JACC Vol. 12, No. 2
August 1988:315–23

Change in Diameter of Coronary Artery Segments Adjacent to Stenosis After Percutaneous Transluminal Coronary Angioplasty: Failure of Percent Diameter Stenosis Measurement to Reflect Morphologic Changes Induced by Balloon Dilation

KEVIN J. BEATT, MRCP, HANS E. LUIJTEN, MD, PIM J. DE FEYTER, MD, MARCEL VAN DEN BRAND, MD, JOHAN H.C. REIBER, PHD, PATRICK W. SERRUYS, MD, FACC WITH THE STATISTICAL ASSISTANCE OF HARALD J. TEN KATEN AND GERRIT A. VAN ES

Rotterdam, The Netherlands

To determine the changes in stenotic and nonstenotic segments of a dilated coronary artery, detailed quantitative angiographic measurements were performed in 342 patients (398 lesions) immediately after angioplasty and at a predetermined follow-up time of 30, 60, 90 or 120 days after the dilation. Measurements of the stenotic segments were expressed as minimal luminal diameter, and the adjacent nonstenotic segments were expressed as interpolated reference diameter (both in millimeters). A follow-up rate of 86% was achieved.

In the patients followed up at 30 and 60 days, there was no significant change in either the mean minimal luminal diameter or the mean reference diameter. However, at 90 and 120 days, there was significant deterioration in both the mean minimal luminal diameter (−0.37 and −0.42 mm, respectively) and the mean reference diameter (−0.17 and −0.26 mm, respectively), all of the changes being highly significant ($p < 0.00001$). The reference diameter is involved in the dilation process and may be subject to the same restenosis process that takes place in initially stenotic segments. Percent diameter stenosis measurements, which are conventionally used to express the change in the severity of a stenosis after angioplasty, will tend to underestimate the change when there is a simultaneous reduction in the reference diameter.

(J Am Coll Cardiol 1988;12:315–23)

The incidence of restenosis after coronary angioplasty has become an important index for defining the long-term success rate of the procedure. The relatively high incidence rate (range 12 to 48% [1–5]) of restenosis, as defined by a number of arbitrary criteria, is regarded as the predominant limiting factor to the long-term success rate of angioplasty.

The usual definition of restenosis (2) is based on changes in percent diameter stenosis. This value is used to reflect the changes in minimal luminal diameter in relation to the so-called normal diameter of the vessel in the immediate vicinity of the obstruction. It assumes that this "normal" or reference diameter of the vessel proximal or distal to the obstruction does not change as a result of angioplasty or during the immediate follow-up period when restenosis of the dilated lesion is a well recognized phenomenon. With this criterion for restenosis, which depends on changes that occur in two independent variables (namely, minimal luminal diameter and "normal" luminal diameter), it is not possible to independently examine the absolute changes in either variable, each of which may be important in its own right. In addition, the selection of an arbitrary reference diameter may introduce a further source of error because the selection procedure is not always well standardized and, in practice, is difficult to reproduce reliably during sequential analysis.

Animal experiments (6) have suggested that balloon dilation of a normal coronary artery is capable of inducing the same fibrocellular response seen after dilation of atheroscle-

From the Thoraxcenter, Erasmus University and University Hospital Dijkzigt, Catheterization Laboratory and Laboratory for Clinical and Experimental Image Processing, Rotterdam, The Netherlands.

Dr. Beatt is the recipient of a Research Fellowship from the British and Netherlands Heart Foundation, London, England. Dr. Luijten is the recipient of a Research Fellowship from the Netherlands Heart Foundation (No. 85-118), The Hague.

Manuscript received October 19, 1987; revised manuscript received February 16, 1988, accepted March 9, 1988.

Address for reprints: Patrick W. Serruys, MD, Thoraxcenter, Erasmus University and University Hospital Dijkzigt, Catheterization Laboratory and Laboratory for Clinical and Experimental Image Processing, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands.

0735-1097/88/$3.50

JACC Vol. 12, No. 2
August 1988:315–23

Table 1. Clinical Characteristics of 342 Patients With Successful Coronary Angioplasty

	Follow-Up Period				
	30 Days	60 Days	90 Days	120 Days	Overall
No. of patients	93	79	82	88	342
No. of lesions	110	89	93	106	398
Mean no. of lesions dilated per patient	1.18	1.13	1.13	1.20	1.16
Age (yr)					
Mean ± SD	57 ± 9	57 ± 9	56 ± 9	57 ± 9	57 ± 9
Range	35 to 75	31 to 75	32 to 74	31 to 74	31 to 75
Gender ratio (M/F)	5.6 (79/14)	5.1 (66/13)	3.3 (63/19)	3.9 (70/18)	4.3 (278/64)
Time from PTCA to F/U (days)					
Mean ± SD	40 ± 7	61 ± 12	102 ± 18	120 ± 32	80 ± 38
Range	18 to 62	11 to 80	33 to 164	4 to 226	4 to 226
Extent of CAD (no. [%])					
One vessel disease	62 (67)	56 (71)	52 (63)	62 (70)	232 (68)
Two vessel disease	25 (27)	20 (25)	21 (26)	16 (18)	74 (22)
Three vessel disease	5 (5)	4 (5)	5 (6)	10 (11)	36 (11)
Previous coronary bypass grafting (no. [%])	9 (10)	7 (9)	6 (7)	8 (9)	30 (9)
Previous myocardial infarction (no. [%])	40 (43)	39 (49)	32 (39)	30 (34)	138 (40)
Previous coronary angioplasty (no. [%])	10 (11)	2 (3)	11 (13)	12 (14)	35 (10)

CAD = coronary artery disease; F = female; F/U = follow-up angiography; M = male; PTCA = percutaneous transluminal coronary angioplasty.

rotic vessels. However, no data exist to show whether this is important in the clinical setting, where the dilating process frequently involves relatively normal coronary artery segments. To determine the changes in stenotic and nonstenotic segments in the period immediately after angioplasty and to assess their importance in relation to the change in diameter stenosis occurring in the same period, we used a computer-generated angiographic measurement system in a detailed follow-up study of patients who had undergone successful angioplasty.

Methods

Study patients. Four hundred consecutive patients who underwent successful coronary angioplasty and agreed to have a follow-up angiogram were entered into an ongoing study on restenosis. Successful coronary angioplasty was defined as: 1) <50% diameter stenosis on visual inspection of the postangioplasty coronary angiogram performed in multiple views; and 2) no in-hospital complications (namely, recurrence of angina, coronary bypass grafting, repeat coronary angioplasty, acute myocardial infarction or death). Patients with stable and unstable angina pectoris, as defined previously (7), were included. Patients with acute myocardial infarction receiving a thrombolytic agent who subsequently had immediate coronary angioplasty were excluded.

Allocation of patients at the time of angioplasty to one of four predetermined times for follow-up angiography was made sequentially according to the study period in which the dilation was performed; patients undergoing angioplasty in the first study period were reinvestigated at 30 days, the second group at 60 days, the third group at 90 days and the fourth group at 120 days. Of the 400 patients who met the inclusion criteria, 342 had repeat angiograms suitable for quantitative analysis. Reasons for failure to complete the study were late death (2 patients), recatheterization contraindicated or refused (38 patients) and angiograms unsuitable for quantitative analysis (18 patients).

Of the total study group of 342 patients (398 lesions), 93 patients underwent repeat catheterization at 30 days (110 lesions), 79 at 60 days (89 lesions), 82 at 90 days (93 lesions) and 88 (106 lesions) at 120 days after angioplasty.

The baseline clinical characteristics in the four groups were comparable for the variables shown in Table 1. The mean time from angioplasty to follow-up angiography in the four study groups was 40, 61, 102 and 120 days, respectively.

When clinically indicated (early recurrence of symptoms), patients were reinvestigated before their preset time, but analysis was performed according to that for their original allocation group. This was done to allow a valid statistical comparison of the changes occurring among the individual groups. We assume that changes seen at the early investigation would be present if a further investigation was performed at the original preassigned time. Most patients restudied early had a further intervention (coronary angioplasty or bypass surgery) and, thus, a further investigation was not appropriate. This method was chosen to avoid biasing the early groups with patients who underwent early investigation because of symptoms and who were thus more likely to show a deterioration in the dilated lesion. Table 2 shows the type of vessel, the number of patients with tandem

Table 2. Type of Vessel Dilated and Number of Patients in the Four Study Groups With Tandem Lesions and More Than One Lesion Dilated

	Follow-Up Period				
	30 Days	60 Days	90 Days	120 Days	Overall
Vessel dilated (no. [%])					
LAD	61 (56)	61 (69)	55 (59)	62 (58)	239 (60)
LCx	18 (16)	16 (18)	19 (20)	16 (15)	69 (17)
RCA	26 (24)	11 (12)	16 (17)	23 (22)	76 (19)
Bypass graft	4 (4)	0 (0)	2 (2)	4 (4)	10 (3)
LMCA	1 (1)	1 (1)	1 (1)	1 (1)	4 (1)
No. of patients with tandem lesion (no. [%])	6 (6)	2 (3)	2 (2)	5 (6)	15 (4)
No. of patients with (no. [%]) >1 lesion dilated	15 (16)	10 (13)	10 (12)	18 (20)	53 (15)

LAD = left anterior descending artery; LCx = left circumflex artery; LMCA = left main coronary artery; RCA = right coronary artery.

lesions and the number of patients with more than one lesion dilated for each study group.

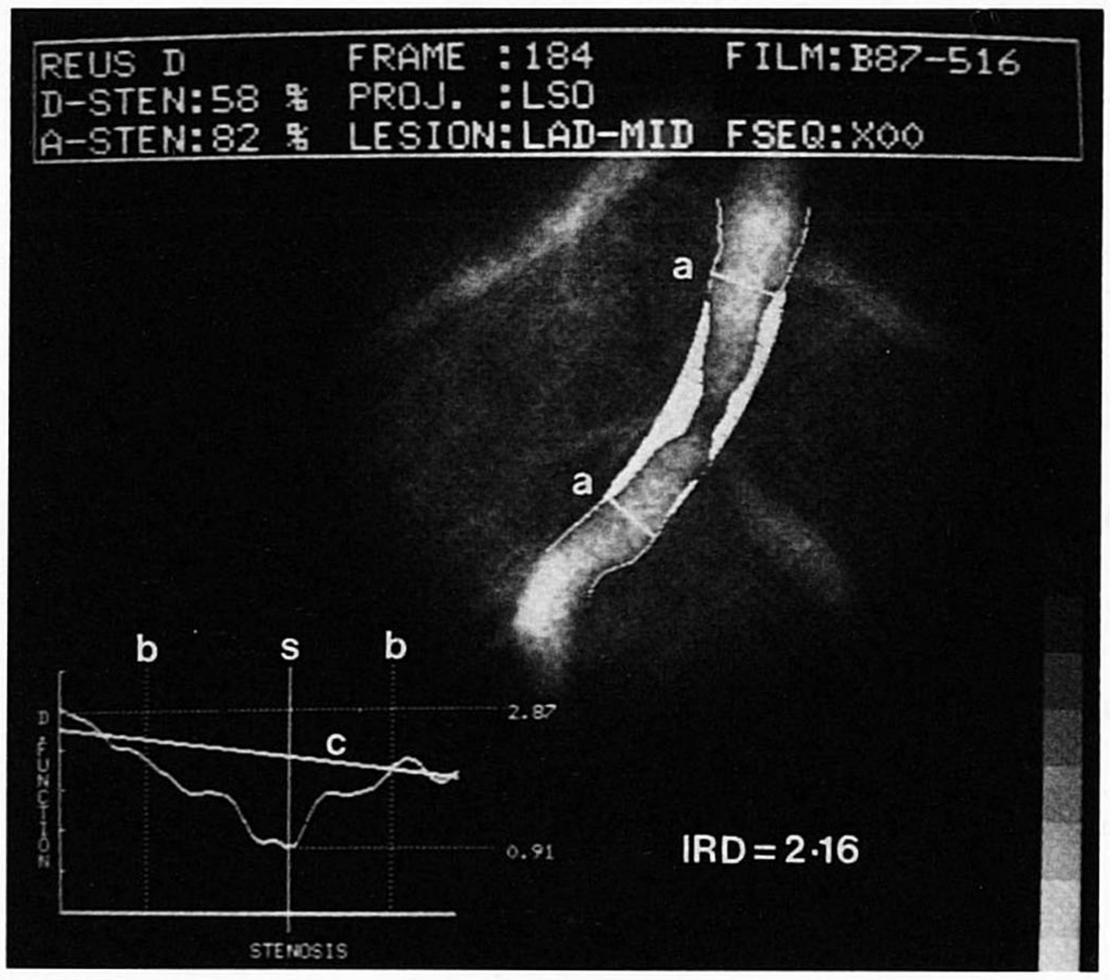
Angioplasty protocol. Coronary angioplasty was performed with a steerable movable guidewire system by means of the femoral route. Details regarding the procedure used in our laboratory have been described previously (7). At the beginning of the procedure, all patients received infusions of heparin, 10,000 IU and aspirin, 500 mg, and a continuous infusion of Rheomacrodex (low molecular weight dextran) was started. After dilation, 10 mg of nifedipine was given orally every 2 h for the first 12 h, and then three to six times a day together with 500 mg/day of aspirin orally until repeat angiography. Beta-adrenergic blocking agents were withdrawn unless indicated for hypertension.

Quantitative coronary angiography. The quantitative analysis of the stenotic coronary artery segments was carried out with the computer-assisted Cardiovascular Angiography Analysis System (CAAS), which has been described in detail (8,9). In summary, to analyze a coronary artery segment in a selected frame of 35 mm cinefilm, an optically magnified portion of the image encompassing that segment is converted into video format by means of a cine-video converter. The region of interest is defined and the contours of the vessel are detected automatically on the basis of the weighted sum of first and second derivative functions applied to the digitized brightness information. Calibration of the diameter data of the vessels in absolute values (in millimeters) is achieved by using the contrast catheter as a scaling device (10). To this end, the contours of a user-defined portion of the optimally magnified catheter (optimal magnification factor $2\sqrt{2}$) are detected automatically and corrected for pincushion distortion caused by the image intensifiers. From the contours, the vessel diameter functions are determined by computing the shortest distances between the two contour positions. All aspects of this process apart from the selection of angiographic frames for analysis are independent of the user and were performed without knowledge of previous results.

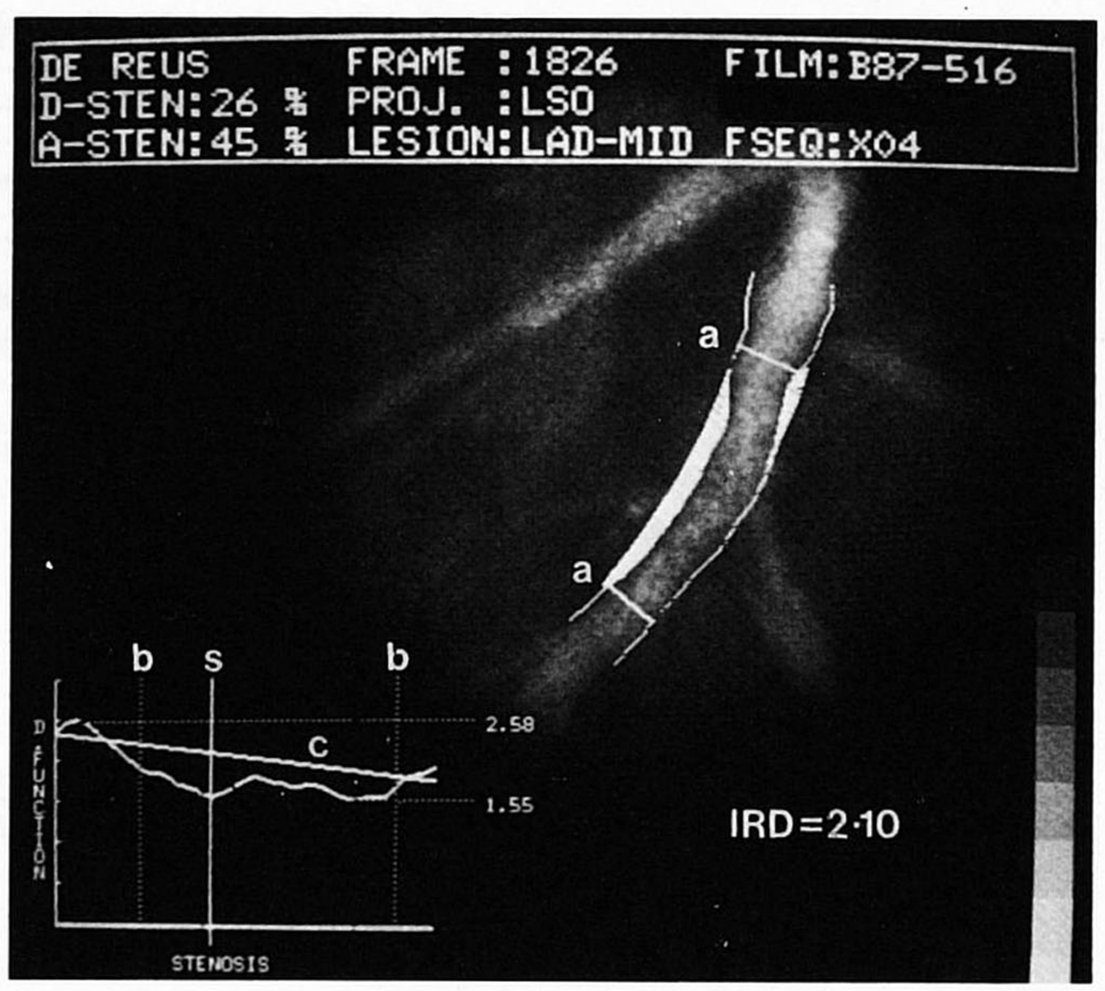
A representative analysis, with the detected contours and the diameter functions superimposed on the original video image, is shown in Figure 1. The reference diameter is difficult to define and is usually selected visually as the nearest coronary artery segment that appears normal. To standardize this measurement and minimize potential errors, we used an "interpolated" reference diameter measurement. This method has the advantage of eliminating the arbitrary choice of a reference diameter, which will vary among individual observers, and also provides a smoothing effect for the segments adjacent to the stenosis so that extreme irregularities in the vessel have little influence on the reference diameter. The principle behind this technique has been described previously (11–13), as have the precision and overall accuracy of the system (13). The method of obtaining angiograms and the precautions taken to reduce error were recently reported (14).

A change ≥ 0.72 mm was taken to represent a significant change. This is based on twice the variability (0.36 mm) of the minimal luminal diameter measurement (in millimeters) when coronary angiography is repeated over an interval of 90 days (8).

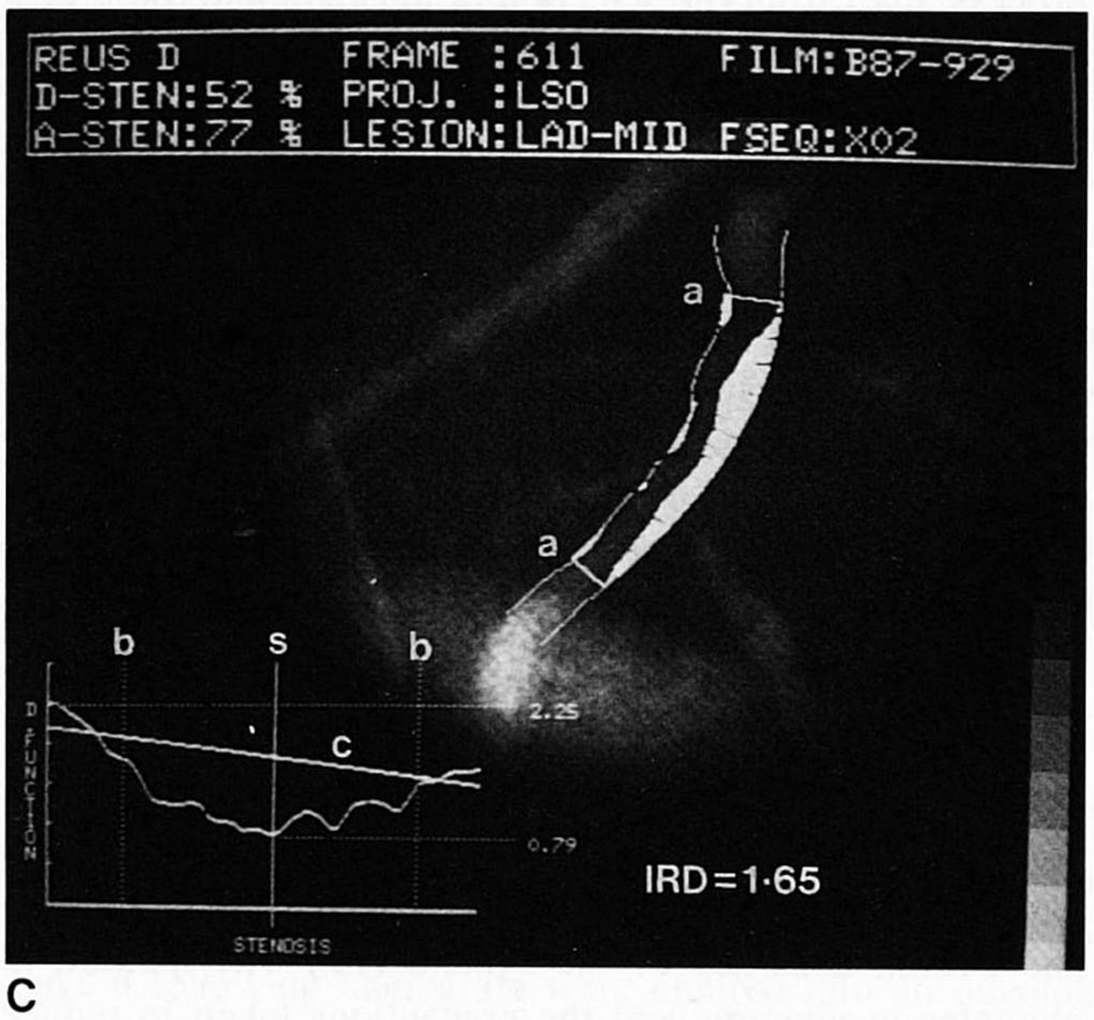
Statistical methods. To test for differences in mean values and proportions among the four follow-up groups with respect to the baseline characteristics (Tables 1 and 2), univariate analysis of variance was performed for the continuous variables, and multiway chi-square analysis for the discrete variables. For the quantitative variables listed in Table 3, univariate analysis of variance was performed (BMDP statistical software, University of California Press, Berkeley, CA, 1985). All statistical tests were two-tailed. A



A



B



C

Figure 1. A series of single frame angiograms of the same left anterior descending coronary lesion, before dilation (**A**), after dilation (**B**) and at 60 days follow-up study (**C**). The interpolated reference diameters (IRD) are shown to the **right** of the diameter function curve, and the corresponding percent diameter stenosis (D-STEN) and percent area stenosis (A-STEN) at the **top left of each frame**. The arterial boundary of the segments of interest is defined by the automated edge detection process, and the length of the lesion is defined automatically by curvature analysis as shown by the **lines** (a,a) proximal and distal to the stenosis and the **vertical lines** (b,b) on the diameter function plot. The interpolated reference contour line (c) is computed from the contours proximal and distal to the lesion, and the reference diameter value is taken at the point coincident with the point of maximal narrowing, shown by the **line** (s). The postangiographic analysis (**B**) shows a satisfactory result. The follow-up analysis (**C**) shows that a significant restenosis has taken place, and the lesion is longer as defined by the computer. However, the adjacent contours outside the boundaries have also become narrower, resulting in a reduction in the reference diameter. This results in an erroneously low percent diameter stenosis of 52%, rather than 70% if the measurement had been based on the reference diameter immediately after angioplasty. The choice of a single reference diameter in such a dynamic setting would be inappropriate and result in misleading errors.

probability (p) value <0.05 was regarded as indicating statistical significance.

Results

Changes in mean minimal luminal diameter and reference diameter. The mean results of quantitative angiography for the 342 patients who completed the study, divided into four follow-up groups, are shown in Table 3 along with the changes that occurred between angioplasty and follow-up study. The changes in mean minimal luminal diameter and mean reference diameter that occurred between postangioplasty and follow-up study are shown in Figure 2. In the groups who underwent follow-up angiography at 30 and 60 days, there were small nonsignificant changes in both minimal luminal diameter and reference diameter, with a small improvement in minimal luminal diameter and a reduction in reference diameter at 30 days and a reduction in both values at 60 days. However, at 90 and 120 days, both minimal luminal diameter and reference diameter show a highly significant ($p < 0.00001$) deterioration, with the values at 120 days being greater than those at 90 days.

Distribution of individual changes in luminal diameter. The individual changes in reference diameter and minimal luminal diameter are represented in Figures 3 and 4, respectively. The progressive shift of the distribution of the minimal

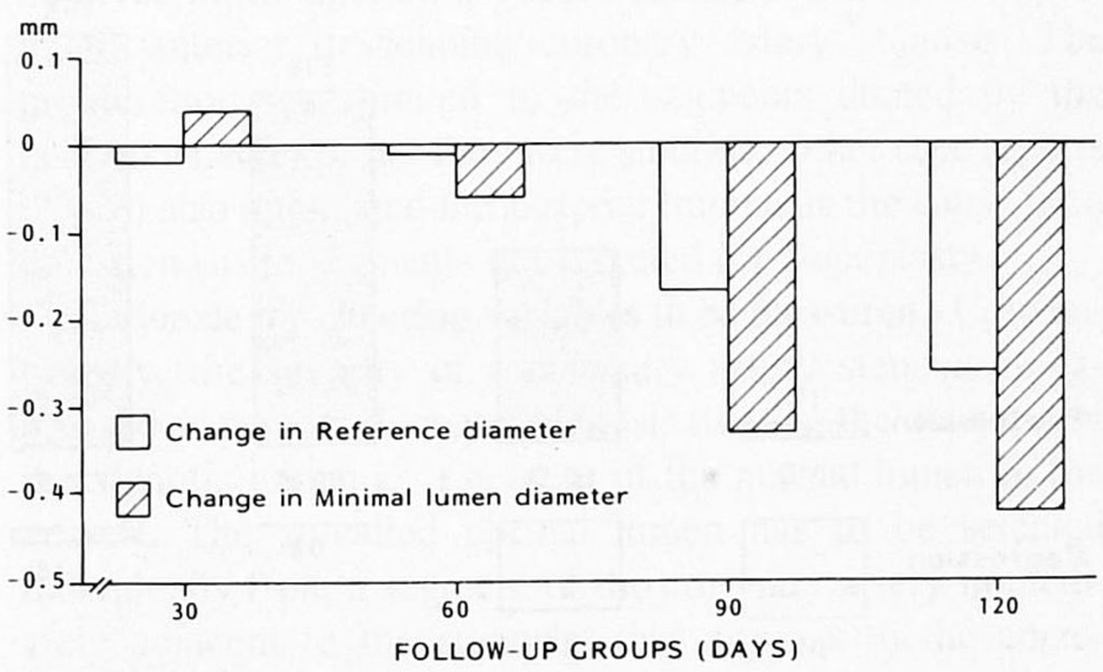
Table 3. Quantitative Coronary Angiographic Findings Postcoronary Angioplasty and at Follow-Up in the Four Study Groups

	Follow-up Period				
	30 Days	60 Days	90 Days	120 Days	p Value
Minimal luminal diameter (mm)					
Post	2.06 ± 0.46	2.00 ± 0.42	2.14 ± 0.42	2.10 ± 0.40	0.17
Follow-up	2.11 ± 0.56	1.93 ± 0.64	1.77 ± 0.58	1.68 ± 0.55	<0.0004
Post to follow-up	+0.04	−0.06	−0.37	−0.42	<0.00001
Reference diameter (mm)					
Post	2.92 ± 0.63	2.91 ± 0.50	3.02 ± 0.56	2.86 ± 0.49	0.34
Follow-up	2.90 ± 0.60	2.92 ± 0.54	2.86 ± 0.55	2.62 ± 0.51	0.84
Post to follow-up	−0.02	−0.01	−0.17	−0.26	<0.00001
Diameter stenosis (%)					
Post	28.5 ± 12.0	31.0 ± 12.0	28.1 ± 11.0	26.3 ± 9.5	0.20
Follow-up	26.9 ± 14.7	33.5 ± 19.8	37.1 ± 18.4	35.4 ± 16.7	<0.0002
Post to follow-up	−1.6	+2.5	+9.0	+9.1	<0.00001

Variables are expressed as mean ± SD. The Post to follow-up values are the mean of the individual differences; the p values are derived from the analysis of variance comparing the four groups.

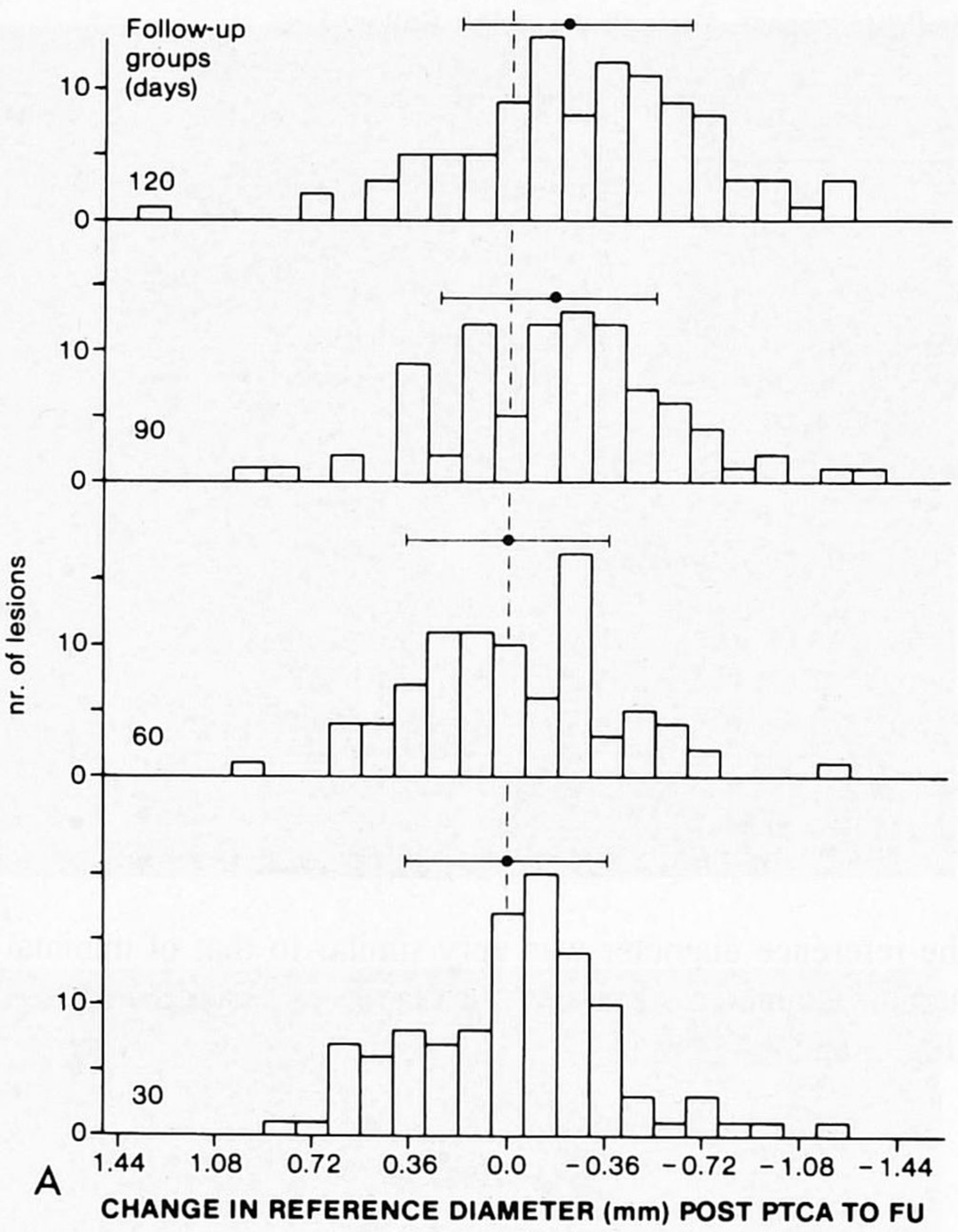
luminal diameter with time to follow-up is evident and shows that it is not just a limited number of lesions that "restenose," but rather almost all lesions deteriorate to some extent by 120 days after angioplasty. The degree of change is normally distributed about the mean value (−0.42 mm at 120 days), and the number of lesions that undergo "restenosis" will depend on the criterion chosen. Figure 4 shows the percent of lesions that undergo change (either progression or regression) if 0.72 mm is used as the criterion for change. For patients who were reinvestigated at 30 days, the percent of individual lesions that achieved the 0.72 mm criterion for regression was 6%, with 1% showing progression. At 60 days, a similar percent showed regression, but the number showing progression had increased to 12%. The rate of progression then increased to 23 and 26%, respectively, in the subsequent two follow-up groups, with virtually no lesions showing regression. The pattern of change for the reference diameter was very similar to that of minimal luminal diameter, although the degree of change was less (Fig. 3 and 4).

Figure 2. Change in reference diameter and minimal luminal diameter for the four follow-up groups. At 90 and 120 days, both these changes are significant ($p < 0.00001$) and are different from the changes at 30 and 60 days ($p < 0.00001$).



Discussion

Change in minimal luminal diameter: mechanism and timing. *Early changes.* The design of this study allows some insight into the course of a dilated coronary lesion after angioplasty. Many of the previously published studies reported mean results for patients with a wide range of follow-up times, so that little information on the behavior of the lesion with time is available. The published data are further distorted by preferential recatheterization of symptomatic patients, who can be expected to show a higher incidence of restenosis. To determine a significant change within individuals, we have taken 0.72 mm, two times the variability for duplicate measurements, as the criterion for change. The variability (0.36 mm) represents 1 SD of the mean difference between duplicate measurements on the same lesion and would result, if used as a criterion for change, in a 16% false positive rate, whereas the use of 2 SD (0.72 mm) as a criterion results in a false positive rate of only 2.5%. When this value is used as the criterion for change, it can be seen that, in patients reinvestigated at 30 and 60 days, the immediate response is variable, with more lesions initially showing regression than progression (Fig. 4). A 30% rate of lesion regression after angioplasty was previously described (14), but only in a small group of patients, with use of different criteria and without specific reference to the time after angioplasty in the selected subgroups. Spontaneous lesion regression may occur as part of the atherosclerotic process (15–18) in undilated coronary artery lesions, but the rapid improvement of 6% of the dilated lesions in our study suggests that some lesions may undergo a remodeling proc-



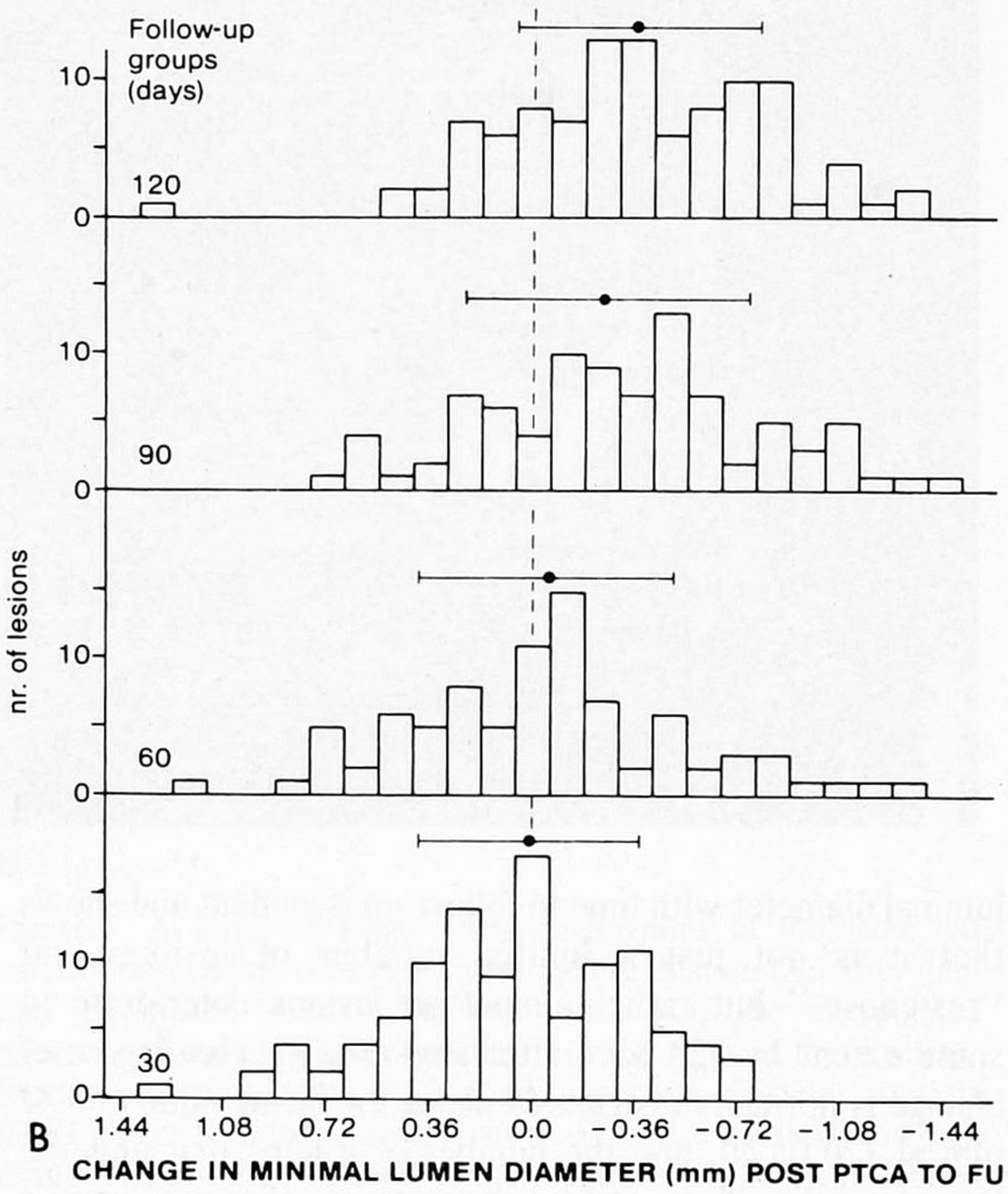


Figure 3. Histograms for the four follow-up groups. **A**, Distribution in the change of reference diameter with time. The **vertical interrupted line** represents no change. The mean value for each follow-up group ± 1 SD is also shown. **B**, Distribution in the change of minimal luminal diameter for the four follow-up groups. FU = follow-up study; nr = number; POST PCTA = postangioplasty.

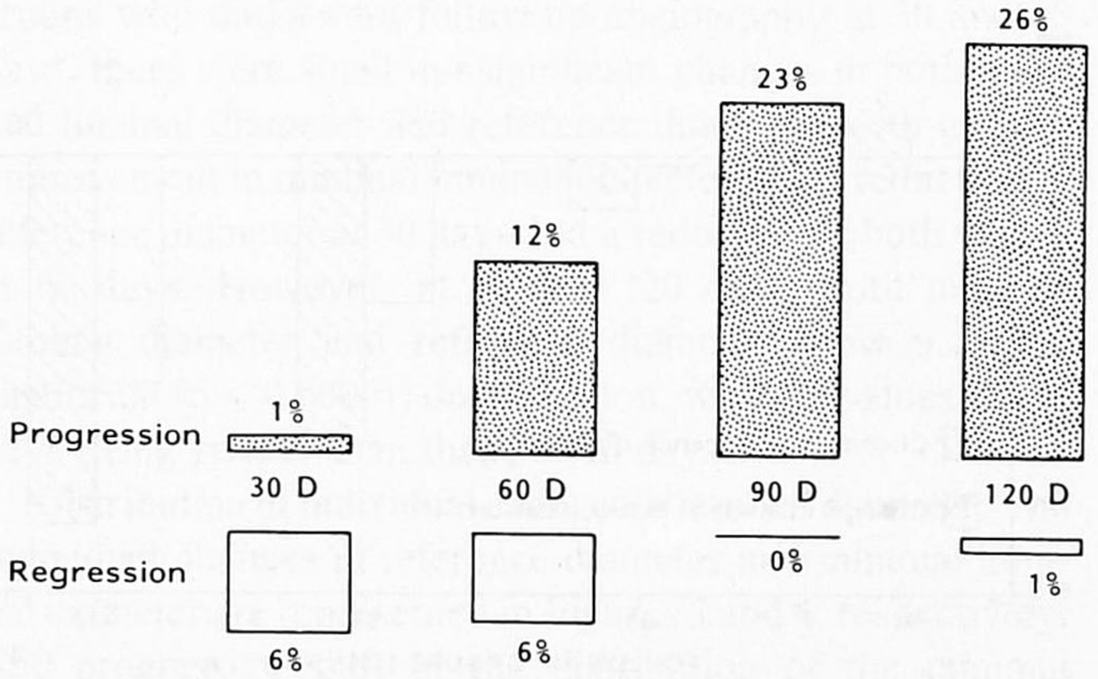
ess early after dilation that is different from the normal atherosclerotic process.

Late changes. At 90 and 120 days, there were virtually no lesions showing regression, indicating that, even after initial improvement, significant progression of stenosis may occur. The more well established trend of lesion progression starts to become evident between 30 and 60 days, but it is not confirmed statistically until 90 days, with some further deterioration at 120 days.

In the pig model, Steele et al. (6) found evidence of smooth muscle proliferation as early as 7 to 14 days after dilation. This same process was identified in at least seven postmortem hearts (19–22) that were examined over a time period (17 to 150 days after dilation) similar to that used in our study. It seems likely that the process also begins early in human patients, but because of the limitations in recognizing small changes even with an accurate system of analysis, we do not see highly significant deterioration until 90 days. Our data suggest that the restenosis process takes place to some extent in virtually all lesions dilated.

Change in reference diameter: response of nonstenotic segments to intraarterial balloon injury. Animal studies (6,23,24) have shown that, after angioplasty of normal carotid arteries, there is initially significant platelet deposition, particularly if a deep intimal tear has occurred, and subsequent proliferation of smooth muscle cells. During angioplasty, the relatively normal coronary artery segments adjacent to the stenosis are inevitably involved in the angioplasty process because the balloon is usually longer than the

Figure 4. Percent of patients within each of the individual follow-up groups who fulfilled the 0.72 mm criterion for change. D = days to follow-up study.



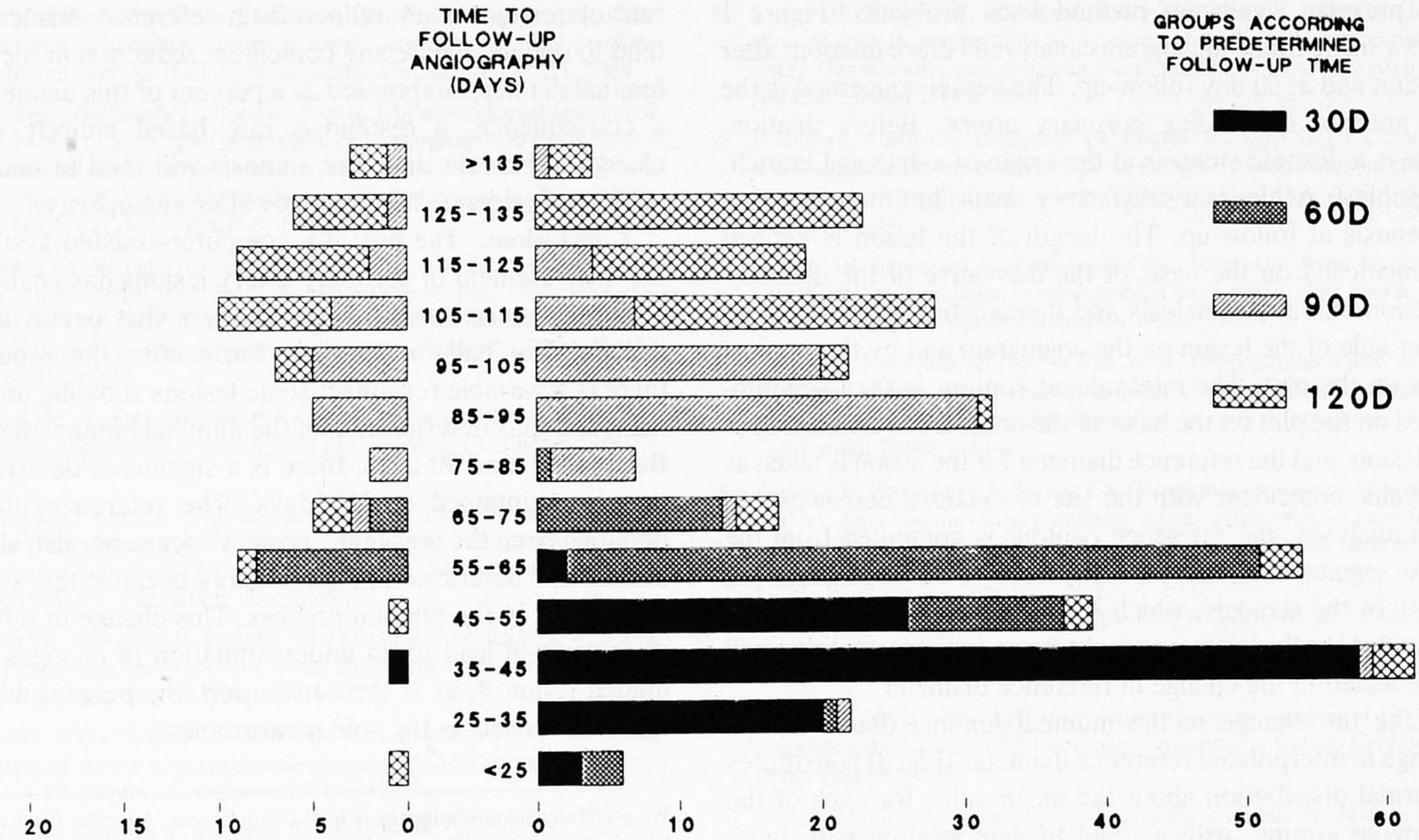


Figure 5. Actual time to follow-up according to predetermined follow-up groups, comparing lesions with restenosis (≧0.72 mm) **(left)** with those without **(right)**. See text for details.

stenosis and positioning of the balloon across the stenosis cannot always be done precisely. The diameter of these adjacent segments (considered to be relatively normal coronary arteries) is conventionally used as the reference diameter because the use of segments at a distance from the stenosis, which are not involved in the dilation process, will no longer reflect the "normal" diameter at the site of the stenosis. In the previously mentioned postmortem studies (19–22), the authors made the distinction between dilated and nondilated segments, but did not differentiate between those having changes within stenotic segments and those who did not. More recently, Waller et al. (21) observed fibrocellular proliferation in the left main stem coronary artery, which was not targeted for angioplasty, but was involved in the dilation process because of the proximity of a left anterior descending coronary artery stenosis. The proliferation was limited to the segments dilated by the balloon whether or not they were stenotic. Other case reports (26–28) also implicated intraarterial trauma as the cause for a new stenosis in segments not targeted for angioplasty.

Rationale for choosing variables to be measured. Conventionally, the severity of a coronary artery stenosis is expressed as percent diameter stenosis (that is, the diameter of the stenotic lumen as a percent of the normal lumen of the vessel). The so-called normal lumen has to be selected individually from a segment of the coronary artery immediately adjacent to the stenosis, that appears to the angiographer to be normal. This approach has several limitations (29,30). The first is that we now know that it is not possible with cineangiography to identify reliably the normal diameter of a coronary artery because of the general compensatory dilation associated with coronary artery disease (31). Also, the presence of diffuse atherosclerotic narrowing may give rise to a normal regular appearance (32), leading to an underestimation of the diameter of the normal arterial segment. Second, because of the normal variation in diameter of diseased coronary arteries composed of stenotic and ectatic segments, the selected normal segment is subject to considerable individual variation; this problem is compounded when sequential analyses are performed on the same lesion. Third, between two analyses the selected normal segment may undergo a significant change that will not be recognized unless the segment is measured quantitatively. The use of the interpolated reference diameter minimizes these potential errors because it is not arbitrarily selected by the angiographer and it is based not on how an artery behaves at one point alone, but reflects the change in the segments adjacent to the stenosis both proximally and distally.

Factors contributing to variability of measurement. Despite these considerations, serial analysis of a dilated lesion

JACC Vol. 12, No. 2
August 1988:315–23

still presents significant methodologic problems. Figure 1 shows single frame angiograms analyzed before dilation, after dilation and at 60 day follow-up. The vessel concerned is the left anterior descending coronary artery. Before dilation, there is a discrete stenosis at the origin of a diagonal branch. Angioplasty achieves a satisfactory result, but there is a long restenosis at follow-up. The length of the lesion is defined automatically on the basis of the derivative of the diameter function curvature analysis and demarcated by the lines on either side of the lesion on the angiogram and by the vertical lines on the plot. The interpolated contour is then superimposed on the plot on the basis of the contours to either side of the lesion, and the reference diameter for the lesion is taken as the value coincident with the site of maximal narrowing. In such analyses, the reference contour is computed from the same segments of the coronary artery, but excluding the length of the stenosis, which is automatically defined by the computer. In this way, any real change in these contours will be reflected in the change in reference diameter.

Like the change in the minimal luminal diameter, the change in interpolated reference diameter (Fig. 3) constitutes a normal distribution about the mean value for each of the follow-up groups, with a trend to deterioration with time. The greatest deterioration is seen between 60 and 90 days, but the trend is still evident between 90 and 120 days. The possibility that this change in reference diameter is artifactual has been addressed; there are reasons why this is unlikely. The first is that the change follows the same trend as that of the minimal luminal diameter, suggesting the underlying causative mechanism is the same. Second, if there was a factor (such as the degree of pharmocologic vasodilation) causing the change, it would be expected that a similar change would be seen in all the follow-up groups and not just in the latter two.

The incidence of restenosis and the timing will be influenced by the selection of patients for reinvestigation, and the selection of symptomatic patients has certainly been relevant to other studies (1,2). It is inevitable that not all patients will be restudied at their originally allocated time, usually because recurrent symptoms dictate early investigation. Figure 5 shows the actual time from angioplasty to follow-up study, comparing those lesions that underwent restenosis with those that did not. Most patients were restudied at or near their preset time. Analysis of the data according to actual time to follow-up study rather than allocated time to follow-up study does not materially alter the results.

Restenosis: implications for follow-up studies. All of the larger follow-up studies after coronary angioplasty have expressed the results in terms of the changes in percent diameter stenosis. Thus, there is little information available on the change in minimal luminal diameter independent of the change in reference diameter. Any change in the reference diameter, as one of the variables on which percent diameter stenosis measurement is based, will influence the rate of restenosis. A reduction in reference diameter will tend to underestimate any coincident reduction in the vessel luminal diameter expressed as a percent of this diameter. As a consequence, a restenosis rate based entirely on the change in percent diameter stenosis will tend to underestimate the incidence of restenosis after angioplasty.

Conclusions. The use of a computer-assisted system for the measurement of coronary artery lesions has enabled the accurate determination of the changes that occur in these lesions after balloon dilation. Early after the procedure, there is a variable response, some lesions showing improvement and thus deterioration of the minimal luminal diameter. Between 60 and 90 days, there is a significant deterioration that is maintained at 120 days. The reference diameter obtained from the adjacent "normal" segment, also shows a similar late deterioration, presumably because this segment is involved in the dilation process. This change in reference diameter will lead to an underestimation of changes in the dilated lesion if, as is the convention, the percent diameter stenosis is used as the sole measurement.

We gratefully acknowledge the help of Gusta Koster, Anja van Huuksloot and Claudia Sprenger de Rover in the preparation of this manuscript.

References

1. Leimgruber PP, Roubin GS, Hollman J, et al. Restenosis after successful coronary angioplasty in patients with single-vessel disease. Circulation 1986;73:710–7.
2. Holmes DR, Vlietstra RE, Smith HC, et al. Restenosis after percutaneous transluminal coronary angioplasty (PTCA): a report from the PTCA Registry of the National Heart, Lung, and Blood Institute. Am J Cardiol 1984;53:77C–81C.
3. Kaltenbach M, Kober G, Scherer D, Vallbracht C. Recurrence rate after successful coronary angioplasty. Eur Heart J 1985;6:276–82.
4. Meyer J, Schmitz HJ, Kiesslich T, et al. Percutaneous transluminal coronary angioplasty in patients with stable and unstable angina pectoris: analysis of early and late results. Am Heart J 1983;106:973–80.
5. Levine S, Ewels CJ, Rosing DR, Kent KM. Coronary angioplasty: clinical and angiographic follow-up. Am J Cardiol 1985;55:673–6.
6. Steele PM, Chesebro JH, Stanson AW, et al. Balloon angioplasty: natural history of the pathophysiological response to injury in a pig model. Circ Res 1985;57:105–12.
7. de Feyter PJ, Serruys PW, van den Brand M, et al. Emergency coronary angioplasty in refractory unstable angina. N Engl J Med 1985;313:342–6.
8. Reiber JHC, Serruys PW, Kooijman CJ, et al. Assessment of short-, medium-, and long-term variations in arterial dimensions from computer-assisted quantitation of coronary cineangiograms. Circulation 1985;71: 280–8.
9. Reiber JHC, Serruys PW, Kooijman CJ, Slager CJ, Schuurbiers JCH, den Boer A. Approaches towards standardization in acquisition and quantitation of arterial dimensions from cineangiograms. In: Reiber JHC, Serruys PW, eds. State of the Art in Quantitative Coronary Arteriography. Dordrecht: Martinus Nijhoff, 1986:145.
10. Reiber JHC, Kooijman CJ, den Boer A, Serruys PW. Assessment of dimensions and image quality of coronary contrast catheters from cineangiograms. Cathet Cardiovasc Diagn 1985;11:521–32.

11. Wijns W, Serruys PW, Reiber JHC, et al. Quantitative angiography of the left anterior descending coronary artery: correlations with pressure gradient and exercise thallium scintigraphy. Circulation 1985;71:273–9.

12. Reiber JHC, Gerbrands JJ, Booman F, et al. Objective characterization of coronary obstructions from monoplane cineangiograms and three-dimensional reconstruction of an arterial segment from two orthogonal views. In: Schwartz MD, ed. Applications of Computers in Medicine. New York: IEEE Cat. No. TH0095-0, 1982:93.

13. Kooijman CJ, Reiber JHC, Gerbrands JJ, et al. Computer-aided quantitation of the severity of coronary obstructions from single view cineangiograms. In: First IEEE Computer Society International Symposium on Medical Imaging and Image Interpretation. New York: IEEE Cat. No. 82 CH1804-4, 1982:59.

14. Serruys PW, Luijten HE, Beatt KJ, et al. Incidence of restenosis after successful angioplasty: a time related phenomenon. Circulation 1988;77: 361–71.

15. Johnson MR, Brayden GP, Ericksen EE, et al. Changes in cross-sectional area of the coronary lumen in the six months after angioplasty: a quantitative analysis of the variable response to percutaneous transluminal angioplasty. Circulation 1986;73:467–75.

16. Kramer JR, Kitazuma H, Proudfit WL, Matsuda Y, Williams GW, Sones FM. Progression and regression of coronary atherosclerosis: relation to risk factors. Am Heart J 1983;105:134–44.

17. Bruschke AVG, Wijers TS, Kolsters W, Landmann J. The anatomic evolution of coronary artery disease demonstrated by coronary arteriography in 256 patients. Circulation 1981;63:527–36.

18. Kramer JR, Matsuda Y, Mulligan JC, Aronow M, Proudfit WL. Progression of coronary atherosclerosis. Circulation 1981;63:519–25.

19. Shub C, Vlietstra RE, Smith HC, Fulton E, Elveback LR. The unpredictable progression of symptomatic coronary artery disease: a serial clinical-angiographic analysis. Mayo Clin 1981;56:155–60.

20. Essed CE, van den Brand M, Becker AE. Transluminal coronary angioplasty and early restenosis: fibrocellular occlusion after wall laceration. Br Heart J 1983;49:393–6.

21. Waller BF, McManus BM, Gorfinkel HJ, et al. Status of the major epicardial coronary arteries 80 to 150 days after percutaneous transluminal coronary angioplasty: analysis of necropsy patients. Am J Cardiol 1983;51:81–4.

22. Austin GE, Ratliff NB, Hollman J, Tabei S, Philips DF. Intimal proliferation of smooth muscle cells as an explanation for recurrent coronary artery stenosis after percutaneous transluminal coronary angioplasty. J Am Coll Cardiol 1985;6:369–75.

23. Hollman J, Austin GE, Gruentzig AR, Douglas JS, King SB III. Coronary artery spasm at the site of angioplasty in the first 2 months after successful percutaneous transluminal coronary angioplasty. J Am Coll Cardiol 1983;2:1039–45.

24. Wilentz JR, Sanborn TA, Handenschild CC, Valeri CR, Ryan TJ, Faxon DP. Platelet accumulation in experimental angioplasty: time course and relation to vascular injury. Circulation 1987;75:636–42.

25. Lam JYT, Chesebro JH, Steele PM, et al. Deep arterial injury during experimental angioplasty: relation to positive indium-III–labeled platelet scintigram, quantitative platelet deposition and mural thrombosis. J Am Coll Cardiol 1986;8:1380–6.

26. Waller BE, Pinkerton CA, Foster CN. Morphologic evidence of accelerated left main coronary artery stenosis: a late complication of percutaneous transluminal balloon angioplasty of the proximal left anterior descending coronary artery. J Am Coll Cardiol 1987;9:1019–23.

27. Hamby RI, Amm HS, Gulotta SJ, Ricciardi R. Coronary artery stenosis complicating coronary angioplasty: report of six cases. Am Heart J 1987;114:639–43.

28. Graft RH, Verani MS. Left main coronary artery stenosis: a possible complication of transluminal coronary angioplasty. Cathet Cardiovasc Diagn 1984;10:163–6.

29. Marcus LM. Physiological effects of a coronary stenosis. In: Marcus LM, ed. The Coronary Circulation in Health and Disease. New York: McGraw-Hill, 1983:260.

30. Harrison DG, White CW, Hiratzka LF, et al. Can the significance of a coronary artery stenosis be predicted by quantitative coronary angiography? Circulation 1981;64:160–3.

31. Glagov S, Weisenberg E, Zarins C, Stankunavicus R, Kolettis GJ. Compensatory enlargement of human atherosclerotic coronary arteries. N Engl J Med 1987;316:1371–5.

32. McPherson DD, Hiratzka LF, Lamber WC, et al. Delineation of the extent of coronary atherosclerosis by high frequency echocardiography. N Engl J Med 1987;316:394–9.