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Predictors of Restenosis After Coronary Stent Implantation

CHRISTOPHE BAUTERS, MD, FACC,* EDOUARD HUBERT, MD,* ALAIN PRAT, MD,* KARIM BOUGRIMI, MD,* ERIC VAN BELLE, MD,* EUGÈNE P. MCFADDEN, MRCPI, FACC,* PHILIPPE AMOUYEL, MD,*† JEAN-MARC LABLANCHE, MD, FACC,* MICHEL BERTRAND, MD, FACC*

Lille, France

Objectives. **We sought to determine predictors of restenosis after coronary stenting (CS) in a consecutive series of patients.**

Background. **Although stenting in highly selected patient groups reduces restenosis, the results of stenting in a heterogeneous patient group and the effects of clinical and procedural factors on stent restenosis are currently unclear.**

Methods. **We analyzed the 6-month angiographic outcome of 500 lesions in 463 consecutive patients undergoing successful CS. Clinical, qualitative and quantitative angiographic variables were correlated with restenosis assessed as both a binary and a continuous variable.**

Results. **Restenosis, defined as the presence of >50% diameter stenosis in the dilated segment, was present in 105 (26%) of the 405 lesions with angiographic follow-up. The mean late lumen loss during the follow-up period was 0.79 ± 0.64 mm. Implantation of multiple stents ($p < 0.0001$) and a high acute gain ($p < 0.0002$) were independently associated with a higher late lumen loss. In contrast, the use of high inflation pressure ($p < 0.02$) and Palmaz-Schatz stents ($p < 0.005$) was independently associated with a lower late lumen loss. When restenosis was defined as a qualitative variable, implantation of multiple stents ($p < 0.001$), stenosis length ($p < 0.01$), small reference diameter ($p < 0.02$) and stent type other than Palmaz-Schatz ($p < 0.01$) were independent predictors of restenosis. None of the clinical variables tested was associated with restenosis.**

Conclusions. **Coronary stenting in an unselected patient group is associated with an acceptable restenosis rate. Although some risk factors were identified, the risk of restenosis was not related to most of the variables tested. This suggests that the superiority of CS over balloon angioplasty, in terms of restenosis, might also apply to subgroups of patients that were not included in the recent randomized studies.**

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Balloon angioplasty (BA) has become an established treatment for patients with coronary artery disease (CAD) but remains plagued by the problem of restenosis (1,2). This has provided the impetus for the development of newer alternative forms of coronary revascularization such as coronary stenting (CS). Follow-up studies after CS have demonstrated relatively low rates of angiographic and clinical restenosis (3–6). Furthermore, two recent randomized studies have shown that CS is associated with a significant reduction in the restenosis rate when compared with BA (7,8); however, these two studies were performed in highly selected study groups. Subsequent insights from intracoronary ultrasound studies in humans have demonstrated different mechanisms of restenosis after BA or after CS: although chronic remodeling (vessel constriction) is the major mechanism of restenosis after BA (9), neointimal thickening is the major mechanism of restenosis after CS, as the stent prevents the remodeling process (10).

Recent improvements in the technique of stent implantation and in antithrombotic regimens have allowed CS to be performed in a high proportion of patients undergoing repeat percutaneous transluminal coronary angioplasty (PTCA) (11,12). CS has been reported in rescue situations (13), in smaller vessels (<3 mm) (14), in diabetic patients (15), in infarct-related lesions (16,17) and for the treatment of chronic coronary occlusions (18). Most of these situations have been associated with high rates of restenosis after BA (19–24); however, data on their impact on restenosis after CS are still sparse (4,5,25,26).

The present study was thus designed to analyze the 6-month angiographic outcome of 500 lesions in 463 consecutive patients undergoing successful CS. Using quantitative angiographic techniques, we determined both the rate and the predictors of in-stent restenosis.

Methods

Study group. Between October 1993 and March 1996, 463 consecutive patients underwent successful CS at the Cardiology Hospital, Lille. Using standard, previously described techniques (11), CS was performed in 500 lesions in these 463 patients. All patients received antiplatelet therapy. Aspirin

From the *University of Lille and Centre Hospitalier Regional et Universitaire and †INSERM CJF 95-05, Institut Pasteur, Lille, France.

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Address for correspondence: Dr. Michel Bertrand, Service de Cardiologie B, Hôpital Cardiologique, Boulevard du Professeur J. Leclercq, 59037 Lille Cedex, France. E-mail: bertrandme@aol.com.

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Abbreviations and Acronyms

ACC = American College of Cardiology
AHA = American Heart Association
BA = balloon angioplasty
CAD = coronary artery disease
CS = coronary stenting
LAD = left anterior descending coronary artery
MLD = minimal lumen diameter
PTCA = percutaneous transluminal coronary angioplasty
TIMI = Thrombolysis in Myocardial Infarction trial

(100 to 300 mg/day) was started at least 24 h before CS and continued indefinitely. Ticlopidine (500 mg/day) was started immediately after CS and continued for 6 weeks. CS was performed as a bail-out procedure after failed BA, if there was a suboptimal result after BA or electively. If a single stent did not entirely cover the lesion, two or three overlapping stents were implanted. The most frequently used stents were the 14-mm, nonarticulated, Palmaz-Schatz stent (PS 154A) and the 16-mm Wiktor stent. Other stents were used in only 7% of lesions. The procedure was considered successful when the residual lumen narrowing immediately after stent implantation, estimated visually, was <30% and when no major complication (electrocardiographic or enzymatic evidence of myocardial infarction, need for coronary artery bypass surgery during the hospital period or in-hospital death) occurred. At the time of stenting, all the patients were asked to return for a 6-month follow-up angiogram, regardless of symptomatic status; angiography was performed earlier if clinically indicated. Angiographic follow-up was performed at a mean of 5.8 ± 1.8 months after CS in 374 patients (405 lesions [81%]).

Angiographic analyses. Qualitative analyses were performed independently by two experienced interventional cardiologists. Disagreements were resolved by a further joint reading. Lesions were classified in accordance with the American Heart Association/American College of Cardiology (AHA/ACC) classification, as modified by Ellis et al. (27). Anterograde blood flow was graded using the Thrombolysis in Myocardial Infarction (TIMI) trial classification (28).

Quantitative computer-assisted angiographic measurements were performed on end-diastolic frames with use of the Computer-Assisted Evaluation of Stenosis And Restenosis (CAESAR) system. A detailed description of this system has been reported previously (29). We routinely perform angiography in at least two projections after intracoronary injection of isosorbide dinitrate (2 mg). These projections are recorded in our data base, and follow-up angiography is performed, after injection of isosorbide dinitrate, in the same projections. The following definitions were used: early gain associated with the procedure was defined as the difference between the minimal lumen diameter (MLD) immediately after the procedure and the MLD before the procedure; late loss during the follow-up period was defined as the difference between the MLD immediately after the procedure and the MLD at follow-up; net gain was defined as the difference between the early gain and the late loss; and restenosis was defined as >50% diameter stenosis at follow-up.

Table 1. Baseline Characteristics: Patient-Related Variables (n = 374)

Age (years)	59 ± 11
Males	322 (86%)
Diabetes mellitus	72 (19%)
Smoker	264 (71%)
Hypertension	142 (38%)
Hypercholesterolemia	222 (59%)
Family history of CAD	185 (49%)
Unstable angina	134 (36%)

Data presented are mean value ± SD or number (%) of patients. CAD = coronary artery disease.

Statistical analysis. Data are presented as the mean value ± SD. For the univariate analysis, continuous variables were divided into tertiles. Comparisons between groups for continuous data were made using the Student *t* test or analysis of variance followed by the Scheffé F test. Differences between proportions were assessed by chi-square analysis. A value of $p < 0.05$ was considered to indicate statistical significance. Multivariate analysis was performed with SAS software (version 6.10; SAS Institute Inc.). To study the relation between a binary outcome variable and multiple categoric and continuous determinants, multiple logistic regression analysis was performed. To study the relation between continuous outcome variables and multiple categoric and continuous determinants, multiple linear regression was done.

Results

Baseline characteristics. Tables 1 and 2 list the baseline characteristics of the study group. Most of the patients were men (mean [±SD] age 59 ± 11 years). Nineteen percent of the patients were diabetics; 36% had CS for unstable angina. The dilated lesion was located in the left anterior descending coronary (LAD) in 50% of lesions. Twenty percent of the lesions were restenotic lesions after BA and 28% were the site of a recent (<1 month) myocardial infarction. A large variety of the lesions, in terms of morphologic characteristics, are shown in Table 2.

CS was performed as a bail-out procedure after failed BA in 14% of patients, because of a suboptimal result after BA in 65% and electively in 21%. Palmaz-Schatz stents were used in most patients (61%). In 85% of patients, a single stent was used. High pressure inflation (>12 atm) was used to deploy the stent in most patients (mean inflation pressure 15 ± 3 atm).

Clinical follow-up. Table 3 shows the major cardiac events during the 6-month follow-up period in the 463 patients who had successful stent implantation. Seven patients died, four had a myocardial infarction, 71 underwent a repeat revascularization procedure (bypass surgery in 2 and PTCA in 69).

Table 2. Baseline Characteristics: Lesion (n = 405) and Procedure-Related Variables

Dilated site	
LAD	203 (50%)
LCx	49 (12%)
RCA	128 (32%)
Saphenous vein graft	25 (6%)
Previous PTCA at same site	80 (20%)
Infarct-related lesion	112 (28%)
ACC/AHA classification*	
A	38 (9%)
B1	105 (26%)
B2	204 (50%)
C	58 (14%)
TIMI flow grade	
0–1	54 (13%)
2	28 (7%)
3	323 (80%)
Calcification	125 (31%)
Eccentric stenosis	183 (45%)
Lesion length (mm)	8.8 ± 5.8
Bifurcation lesion	87 (22%)
Bend location	65 (16%)
Thrombus	73 (18%)
Stent indication	
Rescue	55 (14%)
Suboptimal result	264 (65%)
Elective	86 (21%)
Type of stent	
Palmaz-Schatz	245 (61%)
Wiktor	131 (32%)
Gianturco-Roubin	15 (4%)
Angiostent	6 (1%)
Bard XT	5 (1%)
ACS Multilink	1
NIR Stent	1
Wallstent	1
No. of stents/lesion	1.2 ± 0.4
Inflation pressure (atm)	15 ± 3

*Modified by Ellis et al. (27). Data presented are number (%) of lesions or mean value ± SD. ACC/AHA = American College of Cardiology/American Heart Association; LAD = left anterior descending coronary artery; LCx = left circumflex artery; PTCA = percutaneous transluminal coronary angioplasty; RCA = right coronary artery; TIMI = Thrombolysis in Myocardial Infarction.

Early angiographic results and 6-month angiographic follow-up. The lumen dimensions at baseline, immediately after the procedure and at follow-up are shown in Table 4 and

Table 3. Major Cardiac Events During 6-Month Follow-Up in 463 Patients With Successful Coronary Stenting

Event	<30 Days	>30 Days	Total
Death	1 (0.2%)	6 (1.3%)	7 (1.5%)
MI	2 (0.4%)	2 (0.4%)	4 (0.8%)
Bypass surgery	0	2 (0.4%)	2 (0.4%)
Repeat PTCA			
Target site	2 (0.4%)	67 (14.5%)	69 (14.9%)
Other site	0	30 (6.5%)	30 (6.5%)
Any event	5 (1.1%)	104 (22.5%)	109 (23.5%)

Data presented are number (%) of patients. MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty.

Table 4. Acute Results and 6-Month Follow-Up (405 lesions)

Reference diameter (mm)	
Before	3.04 ± 0.50
After	3.03 ± 0.50
Follow-up	3.03 ± 0.49
Minimal lumen diameter (mm)	
Before	0.78 ± 0.45
After	2.57 ± 0.43
Follow-up	1.78 ± 0.70
Percent diameter stenosis	
Before	73 ± 15
After	10 ± 10
Follow-up	37 ± 22
Acute gain (mm)	1.80 ± 0.56
Late loss (mm)	0.79 ± 0.64
Net gain (mm)	1.01 ± 0.76
Restenosis rate*	105 (26%)
Total occlusion at follow-up	6 (1.5%)

*Diameter stenosis >50% at follow-up. Data presented are mean value ± SD or number (%) of lesions.

Figure 1. CS was associated with an immediate increase in mean MLD, from 0.78 ± 0.45 to 2.57 ± 0.43 mm. Mean percent diameter stenosis decreased from 73 ± 15% to 10 ± 10%. At follow-up angiography, the mean MLD had decreased to 1.78 ± 0.70 mm, and mean percent stenosis had increased to 37 ± 22%. Restenosis, defined as the presence of >50% diameter stenosis in the dilated segment at follow-up, was present at 105 (26%) of the 405 lesions with angiographic follow-up. Of these 105 lesions, 6 (1.5% of the lesions with follow-up angiography) were totally occluded at follow-up.

Predictors of in-stent restenosis. The univariate predictors of in-stent restenosis are shown in Tables 5 to 7. We analyzed both the predictors of lumen narrowing, assessed as a continuous variable (late lumen loss), and the predictors of qualita-

Figure 1. Cumulative distribution curves of MLD at baseline (Pre), immediately after stent implantation (Post) and at 6-month follow-up (F-up).

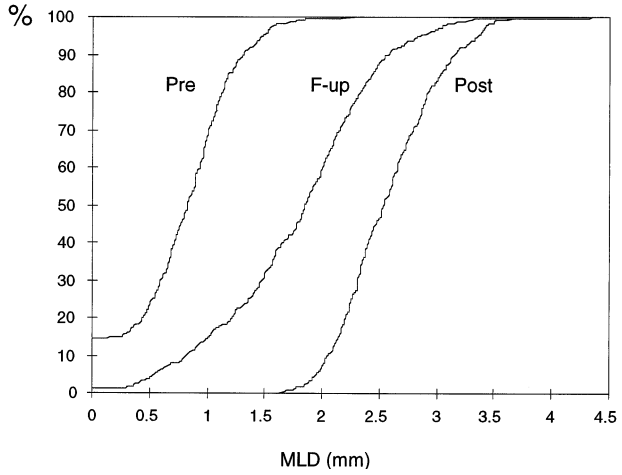

Table 5. Univariate Predictors of Restenosis: Clinical Variables

	Late Loss (mm)*	Restenosis Rate†
Age (yr)		
<53 (n = 129)	0.79 ± 0.61	26%
53–64 (n = 139)	0.84 ± 0.65	27%
>64 (n = 137)	0.75 ± 0.65	25%
Men (n = 350)	0.78 ± 0.64	26%
Women (n = 55)	0.86 ± 0.60	27%
Diabetes mellitus		
Yes (n = 81)	0.82 ± 0.74	26%
No (n = 324)	0.79 ± 0.61	26%
Smoker		
Yes (n = 286)	0.80 ± 0.64	28%
No (n = 119)	0.77 ± 0.63	22%
Hypertension		
Yes (n = 155)	0.81 ± 0.67	30%
No (n = 250)	0.79 ± 0.62	24%
Hypercholesterolemia		
Yes (n = 244)	0.75 ± 0.64	25%
No (n = 161)	0.86 ± 0.64	27%
Family history of CAD		
Yes (n = 198)	0.81 ± 0.66	27%
No (n = 207)	0.78 ± 0.62	25%
Unstable angina		
Yes (n = 145)	0.78 ± 0.66	27%
No (n = 260)	0.80 ± 0.63	25%
Infarct-related lesion		
Yes (n = 112)	0.86 ± 0.62	27%
No (n = 293)	0.77 ± 0.64	26%
Previous PTCA at same site		
Yes (n = 80)	0.82 ± 0.60	31%
No (n = 325)	0.79 ± 0.64	25%

*Mean value ± SD. †Diameter stenosis >50% at follow-up. Abbreviations as in Tables 1 and 3.

Table 6. Univariate Predictors of Restenosis: Lesion-Related Variables

	Late Loss (mm)*	Restenosis Rate†
Dilated site		
LAD (n = 203)	0.76 ± 0.55	25%
LCx (n = 49)	0.90 ± 0.73	39%
RCA (n = 128)	0.81 ± 0.66	24%
Saphenous vein graft (n = 25)	0.78 ± 0.93	20%
ACC/AHA classification‡		
A (n = 38)	0.80 ± 0.58	18%
B1 (n = 105)	0.78 ± 0.62	25%
B2 (n = 204)	0.76 ± 0.63	25%
C (n = 58)	0.93 ± 0.71	34%
TIMI flow grade		
0–1 (n = 54)	0.81 ± 0.69	24%
2 (n = 28)	0.74 ± 0.79	32%
3 (n = 323)	0.80 ± 0.62	26%
Calcification		
Yes (n = 125)	0.72 ± 0.59	24%
No (n = 280)	0.83 ± 0.65	27%
Eccentric stenosis		
Yes (n = 183)	0.77 ± 0.81	25%
No (n = 222)	0.81 ± 0.62	27%
Lesion length (mm)		
<6 (n = 139)	0.61 ± 0.58§	14%§
6–10 (n = 166)	0.86 ± 0.66§	30%§
>10 (n = 100)	0.93 ± 0.68§	37%§
Bifurcation lesion		
Yes (n = 87)	0.80 ± 0.57	33%
No (n = 318)	0.79 ± 0.66	24%
Bend location		
Yes (n = 65)	0.88 ± 0.72	34%
No (n = 340)	0.78 ± 0.62	24%
Thrombus		
Yes (n = 73)	0.84 ± 0.64	26%
No (n = 332)	0.78 ± 0.62	26%
Reference diameter (mm)		
<2.8 (n = 137)	0.73 ± 0.60	28%
2.8–3.2 (n = 127)	0.79 ± 0.61	24%
>3.2 (n = 139)	0.85 ± 0.69	25%
Diameter stenosis before procedure		
<65% (n = 122)	0.69 ± 0.50	20%
65–75% (n = 136)	0.80 ± 0.67	27%
>75% (n = 147)	0.88 ± 0.69	30%

*Mean value ± SD. †Diameter stenosis >50% at follow-up. ‡Modified by Ellis et al. (27). §$p < 0.0001$. Abbreviations as in Table 2.

tive restenosis, defined as >50% diameter stenosis at follow-up.

None of the clinical variables studied were associated with increased late lumen loss or increased restenosis rate (Table 5). In particular, diabetes, unstable angina and CS of an infarct-related lesion were not associated with higher restenosis rates. The outcome at follow-up angiography was also similar for CS performed for a restenotic lesion or for a de novo lesion.

Except for stenosis length, none of the lesion-related variables listed in Table 6 were associated with an increased late lumen loss in MLD or an increased risk of restenosis. Factors such as stenosis location, TIMI flow grade before intervention or the angiographic characteristics of the lesion did not affect the risk of restenosis. Although there was a trend toward a higher late loss in MLD and a higher risk of restenosis in patients with more severe stenoses before CS, these differences did not reach statistical significance.

As shown in Table 7, the implantation of multiple stents in the same vessel, a high early gain and a low residual stenosis after CS were significantly associated with an increased late loss in MLD. The sole procedural factor significantly associated with a higher rate of qualitative restenosis was the implantation of multiple stents.

The results of multivariate analysis are shown in Tables 8 and 9. Implantation of multiple stents and a high early gain were independently associated with a higher late late loss in MLD. The use of high inflation pressure and Palmaz-Schatz stents was independently associated with a lower late loss in MLD. When restenosis was defined as a qualitative variable, implantation of multiple stents, stenosis length, small refer-

Table 7. Univariate Predictors of Restenosis: Procedural Variables

	Late Loss (mm)*	Restenosis Rate†
Stent indication		
Bail-out (n = 55)	0.77 ± 0.62	29%
Suboptimal result (n = 264)	0.81 ± 0.64	26%
Elective (n = 86)	0.76 ± 0.66	23%
Type of stent		
Palmaz-Schatz (n = 245)	0.73 ± 0.61	22%
Wiktor (n = 131)	0.85 ± 0.64	31%
No. of stents		
1 (n = 343)	0.74 ± 0.62‡	22%‡
2 (n = 51)	1.02 ± 0.62‡	39%‡
3 (n = 11)	1.46 ± 0.66‡	72%‡
Inflation pressure (atm)		
<14 (n = 88)	0.92 ± 0.73	31%
14–16 (n = 202)	0.77 ± 0.62	25%
>16 (n = 98)	0.70 ± 0.58	22%
Acute gain (mm)		
<1.5 (n = 138)	0.62 ± 0.52§	26%
1.5–2 (n = 136)	0.86 ± 0.63§	29%
>2 (n = 130)	0.91 ± 0.71§	22%
% DS after stenting		
<5% (n = 143)	0.83 ± 0.64‖	20%
5–15% (n = 147)	0.88 ± 0.68‖	30%
>15% (n = 115)	0.64 ± 0.55‖	29%

*Mean value ± SD. †Diameter stenosis (DS) >50% at follow-up. ‡$p < 0.0001$. §$p < 0.001$. ‖$p < 0.01$.

ence diameter and stent type other than Palmaz-Schatz were independent predictors of restenosis (Table 9).

Discussion

The use of CS has increased dramatically in the past few years. Recent studies, performed in highly selected patient groups, have shown that the risk of restenosis is reduced but not abolished after CS (7,8). Identification of risk factors for in-stent restenosis, as well as comparison with the risk factors for restenosis after BA, may provide a better understanding of the potential of CS to treat patients with CAD. Indeed, as the mechanisms of restenosis after CS differ from those after BA (9,10), factors that have been associated with high restenosis rates after BA will not necessarily affect restenosis after CS.

Previous studies have already described risk factors for in-stent restenosis (Carrozza et al. [4] used the Palmaz-Schatz stent in 250 patients; Ellis et al. [5] used the Palmaz-Schatz stent in 206 patients; Strauss et al. [25] used the Wallstent in 214 patients; Eeckhout et al. [26] used the Wallstent and Palmaz-Schatz and Wiktor stents in 243 patients; de Jaegere et al. [30] used the Wiktor stent in 91 patients). However, at the time these studies were performed, oral anticoagulant agents were given for at least 2 months after the procedure, the rate of subacute thrombosis was high and the importance of high pressure inflations for adequate stent deployment was not widely appreciated. Recent improvements in the technique of stent implantation and the introduction of new antiplatelet regimens, including ticlopidine, have made CS an extremely safe procedure. Because of these advances and the results of randomized studies comparing CS and BA, CS is now performed in a high proportion of patients undergoing PTCA. The present study, reporting the angiographic follow-up of 463 consecutive patients who had high pressure inflation of balloon-expandable coronary stents and who were treated with a combination of ticlopidine and aspirin, is thus likely to reflect the angiographic outcome in patients undergoing CS in current clinical practise.

Table 8. Multiple Linear Regression for the Dependent Variable of Late Loss

Independent Variable	Coeff	SE	p Value
No. of stents	0.34	0.07	0.0001
Acute gain (mm)	0.21	0.06	0.0002
Palmaz-Schatz stent	−0.18	0.06	0.005
Inflation pressure (atm)	−0.02	0.01	0.02

Coeff = coefficient.

Table 9. Multiple Logistic Regression Analysis for the Dependent Variable of Restenosis*

Independent Variable	Coeff	SE	p Value	OR (95% CI)
No. of stents	0.83	0.26	0.001	2.29 (1.37–3.82)
Palmaz-Schatz stent	−0.68	0.25	0.007	0.50 (0.31–0.83)
Stenosis length (mm)	0.05	0.02	0.008	1.06 (1.01–1.10)
Ref diam (mm)	−0.58	0.26	0.02	0.56 (0.34–0.93)

*Diameter stenosis >50% at follow-up. CI = confidence interval; OR = odds ratio; Ref diam = reference diameter.

Diabetes and other CAD risk factors. Multiple studies have tried to relate coronary risk factors to the occurrence of restenosis after BA. In most of these studies, variables such as hypertension, smoking habits or a family history of CAD were not associated with an increased risk of restenosis. In contrast, diabetes has consistently been reported to be a risk factor for restenosis after BA (19–21). In the present study, none of the clinical variables studied were associated with an increased risk of restenosis after CS.

We observed a similar extent of late loss in MLD and a similar binary restenosis rate in diabetic and nondiabetic patients. These results are concordant with those of most previous reports in which diabetes was not found to be a risk factor for in-stent restenosis (5,31), but differ from those reported by Carrozza et al. (15), who suggested that the restenosis rate was indeed increased in diabetic patients undergoing CS. Differences in study groups may account for this discrepancy; in the study of Carrozza et al., a majority of the diabetic patients underwent CS for saphenous vein graft lesions; in the present study, a majority (94%) of the procedures were performed in native vessels. The reasons for the increased restenosis rate after BA in diabetic patients are unknown. It has been suggested that the degree of neointimal hyperplasia might be greater as a consequence of a stimulatory effect of growth factors such as insulin-like growth factor-1 on

vascular smooth muscle cells (32). Alternatively, it has recently been shown that the specific feature of atherectomy specimens from restenotic lesions retrieved in diabetic patients was not enhanced smooth muscle proliferation but rather a greater fibrotic response that may favor vessel constriction (33). Our results showing that diabetes is not a risk factor for restenosis after CS, a situation in which vessel remodeling is abolished and in which restenosis is mainly the consequence of neointimal hyperplasia, do not support the hypothesis that diabetic patients have an increased proliferative response after arterial injury.

Unstable angina, infarct-related lesions, thrombus-containing lesions and total occlusions. High rates of restenosis have been reported when BA is performed in an unstable setting (e.g., unstable angina, infarct-related vessels) (22,23,34). Similar results have been reported when BA is performed in vessels that are totally occluded before the procedure (24) or in lesions that contain thrombus (35,36). The common feature of these subgroups of patients is the unstable nature of the dilated site or the presence of superimposed residual thrombus after angioplasty, or both (35). The higher rate of restenosis in this setting is, at least in part, related to a higher risk (10% to 20%) of total occlusion at the dilated site during the follow-up period (22,23,35,36).

The present study shows that these patients are not at a higher risk of restenosis after CS. This result is, at least in part, a consequence of the very low rate of total occlusion at the dilated site during the follow-up period. Late total occlusion of the stented segment occurred in only six patients (1.5%). The exact mechanism(s) responsible for the effect of stents on late occlusion are not known but may be related to a consolidation of ruptured atherosclerotic plaques, to an improved early result with better postprocedural flow (which would decrease the risk of thrombosis) or to an antithrombotic effect of ticlopidine. Recent studies have shown that the combination of aspirin and ticlopidine—a potent antiplatelet agent (37)—is very effective in preventing subacute stent thrombosis (12); its effect on late occlusion is unknown.

Restenotic lesions. Repeat BA for early restenosis has been associated with high restenosis rates (38,39). Restenotic lesions have a different substrate from that of primary lesions and may predispose to a higher incidence of a second restenosis. Similarly, previous studies have reported a higher restenosis rate after stenting of restenotic versus de novo lesions (5,31). In contrast, in the present study, lumen narrowing after CS was the same whether or not a previous BA had been performed at the target site. Further randomized studies are needed to demonstrate whether CS is superior to BA for restenotic lesions.

Lesion location and angiographic characteristics. As in previous studies (5,31), the location of the stented lesion had no impact on restenosis after CS. Previous studies have suggested that LAD location was a risk factor for restenosis after BA (40). A recent report by Wong et al. (41), suggesting that the antirestenosis effect of stenting versus BA might be greater in LAD vessels, is consistent with these observations.

In the present study, the sole qualitative angiographic variable associated with restenosis after CS was stenosis length. Lesion length has also been cited as a risk factor for restenosis after BA (42).

A small reference diameter was associated with a higher risk of binary restenosis on multivariate analysis; in contrast, it was not associated with a higher late lumen loss. This may be explained by the fact that a given degree of neointimal thickening is more likely to induce >50% diameter stenosis in a small vessel versus a large vessel. A previous meta-analysis of the Belgian Netherlands Stent (BENESTENT) study and Stent Restenosis Study (STRESS) has reported that CS was not significantly better than BA in <2.6-mm vessels (14). Our results again suggest that a small reference diameter is a limitation of CS in terms of restenosis.

Procedural factors. In this study, most of the predictors of restenosis were procedural variables. Previous reports have shown a relation between multiple stents and restenosis (5,25,26). We observed an increasing late lumen loss and restenosis rate with the number of stents implanted. The mechanism by which multiple stents are associated with restenosis is unknown; one explanation may be related to overlapping of the stents, which may provoke a greater degree of neointimal proliferation; alternatively, the increased length of the stented segment may also evoke a greater degree of proliferation. Further studies will have to determine whether the use of longer stents results in an improvement in the method of overlapping stents in the case of long lesions.

A high early gain and its correlate, low residual stenosis after CS, were associated with a higher late loss in MLD. This relation between early gain and late lumen loss has been described for BA and also for CS (43). In contrast, we observed a trend toward a lower rate of restenosis in the case of low residual stenosis. This underscores the fact that, despite the risk of a higher late lumen loss, it is necessary to obtain a high early gain and low residual stenosis to reduce the incidence of restenosis.

The indication for stenting was not found to be a risk factor for restenosis in the present study. The restenosis rate after elective CS was not significantly different from that after bail-out CS or after CS done because of a suboptimal result after BA. Similar results have been reported by Strauss et al. (25) after implantation of the coronary Wallstent. Other procedural variables, such as the type of stent or inflation pressure, had no significant impact on the risk of restenosis by univariate analysis, but were associated with restenosis by multivariate analysis. Previous studies have already suggested that the restenosis rate may be higher with Wiktor stents than with Palmaz-Schatz stents (44), and that the technique of stent implantation may affect the risk of subsequent restenosis (45).

Conclusions. This study demonstrates an acceptable rate (26%) of angiographic restenosis after CS in a series of consecutive patients. Although some procedural risk factors were identified, the risk of restenosis was not related to most of the procedural variables tested. Of particular interest is the lack of effect of variables that have been previously associated

with an increased risk of restenosis after BA, such as diabetes, total occlusion before the procedure, infarct-related vessel and unstable angina. These results suggest a major benefit of CS in these subgroups of patients. This will have to be confirmed by randomized studies.

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