Influence of intimal dissection on restenosis after successful coronary angioplasty

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ABSTRACT We studied 986 patients who underwent follow-up angiography after successful percutaneous transluminal coronary angioplasty (PTCA) to determine the influence of uncomplicated intimal dissection on restenosis rate. Angiographic evidence of intimal dissection after PTCA was present in 248 patients or 25%. After a mean follow-up time of 7 ± 5 months (SD) the restenosis rate in patients without intimal dissection was 30% compared with 24% in patients with intimal dissection (p = .08). Patients with available transstenotic pressure gradients were divided according to the hemodynamic result into two subgroups: those with final gradients at the conclusion of PTCA of 15 mm Hg or less (n = 638) and those with gradients greater than 15 mm Hg (n = 244). Patients with intimal dissection had a significantly lower restenosis rate than patients without intimal dissection if the final gradient was 15 mm Hg or less (19% vs 28%; p < .05). If the final gradient was greater than 15 mm Hg, the presence or absence of intimal dissection had no significant influence on restenosis rate, which was 35% and 39%, respectively (p = NS). We conclude that an uncomplicated intimal dissection after a successful coronary angioplasty has no adverse influence on angiographic restenosis. An excellent angiographic long-term outcome can be expected if the intimal dissection is associated with a favorable hemodynamic result.


PERCUTANEOUS transluminal coronary angioplasty (PTCA) is now an accepted revascularization procedure in the treatment of selected patients with coronary artery disease. The increase in vessel lumen is brought about partially by compression of soft atheromatous material.1, 2 However, stretching of the arterial wall and disruption of intima and media are thought to be the most important contributors in increasing the arterial lumen.3, 4 This process is recognized arteriographically as an intimal tear or intimal dissection. During the healing process, arteriographic irregularities usually regress5, 6 and either improvement (figure 1) or deterioration in luminal narrowing can occur.

The precise relationship between intimal dissection and restenosis after coronary angioplasty, however, is unclear.4, 9 Some investigators have suggested that intimal dissection promotes restenosis,4, 10 while others have indicated that it is a benign arteriographic finding.7 Still others associate intimal dissection with an improved long-term outcome.11

The purpose of this study was to define the hemodynamic importance of an intimal dissection after uncomplicated, successful PTCA and its relationship to arteriographic restenosis.

Methods

Patients. Between July 1980 and January 1984, 1880 patients underwent first, single-vessel PTCA to native coronary arteries. According to a combination of angiographic (≥20% reduction in diameter stenosis)12 and clinical criteria (no electrocardiographic or enzymatic evidence of myocardial infarction, no need for emergency bypass surgery, and no in-hospital death), the procedure was successful in 1650 patients (88%). Of these, the 986 patients (60%) who had angiographic follow-up form the study population. All patients underwent PTCA in accordance with a standard protocol that has been previously described.13 Clinical and angiographic data were prospectively recorded on standard data collection sheets and stored in a relational data base by means of a VAX-750 computer.

Coronary intimal dissection was defined according to the NHLBI PTCA Registry by (1) the presence of angiographically evident intimal damage producing an intraluminal filling defect, (2) extraluminal extravasation of contrast material, (3) linear luminal density or luminal staining.14 Evidence of intimal dis-
section was present in 248 patients (25%). The prevalence of dissection in patients without available follow-up angiograms was not significantly different, 190 of 664 patients (29%). The degree of arterial obstruction was measured in percent diameter with a digital electronic caliper. This method has been previously validated. An individual stenosis was expressed as the mean of the stenoses measured in at least two different orthogonal projections.

A transstenotic pressure gradient was defined as the difference in mean arterial pressure between the tip of the guiding catheter proximal to the stenosis and the tip of the balloon catheter distal to the stenosis undergoing PTCA. Because of technical difficulties in obtaining satisfactory measurements, pressure gradients were not available in all patients (table 1). Follow-up angiograms were available at a mean of 7 ± 5 months (SD). Restenosis was defined as a loss of 50% or more of the initial gain in luminal diameter achieved at PTCA. Long-term gain was defined as the difference between the stenosis before angioplasty and residual stenosis at the time of follow-up angiography.

Patients with intimal dissection were not routinely treated with a prolonged heparin infusion. Discharge medications, which included aspirin and a calcium antagonist, were also similar in patients with dissection as compared with patients without dissection.

Statistical analysis. Statistical analysis was performed with the SPSS-X Program with the chi-square test to assess differences in categorical variables. A one-way analysis of variance was used to assess differences in continuous variables between groups.

In a subset of 882 patients with available transstenotic pressure gradient at the conclusion of PTCA (final gradient), a stepwise linear discriminant analysis was performed to determine the independent influence of uncomplicated intimal dissection and final gradient on restenosis. P values less than 0.05 were considered statistically significant.

Results

Patient characteristics and intimal dissection (table 1). Intimal dissection was identified in 248 patients, or 25% of the study population. The dissection group
TABLE 1

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>No intimal dissection (n = 738)</th>
<th>Intimal dissection (n = 248)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>596 (81%)</td>
<td>177 (71%)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Female</td>
<td>142 (19%)</td>
<td>71 (29%)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Age (yr ± SD)</td>
<td>54.4 ± 9.6</td>
<td>53.5 ± 10</td>
<td>NS</td>
</tr>
<tr>
<td>New-onset angina (≤ 2 mo)</td>
<td>247/657 (33%)</td>
<td>78/221 (35%)</td>
<td>NS</td>
</tr>
<tr>
<td>History of previous MI</td>
<td>193 (26%)</td>
<td>63 (25%)</td>
<td>NS</td>
</tr>
<tr>
<td>History of diabetes mellitus</td>
<td>63 (9%)</td>
<td>26 (10%)</td>
<td>NS</td>
</tr>
<tr>
<td>PTCA-vessel</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LM</td>
<td>2 (0.3%)</td>
<td>1 (0.4%)</td>
<td>NS</td>
</tr>
<tr>
<td>LAD</td>
<td>439 (59.5%)</td>
<td>142 (57.3%)</td>
<td>NS</td>
</tr>
<tr>
<td>RCA</td>
<td>203 (27.5%)</td>
<td>61 (24.6%)</td>
<td>NS</td>
</tr>
<tr>
<td>LCx</td>
<td>94 (12.7%)</td>
<td>44 (17.7%)</td>
<td>NS</td>
</tr>
<tr>
<td>Mean % stenosis (± SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-PTCA</td>
<td>74 ± 12</td>
<td>74 ± 12</td>
<td>NS</td>
</tr>
<tr>
<td>Post-PTCA</td>
<td>25 ± 12</td>
<td>24 ± 11</td>
<td>NS</td>
</tr>
<tr>
<td>Transstenotic gradient (mm Hg ± SD)</td>
<td>50 ± 14 (n = 695)</td>
<td>53 ± 13 (n = 220)</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Pre-PTCA</td>
<td>12 ± 7 (n = 666)</td>
<td>14 ± 8 (n = 216)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Time of follow-up angiogram (mo ± SD)</td>
<td>7 ± 5</td>
<td>7 ± 4</td>
<td>NS</td>
</tr>
</tbody>
</table>

*a* Of 878 patients with typical angina.

*b* When available.

MI = myocardial infarction; LM = left main; LAD = left anterior descending; RCA = right coronary artery; LCx = left circumflex.

contained more women than the group without dissection (29% vs 19%; p < .01). Other clinical characteristics were similar; there were no significant differences in age, presence of new-onset angina, and history of myocardial infarction or diabetes mellitus. The distribution of coronary vessels dilated and the mean diameter stenosis before and after PTCA were also not significantly different. Transstenotic pressure gradients both before and after dilatation were slightly higher in the group with intimal dissection.

**Restenosis rate and intimal dissection.** The overall restenosis rate in the study population was 29%. Restenosis rate in the group with intimal dissection was lower (24%) than that in the group with no dissection (30%), but the difference did not reach statistical significance (p = .08; figure 2).

Mean percent stenosis (± SD) at follow-up in patients with dissection, however, was lower than that in the group with no dissection (34 ± 23% vs 38 ± 23%; p = .01). Conversely, the long-term gain in lumen diameter was greater (40 ± 25% vs 35 ± 26%, p = .01) in the group with dissection (figure 3).

**Intimal dissection and transstenotic pressure gradient.** Patients with intimal dissection had slightly higher transstenotic pressure gradients both before and after PTCA (table 1). Stepwise discriminant analysis revealed that the final gradient and the presence of intimal dissection were both strongly and independently

![FIGURE 2. Angiographic restenosis rate of 738 patients without intimal dissection and 248 patients with evidence of intimal dissection after successful PTCA. There was a trend towards a lower restenosis rate in the group with intimal dissection.](image-url)
related to restenosis. Final gradient appeared to be most significant (table 2).

To determine a final gradient that would best predict restenosis, we analyzed the restenosis rate in subgroups with final gradients 5 or less vs greater than 5 mm Hg, 10 or less vs greater than 10 mm Hg, 15 or less vs greater than 15 mm Hg, 20 or less vs greater than 20 mm Hg, and 25 or less vs greater than 25 mm Hg. There was a significant relationship to restenosis when a final gradient of less or greater than 10, 15, and 20 mm Hg was used. The relationship was strongest (p < .001) when restenosis rate was analyzed in patients with final gradients of 15 or less vs greater than 15 mm Hg. We therefore examined the influence of intimal dissection on restenosis rate in the two subgroups: those with final gradients of 15 mm Hg or less (n = 638) and those with final gradients greater than 15 mm Hg (n = 244; figure 4).

In the subgroup with final gradients of 15 mm Hg or less the group with intimal dissection had a slightly higher mean final gradient (± SD) than the group without intimal dissection (9 ± 4 vs 8 ± 4 mm Hg; p < .05). In the subgroup with final gradients greater than 15 mm Hg the mean final gradient was 21 ± 5 mm Hg in patients without intimal dissection, which was not significantly different from 22 ± 7 mm Hg in the intimal dissection group.

Patients with intimal dissection had a significantly lower restenosis rate than patients without intimal dissections when the final gradient was 15 mm Hg or less (19% vs 28%; p < .05). If, on the other hand, the final gradient was greater than 15 mm Hg, the restenosis rate was not significantly different whether an intimal dissection was present or absent (35% vs 39%; p = NS). The restenosis rate of all patients with final gradients of 15 mm Hg or less was 26% and significantly lower than the restenosis rate of patients with final gradients greater than 15 mm Hg (38%; p < .001).

### Table 2

<table>
<thead>
<tr>
<th>Multivariate discriminant analysis of final gradient and intimal dissection as predictors of restenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canonical discriminant function coefficient</td>
</tr>
<tr>
<td>Final gradient</td>
</tr>
<tr>
<td>Intimal dissection</td>
</tr>
<tr>
<td>Constant</td>
</tr>
</tbody>
</table>

**FIGURE 3.** Mean percent stenosis (± SD) in patients without intimal dissection and in patients with intimal dissection before angioplasty (pre-PTCA), immediately after angioplasty (post-PTCA), and at the time of follow-up angiography (F/U-angio). The long-term gain was 35 ± 26% in patients without intimal dissection and 40 ± 25% in patients with intimal dissection (p = .01).

**FIGURE 4.** Restenosis rate in subgroups of patients with post-PTCA (final) transstenotic pressure gradient of 15 mm Hg or less or greater than 15 mm Hg. Patients with intimal dissection had a significantly lower restenosis rate than patients without intimal dissection in the subgroup with final gradients of 15 mm Hg or less. Intimal dissection had no significant influence on restenosis rate when the final gradient was greater than 15 mm Hg.
of patients with intimal tears or dissections when compared with an overall complication rate of 9.4%. It must be emphasized therefore that data presented in this study refer only to patients with an angiographically and clinically successful PTCA. Patients with intimal dissection leading to major complications (myocardial infarction, bypass graft surgery, or death) are not included.

Concern has been expressed that an intimal dissection during PTCA may contribute to accelerated restenosis. In this study we found no increase in restenosis rate and, in fact, observed an overall trend toward a lower restenosis rate in patients with intimal dissection.

Our results further demonstrate the importance of considering the final gradient when evaluating the significance of an intimal dissection. Similarly, transstenotic pressure gradients have been correlated with improved thallium perfusion abnormalities and coronary vasodilatory flow reserve after PTCA, emphasizing its clinical usefulness.

The mechanism of PTCA in improving blood flow was originally thought to represent compression and compaction of soft atheromatous material. Increasing evidence from experimental and human studies suggests that luminal enlargement of stenosed arteries may also be related to splitting of intima and media and stretching of adventitial tissues. The favorable long-term results seen in our patients with intimal dissection further corroborate these findings. The intimal dissection described in our study is probably anatomically and angiographically different from the classic intramural dissection that occurs within the media and results in a propagating intramural hematoma and subsequent occlusion of the artery. This process appears to occur unpredictably in a small proportion of patients having angiographic evidence of intimal dissection. A low final gradient associated with an intimal dissection may therefore indicate that the intramural hematoma is small and of no hemodynamic significance. This would explain the low restenosis rate of 19% in the subgroup with intimal dissection and associated final gradient of 15 mm Hg or less.

There was a significantly higher proportion of women in our group with intimal dissection, which agrees with the NHLBI PTCA Registry findings. The higher incidence of coronary dissection and intimal tear in women may be related to differences in plaque composition, structural characteristics of the vessel wall, and differences in vessel size. Although women have smaller coronary vessels than men, the same balloon size (3 mm diameter) tended to be used most commonly in both men and women. It is possible that the higher balloon/artery ratio in women induced a higher incidence of intimal dissection. Because a larger balloon size may favorably influence the recurrence rate after PTCA, one is tempted to conclude that the higher incidence of intimal dissection produced by larger balloons may explain the lower restenosis rate reported in women.

Although there was no angiographic evidence of intimal dissection in 75% of patients in this study, we cannot conclude that PTCA did not produce small fractures of plaque and intima. It is therefore likely that some patients had small intimal disruptions not evident on the post-PTCA angiogram. Conclusions from this study must therefore be limited to patients having angiographic evidence of intimal disruptions.

The accuracy of luminal diameter measurements after PTCA, especially if the vascular wall is irregular because of intimal dissection, has been questioned. To minimize this problem, we averaged the stenosis from at least two orthogonal projections. This is important because the definition of restenosis used in this study is based on luminal gain achieved immediately after PTCA. Given this limitation, however, we believe that taking the mean of stenosis measurements in several projections represents the best currently available technique for assessing the anatomic severity of coronary artery stenosis in most patients.

The accurate measurements of transstenotic pressure gradients with a balloon catheter have also been questioned. Because of the relatively large cross-sectional area of the deflated balloon, the gradients could be artifactually increased. Even the smallest catheter across a stenosis will interfere with blood flow and the true gradient may be difficult to measure. A large final gradient after an otherwise successful PTCA may therefore be artifactually elevated. In the absence of significant collateral flow, however, a small final gradient (<15 mm Hg) measured with a balloon catheter should indicate that the true gradient across the residual stenosis is less than 15 mm Hg. These problems notwithstanding, the strong relationship between final gradient and restenosis mentioned earlier emphasizes the clinical usefulness of transstenotic pressure measurements.

Our study population represents only 60% of all patients with successful PTCA (n = 1650) and therefore these results cannot be used to determine overall restenosis rate. However, the restudy rate of all patients with successful PTCA and evident intimal dissection was 57% (248/438), and not significantly dif-
different than that of patients without intimal dissection (61%, 738/1112; p = NS). Because patients who are symptomatic are more likely to have a repeat angiogram, the overall restenosis rate could be expected to be lower than what we found in this population.16

It is possible that heparinization for 12 to 18 hr after PTCA, used more commonly in patients with intimal dissection, may have had an influence on restenosis. The effect of short-term heparinization after PTCA on restenosis, however, is not known and should be determined in a controlled study. Further studies will also be required to define ways to control vessel injury during PTCA, optimizing initial results while keeping short-term complications low and improving long-term success.

In summary, patients with intimal dissection who have an uncomplicated post-PTCA course did not have an increased risk of restenosis. The presence of an intimal dissection appeared to have a beneficial effect on restenosis if the final transstenotic pressure gradient was favorable.

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