precise location of the PCI site. When neither could be found, the entire segment of the artery was interrogated with pulsed Doppler and it was assumed that the greatest velocity recorded within the area where initial lesion was seen on coronary angiography represents the PCI site, while velocity recorded proximal to that site represents the reference part of the coronary artery (see below).

We adopted Doppler criteria valid for peripheral and splanchnic arterial systems, where a ratio of maximal velocities within stenosis and proximal to stenosis above 2 is taken as a sign of significant stenosis. We calculated a ratio of peak diastolic velocities within stenosis and immediately proximal to stenosis. Local velocity increase, with at least doubling of maximal velocity within stenosis in comparison to velocity within the adjacent segment of the artery, was taken as a sign of hemodynamically significant stenosis. Alternatively, when flow velocity within adjacent segments could not be measured, local velocity of at least 2 m/s was taken as a sign of stenosis (Fig. 6). Velocity measurements were corrected for angle of insonation whenever the Doppler angle was up to 60°. When it was impossible to obtain the Doppler angle within 60° the measurement was not performed. Special attention was given to areas where aliasing in color was found.

Figure 4  Coronary angiography of left coronary artery. Division of Cx and LAD into segments: proximal (p) and middle (m); and color Doppler echocardiography of proximal and middle Cx and proximal LAD in parasternal short axis view.
Significant portions of all studies were recorded digitally in a cineloop format or still frames to allow for off-line reviewing.

Coronary angiography

Multiplane coronary angiography was performed in a standard fashion (Judkins technique, views obtained after intracoronary injections of 0.2 mg nitroglycerin, Integris HM3000 digital angiography unit [Philips Medical Systems Nederland BV]) and significant (>50% cross-sectional diameter reduction) stenoses of coronary artery segments were looked for. All projections of the initial angiography were repeated at follow-up. The angiograms were recorded on CDs and S-VHS videotape.

On-line and post-hoc QCA were performed with ACA-DCI system integrated into the angiographic unit by an observer blinded to treatment, not involved in the interventional procedures and unaware of echocardiographic findings.

Computerized quantitative analysis was performed according to edge-detection algorithms, with the guiding catheter diameter used as reference. Reference lumen diameter, minimum lumen diameter (MLD), percent diameter stenosis and lesion length (LL) were measured at baseline and at 9 months of follow-up, with the use of the same angiographic view.

Treatment during the study period

The patients were treated in a standard fashion by the team which was responsible for clinical assessment. All therapeutic decisions—including implementation of coronary interventions before the planned end of the study—were made on clinical grounds and the results of treadmill ECG stress tests.

Statistical analysis

Results are expressed as means±standard deviation. Two-sided t-test is used for parametric and chi-square or sign test for non-parametric comparisons.
The accuracy parameters of restenosis detection by transthoracic echocardiography were defined as follows:

- **Specificity**—number of true-negative (nonstenosed on echocardiography, no stenosis on coronary angiography) coronary segments divided by the sum of true-negative and false-positive echocardiographic diagnoses (stenosis on echocardiography, no stenosis on coronary angiography),

- **Sensitivity**—number of true-positive stenoses (stenosis on echocardiography, stenosis on coronary angiography) divided by the sum of true-positive and false-negative diagnoses,

- **The positive predictive value (PPV)**—number of true-positive diagnoses of stenosis divided by the number of all stenoses diagnosed by transthoracic echocardiography—true-positive plus false-positive diagnoses,

- **The negative predictive value (NPV)**—number of true-negative coronary segments diagnosed by transthoracic echocardiography divided by the number of all nonstenosed segments accordingly to transthoracic echocardiography—true-negative segments plus false-negative segments (no stenosis on echocardiography, stenosis on coronary angiography).

**Results**

Forty patients completed the study. Ten patients were excluded because the artery, which had undergone the PCI could not be visualized on initial transthoracic echocardiographic examination (6 patients with the middle RCA dilated, 1 with both proximal Cx and proximal RCA, 1 with 2 stenoses within middle RCA and 1 with middle RCA and distal RCA). In 1 patient who had proximal LAD and middle RCA PTCA performed, the RCA could not be visualized; observation of his LAD was complete. In 5 out of these 13 arteries stents were implanted, the rest underwent a PTCA alone.

Six patients withdrew their consent (proximal LAD in 4 cases, middle LAD in 1 and distal LAD in 1 case). One patient died of myocardial infarction.
1 month after the PTCA. In 1 case a coronary intervention was performed in another hospital at 5 months (i.e. 2 months after the last transthoracic echocardiographic coronary artery assessment and therefore the patient was excluded from the study). In 1 patient it was impossible to cannulate the femoral artery and perform the final coronary angiography and it was decided to exclude the patient from the study. These 9 patients were included in feasibility of echocardiographic coronary artery visualization, but excluded from accuracy assessment.

Altogether a comparison of transthoracic echocardiographic assessment with coronary angiography was carried out with regard to 44 arterial segments: 15 proximal LAD, 15 middle LAD, 4 proximal Cx, 2 middle Cx, 2 proximal RCA, 5 middle RCA and 1 distal RCA segments (posterior descending coronary artery).

Final angiography

There were 8 restenoses (i.e. stenosis > 50%) found on final coronary angiography—4 within the proximal LAD, and 4 within middle LAD. Additionally, there were 8 new > 50% stenoses found in other arteries or locations than the sites which were originally dilated.

Feasibility of harmonic mode, contrast enhanced transthoracic echocardiography assessment of coronary arteries

All LAD segments were visualized by means of echocardiography. Of 8 Cx segments which were dilated, the echocardiographic assessment could be carried out in 6 cases. With regard to RCA, out of 21 segments only 9 were assessed. Results are given in Table 1.

The final assessment of restenosis was almost exclusively based on velocity ratio (velocity measurements performed both immediately proximal and within the dilated site—41 out of 44 arteries of patients, who completed the study). The remaining 3 arteries (all proximal LAD) were assessed by means of the maximal velocity alone. The reason for not measuring proximal velocity was ostial localization of the dilated site (no reference vessel available for comparison, 2 cases) and the impossibility of obtaining a clear velocity recording proximal to the dilated site (1 case).

Accuracy of harmonic mode, contrast enhanced transthoracic echocardiography assessment of coronary arteries

All the stenosed segments were detected by means of contrast enhanced transthoracic echocardiography. There were 2 false-positive diagnoses of restenosis: one of proximal Cx (in this case the vessel stenosis on coronary angiography was 48.3%) and the other of middle LAD (5% stenosis on coronary angiography—see Table 2).

Specificity of restenosis detection by transthoracic echocardiography was 94% (34/36) while sensitivity was 100% (8/8). The positive predictive value (PPV) was 80% (8/10). The negative predictive value (NPV) was 100% (34/34). Results are shown in Table 3, Figs. 7 and 8.

A separate assessment of accuracy based solely on velocity ratio or on local velocity exceeding 2 m/s was performed.

When velocity ratio was taken as a sign of stenosis, there were 2 false-positive and no false-negative diagnoses of restenosis within the 41 segments studied. Specificity of restenosis detection was 94% (31/33), sensitivity 100% (8/8), PPV 80% (8/10) and NPV 100% (31/31).

When local velocity exceeding 2 m/s was taken as a sign of stenosis, there were 3 false-negative diagnoses and 1 false-positive within the 44 segments studied. Specificity of restenosis detection was 97% (35/36), sensitivity 63% (5/8), PPV 83% (5/6) and NPV 92% (35/38).

<table>
<thead>
<tr>
<th>Coronary artery</th>
<th>Proximal segment</th>
<th>Middle segment</th>
<th>Distal segment</th>
<th>All segments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left anterior descending</td>
<td>20/20</td>
<td>16/16</td>
<td>1/1</td>
<td>37/37 (100%)</td>
</tr>
<tr>
<td>Circumflex</td>
<td>4/5</td>
<td>2/3</td>
<td>—</td>
<td>6/8 (75%)</td>
</tr>
<tr>
<td>Right coronary artery</td>
<td>3/4</td>
<td>5/15</td>
<td>1/2</td>
<td>9/21 (43%)</td>
</tr>
<tr>
<td>Altogether</td>
<td>52/66 (79%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Results are given as a ratio in which the numerator is a number arteries visualized and denominator—number of arteries studied.
Influence of ultrasonic contrast agent enhancement on the feasibility and accuracy of coronary artery restenosis assessment

Ultrasound contrast agent had little impact on final results. The average score for non-contrast enhanced Doppler images was $2.098 \pm 0.386$ and $2.115 \pm 0.52$ for contrast enhanced images ($n = 234$, $p = 0.73$, 2-sided t-test).

However, when the quality of images obtained before and after application of the contrast agent was assessed by the separate method (through direct comparison of contrast enhanced and unenhanced scans) it appeared that the infusion of the contrast agent provided better images in the whole group (66.6% of better images obtained during contrast enhanced examinations, $p = 0.002$ [sign test]). A subgroup analysis of studies of different arteries has shown that the greatest benefit was achieved with regard to the RCA (81.8% of better images obtained during contrast enhanced examinations, $p = 0.006$ [sign test]), while image quality was only insignificantly improved when contrast enhanced scans of the LAD (61.5%, $p = 0.08$) or Cx (66.6%, $p = 0.5$) were analyzed.

In 2 cases the final velocity measurements allowing for comparison with control coronary angiography were possible only after injection of the contrast agent, but in the other 4 we were able to measure velocity only before injection of the contrast agent, because the contrast created a large number of artifacts making measurements impossible. There were no significant differences between velocities recorded before and during infusion of the contrast agent.

In almost all cases qualitative assessment (i.e. stenosis present/absent), based on contrast enhanced and non-enhanced measurements was concordant. However, in 2 cases measurements performed before and after contrast agent injection gave discordant results (i.e. in one case, contrast enhanced image suggested restenosis while contrast unenhanced images suggested that there was no restenosis, while in the other case it was the opposite—see Table 2). In both these cases the diagnoses of restenosis were regarded false positive.

**Discussion**

Application of transthoracic echocardiography for scanning principal coronary arteries in adults has been a subject of numerous studies. Transthoracic measurements of coronary flow velocity were shown to be highly reproducible and correlated with invasive measurements. However, most of the studies dealt with the assessment of the LAD which can now, thanks to the harmonic mode echocardiography and ultrasound contrast agents, be visualized in almost every patient. The interest in scanning the RCA and the Cx was much lower. There are only few single case reports and 3 studies of a series of patients in whom the RCA was examined. In only 1 study of sequential patients scheduled for coronary angiography the Cx was scanned. The RCA and the Cx were studied more often in children.

Our results indicate that examination of all 3 principal coronary arteries by means of harmonic mode, contrast enhanced transthoracic echocardiography is feasible in a substantial number of patients following interventional procedure—PTCA or PTCA with stent implantation. We were able to assess 100% of dilated segments within the LAD, 75% within the Cx and 43% within the RCA.

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**Table 2** Velocity at the angioplasty site and velocity ratio (velocity at the angioplasty site divided by velocity proximal to angioplasty site)

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Maximal velocity at angioplasty site (m/s)</th>
<th>Velocity ratio</th>
<th>Coronary artery stenosis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>13 (Prox Cx)</td>
<td>Without contrast agent 1.35</td>
<td>3.86</td>
<td>48.5</td>
</tr>
<tr>
<td></td>
<td>With contrast agent 2.6</td>
<td>7.45</td>
<td></td>
</tr>
<tr>
<td>54 (Middle LAD)</td>
<td>Without contrast agent 0.86</td>
<td>2.04</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>With contrast agent 0.74</td>
<td>1.76</td>
<td></td>
</tr>
</tbody>
</table>

**Table 3** Accuracy of contrast enhanced, harmonic mode transthoracic echocardiographic assessment of coronary artery restenosis

<table>
<thead>
<tr>
<th>No restenosis/echocardiography</th>
<th>Restenosis/echocardiography</th>
</tr>
</thead>
<tbody>
<tr>
<td>No restenosis/coronary angiography</td>
<td>34</td>
</tr>
<tr>
<td>Restenosis/coronary angiography</td>
<td>0</td>
</tr>
</tbody>
</table>
The present results were better than those obtained in our previous study, and with regard to the LAD the results were similar to the results published by other investigators. In accordance with Watanabe et al., stent implantation did not have a negative effect on the feasibility of coronary artery assessment. Improvement in feasibility may either be due to additional experience (learning curve) by the echocardiographers, availability of coronary angiography films at the time of echocardiographic scanning, and the use of the ultrasound contrast agent.

Limited feasibility of Doppler examination of the principal coronary arteries still remains an important problem. Surprisingly, and contrary to observations made by other investigators, the ultrasound contrast agent had overall a small and insignificant influence on the results. The most pronounced influence was seen when the RCA was scanned. Our general impression was that, once the image quality without contrast was sufficient, little more could be gained with contrast. Since costs of the ultrasound contrast agents are significant, we would recommend that their use should be reserved for cases with insufficient quality of Doppler examination.

The best method of Doppler echocardiographic detection of coronary artery stenosis has not yet been established. Various approaches were used—vessel lumen was assessed in B-mode or color Doppler, color aliasing was sought, flow velocities within and proximal to a stenosis were measured in duplex scan and coronary flow reserve was evaluated in a distal segment of the coronary artery. As the quality of B-mode images of a coronary artery is usually insufficient for the assessment of stenosis and color aliasing along a coronary artery is not a specific finding, the flow velocity and parameters derived from it form the basic tools used in diagnosis of coronary artery stenosis.

When the ratio of velocity within PCI site and velocity proximal to that site is taken as a sign of stenosis > 50%, the harmonic mode, contrast enhanced transthoracic echocardiography appears a highly accurate method of restenosis detection after percutaneous coronary revascularisation. In the present study, comprising 44 arteries, all the non-restenoses were correctly diagnosed and there were only 2 false-positive diagnoses of stenosis. In one of these a Cx stenosis was diagnosed by Doppler echocardiography on the basis of both velocity ratio and maximal flow velocity, while vessel stenosis on coronary angiography was only 48.3%. As the quality of Doppler spectrum in this case was very good and the flow velocity at the PTCA site was abnormal already at 6 month after the PTCA and increased even more by the end of the study (9 months), one may speculate that the stenosis severity could have been underestimated by coronary angiography. Unfortunately, intra-vascular ultrasound examination (IVUS) was not performed. In the other case, stenosis was undoubtedly not present although the Doppler criteria of restenosis were met. Of note, the maximal velocity at the PTCA site in this case was within

Figure 7 Relation between velocity ratio (maximal diastolic velocity at the PTCA site divided by velocity proximal to that site) and coronary artery stenosis at the end of the study.

Figure 8 Relation between maximal diastolic velocity at the PTCA site and coronary artery stenosis at the end of the study. Dashed line intercepts the velocity axis at 1.5 m/s.
normal range\(^1\) and the velocity ratio was only borderline abnormal. It may suggest that the stenosis criteria need further refinement.

Similar results were obtained by other investigators who studied the value of transthoracic echocardiography in diagnosis of restenosis within the LAD. Hozumi et al.\(^2\) measured mean LAD velocity proximal to PTCA site and within the site in 53 patients who had undergone percutaneous coronary intervention. Feasibility of measurement was 77%, while a ratio of prestenotic to stenotic mean velocity < 0.45 (corresponding to 2.22 when an inverse relation, i.e. ratio of mean stenotic to mean prestenotic velocity is calculated) was 93% specific and 86% sensitive in detection of restenosis. However, findings of Hozumi et al.\(^2\) are difficult to compare with our results because in their study mean velocities instead of peak diastolic velocities were used for calculations. Lower feasibility of measurements in this case may be ascribed to the necessity of obtaining a clear velocity spectrum envelope throughout diastole, which might have been more technically demanding than recording of peak diastolic velocity alone. They also found that color aliasing was very sensitive (found in 100% true positive), but not very specific (present in 56% true negative). Of interest, a retrospective analysis of our data has shown that there was no color aliasing in our false-positive case of LAD restenosis. Saraste et al.\(^3\) used a ratio of maximal velocity at the PTCA site to maximal velocity proximal to that site \(> 3\) as a sign of restenosis and found it was 100% specific and sensitive. However, their study group comprised only 9 stenoses of variable severity.

To diagnose restenosis using maximal flow velocity at the PTCA site one has to know velocity and/or pressure gradient at the point of the vessel where its lumen is reduced by 50% (which might allow for calculation of flow velocity using the Bernoulli equation). Claeyts et al.\(^4\) reported that moderate stenoses (i.e. \(47\pm 12\%\)) generated a resting gradient of \(9\pm 6\) mmHg, while Kern et al.\(^5\) found a mean resting gradient of \(10.1\pm 8.8\) mmHg across moderate stenoses of \(54\pm 7\%\). As the accuracy of the simplified Bernoulli equation in estimating pressure gradients across stenoses in small vessels has been questioned\(^5\) so was the validity of invasive, transluminal pressure gradient measurements.\(^6,7\) Therefore, one may only speculate that resting maximal flow velocity at a 50% coronary artery stenosis is around 1.5 m/s. This subject deserves further studies. Interestingly, a retrospective analysis of the present study may also imply that 1.5 m/s threshold discriminates restenoses and non-restenosed arteries slightly better than 2 m/s (Fig. 8) and a cut-off value of 1.5 m/s has already been suggested.\(^1\) Invasive studies show, however, that the pressure gradient at the stenosis depends not only on the severity of stenosis, but also on the total number of stenoses along the artery, the coronary artery wedge pressure,\(^26,27\) the thickness of myocardium, heart rate, coexistent heart disease, medications, perhaps even on vessel involvement in the formation of collateral circulation.\(^20,30,31\) Therefore a universal borderline velocity accurately discriminating normal from abnormal i.e. nonstenosed from stenosed arteries, probably does not exist. Rather a method of “standardization” of velocity should be used. Our data as well as findings of other investigators regarding coronary arteries\(^1,3,25,29,32,33\) and observations concerning peripheral arteries support the conclusion that in stenosis detection a velocity ratio is more reliable than any single velocity measurement.

Coronary flow reserve (CFR) calculations were used in diagnosis of restenosis within the LAD by several investigators and they may soon be used for the same purpose within the RCA.\(^4,10,13,17,20,23,34\) CFR can be assessed in almost every LAD. It is, however, to a certain extent dependent on microvascular vasodilator function. Epicardial stenosis and microcirculation abnormalities may coexist and cumulatively decrease the CFR. In modest abnormalities of CFR, one cannot say which of the 2 is responsible for flow impairment. This makes clinical decision making concerning further treatment (conservative or PCI) difficult. The velocity ratio at the stenosis site is a stenosis-specific measurement and seems to be particularly useful in the functional assessment of the significance of a stenosis.

**Study limitations**

1. Relatively small overall number of vessels examined, overrepresentation of LAD lesions and low restenosis rate make it difficult to draw definite conclusions regarding the accuracy of echocardiographic examination of restenosis after coronary intervention within LAD, Cx or RCA.

2. Stenosis criteria incorporated for the purpose of the study need further validation.

3. The division of coronary arteries into segments does not follow exact angiographic classification. The differences are most pronounced with regard to the RCA, where “middle” and “distal” parts (according to the angiographic classification) form “middle” RCA (according
to the classification proposed in the present study), and where the "posterior interventricular branch" is substituted by "distal" RCA. Differentiation between the LM and proximal LAD is possible only in few patients.

4. Our data do not allow us to draw the conclusion that transthoracic echocardiography can be used to diagnose any stenosis within the principal coronary arteries after the PCI. The protocol of the study limited the assessment to the PCI sites and in fact on control coronary angiography there were 8 new lesions (>50% stenoses) found in other arteries or locations than the sites which were originally dilated.

Conclusions

1. Transthoracic echocardiography allows for restenosis assessment within principal coronary arteries after successful PTCAs. Feasibility of lesion site visualization was 100% for the LAD, 75% for the Cx and 43% for the RCA.

2. The accuracy of restenosis detection is high. Better results are obtained when velocity ratio is used for diagnosis rather than the maximal velocities.

3. Ultrasound contrast agent has only limited influence on the overall feasibility and accuracy of echocardiographic scanning of principal coronary arteries, but improved the quality of images of the RCA.

References


