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Midterm Outcome of Patients With Asymptomatic Restenosis After Coronary Balloon Angioplasty

ROSA ANA HERNÁNDEZ, MD, CARLOS MACAYA, MD, ANDRÉS IÑIGUEZ, MD, FERNANDO ALFONSO, MD, JAVIER GOICOLEA, MD, ANTONIO FERNANDEZ-ORTIZ, MD, PEDRO ZARCO, MD, FACC

Madrid, Spain

Although many patients with restenosis after balloon coronary angioplasty have recurrence of angina, others remain asymptomatic. To assess the clinical implications of asymptomatic coronary restenosis, we analyzed clinical and angiographic characteristics of 277 consecutive patients with restenosis, 133 (48%) of whom were asymptomatic (group I) and 144 (52%) symptomatic (group II). Restenosis was documented 6 to 9 months after the index procedure, or earlier if angina recurred, and was defined as a >50% lumen narrowing (visual estimation). Group I (asymptomatic group) included fewer female (9% vs. 18%, $p < 0.05$) and hypertensive patients (38% vs. 56%, $p < 0.005$) and more patients with a previous myocardial infarction (48% vs. 28%, $p < 0.05$) and single-vessel disease (67% vs. 55%, $p < 0.05$).

Before angioplasty, symptoms had lasted for a shorter period (10 ± 25 vs. 23 ± 42 months, $p < 0.001$), ischemia after a recent infarction was a more frequent indication (21% vs. 10%, $p < 0.05$) and total revascularization more frequently obtained (74% vs. 63%, $p < 0.05$) in group I than in group II patients. Only a normal blood pressure, previous myocardial infarction, single-vessel disease and a shorter duration of symptoms were independent correlates of asymptomatic restenosis. No differences were found in stenosis severity before angioplasty (90% in both groups) or after angioplasty (22% ± 12% vs. 24% ± 16%).

By the time of follow-up angiography, group I patients had exercised more (9.8 ± 2.7 vs. 7.7 ± 3 metabolic exercise equivalents (METs), $p < 0.05$) and had achieved a faster heart rate (140 ± 21 vs. 127 ± 23 beats/min, $p < 0.025$), and more of them had a negative test result (33% vs. 9%, $p < 0.05$). Stenosis was less severe in group I patients (79 ± 15% vs. 86 ± 11%, $p < 0.05$), and 32% of them versus 8% of group II had <75% stenosis. After 17 ± 13 months, 15 asymptomatic patients had recurrence of angina; recurrence was considered related to restenosis in 6 (21%) of 29 patients with exercise-induced ST segment changes, in 4 (9.5%) of 42 without ST changes and in none of the 15 with ST changes and "elective" angioplasty. No group I patient died or was operated on, and only six underwent another angioplasty procedure indicated for angina. By contrast, 6 patients (4%) in group II died, 11 (8%) required surgery and 81 (56%) underwent repeat angioplasty.

It is concluded that asymptomatic coronary restenosis is a frequent phenomenon with a good prognosis mainly in patients with a negative exercise test result. Prospective, randomized studies are required to determine the potential role of repeat angioplasty in asymptomatic patients with documented restenosis and evidence of exercise-induced ST segment changes.

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Coronary restenosis is a frequent phenomenon after successful percutaneous transluminal coronary angioplasty (1–7). Its incidence may be affected by several factors, including the definition (1,4,5), the method used to analyze diameter narrowing, patient or lesion characteristics (3,4), the timing of follow-up angiography (5) and the rate of late angiographic examination (6). Many patients with documented restenosis have recurrence of their symptoms, whereas others remain angina free (1–3,6,7). The proportion of patients with restenosis who remain asymptomatic has been reported to be from rare (6) to as high as 24% in the National Heart, Lung, and Blood Institute Registry (1) or 33% in the Multi-Hospital Eastern Atlantic Restenosis (M-Heart) trial (8). Only small or nonspecifically directed studies (8–11) have addressed the clinical characteristics and prognosis of this subgroup of patients. Asymptomatic patients with restenosis may have silent ischemia (12–22), as has been observed in other subgroups of patients with coronary artery disease, or may not have ischemia at all, if myocardial metabolic requirements are decreased (infarcted areas) or are successfully supplied either by the considered "restenosed" vessel or collateral flow (23). The documentation of silent ischemia in asymptomatic patients with coronary artery disease, during exercise testing or Holter electrocardiographic (ECG) monitoring (20), identifies a subgroup of patients at higher risk for subsequent coronary events (14–19), but the clinical implications of silent ischemia in the subgroup of patients with asymptomatic coronary restenosis are unknown.

The aim of the present study is twofold: 1) to characterize

From the Cardiopulmonary Department, Hospital Universitario San Carlos, Madrid, Spain.

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Address for reprints: Carlos Macaya, MD, Departamento de Exploracion Cardiopulmonar, Hospital Universitario "San Carlos," C/Martín Lagos s/n, Madrid 28040, Spain.

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patients with asymptomatic restenosis, and 2) to determine the usefulness of late exercise testing, follow-up angiography and repeat coronary angioplasty in the management of patients with asymptomatic restenosis after balloon coronary angioplasty.

Methods

Study patients. From March 1985 to November 1990, a total of 1,030 consecutive balloon angioplasty procedures (927 of them were successfully completed, 90% success rate) were performed at our institution. During this period, all patients undergoing coronary angioplasty were enrolled in a prospective study designed to evaluate the impact of several demographic, clinical, anatomic and pharmacologic factors on the incidence of restenosis. According to a protocol approved by our local Clinical Investigation Committee, all patients were recommended to undergo late follow-up angiography (at 6 to 9 months or earlier if clinically indicated); this study was finally obtained in 839 patients (90.5% angiographic follow-up rate). In the remaining 88 patients (9.5%), it was not performed for several reasons, including death (14 patients—7 cardiac and 7 noncardiac), early (<2 months) crossover to surgical treatment (2 patients), severe concomitant disease (10 patients) and patient or referring physician refusal of repeat angiographic examination (47 patients). No further contact could be established with the remaining 15 patients (1.6% of all eligible patients). Therefore, 57 of 88 patients without late angiography were clinically followed up; 55 of them remained angina free and 2 had mild angina when evaluated 6 months after the procedure. No patient with severe angina refused to have follow-up angiography.

Coronary restenosis (stenosis >50%) was documented in 277 patients (33% restenosis rate). At that time, 133 patients (48%, group I) were asymptomatic (no episodes of angina during daily activities or exercise test and no new myocardial infarction since the initial procedure), and 144 patients (52%, group II) had recurrence of their symptoms.

Coronary angioplasty. Our angioplasty protocol has been described in detail elsewhere (24,25). In brief, only patients with angina or evidence of ischemia, or both, underwent coronary angioplasty. Angioplasty was performed with the standard technique only in vessels with a severe lesion (lumen narrowing ≥75% by visual assessment) with the consensus of two well trained invasive cardiologists (who did not perform the angioplasty). All patients had successful dilation of at least one of the segments in which angioplasty was attempted (residual stenosis <50%) in the absence of major complications.

At the beginning of the angioplasty procedure, patients received 10,000 IU of intravenous heparin and 0.2 mg of intracoronary nitroglycerin. Subsequently, a continuous heparin infusion was maintained for 24 h. In elective procedures and starting 2 days before angioplasty, patients received oral aspirin (250 mg), nitrates and a calcium channel blocking agent, usually diltiazem, 60 mg three times/day. At discharge, continued treatment with these three drugs was recommended, although referring physicians occasionally discontinued or changed these medications.

Exercise test. All patients in appropriate cardiac and general condition performed a graded (Bruce protocol), symptom-limited treadmill exercise test within a few days of the angioplasty procedure and at the time of the angiographic follow-up. Medication was not discontinued before the test.

Clinical follow-up. At the time of angiographic follow-up and yearly thereafter, patients were interrogated by a physician during a clinic interview about their clinical condition, the medication they were taking and the presence or absence of coronary events (angina, myocardial infarction, repeat angioplasty or surgical revascularization). Patients who failed to comply with their clinic appointments were contacted by telephone and their clinical status noted; they were strongly encouraged to come to the next scheduled clinic appointment. Patients who died were identified either by these follow-up telephone calls to missing patients or by reports from relatives or physicians. No patient with documented restenosis was lost to follow-up.

Angiographic follow-up. Follow-up coronary angiography was performed 6 to 9 months after the procedure or earlier if angina recurred. Assessment of stenosis severity was made by visual estimation with the consensus of two observers who were unaware of the patient's angioplasty result, clinical condition or follow-up exercise test result. Restenosis was diagnosed if stenosis >50% was present in at least one of the previously dilated segments.

After the restenosis diagnosis was made, the decision whether or not to perform repeat angioplasty was made on the basis of clinical and angiographic findings. Symptomatic patients, excluding most of those with an occluded vessel or with a clear preference for surgical revascularization, underwent repeat angioplasty, usually during the same angiographic procedure. Asymptomatic patients without evidence of ischemia during the exercise test were treated medically and later underwent angioplasty only in the case of clinical recurrence. Asymptomatic patients with significant ST segment changes on exercise or a nondiagnostic exercise test were treated on an individual basis, taking into account the patient's age, work and recreational activities and lesion suitability for angioplasty.

Definitions. The following definitions are used. *Stable angina:* exercise-related angina unmodified for at least 1 month. *Unstable angina:* progressive angina, at rest or of recent onset (<1 month). *Recent myocardial infarction:* myocardial infarction <1 month old. *Postinfarction angina:* angina in the 1st month after a new myocardial infarction. *Atypical chest pain:* chest pain with atypical clinical features for angina. *Multivessel disease:* stenosis >50% in more than one major coronary vessel. *Successful angioplasty:* primary success (residual stenosis <50%) in any of the dilated vessels and no major complication. *Complete revascularization:* no stenosis >50% in any major coronary vessel immediately after the angioplasty procedure. *Clinical recurrence:*

Table 1. Baseline Clinical Characteristics of 839 Patients Undergoing Coronary Angioplasty

	Group I (n = 133)	Group II (n = 144)	p Value*	No Restenosis (n = 562)
Age (yr)	60 ± 9	59 ± 10	NS	59 ± 10
Female gender (%)	9	18	<0.05	15
Hypertension (%)	38	56	<0.005	41
Diabetes (%)	19	25	NS	16
Cigarette smoking (%)	78	69	NS	75
High serum cholest (%)	37	37	NS	38
Medication (%)				
Nitrates	88	83	NS	80
Ca antagonists	79	84	NS	81
Beta-blockers	41	47	NS	39
Previous MI (%)	48	28	<0.05	43
Symptom duration (mo)	10 ± 25	23 ± 42	<0.001	20 ± 34
PTCA indication (%)				
Stable angina	27	24	NS	25
Unstable angina	52	66	<0.05	60
Recent MI + angina	11	9	NS	10
Recent MI, no angina	10	1	<0.05	5

*Group I versus group II, univariate analysis. Ca = calcium; cholest = total cholesterol; Group I = asymptomatic restenosis; Group II = symptomatic restenosis; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty.

stable or unstable angina, new myocardial infarction, revascularization surgery or death. *Positive exercise test result:* ≥1 mm horizontal or downward ST segment depression or typical angina, or both, appearing during or immediately after exercise. *Nondiagnostic exercise test result:* no significant ST segment changes in patients who failed to achieve ≥85% of the theoretical maximal heart rate for age. *Negative exercise test result:* no angina or significant ST segment changes and >85% of maximal heart rate achieved. *Elective angioplasty:* angioplasty performed by the time of follow-up angiography in patients with asymptomatic restenosis.

Data management and analysis. Raw data were prospectively introduced in a computer data base (Angiosystem, Seattle Software and Cormedica). Clinical, exercise test and angiographic data are presented as a percent (discontinuous variables) or as mean values ± SD (continuous variables). For statistical analysis, the Student *t* test was used for comparison of continuous variables and the chi-square test for discontinuous variables. Independent correlates of asymptomatic restenosis were determined by using a stepwise logistic regression analysis (SPSS + V 3.1, Microsoft Corp.).

Results

Baseline clinical characteristics of groups I and II (Table 1). For comparison, data from our general population of patients without restenosis are also included in Table 1. Group II (symptomatic group) included more female patients and more patients with hypertension, unstable angina and symptoms of longer duration; previous (including recent) myocardial infarction was more common in group I (asymptomatic) patients. Multivariate analysis identified only the absence of hypertension ($p = 0.001$), the presence of previous myocardial infarction ($p = 0.0002$) and symptoms of shorter dura-

Table 2. Angiographic Data Before and Immediately After Angioplasty

	Group I (n = 133)	Group II (n = 144)	p Value*	No Restenosis (n = 562)
Single-vessel disease (%)	67	55	<0.05	62
LAD dilation (%)	61	66	NS	51
Collateral circulation (%)	25	21	NS	20
Multivessel dilation (%)	17	15	NS	14
Total revascularization (%)	74	63	<0.05	70
LVEF (%)	63 ± 7	65 ± 8	NS	63 ± 13
Stenosis severity (%)				
Before angioplasty	90 ± 15	90 ± 17	NS	88 ± 8
After angioplasty	22 ± 12	24 ± 16	NS	25 ± 17

*Group I versus group II, univariate analysis. LAD = left anterior descending coronary artery; LVEF = left ventricular ejection fraction. Other abbreviations and definitions as in Table 1.

Table 3. Exercise Test Results at Discharge After Coronary Angioplasty*

	Group I	Group II	No Restenosis
Patients	115 (86%)	130 (90%)	495 (88%)
METs	9.7 ± 2	9.5 ± 2	9.4 ± 4
HR (beats/min)	138 ± 24	136 ± 17	138 ± 20
Angina	0	5 (4%)	5 (1%)
ST segment changes	17 (15%)	20 (15%)	90 (18%)

*p = NS, group I versus group II, univariate analysis. HR = heart rate; METs = metabolic exercise equivalents. Other abbreviations and definitions as in Table 1.

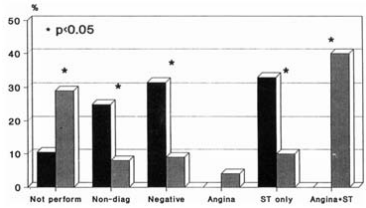

Figure 1. Exercise test results at the time of angiographic follow-up in 277 asymptomatic **(solid bars)** and symptomatic **(hatched bars)** patients. Non-diag = nondiagnostic; Not perform = not performed.

tion (p = 0.003) as independent correlates of the asymptomatic status in patients with coronary restenosis.

Angiographic data before and immediately after angioplasty (Table 2). Group I patients more frequently had single-vessel disease and complete revascularization at the initial angioplasty procedure. On multivariate analysis, only the presence of single-vessel coronary artery disease was found to be an independent correlate of asymptomatic restenosis (p = 0.04). There were no differences between groups in the presence of collateral circulation before the procedure, the rate of multivessel dilation, the left ventricular ejection fraction or stenosis severity before or after angioplasty. For comparison, data concerning our population of patients without restenosis are also included in Table 2.

Exercise test at discharge (Table 3). No significant differences between the two groups were found in exercise capacity, maximal heart rate obtained or exercise-induced ST segment changes. Five patients (4%) in group II had angina that was mild in all cases and considered not to limit patient lifestyle.

Clinical status at the time of angiographic follow-up. By definition, at the time of late angiography (6 to 9 months after angioplasty) all group I patients were, and had been, asymptomatic since the procedure. Patients with chest pain that was atypical, or different from that before angioplasty, were included in the symptomatic group. Group II patients presented with stable angina (n = 49, 34%), unstable angina (n = 69, 48%), acute myocardial infarction (n = 1, 0.7%) or atypical chest pain (n = 25, 7.3%), and at the time of follow-up angiography they were more frequently receiving nitrates (74% vs. 56%, p < 0.05) or a beta-adrenergic blocking agent (16% vs. 8%, p < 0.05) than were group I patients. A similar percent of patients were receiving a calcium channel antagonist (90% of symptomatic and 87% of asymptomatic patients, p = NS).

Exercise test at the time of angiographic follow-up (Fig. 1). Asymptomatic patients exercised more (9.8 ± 2.7 vs. 7.7 ± 3 metabolic exercise equivalents [METs], p < 0.05), achieved a faster heart rate (140 ± 21 vs. 127 ± 23 beats/min, p < 0.025) and had exercise-induced significant ST segment changes less frequently (37% vs. 71% of patients able to perform the test, p < 0.05).

Of 133 asymptomatic patients, 14 (10.5%) were not able to perform the test (because of age >80 years in 3 patients, severe claudication in 2 and invalidating noncardiac disease in 9); in 33 (25%) the test was nondiagnostic, in 42 (31.5%) it was negative and in 44 (33%) there were significant ST changes. Maximal ST depression was <2 mm in 31 (70.5%) of the 44 patients with a positive test, 2 to 3 mm in 8 patients and >3 mm in 5 patients. Significant ischemic changes appeared before 5 METs in only three patients and between 5 and 8 METs in four additional patients. Seventeen (38%) of the 44 asymptomatic patients with a positive exercise test already had significant ST depression on the predischarge exercise test performed a few days after the initial angioplasty procedure. Only 102 (71%) of 144 symptomatic patients performed the exercise test compared with 119 (89.5%) of 133 asymptomatic patients (p < 0.05). In 30 of 42 patients the test was not performed because it was considered too high a risk in the setting of unstable angina. Most of the 49 patients with stable angina had a positive test (40 of 44, 91% of those who performed the test). Of the 69 patients with unstable angina, only 38 (55%) performed the test and in all but 5 patients (94%) the test result was positive. By contrast, only 7 (33%) of 20 patients with atypical chest pain who performed the test had significant ST segment changes, whereas 7 had a negative and 5 a nondiagnostic test result.

Late follow-up angiographic data (Fig. 2). Follow-up angiography was performed a mean of 7.1 ± 1.5 months after initial angioplasty in group I patients and 5.2 ± 3.1 months in group II patients (p < 0.05). Mean stenosis was less severe in asymptomatic (group I) than in symptomatic (group II) patients (79 ± 15% vs. 86 ± 11%, p < 0.05). Total occlusion of the restenotic vessel was present in 19% and 12% of group I and II patients, respectively (p = NS). Excluding patients with an occluded vessel, 40% of asymptomatic versus 9% of symptomatic patients had moderate (>50% and <75%, respectively) stenosis (p < 0.05).

Collateral circulation was evident in a similar percent of patients in both groups (37 [28%] of 133 asymptomatic patients and 35 [24%] of 144 symptomatic patients [p = NS]).

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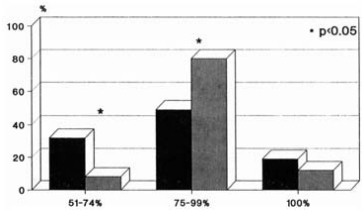

Figure 2. Stenosis severity at the time of angiographic follow-up in asymptomatic (**solid bars**) and symptomatic (**hatched bars**) patients.

Nevertheless, in the subgroup of patients with ≥90% stenosis, collateral circulation was more frequently seen in asymptomatic patients than in their symptomatic counterparts (33 of 48 [69%] and 30 of 60 [50%], respectively) (p = NS).

Long-Term Follow-Up

Asymptomatic patients. Of the 133 asymptomatic patients, 18 (15 with exercise-induced ST segment changes and 3 with a nondiagnostic test result) underwent "elective" repeat angioplasty of the restenotic vessel and none had a recurrence of stenosis. The remaining 115 patients were medically treated. After a mean follow-up interval of 17.1 ± 13 months, 15 of 115 patients had a recurrence of angina, and in 11 (10%) recurrence was thought to be due to the restenotic vessel. The recurrence rate was 9.5% (4 of 42) for patients with a negative exercise test result and 21% (6 of 29) for those with exercise-induced ST changes. Six of the 11 patients with a recurrence of angina underwent repeat angioplasty of the restenotic vessel, and the remaining 5 patients with symptoms thought to originate in the restenotic vessel (2 with total occlusion) did well after antianginal medication was increased. No patient died or required coronary artery bypass grafting.

Symptomatic patients. The 49 patients with stable angina underwent either repeat angioplasty (25 patients, 51%) or revascularization surgery (4 patients, 8%) or were treated with an increase in antianginal medication only (20 patients, 41%). Three patients died, two from the medically treated group (one suddenly and the other of congestive heart failure); the third patient died of postoperative complications after coronary revascularization surgery.

Fifty of 69 patients who presented with unstable angina underwent repeat angioplasty (86% of patients with a patent vessel), 7 (10%) had revascularization surgery and 12 (17%) received antianginal drugs only. Two surgical patients died in the postoperative period.

One patient presented with acute myocardial infarction and died of cardiogenic shock a few hours later after a technically successful emergency angioplasty. All patients with atypical chest pain were event free during follow-up, either with (n = 6) or without (n = 19) elective angioplasty.

In summary, 6 patients (4%) died (1 of acute myocardial infarction, 1 suddenly, 1 of congestive heart failure, 3 of complications related to surgery), 11 (8%) were operated on and 81 (56%) had repeat angioplasty.

Discussion

Asymptomatic coronary restenosis. As confirmed by our study, restenosis after successful coronary angioplasty is not necessarily associated with recurrence of angina, and many patients with restenosis remain asymptomatic. The absence of symptoms in patients with angiographically proved restenosis is associated with a good prognosis, and it occurs more frequently in patients with a normal blood pressure, previous myocardial infarction and a short-term history of angina at the time of angioplasty. Restenosis in this subgroup of patients is also relatively less severe than in patients with recurrent angina.

Because asymptomatic patients tend to have a lower recatheterization rate than do symptomatic patients, an almost complete angiographic follow-up is mandatory to accurately assess the incidence of this phenomenon. The present study, with a high angiographic follow-up rate, constitutes a large series of consecutive patients with restenosis without symptoms. Although most previous studies have reported an incidence rate of asymptomatic restenosis of 24% to 33%, in our study up to 48% of patients with restenosis remained free of angina. Table 4 summarizes the incidence of asymptomatic restenosis reported by several investigators.

Factors influencing the rate of silent restenosis. Several factors influence the rate of silent restenosis. These include:

1. *Definition of restenosis.* The percent of coronary stenosis that more accurately defines the physiologic relevance of a lesion remains to be determined (26–29), but it has been estimated that many lesions >50% and most lesions >70% might eventually cause ischemia. Consequently, several percent values have been used to define restenosis after successful coronary angioplasty (1,5). The definition of restenosis used in the present study (>50% narrowing of lumen diameter) is probably the most frequently used (4,5,8,11).

2. *Method used for quantification of stenosis severity* (visual or caliper assessment versus fully automatic angiographic quantification). Visual assessment, in addition to the well known intra- and interobserver variability, tends to overestimate severe stenosis and to underestimate mild lesions in comparison with results of quantitative analysis (30–32), but whether quantitative analysis better predicts the clinical significance of a coronary restenosis has not yet been established.

3. *Accuracy of the term asymptomatic.* To rule out a sedentary lifestyle or underestimation of symptoms by the

Table 4. Previous Reports on Asymptomatic Restenosis

First Author (ref. no.)	Ang FU (%)	Definition of Restenosis	Restenosis [No. (%)]	AR (%)	Method	Time After PTCA (mo)
Holmes (1)	84	Loss of 50% gain	187 (34%)	24	Visual	6
Levine (6)	92	Loss of 50% gain	37 (40%)	5	Visual	1–11
Ventrovec (8)	—	>50%	237 (—)	33	Visual	>4
Popma (11)	100	>50%	31 (34%)	32	Caliper	3
Present study	92	>50%	277 (30%)	48	Visual	6–9

Ang FU = angiographic follow-up rate; AR = asymptomatic restenosis rate; Loss of 50% gain = >50% loss of the previous gain in lumen diameter obtained with coronary angioplasty; Method = method for assessment of stenosis severity; Ref. = reference. Other abbreviations as in Table 1.

patient as potential causes of the absence of angina, we only considered that a patient was asymptomatic after no chest pain was reported during the treadmill exercise test, which was performed in 89.5% of the asymptomatic patients.

4. *Patient medication.* Antianginal drugs relieve angina, and some patients may eventually become asymptomatic while receiving them. Most of the patients in our study were, from angioplasty to follow-up angiography, receiving two, and some were receiving three, antianginal drugs. This factor may strongly influence symptomatic status.

5. *Patient baseline characteristics.* In general, patients with more extensive and severe coronary artery disease tend to be more symptomatic. In our study, 38% of patients with restenosis had multivessel disease, a percent similar to that of many other angioplasty series and a good representation of the current coronary angioplasty population.

Other independent correlates of restenosis. The absence of systemic high blood pressure and the presence of single-vessel disease and of a previous myocardial infarction were independent correlates of asymptomatic restenosis in the present series. Although it is not clear why patients with systemic high blood pressure tend to be more symptomatic should restenosis occur, it seems reasonable that an increase in cardiac mass will unfavorably affect the balance of myocardial need and supply (33,34). The absence of angina in patients with severe coronary lesions perfusing infarcted areas is a well known phenomenon. Although the rate of previous myocardial infarction in our study patients undergoing coronary angioplasty was similar to that of other angioplasty series (1,3,4), it was higher in asymptomatic than in symptomatic patients. In 50% of the patients with a previous infarction, the event was recent (within 1 month after infarction). Even though it is our current practice to perform angioplasty after recent myocardial infarction only in patients with angina or with evidence of exercise-induced ischemia, or both, some patients may have had, at the time of the initial angioplasty procedure, nonviable myocardium that was being perfused by the dilated vessel. In addition, it is not surprising that in asymptomatic patients single-vessel disease was more common and complete revascularization was obtained more frequently with angioplasty.

Concerning asymptomatic patients with restenosis, the most clinically relevant question to be answered is whether they have silent or no ischemia at all. Ischemia may be absent if coronary flow (either anterograde or by collateral circulation) meets myocardial metabolic requirements, even during exercise. Asymptomatic patients tended to have milder stenosis, as has previously been reported (8–11). Up to 32% of our patients had moderate (<75%) stenosis at the time of restenosis diagnosis. Therefore, it is possible that some patients with restenosis would not have been classified as having restenosis if another definition or quantification method had been used. Although Popma et al. (11) reported that 55% of asymptomatic patients had collateral circulation compared with 10% of symptomatic patients, we did not find a significant difference in collateral circulation between the two groups, even when patients with more severe stenosis were separately analyzed.

Role of exercise testing. Silent ischemia is frequent in patients with coronary artery disease (12–22), either alone or coexisting with painful episodes. In one-third of our asymptomatic patients and in 21% to 41% of those reported by others (10,35,36), there was evidence of painless, exercise-induced significant ST segment changes. Because the ECG exercise test has a limited sensitivity (approximately 50%) in patients with single-vessel disease (37–39), as observed in 67% of our asymptomatic patients, and test sensitivity may even be decreased by antianginal medication (37), at least some patients with significant stenosis would be expected to have a false negative or a nondiagnostic test. Another exercise test after drug withdrawal, performed with or without thallium scintigraphy, might have improved the sensitivity of the test for detecting ischemia (36,40,41). The specificity of an ECG exercise test is also limited, even in patients with known coronary artery disease (37–39), and false positive results are not uncommon in female or hypertensive patients. It should be remarked that 50% of our asymptomatic patients with a positive exercise test, most of them with complete revascularization, had already exhibited significant ST changes during the predischarge exercise test performed a few days after angioplasty. In some patients, ST changes may be due to coronary disease in one or more additional vessels, but in others the test is more likely to be false positive (42–47).

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Role of coronary angiography and indications for repeat angioplasty. Midterm prognosis of patients with asymptomatic restenosis was relatively good (11.3% recurrence rate after a mean follow-up interval of 17 months) and quite similar to the rate of 5% of patients per year reported elsewhere (9,36). The recurrence rate of angina related to the restenosed vessel was 9.5% for patients with a negative exercise test result and 21% for those with exercise-induced ST segment changes. Such a good prognosis supports the general practice of not performing routine coronary angiography in asymptomatic patients without evidence of ischemia. Nevertheless, in our experience, asymptomatic patients with restenosis and evidence of ischemia during exercise testing have a twofold angina recurrence rate, as has been previously reported (9,36), and should probably undergo a repeat angiographic examination to document restenosis or progression in coronary artery disease, or both.

Whether these patients should also undergo repeat angioplasty of the restenosed vessel (48) or should be conservatively managed cannot be determined from our study, because only 5% of patients initially treated medically eventually underwent repeat angioplasty for angina. The usefulness of elective angioplasty is supported by the absence of recurrent symptoms in all 15 patients with a positive exercise test result who underwent elective angioplasty at the time of restenosis documentation and by the presence of angina on midterm follow-up in 21% of those who did not undergo angioplasty. Even if angioplasty can be safely deferred until recurrence of angina (no patient died or had a myocardial infarction related to the dilated vessel), the cost of another procedure and the eventual need for hospital admission should be taken into consideration at the time of restenosis documentation.

Limitations of the study. Although the use of visual assessment to estimate stenosis severity may be a limitation of the study, the conclusions drawn from it will still apply to restenosis diagnosed by visual assessment, the most frequently used method worldwide. A thallium perfusion study, in addition to the ECG, might have improved the sensitivity and specificity of the exercise test to detect the presence of ischemia. Nevertheless, a simple ECG exercise test is the technique most frequently used to evaluate patients with previous angioplasty, and our results should prove useful in the decision-making process involved in managing patients with restenosis evaluated in this conventional way.

Conclusions. The lack of symptoms in patients who have documented restenosis while receiving antianginal medication is a frequent phenomenon (48% in our study). Patients with single-vessel disease, previous myocardial infarction and complete revascularization at angioplasty are more frequently asymptomatic should restenosis occur. Mild restenosis, dilation of a vessel perfusing nonviable myocardium, collateral circulation and silent ischemia are potential mechanisms to explain the asymptomatic status of these patients with documented restenosis. Although the overall prognosis is relatively good, patients with asymptomatic restenosis and a positive exercise test result are at higher risk for recurrence of angina. The potential role of repeat elective angioplasty in patients with asymptomatic restenosis remains to be defined.

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