Intravascular Ultrasound Predictors of Side Branch Occlusion in Bifurcation Lesions After Percutaneous Coronary Intervention

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Background  Percutaneous coronary intervention (PCI) of bifurcation lesion has been associated with a low success rate and a high incidence of procedural complications, including side branch occlusion and myocardial infarction. It remains controversial whether preintervention intravascular ultrasound (IVUS) findings can help to identify side branches likely to occlude after PCI of bifurcation lesions.

Methods and Results  From our IVUS database we identified 81 bifurcation lesions in 72 patients. Side branches were classified into 2 groups: group 1 had ostial side branch stenosis due to atherosclerotic plaque only in the main vessel (n=61), and group 2 had plaque truly involved in the side branch ostium (n=20). There was no significant difference between the 2 groups in the extent of ostial stenosis as assessed by angiography. After PCI, 7 side branches occluded in group 2, compared with 5 side branches occluded in group 1 (35% vs 8%, p=0.003).

Conclusion  Ostial plaque distribution as assessed by IVUS may be one of the consistent predictors of side branch occlusion after PCI. (Circ J 2005; 69: 325–330)

Key Words:  Atherosclerosis; Coronary angioplasty; Ultrasonics

Although success rates of percutaneous coronary intervention (PCI) are high, PCI of bifurcation lesions is associated with a relatively low success rate and a relatively high incidence of procedural complications, including side branch occlusion and myocardial infarction. It remains controversial whether preintervention intravascular ultrasound (IVUS) findings can help to identify side branches likely to occlude after PCI of bifurcation lesions.

Lesions and the Patient Population
The study group consisted of 105 bifurcation lesions in 96 patients with coronary artery disease, all of which had undergone preintervention IVUS examination in the native coronary artery. No directional coronary atherectomy, rotational atherectomy, nor thrombectomy were performed. The clinical diagnoses included: acute myocardial infarction (AMI) (57%), stable angina pectoris (17%), unstable angina pectoris (15%), and previous myocardial infarction (11%). We studied bifurcation lesions involving the main branch and the ostium of the side branch. Only side branches with an estimated reference luminal diameter of 1 mm or greater were considered. Twenty-four lesions were excluded for the following reasons: kissing balloon technique or sequential dilatation was performed (n=6) and extensive target lesion calcification or artifacts which precluded accurate cross-sectional evaluation of the vessel involved (n=18). The remaining 81 bifurcation lesions in 72 patients were studied.

Side branch occlusion was defined as a thrombolysis in myocardial infarction (TIMI) flow of ≤2 by the final angiogram after PCI procedures.

Quantitative Coronary Angiography
Angiograms were reviewed before introduction of coronary guidewire and after balloon dilation or stent deployment. The coronary flow pattern of side branches was graded according to the classification system of the TIMI trial.
Reference diameter and diameter stenosis at end-diastole before intervention were calculated on the computer monitor with the use of the view that showed the ‘worst’ luminal narrowing, using a guiding catheter for magnification calibration reference. A value of 0 mm was assigned to the minimal lumen diameter of totally occluded vessels. The angiography reviewer was blinded to the IVUS findings.

**IVUS Imaging**

IVUS studies were performed before and immediately after PCI, using a 30- or 40-MHz, and 2.9- or 3.2-F monorail intracoronary ultrasound catheter (CVIS-Boston Scientific, Natick, MA, USA). A 0.014-inch coronary guidewire was introduced into the target coronary artery. To avoid spasm and to obtain optimal vasodilatation, 1.5 to 2.5 mg of isosorbide dinitrate was administered before insertion of the IVUS catheter through a coronary guiding catheter. After the IVUS catheter had advanced more than 10 mm beyond the target lesion, a motorized auto pullback was performed at 0.5 or 1 mm/s to the aorto-ostial junction under fluoroscopic guidance. Ultrasound images were recorded on S-VHS videotapes for off-line analysis.

**IVUS Analysis**

Computer planimetry software (Tape Measure, INDEC Systems, Inc Mountain View, CA, USA) was used to measure the cross-sectional areas (CSA) of the external elastic membrane (EEM) and lumen at the culprit lesion site. Cross-sectional ultrasound measurements were performed at the lesion site, which is the image slice with the smallest lumen CSA prior to interventions; if there were several image slices with an equally small lumen, the image slice with the largest EEM CSA and plaque plus media CSA (EEM CSA – lumen CSA) was analyzed. The reference
IVUS and Side Branch Occlusion After PCI

sites were defined as those cross sections with the largest lumen and the least plaque within 10 mm proximal and distal to the lesion before any originating branches. A lesion in which EEM CSA was greater than that of proximal reference site was defined as positive remodeling. Remodeling index (lesion EEM CSA divided by proximal reference EEM CSA) was calculated.

Thrombus was an intraluminal mass having a layered or lobulated appearance, evidence of blood flow (microchannels) within the mass, and sparkling or scintillation.\(^\text{13}\) Calcium was detected as bright dense echoes (brighter than the reference adventitia) with acoustic shadowing of underlying tissue.\(^\text{14}\)

Intravascular ultrasound studies were reviewed separately by K.H., who had no knowledge of the outcome of angioplasty.

**Side Branch Analysis**

To determine whether side branches with 50% or more diameter stenosis are at increased risk for occlusion resulting from PCI of the main vessel, the outcome of PCI was compared between branches with 50% or more diameter stenosis at their origin (n=48) and those with less than 50% diameter stenosis (n=33).

Side branches were classified into 2 groups according to the IVUS findings: group 1, where the angiographic ostial side branch stenosis was due to atherosclerotic plaque only in the main vessel (n=61), and group 2, where atherosclerotic plaque truly involved the side branch ostium (n=20).

As shown in Fig 1, we further subdivided group 2 according to whether the ostial plaque was predominantly located on the proximal side of the side branch (group 2P, n=14) or had diffusely developed around the ostium (group 2D, n=6).

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**Table 2 Preintervention IVUS Findings**

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=61)</th>
<th>Group 2 (n=20)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Plaque morphology</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-echoic plaque (%)</td>
<td>32 (52.5%)</td>
<td>11 (55.0%)</td>
<td>0.843</td>
</tr>
<tr>
<td>Eccentric plaque (%)</td>
<td>34 (55.7%)</td>
<td>12 (60.0%)</td>
<td>0.738</td>
</tr>
<tr>
<td>Thrombus (%)</td>
<td>37 (58.6%)</td>
<td>19 (52.6%)</td>
<td>0.506</td>
</tr>
<tr>
<td>Calcium (%)</td>
<td>21 (34.4%)</td>
<td>14 (70.0%)</td>
<td>0.012</td>
</tr>
<tr>
<td><strong>Proximal reference</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vessel CSA (mm(^2))</td>
<td>18.6±6.6</td>
<td>17.2±6.4</td>
<td>0.438</td>
</tr>
<tr>
<td>Lumen CSA (mm(^2))</td>
<td>10.0±4.8</td>
<td>7.9±3.0</td>
<td>0.081</td>
</tr>
<tr>
<td>Plaque + Media CSA (mm(^2))</td>
<td>8.6±4.4</td>
<td>9.3±5.2</td>
<td>0.569</td>
</tr>
<tr>
<td><strong>Lesion</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vessel CSA (mm(^2))</td>
<td>15.3±5.8</td>
<td>14.3±5.8</td>
<td>0.482</td>
</tr>
<tr>
<td>Lumen CSA (mm(^2))</td>
<td>2.5±1.3</td>
<td>2.3±0.8</td>
<td>0.389</td>
</tr>
<tr>
<td>Plaque + Media CSA (mm(^2))</td>
<td>12.8±5.6</td>
<td>12.0±5.9</td>
<td>0.593</td>
</tr>
<tr>
<td><strong>Distal reference</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vessel CSA (mm(^2))</td>
<td>14.0±5.8</td>
<td>12.1±4.5</td>
<td>0.281</td>
</tr>
<tr>
<td>Lumen CSA (mm(^2))</td>
<td>7.7±4.0</td>
<td>6.2±2.8</td>
<td>0.226</td>
</tr>
<tr>
<td>Plaque + Media CSA (mm(^2))</td>
<td>6.3±3.3</td>
<td>5.9±3.0</td>
<td>0.657</td>
</tr>
<tr>
<td>Remodeling index</td>
<td>0.95±0.19</td>
<td>1.03±0.30</td>
<td>0.359</td>
</tr>
</tbody>
</table>

**IVUS**, intravascular ultrasound; CSA, vessel cross-sectional area.

**Table 3 The Frequencies of Side Branch Occlusion in Prespecified Study Subgroups**

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=61)</th>
<th>Group 2 (n=20)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ostial stenosis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥50% (n=48)</td>
<td>3/32 (9.4%)</td>
<td>7/16 (43.8%)</td>
<td>0.010</td>
</tr>
<tr>
<td>&lt;50% (n=33)</td>
<td>2/29 (6.9%)</td>
<td>0/4 (0%)</td>
<td>0.588</td>
</tr>
<tr>
<td><strong>Plaque distribution</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concentric (n=35)</td>
<td>3/27 (11.1%)</td>
<td>3/8 (37.5%)</td>
<td>0.117</td>
</tr>
<tr>
<td>Eccentric (n=46)</td>
<td>2/34 (5.9%)</td>
<td>4/12 (33.3%)</td>
<td>0.033</td>
</tr>
<tr>
<td>Same side (n=21)</td>
<td>1/17 (5.9%)</td>
<td>2/4 (50.0%)</td>
<td>0.080</td>
</tr>
<tr>
<td>Opposite side (n=25)</td>
<td>1/17 (5.9%)</td>
<td>2/8 (25.0%)</td>
<td>0.231</td>
</tr>
</tbody>
</table>

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As shown in Fig 1, we further subdivided group 2 according to whether the ostial plaque was predominantly located on the proximal side of the side branch (group 2P, n=14) or had diffusely developed around the ostium (group 2D, n=6).

Fig 2. Frequency of side branch occlusion after percutaneous coronary intervention (PCI).
n=6). To evaluate the potential effect of plaque distribution of main vessel on side branch occlusion resulting from PCI of the main vessel, we classified side branches based upon the plaque morphology of the main vessel and the origin of the side branch. The outcome of PCI was compared among lesions with concentric plaques in their main vessel (n=35), those with eccentric plaque with the side branch originating from the plaque side (n=21), and those with eccentric plaque with the side branch originating from the opposite side of the plaque (n=25).

**Statistical Analysis**
Quantitative data are expressed as mean values ± SD. Comparisons among groups were performed using chi-squared statistics and Fisher’s exact test for categorical variables. Continuous variables were compared by means of unpaired t-tests. Differences were considered significant when p-values were <0.05.
Results

The clinical characteristics of the patients and the results of quantitative coronary angiography are summarized in Table 1. There was no significant difference between the 2 groups with regard to the clinical characteristics, percentage of stent use, reference vessel diameter, side branch diameter, or the extent of ostial stenosis as assessed by angiography. The mean diameter of the side branches was 1.75±0.48 mm (range: 1.01–3.64 mm).

Qualitative and quantitative IVUS findings of the parent vessel are summarized in Table 2. Calcium was more frequent in group 2 than in group 1 (70.0% vs 34.4%, p=0.012). There was no difference in the CSA for vessel lumen, nor plaque plus media of the main branch lesions between the 2 groups.

Twelve side branches occluded (14.8%). The rate of side branch occlusion was similar between patients with AMI and those with angina pectoris (16.7% vs 12.8%, p=0.862). Ten of the 48 side branches with more than 50% stenosis at the ostium occluded after PCI, as compared with 2 of the 33 side branches with less than 50% stenosis at the ostium (20.8% vs 6.1%, p=0.049). In the subgroups of lesions with side branches with more than 50% stenosis at the ostium and those with eccentric plaque in their main vessel, the frequencies of side branch occlusion were still significantly higher in group 2 than in group 1 (Table 3).

As shown in Fig 2, 7 side branches (35.0%) occluded in group 2 after PCI, whereas 5 side branches (8.2%) occluded in group 1 (p=0.003). When we subdivided group 2 according to the plaque distribution as shown in Fig 1, only 1 of the 14 side branches (7.1%) occluded after PCI in group 2P, whereas all 6 (100%) side branches occluded in group 2D (group 1 vs 2P vs 2D, p<0.001).

Fig 3 illustrates a side branch that originated from stenosis of the main branch but was not affected by angioplasty of the lesion involved. Fig 4 shows an example of side branches that occluded after PCI of the parent vessel.

Discussion

The present study showed that IVUS can identify side branches likely to occlude after PCI. Side branches having diffuse plaque around their ostium were at the greatest risk. On the contrary, if side branches did not have plaque involving their ostium, side branch occlusion was uncommon after PCI (<10%).

Angiographic evidence of ostial side branch stenosis has been found to be a strong predictor of side branch occlusion. The current study confirmed that side branches with ≥50% ostial stenosis were at higher risk for occlusion than those without ostial stenosis. Since the beginning of the stent era, stent implantation in coronary lesions involving side branches has been recognized as a potential source of acute complications. One of the largest studies of Palmaz-Schatz stents, involving 182 lesions with 224 side branches, showed the results of the side branch occlusion rate was 19%. Poerner et al reported that independent predictors of acute side branch occlusion after stent implantation included reference side branch diameter at baseline, ostial side branch stenosis before stenting and involvement of the side branch origin within the lesion of the parent vessel. Among side branches at high risk, however, it is difficult to distinguish which side branches are most likely to occlude after PCI solely on the basis of angiographic findings. To our knowledge, this is the first study to examine IVUS predictors of side branch occlusion after currently used techniques for PCI in patients with coronary artery disease.

We found no side branches with demonstrable ostial atherosclerotic plaque only on the distal side of the side branch. Badak et al described characteristic patterns of plaque distribution at coronary bifurcations, derived from the results of volumetric IVUS analysis. They showed that distal segments had smaller plaque volume than proximal segments. Atherosclerotic coronary plaque develops at specific locations in the arterial tree characterized by low or oscillating shear stress.

Previous IVUS studies have shown that stent implantation may cause axial redistribution of plaque from the lesion into the reference segments. Thus, balloon dilatation at a complex bifurcation stenosis may cause the plaque to shift to a side branch vessel, compromising the ostium of the side branch. Vetrovec et al showed that the single predictive factor of side branch occlusion is the presence of pre-existing branch ostial disease. Poerner et al suggested that the most common cause of side branch occlusion is ‘snowplowing’ of atherosclerotic plaque into branch vessels. In the current study, side branches in which diffuse atherosclerotic plaque truly involved the ostium had a higher occlusion rate than those in which angiographic ostial stenosis was due to atherosclerotic plaque only in the main vessel. This finding suggests that a ‘snowplowing’ phenomenon may be pronounced when diffuse atherosclerosis directly involves the ostium of a side branch. Calcium was more frequent in lesions with atherosclerotic plaque involving their side branch ostium than in those involving their parent vessel only. Although a previous study suggested that calcified plaque may be a marker of more advanced atherosclerosis, there is little information regarding the evolution of calcium in bifurcation lesions.

To protect side branches, kissing balloon angioplasty, segmental dilatation, T-stenting, cutting balloon angioplasty, or debulking of the atherosclerotic plaque may be performed. However, these techniques require more time and higher technical expertise than conventional procedures, and are potentially dangerous. Specialized procedures may therefore only be warranted when the risk of side branch occlusion is particularly high. Especially in the setting of AMI, in which complex procedures may lead to additional thrombus formation, simplified strategies may be favored. This is important even in the current era of drug-eluting stents, because a recent study demonstrated that the frequency of acute side branch occlusion was similar after sirolimus-eluting stent implantation and uncoated metal stent implantation.

Study Limitations

The present retrospective study had several limitations. The IVUS measurements were performed only in cases in which the vessel boundary could be clearly visualized for the entire length of the target segment. Moderately calcified lesions with heavy acoustic shadowing or severely fibrotic lesions with marked ultrasound attenuation were therefore excluded from analysis. Lesions dilated by the kissing balloon technique were excluded, which may have biased our findings. Thrombus may affect the frequency of side branch occlusion in patients with AMI. In the present study, the side branch occlusion rate was similar in patients with AMI and those with angina pectoris.
thrombolytic therapy in the patients with AMI may have modified our findings. Twenty-one patients with AMI (50%) received bolus low-dose tissue-type plasminogen activator before catheterization, which may have reduced thrombus formation. Additionally, IVUS had limited ability to distinguish hypoechoic plaque and thrombus. Finally, we did not perform IVUS examination in side branches. However, IVUS interrogation in side branches is uncommon in the catheterization laboratory and ‘dotter effect’ caused by this procedure may have biased the probability of side branch occlusion.

Conclusions

Our results suggest that side branch occlusion after PCI in patients with coronary artery disease is associated with ostial lesion location and plaque distribution. The technique of IVUS may therefore provide information not available by angiography alone. It can be used to predict side branch occlusion after PCI.

References