

Comparative Results of Percutaneous Transluminal Coronary Angioplasty in Patients With Dynamic Versus Fixed Coronary Stenosis

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This study compares the results of percutaneous transluminal coronary angioplasty in a group of 132 patients (group A) with fixed atherosclerotic narrowing (no spontaneous or ergonovine-provoked spasm) and in a group of 97 patients (group B) with dynamic coronary stenosis (spasm superimposed on the stenosis). All these patients underwent complete follow-up angiography. The rate of restenosis (defined as a loss of 50% of the initial gain) was significantly higher in patients in group B (dynamic coronary stenosis) than in group A (fixed narrowing) (35

versus 22%, $p < 0.05$). Despite treatment with a calcium antagonist, coronary artery spasm persisted in 44% of the patients in group B and was detected for the first time in 15% of the patients in group A.

Thus, in patients with dynamic coronary stenosis, the results of coronary angioplasty were less satisfactory than in patients with fixed narrowing, and in both groups coronary artery spasm was frequently (64%) superimposed on the restenosis.

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Percutaneous transluminal coronary angioplasty is a new approach to the treatment of atherosclerotic coronary stenosis. The efficacy of this technique is well established but restenosis can occur in 20 to 28% of cases and could limit the long-term benefit of the procedure. Recent follow-up data from the Percutaneous Transluminal Coronary Angioplasty (PTCA) Registry of the National Heart, Lung, and Blood Institute (1) shows a restenosis value of 33.6% among 557 patients with angiographic follow-up. However, some studies (2,3) have shown that the results of coronary angioplasty were less satisfactory in patients with Prinzmetal's variant angina than in other patients. Therefore, the purpose of this study was to compare the results obtained with coronary angioplasty in patients with dynamic coronary stenosis and in those with fixed atherosclerotic narrowing.

Methods

Patients. From December 1981 to September 1985, 522 patients with significant coronary artery narrowing ($\geq 60\%$) underwent percutaneous transluminal coronary angioplasty in our institution: 478 (83%) had a primary successful result, defined as an improvement of at least 20% in the angio-

graphic appearance of the stenosis without complications. Our protocol included a systematic restudy with coronary angiography 6 to 8 months after the procedure, and 275 patients completed this angiographic follow-up. Among these patients, 229 were selected because all (except those with spontaneous spasm) had undergone a provocative test with ergonovine at the time of the first coronary angiographic study.

These patients were classified into two groups: Group A included 132 patients with a fixed atherosclerotic coronary narrowing, that is, nonmodified by ergonovine. Group B included 97 patients with dynamic coronary stenosis, characterized by spontaneous ($n = 14$) or provoked ($n = 83$) coronary artery spasm superimposed on atherosclerotic stenosis.

Definition of spasm. Coronary spasm was defined as a transient (reversible with intracoronary injection of isosorbide dinitrate) total occlusion of the vessel at the site of the narrowing that had been dilated. The two groups had equivalent severity of atherosclerotic narrowing ($70 \pm 13\%$ in group A, $72 \pm 13\%$ in group B). The patients in both groups were discharged on a daily regimen of dipyridamole (150 mg) and nifedipine (40 to 60 mg). All of these patients (symptomatic or asymptomatic) underwent a second coronary angiographic study 6 to 8 months later and the procedure was completed by an ergometrine test in 210 patients.

Follow-up angiography. During follow-up angiography the preceding definition of spasm was applied to the patients

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with restenosis (defined as a loss of 50% of the initial gain achieved at angioplasty). In patients without restenosis, coronary spasm was defined as either a total transient occlusion of the vessel or the appearance of a transient significant (>60%) narrowing of the previously dilated segment. The protocol of the ergonovine test has been previously reported (4). The lesions before and after angioplasty were carefully measured with an automated digital caliper using a 6502 microprocessor (5). For each narrowing, at least two measurements were performed in different projections and the results were expressed as a mean of these two values.

Statistical analysis. All results were expressed as mean \pm SD. Differences between the two groups with respect to the frequency of an event were determined by chi-square analysis. Comparisons were performed between two means using the unpaired Student's *t*-test. A probability (*p*) value of less than 0.05 was considered statistically significant.

Results

Patient characteristics (Table 1). The 113 men and 19 women in Group A had a mean age of 53 ± 13 years. This

Table 1. Clinical and Angiographic Data in 229 Patients

| | Group A | Group B |
|---|-------------|-------------|
| No. of patients | 132 | 97 |
| Age (yr) (\pm SD) | 53 ± 13 | 50 ± 9 |
| Sex (M/F) | 113/19 | 90/7 |
| Symptoms | | |
| Effort angina | 52 | 18 |
| Angina at rest | 26 | 25 |
| Mixed angina | 13 | 11 |
| Prinzmetal variant angina | 0 | 20 |
| Unstable angina | 24 | 16 |
| Atypical chest pain | 17 | 7 |
| No. of diseased vessels | | |
| 1 | 89 | 79 |
| 2 | 38 | 17 |
| 3 | 5 | 1 |
| Dilated vessel | | |
| LAD | 110 | 74 |
| RCA | 22 | 22 |
| LCx | 14 | 8 |
| Location of spasm | | |
| LAD | — | 63 |
| RCA | — | 22 |
| LCx | — | 11 |
| LAD + LCx | — | 1 |
| Stenosis (%) | | |
| Before PTCA | 70 ± 13 | 72 ± 13 |
| After PTCA | 23 ± 39 | 21 ± 48 |
| Transstenotic pressure gradient (mm Hg) | | |
| Before PTCA | 53 ± 27 | 57 ± 23 |
| After PTCA | 9 ± 10 | 8 ± 8 |

F = female; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; M = male; PTCA = percutaneous transluminal coronary angioplasty; RCA = right coronary artery.

was not significantly different from the mean age 50 ± 9 years in the 90 men and 7 women in Group B. Symptoms in the two groups were significantly different ($p < 0.001$): group B was characterized by an important proportion of patients with angina at rest or typical Prinzmetal variant angina, whereas exertional angina was the common clinical feature observed in group A. There was also a significant difference ($p < 0.05$) in the extent of coronary artery disease. In group B, 79 (81%) of 97 patients had single vessel disease whereas 33% of patients in group A had double (29%) or triple (4.5%) vessel disease. In patients with dynamic coronary stenosis (group B) the spasm involved the left anterior descending coronary artery in 63 cases, the right coronary artery in 22 and the left circumflex branch in 11. In one patient, spasm involved simultaneously the left anterior descending coronary artery and the circumflex branch. In groups A and B, 146 and 114 coronary vessels were dilated respectively. There were no significant differences in the locations of the stenoses that were to be dilated in both groups.

Coronary angioplasty procedure. Percutaneous transluminal coronary angioplasty was performed with the method of Grüntzig et al. (6,7). Until July 1983, we used Dilaca's catheter and the subsequent cases were treated with the steerable guide wire. The number, maximal pressure and total duration of inflations were similar in the two groups. However, there was a significant difference in the size of the balloon. In group B, the vessels were dilated with a 3.7 mm balloon in 46% of the patients versus only 27% of the patients in group A. A 3 mm balloon was most commonly used (68% of cases) in group A but was employed in only 49% of the patients in group B.

Immediate results. The gain in luminal patency was similar in groups A and B ($48.6 \pm 18\%$ in group A versus $50.8 \pm 15\%$ in group B) ($p = \text{NS}$). After angioplasty the degree of residual stenosis was $23 \pm 39\%$ in group A and $21 \pm 48\%$ in group B ($p = \text{NS}$). The transstenotic pressure gradient (obtained in 150 patients) was significantly and equally reduced in both groups: from 53 ± 27 to 9 ± 10 mm Hg in group A and from 57 ± 23 to 8 ± 8 mm Hg in group B; again there was no difference between groups A and B.

Clinical follow-up. At the time of follow-up angiography, 62% of patients in group A and 56% of patients in group B were asymptomatic. In group B, 11 had anginal pain at rest while 4 complained of pain during effort and at rest; only 4 of them had effort angina alone and 3 had unstable angina.

Follow-up angiography. At the time of reinvestigation, 29 (22%) of the 132 patients in group A had a restenosis defined as a loss of 50% of the initial gain. In contrast, 34 (35%) of the 97 patients in group B had restenosis, a significantly higher rate than in group A ($p < 0.05$). However, 11 (38%) of the 29 patients in group A with restenosis were

Table 2. Follow-Up Data in 43 Patients With Restenosis

| | Group A | Group B |
|-------------------------------------|----------|----------|
| Restenosis | 29 (22%) | 34 (35%) |
| Asymptomatic with restenosis | 11 | 5 |
| Symptoms associated with restenosis | | |
| Effort angina | 6 | 5 |
| Angina at rest | 4 | 4 |
| Mixed angina | 1 | 7 |
| Prinzmetal variant angina | — | 1 |
| Unstable angina | 4 | 5 |
| Atypical chest pain | 3 | 7 |
| Ergonovine tests | | |
| No. of cases | 20 | 27 |
| Positive test | 19 | 38 |
| Spasm superimposed on restenosis | 8 | 22 |

totally free of symptoms; the others (62%) experienced symptoms listed in Table 2. In group B, only 15% of patients with angiographic evidence of restenosis were asymptomatic and 85% of them had recurrence of symptoms. Thus, the incidence of patients with recurrence of symptoms associated with angiographic evidence of restenosis was significantly higher in group B (dynamic coronary stenosis) than in group A (30 versus 14%, $p < 0.01$).

Provocative test with ergonovine. The provocative test was repeated during coronary angiography in 123 patients in group A and 87 patients in group B. In the patients with dynamic coronary stenosis (group B) coronary artery spasm was induced in 38 (44%). In patients with previously fixed coronary stenosis (group A) 19 (15%) of 123 had coronary artery spasm at the time of reinvestigation.

Among the 29 patients in group A with restenosis, a provocative test was performed in 20 and induced spasm in 8 (40%). In 34 patients in group B with restenosis, 27 underwent an ergonovine test: 22 (81.5%) had spasm at the site of the dilation. Thus, for the whole group of 47 patients with restenosis who underwent the ergonovine test, 30 (64%) had spasm superimposed on restenosis.

Discussion

Previous studies in coronary angioplasty. In 1976, Selzer (8) discussed the concept of dynamic coronary ste-

nosis characterized by spasm superimposed on atherosclerotic narrowing: both dynamic and fixed components could contribute variably to the degree of obstruction. The fixed obstruction can be treated with coronary angioplasty, and in 1982, David et al. (2) demonstrated that coronary angioplasty was technically feasible in patients with Prinzmetal's variant angina. However, the symptoms recurred after successful treatment with coronary angioplasty in 5 of 13 patients and, within 4 months of the procedure, 5 of the patients had restenosis and 2 others developed severe lesions adjacent to the site of angioplasty. More recently, Hollman et al. (9) reviewed the clinical course of five patients manifesting coronary spasm at the site of previous successful coronary angioplasty. In all five cases spasm was observed on a hemodynamically insignificant obstruction. Four patients did not respond to therapy with a calcium antagonist and subsequently developed restenosis. One patient died and pathologic study revealed new atherosclerotic disease. Corcos et al. (3) described a series of 21 patients with Prinzmetal's variant angina treated with coronary angioplasty: the procedure was successful in 19 but angina persisted or recurred 1 to 4 months after coronary angioplasty in nine patients (47%) who had restenosis.

Present results of coronary angioplasty in patients with variant angina. Thus, our study is the fourth report concerning coronary angioplasty in a large series ($n = 97$) of patients with coronary artery spasm superimposed on atherosclerotic narrowing. However, our presentation differs from the preceding studies in that spasm was demonstrated before the procedure while it was recognized beforehand in only 5 of the 15 cases of David et al. (2). This resulted from our systematic approach and search for spasm with provocative testing as described in 1982 (4). Coronary artery spasm persisted in 44% of our patients of group B (patients with dynamic stenosis) despite treatment with a calcium antagonist although all the patients received nifedipine, 40 to 60 mg daily. However, treatment with this drug was discontinued 12 to 18 hours before follow-up catheterization.

Among patients of group A (patients with fixed atherosclerotic narrowing), 15% had spasm involving the segment of the dilated vessel 6 to 8 months after coronary angioplasty. This is not totally unexpected: experimental studies

Table 3. Clinical and Angiographic Characteristics of Patients With or Without Restenosis

| | Group A (n = 132) | | Group B (n = 97) | |
|---------------------------|--------------------|-----------------|--------------------|-----------------|
| | Without restenosis | With restenosis | Without restenosis | With restenosis |
| No. of patients | 103 | 29 | 63 | 34 |
| Age (yr) (\pm SD) | 52 \pm 8.7 | 51 \pm 7.7 | 50 \pm 9.7 | 51 \pm 8.2 |
| Duration of symptoms (mo) | 5.7 \pm 3.7 | 5.6 \pm 9.1 | 3.3 \pm 4.3 | 4 \pm 8 |
| Stenosis before PTCA (%) | 71 \pm 12 | 72 \pm 11 | 73 \pm 14 | 71 \pm 11 |

PTCA = percutaneous transluminal coronary angioplasty.

(10) have shown that after coronary angioplasty, the endothelium is damaged and denuded, exposing the neointima to platelet adhesion. This could lead to the release of platelet factors such as adenosine diphosphate (ADP), platelet growth factor 4 and thromboxane, the latter being a potent vasoconstrictor agent. Therefore, coronary angioplasty can exaggerate the vasomotor reactivity of the dilated segment, leading to residual spasm.

Restenosis after coronary angioplasty. For the total group, the rate of restenosis (63 of 229 patients or 27.5%) is comparable with that of other series. However, the differences in our two groups are noteworthy; the incidence of restenosis was higher when coronary angioplasty was performed on a dynamic narrowing (group B) than on a fixed atherosclerotic stenosis (group A). When restenosis occurred, coronary artery spasm was frequently (64%) superimposed on this segment.

Restenosis is a common complication of coronary angioplasty and could limit the long-term benefit of this procedure. Several studies have emphasized the role of repeated angioplasty in patients who had recurrent stenosis after the first attempts; reliable means of preventing recurrence are needed but the mechanisms of restenosis are still unclear. A report from the National Heart, Lung, and Blood Institute's Percutaneous Transluminal Coronary Angioplasty registry (1) selected, with multivariate analysis, four factors associated with restenosis: male sex, angioplasty of bypass graft, severity of angina before angioplasty and no history of prior myocardial infarction. The report (1) mentioned that patient age, duration of symptoms before angioplasty and severity of stenosis were important determinants of successful coronary angioplasty. However, in our study, the restenosis rate in the two patient groups was not affected by these factors (Table 3).

Some reports (11,12) emphasized the role of the angioplasty technique (size of the balloon, pressure and inflation time). In our study, there was only a significant difference between the two groups concerning the size of the balloon. David et al. (11) selected, with a stepwise logistic regression, variant angina, severity and the length and geometry of the stenosis as the baseline characteristics that were the most predictive of restenosis.

These conclusions and our findings underline the role of spasm in the pathogenesis of restenosis. Chahine and Raizner (13) in 1977 and Marzilli et al. (14) in 1980 suggested that recurrent vasospastic episodes in an angiographically normal or minimally diseased coronary segment could result in a more rapid progression of the atherosclerotic process. Although this provocative affirmation needs confirmation, our results could support this hypothesis.

Clinical implications. Our study demonstrates the less satisfactory results obtained with coronary angioplasty in patients with dynamic coronary stenosis. More than 10 years ago, Gaasch et al. (15) reported that the results of coronary

bypass surgery were not as good in patients with variant angina as in patients with classical effort angina. These results (before the era of calcium channel blockers) are analogous to our results. The role of drugs to prevent restenosis is unclear: in our study all the patients received a calcium antagonist, but in the study of Corcos et al. (3) concerning coronary angioplasty in variant angina, restenosis occurred only in patients not treated with calcium channel blockers. In contrast, a randomized study by the same group (16) was unable to show a significant difference in restenosis in two groups treated or not treated with calcium antagonists. Faxon et al. (17) have shown that lower recurrence rates than are recorded in control animals can be achieved with antiplatelet drugs. Aspirin has been shown to be at least as effective as warfarin in the treatment of patients with recurrent stenosis, and overall the study showed a lower incidence of recurrent stenosis among aspirin-treated patients. Our two groups of patients received dipyridamole, but only a low dose was administered. Finally, these observations emphasize the need for further randomized studies to detect appropriate drug prevention of restenosis after successful angioplasty.

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References

1. Holmes DR, Vliestra RE, Smith HC, et al. Restenosis after percutaneous transluminal coronary angioplasty (PTCA): a report from the PTCA registry of the National Heart, Lung, and Blood Institute. *Am J Cardiol* 1984;53:77C-81C.
2. David PR, Waters DD, Scholl JM, et al. Percutaneous transluminal coronary angioplasty in patients with variant angina. *Circulation* 1982;66:695-702.
3. Corcos T, David PR, Bourassa MG, et al. Percutaneous transluminal coronary angioplasty for the treatment of variant angina. *J Am Coll Cardiol* 1985;5:1046-54.
4. Bertrand ME, Lablanche JM, Tilmant PY, et al. Frequency of provoked coronary arterial spasm in 1089 consecutive patients undergoing coronary arteriography. *Circulation* 1982;65:1299-306.
5. Bertrand ME, Lablanche JM, Thieuleux FA, Fourrier JL, Traisnel G. Mesure du diamètre des artères et des sténoses coronaires. Présentation de deux méthodes. *Ann Cardiol Angeiol (Paris)* 1985;34:615-9.
6. Gruentzig A, Senning A, Siegenthaler WE. Nonoperative dilation of coronary artery stenosis. Percutaneous transluminal coronary angioplasty. *N Engl J Med* 1979;301:61-3.
7. Gruentzig AR. Technique of percutaneous transluminal coronary angioplasty. In: Hurst JW, Logue RB, Rocklly CE, eds. *The Heart*. New York: McGraw-Hill, 1982:1904-10.
8. Selzer A. Clinical syndrome of variant angina with normal coronary arteriogram. *N Engl J Med* 1976;295:1343-7.
9. Hollman J, Austin GE, Gruentzig AR, Douglas JS Jr, King SB III. Coronary artery spasm at the site of angioplasty in the first 2 months after successful percutaneous transluminal coronary angioplasty. *J Am Coll Cardiol* 1983;2:1039-45.
10. Faxon DP, Sanborn TA, Handenschild CC, et al. Effect of antiplatelet therapy on restenosis after experimental angioplasty. *Am J Cardiol* 1984;53:72C-76C.
11. David PR, Renkin J, Moise A, Dangoisse V, Val PG, Bourassa MG.

- Can patient selection and optimization of technique reduce the rate of restenosis after percutaneous transluminal coronary angioplasty (abstr)? *J Am Coll Cardiol* 1984;3:470.
12. Meier B, Hollman J, Gruentzig A, Ischinger T, Bradford J, Galan K. Does higher balloon pressure increase the success of coronary angioplasty (abstr)? *J Am Coll Cardiol* 1983;1:644.
 13. Chahine RA, Raizner AE. Another look at Prinzmetal's variant angina. *Eur J Cardiol* 1977;6:71-4.
 14. Marzilli M, Goldstein S, Trivella MG, et al. Some clinical considerations regarding the relation of coronary vasospasm to coronary atherosclerosis. A hypothetical pathogenesis. *Am J Cardiol* 1980;45:882-6.
 15. Gaasch W, Lufschavoski R, Leachman RD, Alexander JK. Surgical management of Prinzmetal's variant angina. *Chest* 1974;66:614-7.
 16. Corcos T, David PR, Renkin J, et al. A randomized trial of diltiazem for prevention of restenosis after percutaneous transluminal coronary angioplasty (abstr). *Circulation* 1984;70(suppl II):II-175.
 17. Faxon DF, Sanborn TA, Haudenschild CC, Ryan TJ. Effect of antiplatelet therapy on restenosis after experimental angioplasty. *Am J Cardiol* 1984;53:72C-75C.