Value of Acceleration Flow and the Prestenotic to Stenotic Coronary Flow Velocity Ratio by Transthoracic Color Doppler Echocardiography in Noninvasive Diagnosis of Restenosis After Percutaneous Transluminal Coronary Angioplasty

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OBJECTIVES The study evaluated the value of coronary flow velocity measurement by transthoracic color Doppler echocardiography (TTCDE) for the noninvasive diagnosis of restenosis after percutaneous transluminal coronary angioplasty (PTCA) for left anterior descending coronary artery (LAD) lesions.

BACKGROUND Recent advances in TTCDE provide coronary flow velocity measurements in the LAD under the guidance of color flow mapping.

METHODS We studied 53 patients who underwent successful PTCA for LAD lesions and follow-up coronary angiography (18 patients with restenosis [Group-R], 35 patients without restenosis [Group-N]). We searched localized color aliasing corresponding to local flow acceleration to obtain coronary flow velocity at PTCA sites in the LAD. When localized aliasing was detected, we measured coronary flow velocity at the aliasing (stenotic site) and the prestenotic site.

RESULTS Using TTCDE, it was possible to measure mean diastolic velocity (MDV) in the LAD in 41 (77%) of 53 patients (14 of 18 patients in Group-R; 27 of 35 patients in Group-N). Localized aliasing was displayed by color flow mapping in 14 (100%) of 14 patients in Group-R, and 15 (56%) of 27 patients in Group-N. Stenotic MDV in Group-R was significantly higher than that in Group-N (60.3 ± 21.1 vs. 35.1 ± 7.6 cm/s, p < 0.01), although prestenotic MDV did not differ between Group-R and Group-N (20.2 ± 3.0 vs. 19.6 ± 2.3 cm/s). There were significant differences in the prestenotic to stenotic MDV ratio between Group-R and Group-N (0.36 ± 0.10 vs. 0.57 ± 0.09, p < 0.001). Localized aliasing with the prestenotic to stenotic MDV ratio <0.45 as the optimal cutoff value had a sensitivity of 86% and a specificity of 93% for the presence of restenosis in LAD lesions.

CONCLUSIONS Detection of localized color aliasing and measurement of the prestenotic to stenotic MDV ratio in the LAD by TTCDE are useful in the noninvasive diagnosis of restenosis after PTCA for LAD lesions. (J Am Coll Cardiol 2000;35:164–8) © 1999 by the American College of Cardiology

Restenosis after percutaneous transluminal coronary angioplasty (PTCA) during follow-up period has been an important issue (1–3). Several reports have shown that coronary flow velocity measurement at the stenosis by transesophageal Doppler echocardiography is useful in the assessment of significant stenosis in the left anterior descending coronary artery (LAD) (4–6). Recent advances in transthoracic color Doppler echocardiography (TTCDE), which is noninvasive and widely used in the clinical setting, provide coronary flow velocity measurement in the LAD under the guidance of color flow mapping (7,8). Coronary flow velocity measurement at PTCA sites using TTCDE may be useful in the noninvasive diagnosis of restenosis after PTCA. The purpose of this study was to evaluate the value of coronary flow velocity measurement by TTCDE for the
noninvasive diagnosis of restenosis after PTCA for LAD lesions during the follow-up period.

**METHODS**

**Study population.** The initial study population consisted of 58 consecutive patients who underwent successful PTCA (residual diameter stenosis <50% immediately after PTCA) for LAD lesions. Patients with unstable hemodynamic conditions (systolic blood pressure <80 mm Hg) (n = 3), myocardial infarction during follow-up period (n = 1) or atrial fibrillation (n = 1) were excluded. In the 53 remaining patients (43 men, 10 women; mean age, 62 ± 8 years), 41 patients had no significant stenosis (diameter stenosis >70%) in the other coronary arteries. Seven patients had a significant stenosis in the right coronary artery, and five in the circumflex branch. The underlying diseases were angina pectoris in 16 patients and myocardial infarction in 37 (anterior infarction in 34 and inferior in 3). The PTCA site was located in the mid-LAD in 34 patients and in the proximal LAD in 19. In 18 of 53 patients, restenosis (diameter stenosis ≥50%) was diagnosed by follow-up angiography at six months after PTCA (Group-R). In the remaining 35 patients, follow-up angiography did not reveal restenosis (Group-N). Collateral channels were not observed by coronary angiography in any patients. All participants gave informed consent to the protocol approved by the Committee for the Protection of Human Subjects in Research at Kobe General Hospital.

**Coronary flow velocity measurements by TTCDE.** The TTCDE was performed within two days before follow-up angiography with Acuson Sequoia (5.0 or 3.5 MHz), ATL 3000 or 5000 (4 to 7 MHz), or GE Logic 500 (3.5 to 8.0 MHz) digital ultrasound systems. In color flow mapping, velocity range was set in the range of ±16.0 to ±32.0 cm/s in the Acuson system, ±19.2 to ±28.8 cm/s in the ATL system, and ±17.4 to ±30.5 cm/s in the GE system for the purpose of visualization of coronary flow signal. To obtain coronary flow velocity in the mid-LAD, the acoustic window was around the midclavicular line in the fourth or fifth intercostal spaces or the parasternal third or fourth costal space in the left lateral decubitus position. First, the left ventricle was imaged in the long-axis cross section, and then the ultrasound beam was inclined laterally. Next, LAD flow was searched under the guidance of color flow mapping (7,8). To obtain coronary flow velocity in the proximal LAD, a short-axis view of the aortic valve was visualized as described in previous reports (9–11). Proximal to mid-LAD flow was obtained by scanning from the aortic valve to the basal left ventricle. We searched LAD flow using color flow mapping.

We searched localized color aliasing corresponding to local flow acceleration to obtain coronary flow velocity at PTCA sites in the LAD. When localized aliasing was detected, we set the sample volume (2.0 mm wide) at the aliasing (stenotic site). Then, the sample volume was moved slightly upstream from the aliasing to measure coronary flow velocity.

**Figure 1.** An example of coronary flow velocity recordings in the proximal left anterior descending coronary artery (LAD) by transthoracic color Doppler echocardiography shows localized aliasing in the proximal LAD (upper panel). Pulsed Doppler recording is shown at the color aliasing (lower left panel) and upstream from the color aliasing (lower right panel).
velocity at the prestenotic site. Doppler spectral tracings of coronary flow velocity at stenotic and prestenotic sites were recorded on 1/2-inch super-VHS videotape (Fig. 1). Angle correction was performed in each Doppler measurement (incident angle: 32 ± 15°). Measurements of mean diastolic velocity (MDV) at prestenotic and stenotic sites were performed by tracing the contour of spectral Doppler signals using the computer incorporated in the ultrasound system by one investigator unaware of other patient data. An average of the measurements was obtained in three cardiac cycles. The prestenotic to stenotic MDV ratio was calculated.

Coronary angiography. Coronary angiography was performed by the Judkins technique. The PTCA was performed in a routine manner using balloon catheters. Coronary stenosis was evaluated using multiple projections by one investigator unaware of the TTCDE data. Quantitative analysis of % diameter stenosis was done using CMS analysis software (Medical Imaging Systems) (12). Follow-up angiography was performed at six months after PTCA. Successful PTCA was defined as a residual diameter stenosis <50%. Restenosis was defined as ≥50% diameter stenosis on follow-up angiography.

Data analysis. Mean and standard deviation (SD) are expressed for the parametric data. Comparisons between the two groups for the parametric data were made with an unpaired two-tailed t test. Differences between proportions were assessed by chi-square analysis. A probability value <0.01 was considered statistically significant. We examined the sensitivity and specificity of various cutoff points of the prestenotic to stenotic MDV ratio for diagnosis of restenosis. Using receiver operating characteristic (ROC) curves, i.e., plots of sensitivity versus (1-specificity) (13), we defined the best cutoff value for diagnosis of restenosis.

Interobserver and intraobserver variabilities were assessed for MDV in 10 randomly selected recordings. Interobserver variability was calculated as the SD of the differences between the measurements of two independent observers unaware of the other patient data and expressed as a percent of the average value. Intraobserver variability was calculated as the SD of the differences between the first and second determination (three-week interval) for a single observer and expressed as a percent of the average value.

RESULTS

Using TTCDE, it was possible to measure MDV in the LAD in 41 (78%) of 53 study patients (14 of 18 in Group-R; 27 of 35 in Group-N). Table 1 shows clinical characteristics and angiographic data in these 41 patients.

Detection of localized aliasing. Localized aliasing corresponding to local flow acceleration in the LAD was displayed by color flow mapping in 14 (100%) of 14 patients in Group-R and in 15 (56%) of 27 patients in Group-N. In Group-N, % diameter stenosis on follow-up angiography in patients with localized aliasing was greater than that in patients without aliasing (40 ± 5% vs. 25 ± 6%, p < 0.001).

Coronary flow velocity measurements. In 29 patients with localized aliasing (14 patients in Group-R, 15 patients in Group-N), coronary flow velocity were measured by TTCDE (Table 2). The prestenotic MDV did not differ between Group-R and Group-N (20.2 ± 3.0 vs. 19.6 ± 2.3 cm/s). The stenotic MDV in Group-R was higher than that in Group-N (60.3 ± 21.1 vs. 35.1 ± 7.6 cm/s, p < 0.01). There was a significant difference in the prestenotic to stenotic MDV ratio between Group-R and Group-N (0.36 ± 0.10 vs. 0.57 ± 0.09, p < 0.001). Figure 2 shows the relation between the prestenotic to stenotic MDV ratio and % diameter stenosis on follow-up angiography in 29 patients with localized aliasing by color flow mapping.

Diagnosis of restenosis after PTCA by localized aliasing and prestenotic to stenotic coronary flow velocity. Although localized aliasing had a high sensitivity for detection of restenosis (100%; 14 of 14 patients in Group-R), specificity was low (44%; 12 of 27 patients in Group-N). Considering localized aliasing with the prestenotic to stenotic MDV ratio <0.45 for diagnosis of restenosis as a positive criterion, positive test was detected in 12 of 14 patients in Group-R (sensitivity 86%) and in 2 of 27 patients in Group-N (specificity 93%).

Table 1. Clinical Characteristics and Angiographic Data

<table>
<thead>
<tr>
<th></th>
<th>Group-R (n = 14)</th>
<th>Group-N (n = 27)</th>
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<tbody>
<tr>
<td>Clinical characteristics</td>
<td></td>
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<tr>
<td>Age (yrs)</td>
<td>64 ± 10</td>
<td>62 ± 7</td>
</tr>
<tr>
<td>Men</td>
<td>12 (86%)</td>
<td>24 (89%)</td>
</tr>
<tr>
<td>Hypertension*</td>
<td>5 (36%)</td>
<td>9 (33%)</td>
</tr>
<tr>
<td>Hypercholesterolemia**</td>
<td>3 (21%)</td>
<td>6 (22%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>4 (29%)</td>
<td>8 (30%)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>10 (71%)</td>
<td>20 (74%)</td>
</tr>
<tr>
<td>Angiographic data</td>
<td></td>
<td></td>
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<tr>
<td>% Diameter stenosis</td>
<td></td>
<td></td>
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<tr>
<td>Immediately after PTCA</td>
<td>30 ± 5***</td>
<td>21 ± 6</td>
</tr>
<tr>
<td>Follow-up</td>
<td>66 ± 8****</td>
<td>33 ± 9</td>
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</table>

*p < 0.001 vs. Group-N; **p < 0.001 vs. Group-N.

TTCDE = transthoracic color Doppler echocardiography; MDV = mean diastolic velocity.

Table 2. Coronary Flow Velocity Measurements by TTCDE

<table>
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<tr>
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<th>Group-R (n = 14)</th>
<th>Group-N (n = 27)</th>
</tr>
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<tbody>
<tr>
<td>Prestenotic MDV (cm/s)</td>
<td>20.2 ± 3.0</td>
<td>19.6 ± 2.3</td>
</tr>
<tr>
<td>Stenotic MDV (cm/s)</td>
<td>60.3 ± 21.1*</td>
<td>35.1 ± 7.6</td>
</tr>
<tr>
<td>Prestenotic to stenotic MDV ratio</td>
<td>0.36 ± 0.10**</td>
<td>0.57 ± 0.09</td>
</tr>
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</table>

*p < 0.001 vs. Group-N; **p < 0.001 vs. Group-N.
Recent TTCDE and 2) TTCDE facilitated the positioning of the sample volume in the LAD flow under the guidance of color flow mapping when compared with previous studies that employed only two-dimensional imaging.

Detection of localized aliasing in the LAD. For coronary flow velocity measurements at PTCA sites, we searched localized color aliasing corresponding to local flow acceleration by color flow mapping in the present study. Aragam et al. (16) have reported that localized aliasing, which reflects increased velocity over the velocity range in color flow mapping along the flow direction, could be displayed at the stenotic human coronary artery in vitro by color flow mapping. Other investigators also demonstrated that the localized aliasing with higher flow velocity than normal velocity was found at the stenosis in the LAD using transesophageal Doppler echocardiography (4–6). In the present study, detection of localized aliasing by color flow mapping was helpful in searching for the stenotic site.

Diagnosis of coronary stenosis by prestenotic to stenotic velocity ratio. The present study also showed that MDV measured by TTCDE at the aliasing was higher in patients with restenosis than that in patients without restenosis. However, MDV at the stenosis may be modified by different hemodynamic conditions because it is dependent on several physiologic variables such as aortic pressure, heart rate, myocardial contractility and so on. Therefore, we calculated the prestenotic to stenotic MDV ratio to evaluate restenosis. In the previous reports using transesophageal Doppler echocardiography, a similar index was used for the assessment of significant stenosis of LAD (5,6). Caiati et al. (5) reported that % coronary flow velocity increase ≥50% at the stenotic site are highly sensitive (92%) and specific (100%) for diagnosing significant stenosis (diameter stenosis ≥50%). Recently, Isaaz et al. (6) reported that the prestenotic to stenotic MDV ratio <0.5 predicted diameter stenosis ≥50%, with 100% sensitivity and 90% specificity. In the present study, localized aliasing with the prestenotic to stenotic MDV ratio <0.45 had a high sensitivity (86%) and a high specificity (93%) for diagnosis of restenosis (diameter stenosis ≥50%). Our results suggest that coronary flow velocity measurements at the stenotic and prestenotic sites using TTCDE can diagnose restenosis after PTCA.

Study limitations. It was difficult to measure MDV in the LAD in 12 (23%) of 53 patients because of poor echocardiographic images or Doppler recordings. To improve success rate in detecting coronary flow velocity by TTCDE, peripheral injection of lung-crossing contrast agents may be helpful (5,17).

Although we applied the present method using TTCDE to PTCA lesions in the LAD, the present method was not applied to PTCA sites in the other coronary vessels. Further investigations are necessary to demonstrate whether the present method can be applied in the other coronary lesions. However, the LAD is a major coronary artery as it vascularizes a large amount of myocardium. Noninvasive diagno-
sis of restenosis in the major coronary artery by the present method should contribute to follow-up in patients who underwent PTCA.

In addition, reducing the velocity range in color flow mapping could create aliasing within the central lumen of normal coronary artery. However, this appearance extended uniformly along the length of the vessel in contrast to the localized aliasing at stenosis (16). We searched only localized aliasing corresponding to local flow acceleration at stenosis by adjusting velocity range in color flow mapping.

In the present study, patients with stents were not included. Concerning the applicability of the present method to patients with stents, further investigations are needed.

Finally, the present study contained a relatively small number of patients. A larger number of patients should be examined by a prospective randomized fashion in future investigations.

Conclusions. Detection of localized color aliasing and measurement of prestenotic to stenotic MDV ratio in the LAD using TTCDE are both useful in the noninvasive diagnosis of restenosis after PTCA for LAD lesions.

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REFERENCES