RESTENOSIS AFTER SUCCESSFUL CORONARY ANGIOPLASTY: KOŞUYOLOU EXPERIENCE

Ö. KOZAN, M.D., *
O. ERGENE, M.D., *
T. OKAY, M.D., *
İ. DİNDAR, M.D., *
N. ÇAĞLAR, M.D., *
A. ĐİRİÇAN, M.D., **
M. ÖZDEMİR M.D., *
O. PEKTAŞ, M.D.*

From: *Koşuyolu Heart and Research Hospital
** Cerrahpaşa Medical School Biostatistic Division

Adress for reprints:
Ömer KOZAN M.D.
Koşuyolu Heart and Research Hospital
İstanbul-TÜRKİYE

The PTCA procedure was performed to 444 patients successfully, until end of January 1991; of these, angiographic follow-up was available in 320 (72%) patients. The mean age was 51±7 years, 282 (88.1%) of these were men. 374 lesions were dilated. 47 patients of this group had to undergo PTCA for the second or third time. Global restenosis rate was 32.8% (105 patients). Lesion restenosis rate was 33.7% (126 lesions). Restenosis rate was 38.6% in the left anterior descending, 20.4 in the right coronary artery, 7.3% in the circumflex artery (p<0.001). It was 56% in the proximal part of the anterior descending. In %81.9 of the patients, restenosis was seen in the first three months after the PTCA procedure.

Key words: restenosis, percutaneous transluminal coronary angioplasty

Although the initial outcome for coronary angioplasty procedures has improved progressively over the last 10 years, the incidence of restenosis over the first 6 to 8 months after dilation has remained unchanged at approximately 30%. We report the angiographic and long term clinical results in our patients who were treated with percutaneous transluminal coronary angioplasty (PTCA) at Koşuyolu Heart and Research Hospital between December 1989 and January 1991.

Methods
The PTCA procedure was performed to 444 patients successfully. Mean age was 51±7 years, 282 (88.1%) of these were male, 38 (11.9%) were female. Control angiography was performed to 320 (72%) patients.
The PTCA technique used has been described elsewhere. The patients were premedicated with aspirin (150-300mg/day) and heparin (10,000-15,000U) immediately after insertion of the arterial sheath. An additional 5,000 U of heparin were administered hourly during the...
angioplasty procedure, when activated clotting time was lower than 300 seconds. Intravenous infusion of heparin was usually administered overnight when angiographic evidence of a coronary dissection or thrombus was seen. In the post-angioplasty period, each patient was monitored and usually discharged at the third day. In general, patients continued to receive aspirin and calcium channel antagonist after PTCA.

A successful angioplasty procedure is defined as one in which a ≥ 20% or more change in luminal diameter is achieved with the final diameter stenosis less than 50% and without the occurrence of death, acute myocardial infarction or the need for emergency bypass operation.

Follow-up coronary angiography was performed six months after coronary angioplasty. Any recurrence of symptoms within 6 months prompted earlier angiography. In patient with repeat coronary angiography during follow-up, the presence of a residual stenosis more than 50% at the site initially dilated was considered as restenosis regardless of the patients symptoms. Nominal data were analyzed using chi-square equations.

Results

The PTCA procedure was performed to 444 patients successfully. Follow-up coronary angiography was performed to 320 (72%) patients, 221 (66.3%) of these had one vessel disease, 108 (33.7%) had multivessel disease. Mean follow-up period was 11±2 months (range: 2-26 months). 374 stenosis was dilated in 320 patients.

Incidence of restenosis:
Restenosis was documented in 105 of 320 patients in whom follow-up coronary angiography was performed. The observed restenosis rate per patient was 32.8%.
A total of 126 of 374 successfully dilated segments were restenosed at follow-up angiography. The observed restenosis rate per segment was 33.7%.

Clinical characteristics predictive of restenosis (Table-1):
Among the 7 clinical variables evaluated in our study, male gender, diabetes, smoking, multivessel disease, and angina class (III, IV according to Canadian Heart Association Angina Classification) were associated with restenosis in the univariate analysis. Hypertension, female gender, unstable angina and single vessel disease were not significantly different in patients with or without restenosis.

Angiographic characteristics predictive of restenosis (Figure-1, Table-2).
Restenosis related significantly with the vessels performed PTCA. Restenosis rate was found 38.6% in left anterior descending artery (LAD), 20.4% in right coronary artery (RCA), 17.3% in circumflex artery (Cx) (p<0.01). In the proximal part of the LAD(from separation of Cx artery to the first septal or/and diagonal artery), restenosis rate was 56%. Whereas, in the distal segments of the proximal part of the LAD, restenosis rate was found 30%. Of the 215 patients, in whom restenosis was not found in follow-up angiography, the degree of stenosis at the previously dilated segments was found lower in Cx (13.2±14.6%). Whereas, it was found significantly higher in LAD (24.7±20.4%) and RCA (25.9±20.8%) (p< 0.001).

Time course of restenosis (Figure-2)
Mean time for development of restenosis was 8.2±5.4 weeks. Restenosis developed in 82% of the patients within the first 3 months.

Follow-up of restenosis (Table-3):
After the 3rd PTCA procedure has been performed, the restenosis developed patients was given to the bypass graft operation.

Discussion

Major technologic advances and high early clinical and angiographic success rates have led to rapid expansion of coronary angioplasty indications. However, restenosis is frequent and this problem remains a major concern2,3.
Table 1: Categorical baseline clinical characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Observed Restenosis Rates</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>%</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>96/282</td>
<td>34</td>
</tr>
<tr>
<td>female</td>
<td>9/38</td>
<td>23.7</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>93/285</td>
<td>32.6</td>
</tr>
<tr>
<td>Yes</td>
<td>12/35</td>
<td>34.2</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>97/300</td>
<td>32.3</td>
</tr>
<tr>
<td>Yes</td>
<td>8/20</td>
<td>40</td>
</tr>
<tr>
<td>Unstable Angina</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>93/284</td>
<td>31</td>
</tr>
<tr>
<td>Yes</td>
<td>12/36</td>
<td>33.3</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>76/256</td>
<td>29.7</td>
</tr>
<tr>
<td>Yes</td>
<td>29/64</td>
<td>45.3</td>
</tr>
<tr>
<td>Single or Multivessel disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>65/216</td>
<td>30</td>
</tr>
<tr>
<td>2, 3</td>
<td>40/104</td>
<td>38.5</td>
</tr>
<tr>
<td>Angina Class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I,II</td>
<td>67/201</td>
<td>33.3</td>
</tr>
<tr>
<td>III,IV</td>
<td>38/83</td>
<td>45.8</td>
</tr>
</tbody>
</table>

The search for correctable factors and drugs that will reduce its incidence has not provided conclusive results. In recent reports, restenosis rates varied from 15% to 47%. This wide variability is due to several factors. Different clinical and angiographic characteristics of the group of patients undergoing the procedure and different procedural factors may influence observed restenosis rates after coronary angioplasty. The early and late histologic appearance of the coronary angioplasty site are established. Immediately after angioplasty, there is substantial evidence of vascular injury; the intimal surface is denuded, the atheroma has fissures, and the normal segment of the vessel circumference is stretched.

The major milestones in the temporal sequence of restenosis are platelet aggregation, inflammatory cell infiltration, release of growth factors, medial smooth muscle cell modulation and proliferation, proteoglycan synthesis and matrix remodeling. When restenosis develop at 1 to 4 months, the histologic appearance of the restenotic lesion is intimal hyperplasia. Given this end-point, it was theorized that the proximate cause of restenosis is denuding and stretching vascular injury. Several previous studies have shown that class III or IV angina and recent angina are predictive...
of restenosis after coronary angioplasty. Some investigators also suggested that unstable angina was associated with an increased incidence of restenosis. However, other investigators did not find a relation between severity of angina and restenosis after coronary angioplasty. Male gender was found to be associated with an increased rate of restenosis by some investigators, but this relation was not confirmed by others. Several investigators have suggested that there is a relation between diabetes and restenosis, whereas others have not. Some have reported a relation with cigarette smoking whereas others have not. In general, systemic hypertension was not found to be associated with increased restenosis rates after coronary angioplasty. In our study, smoking, multivessel disease, and III, IV angina class were associated with restenosis.

Other investigators have reported a higher restenosis rate when the LAD was successfully dilated or when distal versus proximal segments were successfully dilated. We have shown that the incidence of restenosis was higher in patients with multivessel disease than in patients with single vessel disease. Other investigators have reported a lower restenosis rate when the Cx was successfully dilated.

Of the 215 patients, in whom restenosis hasn't been found in follow-up angiography, the degree of stenosis at the previously dilated segments was found lower in Cx.

<table>
<thead>
<tr>
<th>Table 2. Restenosis per diseased vessel</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>----------------------------------------</td>
</tr>
<tr>
<td>Lesion</td>
</tr>
<tr>
<td>Patient</td>
</tr>
</tbody>
</table>
Figure 2. Time course of restenosis

±14.6%). Whereas, it was found significantly higher in LAD (24.7 ± 20.4%) and RCA (25.9 ± 20.8%) (P < 0.001).

Conclusion

We have shown that restenosis rate was higher in patients with LAD disease (especially proximal LAD disease) and lower in patients

Table 3. Follow-up of restenosis

LAD (87)

MEDICAL (5) → OPEN (18)

2. PTCA (35) → CABG (10)

CABG (47) → 3. PTCA (7)

RCA (10)

MEDICAL (4) → OPEN (2)

2. PTCA (6) → 3. PTCA (4)

CX (8)

MEDICAL (2) → OPEN (2)

2. PTCA (6) → 3. PTCA (4)
with Cx disease. 81.9% of restenosis was developed within the first three months after the procedure. In our study, smoking, multivessel disease, and III-IV angina class were associated with restenosis.

References


