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Restenosis After Directional Coronary Atherectomy and Balloon Angioplasty: Comparative Analysis Based on Matched Lesions

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Objectives. Late lumen narrowing after directional coronary atherectomy was assessed by quantitative coronary angiography and compared with that after balloon angioplasty.

Background. Directional coronary atherectomy has been introduced as an alternative technique for balloon angioplasty and may reduce the incidence of restenosis.

Methods. A prospectively collected consecutive series of 87 native coronary artery lesions successfully treated with atherectomy were matched with 87 coronary artery lesions selected from a consecutive series of lesions that had been successfully dilated by balloon angioplasty. Late angiographic analysis was performed in 158 lesions. The net gain index represents the ultimate gain in minimal lumen diameter at follow-up study, normalized for the vessel size. This index is the result of the relative gain attained during the procedure (the ratio of the change in minimal lumen diameter and reference diameter) and the relative loss observed during the follow-up period (the ratio of the change in minimal lumen diameter during the follow-up period and the reference diameter).

Results. Matching for clinical and angiographic variables resulted in two comparable groups with similar baseline stenosis characteristics. Atherectomy resulted in a more pronounced increase in minimal lumen diameter than did balloon angioplasty (mean ± SD 1.17 ± 0.29 to 2.44 ± 0.42 mm vs. 1.21 ± 0.38 to 2.00 ± 0.36 mm, $p < 0.001$). However, this favorable immediate result was subsequently lost during late angiographic follow-up, so that the minimal lumen diameter at follow-up and the net gain index did not differ significantly between the two groups (1.76 ± 0.62 vs. 1.77 ± 0.59 mm, $p = 0.93$, and 0.18 ± 0.19 vs. 0.17 ± 0.17, $p = 0.70$). Consequently, the relative gain and relative loss were higher in the atherectomy group. For both techniques, the relative gain was linearly related to the relative loss but the slope of the regression line was steeper for atherectomy, suggesting that the relative loss in the atherectomy group is proportionally even larger for a given relative gain compared with that in the angioplasty group.

Conclusions. In matched groups of patients, atherectomy induces a greater initial gain in minimal lumen diameter than does balloon angioplasty. However, the vascular wall injury induced by the device is of a different nature (debulking vs. dilating) that leads to more relative loss over the follow-up period in the atherectomy group.

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Restenosis after intracoronary interventions remains the most problematic limitation of these techniques (1–4). In the past 5 years, atherectomy, stenting and laser techniques have been introduced as an alternative or adjunct to balloon dilation and as potentially safer techniques with better immediate and late results. Considerable difficulty exists in making valid comparisons among the different techniques with regard to outcome. We (4) have previously shown that, directional coronary atherectomy yields a superior immediate improvement in coronary lumen diameter than does balloon angioplasty as judged by quantitative coronary angiography. Because of the differing methods of action, this discrepancy is not unexpected. Whether directional atherectomy indeed has a more favorable long-term result has not been proved. Therefore, we studied the long-term results after directional atherectomy and compared them with those of balloon angioplasty as assessed by quantitative angiography. Because the restenosis phenomenon seems to be a systematic process affecting virtually every dilated stenotic lesion (2,3), it should be assessed by a continuous analytic approach rather than applying categoric definitions of restenosis when comparing the long-term results of two different types of interventions, such as directional coronary atherectomy and balloon angioplasty. For the purpose of this quantitative angiographic study, the initial consecutive 87 successfully treated primary atherectomy lesions (83 patients) were matched for clinical and quantitative angiographic variables with 87 coronary artery lesions that were

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selected from a consecutive series of successfully dilated primary angioplasty lesions. Three recently conceived angiographic end points (minimal lumen diameter, relative gain vs. relative loss and net gain index) at follow-up were assessed to compare the long-term results of directional coronary atherectomy and balloon angioplasty.

Methods

Patient group. From September 1989 through January 1992, 111 patients completed a 6-month follow-up period after 117 atherectomy procedures for coronary artery disease. Of these, 4 patients (4 lesions) had an atherectomy procedure for bypass graft stenosis and 18 patients (19 lesions) underwent atherectomy for restenosis after a previous percutaneous intervention. Therefore, for the purpose of this study, 89 patients (94 lesions) underwent an atherectomy procedure for native primary coronary artery disease. However, during hospitalization, one patient died as a result of cardiac tamponade (5), four patients (five lesions) underwent emergency surgery after an unsuccessful procedure and one patient (one lesion) had surgery because of presumed pericardial tamponade.

Ultimately, 83 patients with 87 primary coronary artery lesions who underwent successful atherectomy were eligible for a 6-month follow-up evaluation and were individually matched with patients undergoing successful balloon angioplasty. Late angiographic follow-up study and the final late comparative analysis were obtained in 75 patients (90%) or 79 of 87 lesions (angiographic follow-up rate 91%) in each group. The mean age ± SD of the 83 patients was 58 ± 10 years. The site of obstruction of the 87 lesions was the left anterior descending coronary artery in 56 cases, the right coronary artery in 18 and the left circumflex coronary artery in 13. Clinical and angiographic details of the matched groups are described in Table 1.

Table 1. Patient and Lesion Demographic Data for the Matched Groups

	Atherectomy Group (87 lesions)	Angioplasty Group (87 lesions)
Patient characteristics		
Age (yr)	58 ± 10	57 ± 8
% male	82	82
Vessel treated (%)		
LAD	65	65
RCA	19	19
LCx	16	16
Unstable angina (%)	43	43
Diabetes (%)	3	3
Hypercholesterolemia (%)	4	4
Lesion characteristics		
Lesion length (mm)	6.4 ± 2.5	6.5 ± 2.4
Plaque area (mm^2)	9.3 ± 6.8	9.2 ± 4.2
Reference diameter (mm)	3.22 ± 0.60	3.18 ± 0.56
Minimal lumen diameter (mm)	1.16 ± 0.38	1.19 ± 0.28
Diameter stenosis (%)	64 ± 12	62 ± 8
Reference area (mm^2)	8.72 ± 4.03	8.18 ± 2.75
Area stenosis (%)	85 ± 10	86 ± 10
Cross-sectional area (mm^2)	1.27 ± 0.94	1.11 ± 0.80

p = NS for all variables. Unless otherwise indicated, data are expressed as mean value ± SD. LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; RCA = right coronary artery.

Atherectomy. The atherectomy procedure was performed as described previously (4). The atherectomy device was directed over the guide wire and positioned across the stenosis. The support balloon was then inflated up to 7.5 psi, the cutter retracted and balloon inflation pressure increased from 7.5 to 45 psi. The driving motor was activated and the rotating cutter was slowly advanced to cut and collect the protruding atherosclerotic lesion in the collection chamber located at the tip of the catheter. After every pass, the balloon was deflated and either removed or repositioned. On average, 5.6 ± 2.2 passes in multiple directions were performed across a stenosis, resulting in tissue retrieval in all cases. Atherectomy was considered successful when the residual stenosis was <50% after tissue retrieval. Before and after the procedure, intracoronary nitroglycerin was administered to prevent coronary spasm. Predilation with a conventional balloon was performed in two patients, and in 4 cases balloon angioplasty was performed after atherectomy because there was persistent haziness on angiography after a successful atherectomy procedure. After atherectomy, the arterial and venous sheaths were usually left in place for 6 h. Patients were monitored for 24 h and an electrocardiogram and cardiac enzyme levels were obtained twice a day. Nifedipine was given every 2 h for 24 h after the procedure and patients were maintained on aspirin therapy for 1 year.

Follow-up evaluation. After a successful atherectomy or angioplasty procedure (that is, <50% postprocedural diameter stenosis on visual angiographic inspection), the patients were seen at 1 month for clinical evaluation in the outpatient clinic. An exercise test was performed 2 weeks before the 6-month follow-up coronary angiogram. Angiography was performed earlier for symptomatic recurrence within 6 months.

Quantitative coronary angiography. Quantitative analysis of the coronary segments was performed with the computer-based Coronary Angiography Analysis System (CAAS), previously described in detail (1,4,6–8). In essence, boundaries of a selected coronary artery segment are detected automatically from optically magnified and video-digitized regions of interest (512 × 512 pixels) of a cine frame. The absolute diameter of the stenosis (in mm) is determined using the guiding catheter as a scaling device. Each individual catheter is measured by a micrometer and used as a scaling device. Correction for pincushion distortion is performed. The computer estimation of the original dimension of the artery at the site of the obstruction is used to define the interpolated reference diameter. The percent diameter and area stenosis as well as the cross-sectional area (in mm^2) are then calculated. The length of the lesion (in mm) is deter-

mined from the diameter function on the basis of a curvature analysis. Symmetry is defined as the coefficient of the left-hand distance between the reconstructed interpolated reference diameter and actual vessel contours and the right-hand distance between reconstructed and actual contours at the site of the obstruction. The symmetry index ranges from 0 (totally eccentric stenosis) to 1 (symmetric stenosis). The area between the actual and reconstructed contours at the obstruction site is defined as the area plaque (in mm^2). To standardize the method of analysis of the interventional and follow-up angiograms, the following measures were taken (8). 1) The X-ray system was positioned exactly as noted at the time of the intervention. 2) All study frames to be analyzed were selected at end-diastole to minimize foreshortening. 3) The user-determined beginning and end points of a segment of a major coronary artery were identified according to the definitions of the American Heart Association. Finally, Polaroid photographs were taken of the video image, with the detected contours superimposed to ensure that the same coronary segments were analyzed on the consecutive angiograms. At follow-up catheterization, the administration of intracoronary nitrates was recommended before angiography.

Categoric approach. Two criteria were used to define restenosis. We (1,4,6–8) have found a change in minimal lumen diameter ≥0.72 mm to be a reliable indicator of angiographic progression of vessel narrowing. This value takes into account the limitations of coronary angiographic measurements and represents the long-term variability for repeat measurements for a coronary stenosis using the Coronary Angiography Analysis System. The second criterion for restenosis chosen was an increase in the diameter stenosis from <50% after an intervention to ≥50% at follow-up because in clinical practice lesion severity is still assessed using percent stenosis.

Continuous approach. Three criteria were defined to assess the long-term efficacy of directional coronary atherectomy and balloon angioplasty using a continuous approach. We (2,9,10) and others (11) have found that the minimal lumen diameter at follow-up is associated with the onset of exercise-induced thallium perfusion defects and symptoms. The second criterion relates the gain achieved during an intervention and the observed loss during follow-up to the vessel size, allowing a comparison among vessels of different sizes (9,12). The relative gain is defined as the change in minimal lumen diameter (MLD) normalized for vessel size by the following equation: Relative gain = (Postintervention MLD − Preintervention MLD)/Vessel size. The relative loss is defined as the change in minimal lumen diameter (MLD) during follow-up normalized for vessel size by the following equation: Relative loss = (Postintervention MLD − Follow-up MLD)/Vessel size.

The third criterion relates the final outcome of a procedure to the reference diameter. The net gain index represents the net gain in lumen improvement at follow-up normalized for vessel size and is described by the following equation: Net gain index = (Follow-up MLD − Preintervention MLD)/Vessel size (= relative gain − relative loss).

Matching process. The coronary artery tree was subdivided into 15 segments according to American Heart Association guidelines, and the lesions were individually matched according to stenosis location, reference diameter, minimal lumen diameter as well as the clinical variables of gender, angina status, diabetes and hypercholesterolemia. Unstable angina was defined as chest pain at rest while the patient was hospitalized and treated with intravenous nitroglycerin or heparin, or both. Hypercholesterolemia was defined as serum cholesterol levels >6.5 mmol/liter requiring treatment with lipid-lowering drugs (13). The principles of matching by quantitative angiography are threefold: 1) the angiographic dimensions of matched lesions are assumed to be identical, 2) the observed difference between the two identical lesions must be within the range of the Coronary Angiography Analysis System's reproducibility of 0.1 mm (= 1 SD), and 3) the reference diameter of the lesions to be matched are selected within a range of ±0.3 mm (= 3 SD; 99% confidence limits) (4,14,15).

To compare the results of atherectomy and balloon angioplasty, 87 coronary artery lesions from a consecutive series of 2,500 successfully dilated balloon angioplasty lesions (residual stenosis <50% on visual inspection) were selected by an independent analyst according to the selection criteria of matching just mentioned. These lesions were matched with the prospectively collected consecutive series of 87 native coronary artery lesions successfully treated with atherectomy. Late comparative analysis between atherectomy and angioplasty procedures was performed in 79 lesions because 8 lesions in the atherectomy group did not undergo late angiographic follow-up. Consequently, the eight twin-matched angioplasty-treated lesions were also not eligible for comparative follow-up analysis. At the time of lesion selection, the analyst was unaware of the 6-month angiographic outcome of these lesions. The Thoraxcenter angiographic data base has now accumulated quantitative angiographic data on 2,500 lesions treated by angioplasty, 535 lesions treated with intracoronary stenting, 153 lesions treated with directional or rotational atherectomy and 73 lesions treated with laser angioplasty. Because neither angiographic nor clinical benefit of the tested compounds could be demonstrated in the previous angioplasty restenosis trials (8,10), the placebo and active treatment groups were pooled for the present study.

Statistical analysis. The unit of analysis reported here is the stenotic lesion, not the patient. All values are expressed as mean value ± 1 SD. Comparisons of the severity of minimal lumen diameter, area plaque, diameter stenosis, symmetry index and length between the two groups were performed using analysis of variance and the paired Student *t* test. Levene's test for variance was used to examine the equality of group variability; if a significant difference was found, the Welch and Brown-Forsythe tests for equality of means were applied. The Bonferroni correction was applied

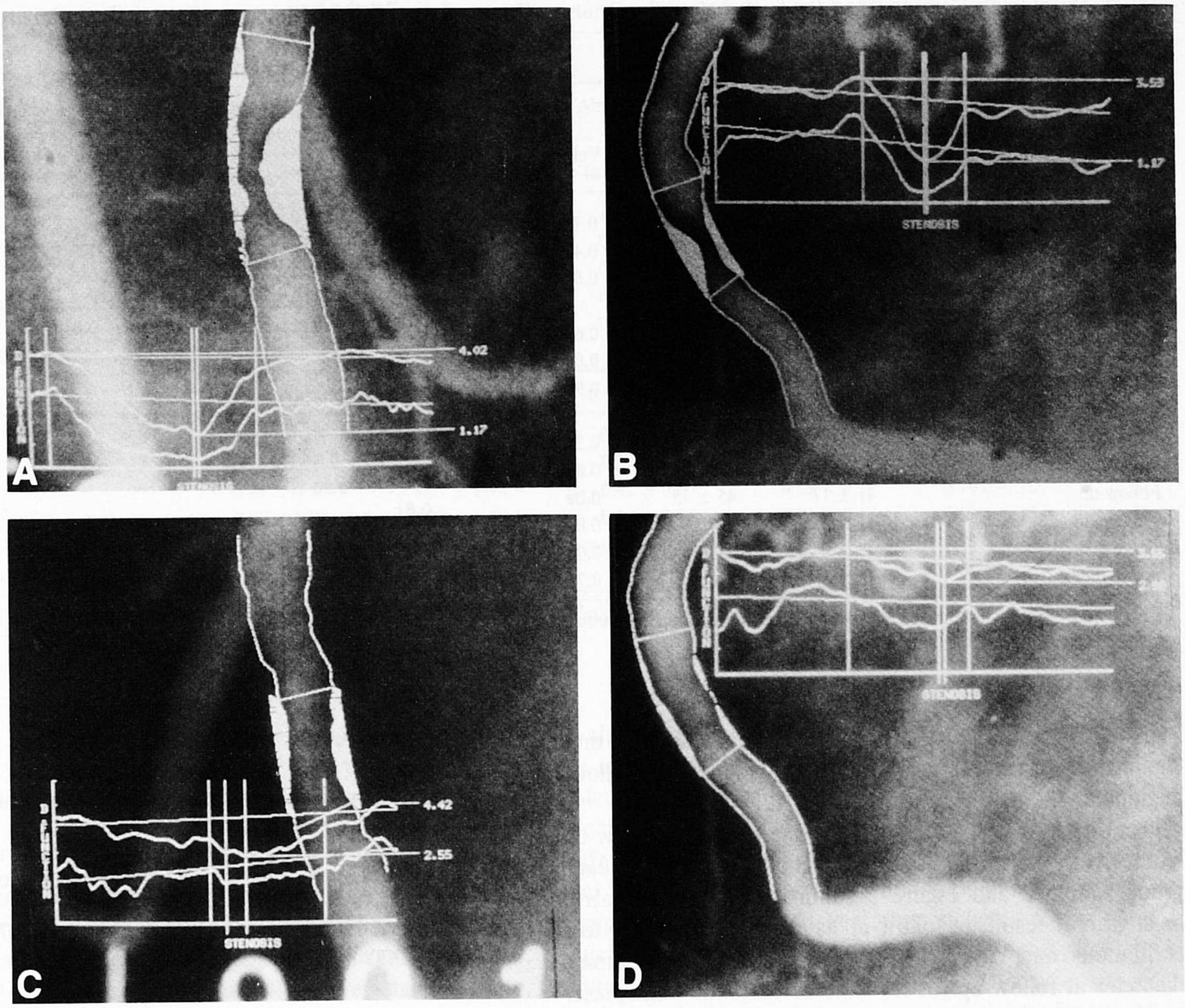

Figure 1. Representative examples of an angiogram of matched lesions in the right coronary artery before atherectomy (**A**) or balloon angioplasty (**B**) and after atherectomy (**C**) or balloon angioplasty (**D**). Edge contour and densitometric analysis of the severity of the obstruction are superimposed. The graphs show the diagnostic diameter function (**upper curve**) and densitometric area function (**lower curve**). **Lower vertical line** is the minimal lumen diameter (1.17 mm in **A and B**). **Outside vertical lines** on the graph and the **two lines on the angiogram** are lesion boundaries. The mean reference diameter measured in the orthogonal projections is 3.55 mm (**A**) and 3.56 mm (**B**). There was a larger gain in minimal lumen diameter after directional atherectomy (**C**) than after balloon angioplasty (**D**).

for multiple comparisons. Linear regression analysis by groups was performed (BMDP statistical package, program 1R) as a formal test for comparison of correlations and slopes. Differences were considered statistically significant when the p value was < 0.05.

Results

Matching. Baseline clinical and quantitative angiographic variables of the matched patient groups are listed in Table 1. No difference in gender, angina status or stenosis location were observed. Minimal lumen diameter and reference diameter measurements were not significantly different in the lesions treated with atherectomy or angioplasty (1.16 ± 0.38 and 3.22 ± 0.60 mm, respectively, for the atherectomy group and 1.19 ± 0.28 and 3.18 ± 0.56 mm for the angioplasty group (p = NS). The use of this matching technique resulted in the selection of patients treated by two different interventional techniques with similar clinical and preprocedural stenosis variables (Table 1). Figure 1 shows an example of two matched lesions treated with atherectomy or angioplasty.

Immediate results (Table 2). The reference diameter did not change significantly after either atherectomy or balloon angioplasty (from 3.26 ± 0.62 to 3.29 ± 0.41 mm atherectomy group vs. 3.23 ± 0.60 to 3.23 ± 0.58 mm in the angioplasty group). Atherectomy resulted in a greater increase in minimal lumen diameter than did balloon angioplasty, with consequently greater initial gain (1.27 ± 0.48 vs. 0.79 ± 0.34 mm, $p < 0.001$) and postprocedural minimal lumen diameter (2.44 ± 0.42 vs. 2.00 ± 0.36 mm, $p < 0.001$) and concomitantly lower percent diameter stenosis ($25 \pm$

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Table 2. Quantitative Comparison of the Immediate and Long-Term Results of Atherectomy and Balloon Angioplasty in 79 Stenoses

	Atherectomy Group (n = 79)	Angioplasty Group (n = 79)	p Value
Reference diameter (mm)			
Pre	3.26 ± 0.62	3.23 ± 0.60	0.71
Post	3.29 ± 0.41	3.23 ± 0.58	0.45
Follow-up	3.02 ± 0.55	3.21 ± 0.63	0.05
Minimal lumen diameter (mm)			
Pre	1.17 ± 0.29	1.21 ± 0.38	0.67
Post	2.44 ± 0.42	2.00 ± 0.36	< 0.001
Follow-up	1.76 ± 0.62	1.77 ± 0.59	0.93
Diameter stenosis (%)			
Pre	64 ± 12	62 ± 9	0.28
Post	25 ± 11	37 ± 10	< 0.001
Follow-up	41 ± 17	45 ± 15	0.09
Relative gain	0.41 ± 0.20	0.25 ± 0.12	< 0.001
Relative loss	0.23 ± 0.24	0.08 ± 0.16	< 0.001
Net gain index	0.18 ± 0.19	0.17 ± 0.17	0.70

Follow-up = long-term results; Post = after intervention (immediate results); Pre = results before intervention.

11% vs. 37 ± 10%, $p < 0.001$). The relative gain was thus significantly greater after atherectomy than after balloon angioplasty (0.41 ± 0.20 vs. 0.25 ± 0.12, $p < 0.001$).

Long-term results (Table 2). Angiographic follow-up studies were performed in 90% of eligible patients in each group. Table 2 and Figure 2 summarize the quantitative angiographic results at follow-up as analyzed according to a continuous and categoric approach. The minimal lumen diameter at follow-up for the atherectomy and angioplasty groups was not significantly different (1.76 ± 0.62 vs. 1.77 ± 0.59 mm, $p = 0.93$) nor was the net gain index (0.18 ± 0.19 vs. 0.17 ± 0.17, $p = 0.70$). The relative gain was greater in the atherectomy group than in the balloon angioplasty group (Fig. 3). A linear relation existed between the relative gain and relative loss for each treatment group, although the coefficient of correlation was superior in the atherectomy group ($r = 0.65$ vs. $r = 0.26$). Thus, the amount of loss during follow-up was more clearly related to the gain achieved at intervention with respect to atherectomy. Furthermore, the slope of the regression line was steeper in the atherectomy group (0.77) than in the balloon angioplasty group (0.35),

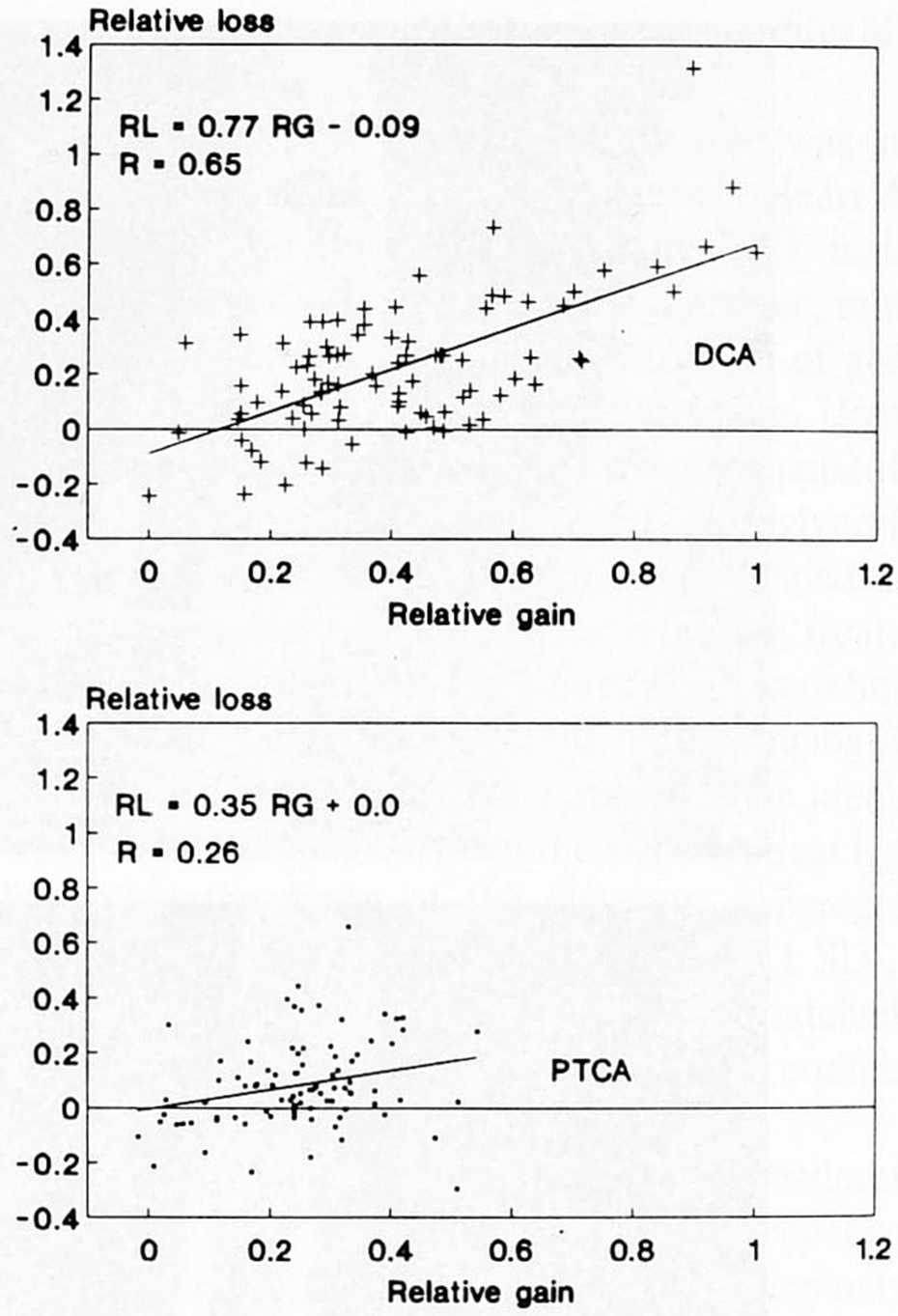

Figure 3. Scattergram of values obtained for relative gain (RG) after directional coronary atherectomy (DCA) or balloon angioplasty (PTCA) and relative loss (RL) during the follow-up period. A linear relation emerges for both techniques; however, a higher coefficient of correlation ($r = 0.65$ vs. 0.26; $p < 0.001$ vs. $p = 0.007$, respectively) and a steeper slope (0.77 vs. 0.35; $p = 0.07$) is found in the atherectomy group.

although this difference was not statistically significant ($p = 0.07$) because of a large scatter in the angioplasty group. However, the relation between relative gain and relative loss suggested that the vessel wall injury as well as the reactive hyperplasia were more intense for the same amount of gain. Finally, vessel size played an important role in the amount of relative gain and relative loss (Table 3). It appears that the relative gain observed during the procedure and the relative loss at follow-up were both decreasing in vessels of increasing size. As analyzed by the categoric approach using the >50% diameter stenosis criterion, 27% of the atherectomy

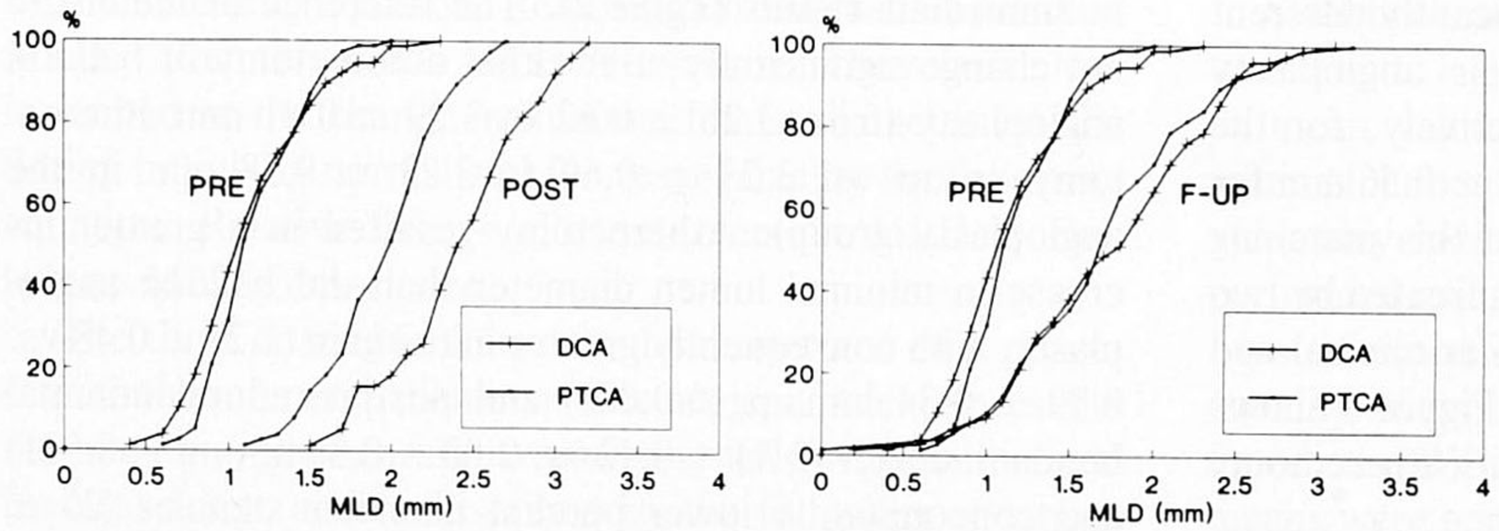

Figure 2. Cumulative frequency curves to illustrate the immediate and follow-up effects in minimal lumen diameter (MLD) of directional coronary atherectomy (DCA) as assessed by quantitative coronary angiography (PTCA). F-UP = at follow-up study; POST = after intervention; PRE = before intervention.

Table 3. Relative Gain, Relative Loss and Net Gain per Reference Diameter Group

Reference Diameter (mm)	No.	Absolute Gain (mm)	Relative Gain	Absolute Loss (mm)	Relative Loss	Net Gain	DS at F-UP ≥50% (%)
			Atherectomy Group (n = 79)				
<2.5	8	1.68 ± 0.45	0.79 ± 0.16	1.40 ± 0.49	0.68 ± 0.27	0.11 ± 0.28	50
2.5 to 3.0	16	1.28 ± 0.54	0.46 ± 0.20	0.67 ± 0.49	0.24 ± 0.18	0.22 ± 0.21	25
3.0 to 3.5	27	1.15 ± 0.49	0.36 ± 0.15	0.51 ± 0.52	0.16 ± 0.16	0.20 ± 0.16	22
3.5 to 4.0	19	1.25 ± 0.38	0.34 ± 0.11	0.48 ± 0.55	0.13 ± 0.15	0.21 ± 0.18	26
>4.0	9	1.26 ± 0.56	0.29 ± 0.14	0.99 ± 0.80	0.23 ± 0.19	0.06 ± 0.14	44
Analysis of variance		0.1171	0.0000	0.0007	0.0000	0.1951	
			Angioplasty Group (n = 79)				
<2.5	10	0.59 ± 0.48	0.27 ± 0.21	0.24 ± 0.22	0.16 ± 0.19	0.11 ± 0.10	10
2.50 to 3.0	17	0.78 ± 0.24	0.27 ± 0.09	0.27 ± 0.38	0.09 ± 0.13	0.18 ± 0.18	18
3.0 to 3.5	27	0.88 ± 0.34	0.27 ± 0.10	0.42 ± 0.56	0.13 ± 0.17	0.14 ± 0.16	37
3.5 to 4.0	18	0.84 ± 0.33	0.23 ± 0.09	0.14 ± 0.64	0.04 ± 0.17	0.19 ± 0.17	39
>4.0	7	0.66 ± 0.40	0.16 ± 0.10	−0.34 ± 0.37	−0.08 ± 0.09	0.23 ± 0.15	0
Analysis of variance		0.1676	0.1272	0.0045	0.0194	0.7401	

DS at F-UP = diameter stenosis at follow-up atherectomy or angioplasty. See Methods for definition of relative loss and gain and net gain.

group and 29% of the angioplasty group had restenosis (Fig. 4).

Discussion

The ubiquitous phenomenon of restenosis has been the subject of much attention since the introduction of percutaneous transluminal coronary angioplasty as a treatment for symptomatic coronary artery disease. Over the last few years, various new devices, including directional atherectomy (4,14–18), stenting (6,7,19), rotational ablation (20) and laser therapy (21), have been introduced to reduce the acute complication rate after balloon angioplasty and, more important, to lower the restenosis rate. Furthermore, a variety of pharmacologic agents, presumably likely to prevent restenosis, have been tested in randomized clinical trials (22,23) to reduce the restenosis rate. Unfortunately, none of these trials or device registries convincingly demonstrated a significant reduction in the restenosis rate. However, many of these studies (24) had methodologic problems and the interpretation of the results are confounded by the variety of definitions of restenosis used, rendering any comparison invalid.

Matching: comparing the comparable. With the introduction of various new intracoronary devices, it is critical to assess the relative merits of each system. We have introduced and validated the concept of matching as a surrogate for true randomized trials (4,14,15), anticipating their eventual results or at least allowing a more accurate calculation of power of upcoming randomized trials. The present study confirms that the long-term beneficial effect of directional atherectomy might be less pronounced than expected and, indeed, important information may be derived from the evaluation of matched lesions, which may be useful for the design of future randomized trials. For example, it can be calculated from this study how many patients should be included in a randomized trial to demonstrate a statistical difference in minimal lumen diameter between angioplasty and atherectomy. However, this should not preclude attempting a randomized trial that includes fewer patients (such as the Coronary Angioplasty Versus Excisional Atherectomy Trial [CAVEAT] [24a]) because subgroup analysis might nevertheless reveal a subset of patients or lesions that may especially benefit from the new intervention.

Dynamic versus static restenosis criteria. Restenosis criteria currently in use can be separated into those that describe the change in lesion severity during follow-up (dynamic criterion) and those that merely describe lesion severity at follow-up (static criterion). Examples of the first category are the loss of >0.72 mm in lumen diameter (4,6–8) and a change in percent diameter stenosis. Examples of the second category are the criterion of >50% diameter stenosis at follow-up and minimal lumen diameter >1.4 mm at follow-up (11). In the present study, we carefully selected comparable patient groups with identical stenoses by matching for clinical and angiographic variables. However, this technique does not reconcile the discrepancy arising from the divergent immediate effects of two different interventional techniques, rendering the dynamic restenosis criteria that describe a change in lesion severity from postintervention to follow-up angiography inappropriate. Therefore, a static restenosis variable that describes the lesion severity at follow-up angiography should be used when comparing two different interventional techniques such as directional coronary atherectomy and balloon angioplasty.

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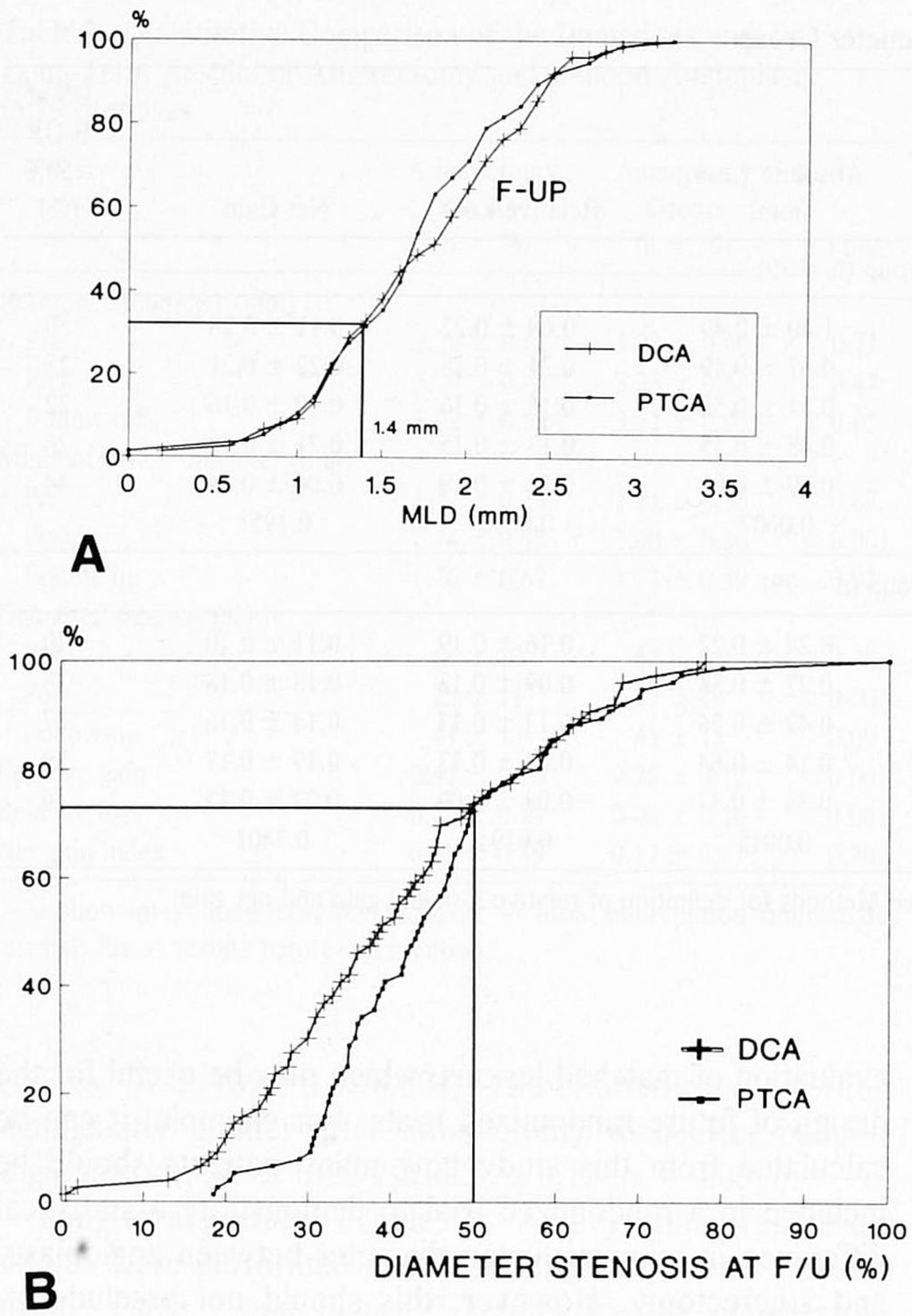

Figure 4. Static and dynamic assessment of long-term angiographic outcome after directional coronary atherectomy (DCA) and balloon angioplasty (PTCA) as determined by three categoric cutoff points: minimal lumen diameter (MLD) *at* follow-up (F/U, F-UP) = 1.4 mm (**A**), diameter stenosis (DS) <50% *at* follow-up (**B**) and ≥0.72-mm change in minimal lumen diameter *during* follow-up (**C**).

Minimal lumen diameter at follow-up: the quantitative angiographic end point. Of all directly acquired measurements by quantitative coronary angiography, the absolute value of the minimal lumen diameter has been shown to be the greatest single determinant of the hemodynamic consequence of a stenosis and is therefore the only nonambiguous, objective and reproducible variable with which to describe the caliber of a coronary artery and changes therein after an intervention (25). In placebo-controlled restenosis prevention trials after coronary angioplasty, the change in minimal lumen diameter during follow-up has traditionally been used assess the value of a new pharmacologic strategy (8,10). This approach was justified because the degree of lumen enlargement was, by definition, comparable in the two arms of the trial. Because of the different nature of the two interventions applied here (atherectomy and angioplasty), the immediate postprocedural results are different and no longer comparable. This is clearly shown in the cumulative distribution curve (Fig. 2). Because atherectomy induces a larger gain in minimal lumen diameter than does angioplasty, the immediate postprocedural characteristics are dissimilar so that the loss during follow-up is no longer a helpful indicator of the long-term benefit. The most valid variable for the comparison of two interventional devices is the minimal lumen diameter at follow-up because this static variable in itself represents the final lumen improvement. Moreover, the minimal lumen diameter at follow-up may have some functional component. In accordance with Danchin et al. (11), we (26) found that a minimal lumen diameter of 1.45 mm correlates with the recurrence of angina pectoris (sensitivity and specificity 72%). This information suggests that the absolute value of the minimal lumen diameter at follow-up may prove to be even more useful than variables obtained by clinical examination or exercise testing. In this study comparing two patient groups with similar clinical and preprocedural stenosis characteristics, using quantitative angiographic variables of 158 coronary lesions, there was no significant difference in minimal lumen diameter at follow-up between the atherectomy and balloon angioplasty group.

Continuous versus categoric approach. Restenosis has been shown to be a proliferative response, affecting virtually all lesions that have been subjected to the trauma of an intracoronary intervention (16,27–30). Using quantitative angiography, our group previously demonstrated that a loss in minimal lumen diameter occurs in all treated lesions, irrespective of localization in the coronary artery tree (12) and, more important, that narrowing after balloon angioplasty follows a near-gaussian distribution (2). Therefore, restenosis should be viewed as the tail end of an approximately gaussian-distributed phenomenon rather than a unique disease entity, occurring in some lesions but not in others (2,3). Given these facts, analysis with parametric statistical tests is appropriate and by using a continuous approach, we can take advantage of all information made available by follow-up angiographic studies.

Relative gain as an injury score and relative loss as an index of neointimal hyperplasia. The important observation that a greater gain in lumen (that is, injury) is associated with a greater loss (that is, repair) during follow-up was previously

described by Schwartz et al. (31,32). In a domestic swine model with stenting that accurately mimics the proliferative nature of human restenosis, the extent of the proliferative response was strongly associated with rupture of the internal elastic lamina as induced by oversized and overpressurized balloon inflations with or without coil implantation (31,32). To test this hypothesis in a clinical setting, we replaced the concepts of "injury score" and "neointimal hyperplasia" as observed in the animal model with the angiographically derived variables of relative gain and relative loss. Quantitative angiographic analysis (8) of 522 coronary artery lesions treated by balloon angioplasty with a 95% angiographic follow-up reveals a linear relation between relative gain and relative loss, although the coefficient of correlation is low (0.4). The present study indeed confirms these observations for balloon angioplasty but unveils a stronger correlation between relative gain and relative loss for atherectomy compared with balloon angioplasty. More important, the slope of the regression line is steeper in the atherectomy group than in the angioplasty group, implying not only that the relative gain is greater in the atherectomy group, but also that the reactive response (that is, relative loss) is more pronounced after atherectomy than after angioplasty. As seen in Figure 3, the slope of the regression line between relative gain and relative loss, which reflects the inherent relation between the degree of wall injury and the degree of repair, represents an index of lumen renarrowing specific for each treatment (that is, atherectomy and balloon angioplasty). Furthermore, the reference diameter emerged as a potentially important variable that may affect procedural outcome because the relation between relative gain and relative loss appears to be a function of vessel size, with less gain during the procedure but also less loss during follow-up in larger vessels (Table 3). Indeed, an earlier observation from our group (9,12) demonstrated that relative loss is significantly smaller in vessels with a reference diameter >3.5 mm. This phenomenon might be related to less medial disrupture and a better artery/device ratio.

Limitations of the study. Several limitations of this study must be acknowledged. 1) It is an uncontrolled observational study limited to a subset of patients with successful coronary atherectomy or balloon angioplasty without inclusion of patient- and procedure-related variables. 2) It is based on the relative early experience with atherectomy. Careful patient selection, future design changes and improved operator experience may further improve the immediate and long-term results. Controlled clinical trials, such as the CAVEAT (24a), will be required to determine the immediate angiographic result, the long-term efficacy of these interventions and the benefit, if any, in particular patient subgroups. These studies should also address the presumed time frame for restenosis after any particular intervention.

Practical implications. At present, debate exists whether atherectomy should be performed while aiming at the maximal achievable result. Although studies (33) have reported that "bigger is better" (a bigger gain in lumen size yields a better late angiographic result), controversy still exists regarding the influence of medial or adventitial tissue retrieval on the final restenosis rate (30,34,35). Animal studies (31,32) suggest a direct relation between intimal hyperplasia and vessel wall injury at intervention. In this clinical study introduction of quantitative angiographic correlates for these variables (relative loss and relative gain, respectively) clearly supports this hypothesis in the context of directional atherectomy and balloon angioplasty. The biologic control of the healing process has to be elucidated before we may take full advantage of the superior initial gain provided by this powerful interventional technique.

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