JACC Vol. 27, No. 6
May 1996:1398–405

Repeat Interventions as a Long-Term Treatment Strategy in the Management of Progressive Coronary Artery Disease

KENNETH G. LEHMANN, MD, FACC, ARTHUR C. MAAS, MD,* RON VAN DOMBURG, MS,* PIM J. DE FEYTER, MD, PHD, FACC,* MARCEL VAN DEN BRAND, MD, PHD, FACC,* PATRICK W. SERRUYS, MD, PHD*

Rotterdam, The Netherlands and Seattle, Washington

Objectives. **This study investigates whether repeat coronary interventions, applied over an extended time period, can successfully curtail the progression of ischemic symptoms and angiographic lumen narrowing.**

Background. **Coronary artery disease is a chronic and generally progressive disorder, and potential treatment strategies should be examined and compared with this chronicity in mind. Percutaneous interventional revascularization procedures could theoretically be useful in controlling progression of the disease through repeated use as new coronary lesions arise. However, the outcome of this long-term management concept has not previously been subjected to detailed investigation.**

Methods. **From a consecutive series of 4,357 interventional cardiac procedures, 544 patients were identified who received two or more interventions during the 13-year study period. These patients were categorized into one of three groups: *restenosis* (repeat interventions limited to the same target segment, n = 261), *new stenosis* (all repeat interventions directed to stenoses not previously treated, n = 155) or *both* (repeat interventions directed both to the same and to different target lesions, n = 128).**

Results. **Two to five procedures were performed per patient; the time period (mean ± SD) separating each procedure was significantly less (p < 0.0001) for the restenosis group (4.2 ± 2.3 months) than for the new stenosis (24.2 ± 23.5 months) or the "both" groups (11.4 ± 11.0 months). Despite the need for repeat procedures, the severity of angina (mean New York Heart Association functional class 1.6 ± 0.9) after 6.2 ± 2.3 years of follow-up was substantially better than before the initial procedure (mean functional class 3.2 ± 0.8), with a similar magnitude of change found in all three groups. This long-term functional improvement was mirrored by a corresponding anatomic improvement, with the mean number of diseased vessels remaining constant at the time of each procedure (1.5 ± 0.7, 1.5 ± 0.7 and 1.6 ± 0.7, respectively, for the first, second and third procedures, p = NS). The restenosis and the new stenosis groups also demonstrated statistically similar annual rates of mortality (1.9% vs. 1.8%) and coronary surgery (2.3% vs. 2.6%), although the restenosis group had a lower rate of infarction (1.4% vs. 3.2%, p = 0.002).**

Conclusions. **Repeat interventional treatment of newly acquired stenoses provides a rational approach for the long-term management of chronic coronary artery disease. In addition to yielding a favorable late outcome, the use of this strategy can result in sustained functional improvement and can check the progression of clinically significant stenoses.**

(J Am Coll Cardiol 1996;27:1398–405)

The use of coronary angioplasty and related interventional procedures has proved (1) to be clinically helpful in the management of the acute manifestations of coronary artery disease. Relative to medical therapy, continued subjective and objective improvement have been documented (2) for ≥6 months after the procedure. Retrospective uncontrolled analyses (3–6) have also provided insight into effectiveness of this strategy 5 to 10 years later.

The primary alternative to percutaneous intervention is coronary artery surgery. When opting for a surgical approach, a significant reduction of symptoms can be anticipated on the basis of results of several randomized trials (7,8). However, this benefit appears to be finite in duration. Ten-year follow-up data (7–9) reveal an unfortunate trend toward loss of the initial angina relief and improved activity tolerance gained through the operation. This pattern probably stems from the well recognized tendency of many venous bypass conduits to occlude within 10 years of implantation (10). The recent preferential use of arterial conduits may improve the long-term patency in coronary arteries grafted with these vessels, but total arterial revascularization remains uncommon (11). Repeat operation can be undertaken, but increased mortality and reduced success can accompany additional bypass procedures (12,13).

Repeat percutaneous intervention has long been considered the therapy of choice for appropriate persons experiencing coronary restenosis within the 1st year after angioplasty

From the University of Washington School of Medicine, Seattle, Washington; and *The Thoraxcenter, Erasmus University, Rotterdam, The Netherlands.
This work was presented in part at the 67th Scientific Sessions of the American Heart Association, Dallas, Texas, November 1994.

Manuscript received August 10, 1995; revised manuscript received December 14, 1995, accepted December 22, 1995.

Address for correspondence: Dr. Patrick W. Serruys, Thoraxcentrum Cardiologie (Bd 418), Academisch Ziekenhuis-Rotterdam-Dijkzigt, DR Molewater Plein 40, 3015 GD Rotterdam, The Netherlands.

0735-1097/96/$15.00
PII S0735-1097(96)00002-3

(14). However, repeat procedures can also be used to treat new coronary stenoses that may arise years after a successful initial intervention. Relative to a second or third coronary operation, repeat percutaneous intervention provides a potentially more attractive approach for several reasons. 1) Medical expenses and patient recovery time are generally lower (15–17), reducing the financial and social burden of multiple additional procedures. 2) Repeat intervention can be attempted with anticipated success and complication rates comparable to those of patients undergoing a first intervention. 3) Repeat percutaneous procedures can probably be continued in the future even as a patient ages or acquires comorbidities, factors that could preclude candidacy for repeat bypass operation (18–20).

Despite its inherent appeal, the utility of repeat percutaneous coronary intervention as a long-term management strategy for new lesions has not previously been subjected to detailed formal investigation. This issue is examined in the present study derived from the 13-year experience of a high volume center.

Methods

Study patients. Participants in this investigation were derived from the 4,357 consecutive interventional cardiac procedures performed at the Thoraxcenter between September 1980 and April 1991. This latter date provided a minimum of 2.5 years of follow-up for every patient in the study. Additional criteria for entrance into the current study consisted of 1) two or more interventional procedures performed at this or another facility; 2) a minimum of 7 days separating each procedure to help eliminate planned staged procedures or unplanned repeat intervention due to complications arising from the initial procedure; and, 3) first interventional procedure performed for either stable or unstable angina but not for evolving myocardial infarction. Potential candidates were identified using the Thoraxcenter interventional data base, with final acceptance contingent on verification and thorough review of all clinical and procedural records. The 544 patients who satisfied all these criteria form the basis of this report.

Patient classification. Each enrolled patient was assigned to one of three mutually exclusive groups based on location of the target lesion or lesions. The *restenosis group* had repeat interventions limited to the same target segments treated during the initial procedure for each and every subsequent intervention. In the *new stenosis group*, all subsequent interventions occurred in coronary segments not treated at any time previously. The *both* group included all remaining patients and consisted of those undergoing repeat interventions directed both to the same and to different target segments; these interventions may or may not have been performed during the same repeat procedure. Target coronary segments treated >12 months after the last intervention in that same segment were considered new stenoses and not restenosis (21). Coronary segmentation was based on the classification scheme of the American Heart Association (22), with stenoses >50% considered clinically significant. All patients with one or more repeat procedures performed in a contiguous coronary artery segment (such as the proximal left anterior descending artery in the first procedure and the mid left anterior descending artery in the second) were analyzed for possible target segment misclassification. Those found by careful analysis of records and cine films to be categorized incorrectly were reassigned to the appropriate group.

Long-term follow-up. Follow-up data were obtained by using two complementary strategies. First, written inquiries on patient whereabouts and vital status were sent to the local Civil Registration Service for each of the 544 participants using their last known address. In The Netherlands, municipal records such as these are generally quite accurate and complete. For patients who had moved to new areas, additional inquiries were undertaken until the location of their current residence was firmly established. Questionnaires were then mailed to all living participants. Patients were queried as to current angina status with the use of a series of questions designed to reliably replicate the New York Heart Association classification scheme. Information on the occurrence, location and timing of cardiac admissions, myocardial infarctions, repeat revascularization procedures and medication use was also requested. Nonresponders were contacted by repeated mailings and ultimately by telephone. Ambiguous responses were also clarified by phone. Overall, 92.7% of personal patient responses were obtained.

Second, additional follow-up data were obtained by record review. This source was used to verify positive patient responses to questions on interval myocardial infarctions and revascularization procedures. Outside records were also sought and obtained for infarctions and procedures occurring at other medical centers. Because of the inherent inaccuracy of the remote recall of symptoms, the medical record was used as the sole source of data regarding the presence and severity of angina pectoris preceding each interventional procedure. The follow-up rate by record review was 97.2%.

Data analysis. The data were analyzed by using the CLINT data base system (23) in conjunction with Biomedical Data Processor version 7.0. Categoric data were compared by using the chi-square statistic. Continuous variables were analyzed by using one-way analysis of variance, with the Tukey multiple range test employed for post hoc intergroup comparisons. Life tables were calculated according to the Kaplan-Meier method, and the generalized Wilcoxon test was selected to detect potential differences between groups. Plus over minus values represent mean value ± SD. Mean differences associated with a p value ≤ 0.05 were deemed statistically significant.

Results

Baseline patient characteristics. Of the 544 enrolled patients who underwent repeat procedures, 261 (48%) had all subsequent interventions limited to retreatment of their initial target stenosis or stenoses (restenosis group), 155 (28%) underwent repeat interventions limited to stenoses that had

Table 1. Patient Characteristics at Initial Procedure

	Group		
	Restenosis (n = 261)	New Stenosis (n = 155)	Both (n = 128)
Age (yr) (mean;range)	58;30-83	56;33-84	56;31-79
Men	207 (79)	117 (75)	103 (80)
Previous MI	93 (36)	65 (42)	52 (41)
Previous CABG*	23 (9)	16 (10)	22 (17)
Angina severity (NYHA class)			
I	1 (0)	2 (1)	0 (0)
II	57 (24)	43 (29)	22 (18)
III	79 (33)	51 (34)	45 (37)
IV	105 (43)	54 (36)	56 (45)
Indication for procedure			
Unstable angina	120 (46)	56 (36)	49 (38)
Stable angina	141 (54)	99 (64)	79 (62)
Coronary disease severity†			
Single vessel	172 (66)	86 (56)	68 (53)
Double vessel	62 (24)	55 (35)	37 (29)
Triple vessel	27 (10)	14 (9)	23 (18)
Extent of procedure*			
Single lesion/single vessel	175 (67)	124 (80)	84 (65)
Multilesion/single vessel	48 (18)	16 (10)	25 (20)
Multilesion/multivessel	38 (15)	15 (10)	19 (15)
Angiographic procedural success			
Yes	256 (98)	146 (94)	119 (93)
Partial‡	5 (2)	2 (1)	2 (2)
No	——	7 (5)	7 (5)
Major complications			
Urgent operation	0 (0)	2 (1)	3 (2)
Acute MI	2 (1)	3 (2)	4 (3)

*$p < 0.05$. †$p < 0.01$. ‡Successful treatment of some but not all attempted target stenoses. Values represent means of continuous variables and counts of categoric variables, with percentages indicated by parentheses. CABG = coronary artery bypass surgery; MI = myocardial infarction; NYHA class = New York Heart Association functional class.

not been treated previously (new stenosis group) and 128 (24%) had subsequent procedures directed both to prior target stenoses and to new target stenoses ("both" group). As detailed in Table 1, the three groups were similar with respect to mean age (57 years), gender (78% men) and the presence of previous myocardial infarction (39%). Prior coronary artery surgery was slightly more common ($p < 0.05$) in patients in the "both" group. Most patients had severe angina pectoris before intervention (72% in New York Heart Association class III or IV), but the pain pattern was deemed stable in the majority (59%). No statistically significant differences in angina severity or stability were found between groups.

At the time of the initial procedure (Table 1), single-vessel disease was more prevalent in the restenosis group than in either the new stenosis or the "both" group (66% vs. 56% and 53%, respectively, $p < 0.01$). This observation might be explained in part by a greater propensity of patients with initially more severe disease to develop new lesions requiring intervention in the future. Despite more single-vessel disease, patients in the restenosis group initially received more multilesion angioplasty (33% vs. 20% for the new stenosis group, $p < 0.05$).

Complete angiographic success rates for the initial procedures were high overall (98% vs. 94% vs. 93%, p = NS). The complete failure rate of 0 for the restenosis group reflects the study's requirement of angiographic success in at least one target stenosis in all patients experiencing restenosis in the future. Major complications consisted of urgent coronary bypass surgery in five patients and acute myocardial infarction in nine, with differences between groups statistically nonsignificant.

Repeat procedures. On average, each patient underwent 2.36 interventional procedures; 13 patients underwent the maximal number of 5 interventions. In addition to the per patient analyses described, the data on all 740 repeat procedures were analyzed on a per procedure basis (Table 2). A total of 946 target stenoses were treated during these procedures; the mean number of target stenoses per procedure ranged from 1.08 for the restenosis group to 1.52 for the "both" group.

Single-vessel disease at the time of the repeat procedures was substantially more common in the restenosis group (73% vs. 56% for the new stenosis and 51% for the "both" group, $p < 0.0001$) as were single-lesion interventional procedures (93% vs. 76% and 56%, respectively, $p < 0.0001$). The left anterior descending artery was a more typical target in the restenosis group (54% vs. 31% and 38%, $p < 0.0001$). Balloon angioplasty was the sole device used in 86% of repeat interventions, a finding consistent with the era selected for patient enrollment. The use of other devices was equally distributed among groups (p = NS).

Complete angiographic success was significantly less frequent ($p < 0.0001$) in the new stenosis group (79%) than in the restenosis (91%) or the "both" (89%) group. However, major complications were rare in all three groups (p = NS).

The mean time interval separating each interventional procedure differed considerably among groups ($p < 0.0001$) (Fig. 1). Whereas patients with restenosis had an interprocedural interval averaging 4.2 ± 2.3 months, patients with new stenosis underwent intervention after a much longer interval of 24.2 ± 23.5 months. Patients in the "both" group had an intermediate interprocedural interval (11.4 ± 11.0 months).

Long-term effect on symptoms and disease severity. Overall, the strategy of repeat interventions appears to have had a favorable impact on angina status (Fig. 2). For this analysis, we censored patients who had incomplete data on initial or final angina status; however, the results were virtually identical when the analysis was repeated without censoring. At the end of 6.2 ± 2.3 years of follow-up, 211 patients (57%) were in functional class I. This group includes 61% of the patients who were in class III or IV before their initial procedure. The mean initial functional class of 3.2 ± 0.8 decreased to 1.6 ± 0.9 at the end of follow-up ($p < 0.0001$).

This analysis can be further expanded by considering symptom status segregated by groups and stratified by time. Figure 3 reveals that mean functional class was visually and statisti-

Table 2. Characteristics of Repeat Procedures

	Group		
	Restenosis	New Stenosis	Both
Procedures (no.)	316	177	247
Target stenoses (no.)	341	230	375
Mean target stenoses/procedure	1.08	1.30	1.52
Coronary disease severity*			
Single vessel	230 (73)	100 (56)	126 (51)
Double vessel	53 (17)	53 (30)	73 (30)
Triple vessel	33 (10)	24 (14)	48 (19)
Indication for procedure†			
Acute MI	4 (1)	10 (6)	7 (3)
Unstable angina	73 (23)	41 (23)	76 (31)
Stable angina	239 (76)	126 (71)	164 (66)
Extent of procedure*			
Single lesion/single vessel	293 (93)	135 (76)	139 (56)
Multilesion/single vessel	14 (4)	25 (14)	64 (26)
Multilesion/multivessel	9 (3)	18 (9)	44 (18)
Type of procedure			
Balloon angioplasty	265 (84)	159 (90)	215 (87)
Coronary stent	30 (9)	11 (6)	19 (8)
Directional atherectomy	19 (6)	4 (2)	7 (3)
Other	2 (1)	3 (2)	6 (2)
Angiographic procedural success‡			
Yes	287 (91)	140 (79)	220 (89)
Partial	1 (0)	6 (3)	14 (6)
No	28 (9)	31 (18)	13 (5)
Major complications			
Death	3 (1)	0 (0)	1 (1)
Urgent operation	6 (2)	6 (3)	4 (2)
MI	9 (3)	14 (8)	10 (4)
Target vessel (946 lesions)*			
RCA	83 (24)	81 (35)	123 (33)
LAD	184 (54)	71 (31)	141 (38)
LCx	52 (15)	67 (29)	80 (21)
Graft	22 (6)	11 (5)	31 (8)
Prior procedures (no.)*			
One	261 (82)	155 (88)	128 (52)
Two	44 (14)	22 (12)	79 (32)
Three	9 (3)	0 (0)	29 (12)
Four	2 (1)	0 (0)	11 (4)
Time interval between procedures (mo)*			
Procedure 1 vs. 2	4.2 ± 2.3	23.5 ± 23.8	11.5 ± 17.2
Procedure 2 vs. 3	4.4 ± 4.0	32.0 ± 23.2	15.5 ± 20.7
Procedure 3 vs. 4	6.8 ± 5.3	—	16.6 ± 19.5
Procedure 4 vs. 5	4.3 ± 1.5	—	19.3 ± 15.8

*$p < 0.0001$. †$p < 0.05$. ‡Successful treatment of some but not all attempted target stenoses. Values represent means of continuous variables and counts of categoric variables, with percentages indicated by parentheses. LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; MI = myocardial infarction; RCA = right coronary artery.

cally similar just before each procedure (3.2, 2.9 and 3.2 before the first, second and third procedures, respectively, p = NS). More important, no significant differences in angina severity were observed at any time among the three groups.

We sought to assess whether this substantial functional improvement in coronary disease severity was mirrored by a corresponding anatomic improvement. Figure 4 displays overall coronary disease severity (quantified by using the mean number of vessels containing significant stenoses) at six different points in time (before and immediately after the first, second and third procedures). As shown, each procedure is accompanied by a statistically similar improvement in disease severity. Moreover, the severity at the start of each procedure does not increase with time but remains relatively constant (1.5 ± 0.7 for the first, 1.5 ± 0.7 for the second and 1.6 ± 0.7 for the third procedure, p = NS).

Prognosis and clinical end points. The occurrence of major clinical events (death, coronary artery surgery and nonfatal

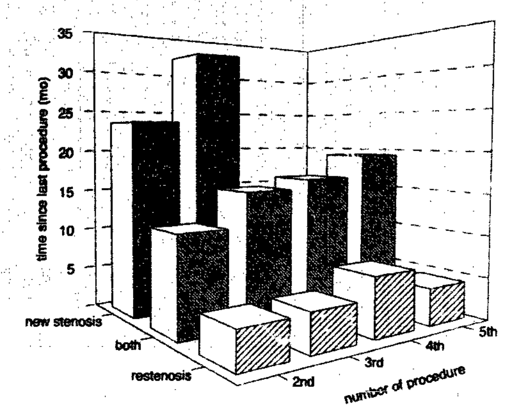


Figure 1. Three-dimensional bar graph depicting the mean time interval separating the current percutaneous coronary interventional procedure from its most immediate predecessor. The procedure number is displayed on the x axis, patients segregated into groups on the y axis, and the number of months since the last procedure on the z axis. The difference between groups was highly significant for each procedure number ($p < 0.0001$), whereas the apparent trend toward greater mean time intervals with later procedures was statistically nonsignificant. There were no fourth or fifth procedures in the new stenosis group.

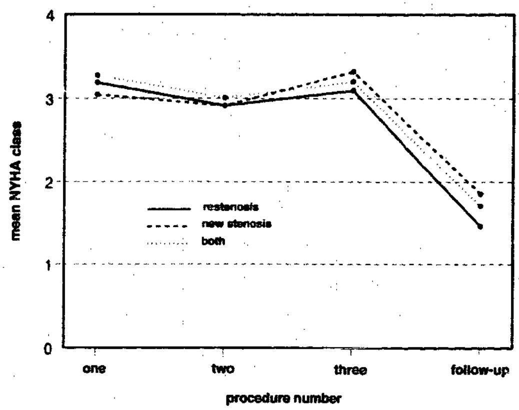
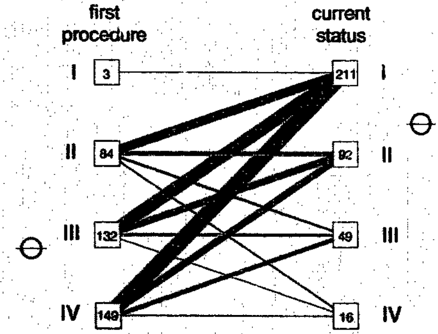


Figure 3. Angina severity represented by mean New York Heart Association (NYHA) class, grouped by patients in the restenosis, new stenosis or "both" groups. Data are presented for before the first procedure (one), before the second procedure (two), before the third procedure (three) and for final follow-up (follow-up). The small number of patients undergoing more than three procedures precluded inclusion of additional data points. The groups did not differ significantly from one another at any time point, nor did the overall data differ significantly among the first, second and third procedures. However, the differences between angina status before each procedure and angina status at final follow-up were all highly significant ($p < 0.0001$).

myocardial infarction) experienced at any time during the study period was determined for 97.2% of participants. Figure 5 provides 10-year survival curves for each group based on Kaplan-Meier estimates. Although the new stenoses group shows a nonsignificant trend toward improved survival during the 1st 4 years, the overall annual mortality rates were similar (1.9%, 1.8% and 2.9% per year, respectively, for the restenosis, new stenosis and "both" groups, p = NS). Figure 6 presents analogous curves based on the performance of coronary bypass surgery during follow-up. For these analyses, the 61 patients (11%) who had undergone coronary surgery before their first percutaneous intervention were excluded, because this preenrollment event could have easily influenced the decision for or against surgery during follow-up. Again, the restenosis and new stenosis groups demonstrated similar event rates (2.3% vs. 2.6%). The surgery rate for the "both" group was slightly but nonsignificantly higher (4.5%, p = NS). Figure 7 provides data on the rates of nonfatal myocardial infarction. Unlike previous analyses, a significant difference was observed between groups, with a lower annual infarction rate observed for patients in the restenosis group (1.4% vs. 3.2% and 2.8%, respectively; $p = 0.002$).

Figure 2. New York Heart Association classification of angina severity in 368 patients assessed immediately before the initial procedure and at final follow-up. Patients with incomplete data on angina status for either period were excluded. The **columns of Roman numerals** represent angina classes I through IV; the **values in the squares** represent the number of patients in that specific angina class at each time period; the **thickness of the lines** interconnecting the boxes is directly proportional to the number of patients involved; **the outermost circles** present mean values of angina class for the two periods. The overall changes observed were highly significant ($p < 0.0001$).



Discussion

Characteristics of repeat procedures. The clinical decision to attempt repeat intervention obviously depends on many factors, including the likelihood of success, the anticipated frequency of complications and the viability of alternative modes of treatment. Nevertheless, in the current study the threshold for percutaneous intervention, as gauged by preprocedural angina severity, proved to be similar between the initial procedure and all subsequent repeat procedures. This pattern was found with both restenosis and new stenosis. In contrast, the timing of the repeat procedures was quite different.

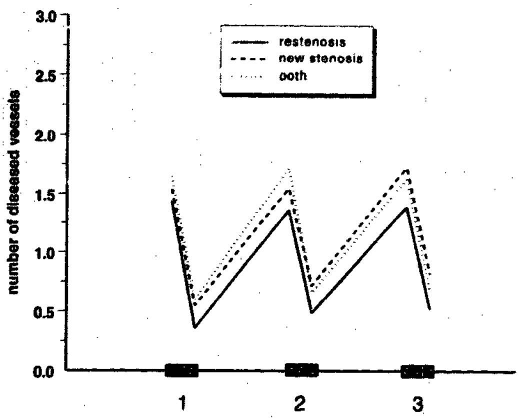
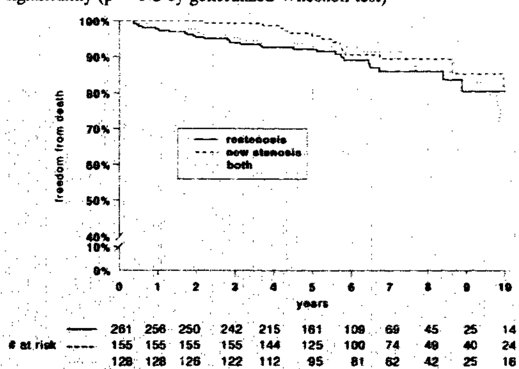


Figure 4. Overall coronary disease severity, represented by the mean number of major coronary arteries (or their branches) possessing stenoses with >50% diameter reduction. Values for each group are presented at six time points—immediately before and after the first, second and third interventional procedures. The small number of patients undergoing more than three procedures precluded inclusion of these additional data points. The groups did not differ significantly from one another at any point in time, nor did the overall data differ significantly when comparing preprocedural values with one another or when comparing postprocedural values with one another. However, all reductions in severity of angiographically assessed disease observed at each procedure were highly significant ($p < 0.0001$).

Additional procedures for restenosis occurred on average 4 months after the previous procedure, a time course consistent with the process of late lumen narrowing (21). However, repeat procedures directed to new stenoses were performed on average 2 years after the previous intervention. Knowledge of this time frame might prove useful when assessing the practicality of repeat interventions as a long-term strategy.

Figure 5. Survival curves for all three groups depicting freedom from death from any cause for the 1st 10 years of follow-up, based on Kaplan-Meier estimates. The numbers of patients at risk at each year are shown immediately below the graph. None of the curves differ significantly (p = NS by generalized Wilcoxon test)



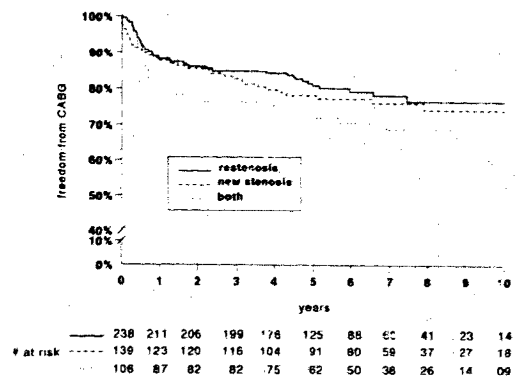
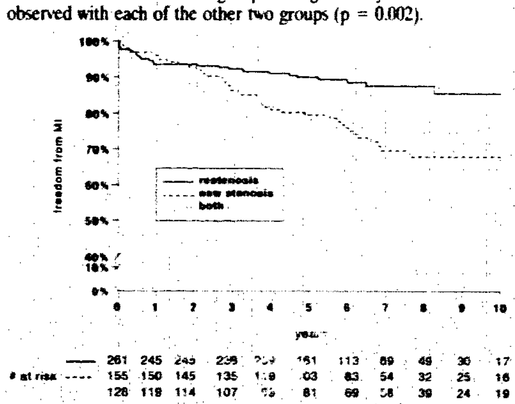


Figure 6. Curves for all three groups representing freedom from coronary artery bypass surgery (CABG) for the 1st 10 years of follow-up, based on Kaplan-Meier estimates. Patients who had undergone coronary surgery before their first percutaneous interventional procedure were excluded. The numbers of patients at risk at each year are presented immediately below the graph. None of the curves differed significantly (p = NS by generalized Wilcoxon test).

The angiographic success rate for repeat intervention in this study was not as high ($p < 0.0001$) for new as for restenotic target lesions. This finding could be anticipated, as it is known (14) that procedures directed to restenotic lesions have higher initial success rates. A more useful comparison to assess the merit of this approach may be with the initial intervention of new lesions treated over the same period as the current cohort. The National Heart, Lung, and Blood Institute registry of coronary angioplasty reported complete angiographic success rates of 65% and 82%, respectively, during the early (1977 to 1981) and late (1985) phase of the study. These rates compare with the 79% complete success rate seen for new stenoses in

Figure 7. Curves for all three groups depicting freedom from nonfatal myocardial infarction (MI) for the 1st 10 years of follow-up, based on Kaplan-Meier estimates. The numbers of patients at risk at each year are presented immediately below the graph. The overall risk of infarction for the restenosis group was significantly less than the risk observed with each of the other two groups ($p = 0.002$).



the current study, and suggest that the anticipated success rates for repeat interventions of new stenoses may be comparable to that of initial interventions of new lesions.

Impact on symptoms and adverse events. The strategy of repeat percutaneous interventions proved to be quite capable of lessening symptoms of angina pectoris over the long term, with treatment of new stenosis as successful in this regard as treatment of restenosis. During a follow-up interval extending to 13 years, 58% of patients with angina class III or IV initially changed to class I. Each repeat procedure on average was able to reestablish the magnitude of angina relief experienced with the initial intervention.

Outcomes analysis also established a relatively low rate of adverse events for all groups in the study. The 10-year survival rate for our restenosis (81%) and new stenosis (82%) groups was similar to the survival figures observed in the Coronary Artery Surgery Study (24) for both the medical (79%) and the surgical (82%) cohort, although disease severity was probably different in these two studies. The rate of bypass surgery was also statistically similar among three patient groups. Overall, despite a higher prevalence of multivessel disease at baseline, the patients undergoing repeat procedures for new stenoses did as well in three outcome domains (death, bypass surgery and symptomatic relief) as did those who underwent repeat procedures for restenosis, the latter representing a well established and widely accepted treatment strategy.

The observation of a somewhat higher rate of infarction in the new stenosis group than in the restenosis group remains both intriguing and unexplained. It is due in part to the higher rate of periprocedural myocardial infarction observed in the former group during repeat procedures and to the more frequent use of interventional procedures for the treatment of acute infarction in previously untreated stenoses. However, these two factors combined account for only a 10% difference in the observed 10-year infarction rates. Other contributory factors may include a higher prevalence of multivessel disease at baseline and the possibility of "more aggressive" disease associated with the rapid development of new lesions.

Impact on coronary anatomy. Ideally, repeat interventional procedures performed solely for restenosis might be expected to maintain the overall extent of coronary disease at or near a constant level over a prolonged period. In the current study this theory was borne out by the patients in whom this approach was used. In addition, interventions directed exclusively to newly developed stenoses accomplished this same goal. Patients in the new stenosis group had an average of 1.54 vessels with significant disease before the initial intervention, but this number was statistically similar before the second (1.55) and third (1.73) procedures despite a time span of several years. Similarly, the mean number of diseased vessels was 0.55, 0.72 and 0.82, respectively, immediately after the first, second and third interventional procedures. The treatment strategy of multiple repeat percutaneous intervention may therefore be able to check the progression of coronary disease in selected patients over the lifetime of the patient.

Potential limitations of the study. Among possible limitations of the present study is the fact that precise categorization of a newly visualized lesion as either restenotic or new can be difficult or impossible if the stenosis develops near the site of an earlier interventional procedure. Although a prospective investigation of this issue would have enhanced the reliability of our findings, it would probably have proved logistically difficult. Second, our conclusions are directly applicable only to the subset of patients whose coronary anatomy and clinical status permit serial interventions. Third, the outcomes observed are derived from procedures performed up to a decade or more in the past. Because interventional cardiology is such a rapidly evolving field, conclusions derived from work done in the 1980s may not be directly applicable to the 1990s. Nevertheless, relative to the current study, the superior safety and efficacy of modern percutaneous interventions may predict an even more favorable outcome for repeat interventional procedures in the future.

Clinical implications. The acute manifestations of coronary artery disease, such as unstable angina pectoris or myocardial infarction, rightly command the greatest attention of cardiologists and cardiac interventionalists. However, this focus often overshadows the inherently chronic nature of the underlying atherosclerotic process. When coronary atherosclerosis is viewed as a lifelong disease, it becomes obvious that procedures performed during a period of heightened symptoms should be considered not in isolation but rather as a single step in a long-term management strategy that may span several decades.

This study helps validate the use of repeat interventional procedures in the management of progressive coronary artery disease. This approach resulted in a clear decrease in symptoms during follow-up of up to 13 years, a period during which coronary bypass surgery used as a single procedure tends to lose its effectiveness (4). Adverse events were relatively infrequent, with a good 10-year survival rate observed. Perhaps most remarkable was the ability of this strategy of multiple repeat procedures to maintain the severity of angiographic disease below its level at initial presentation, even though new stenoses developed during follow-up with regular frequency. These data suggest that the use of repeat coronary interventions should be considered a rational long-term treatment strategy for appropriate patients with atherosclerotic heart disease.

References

1. Detre K, Holubkov R, Kelsey S, et al. Co-investigators of National Heart, Lung and Blood Institute's Percutaneous Transluminal Coronary Angioplasty Registry. Percutaneous transluminal coronary angioplasty in 1985–1986 and 1977–1981: The National Heart, Lung, and Blood Institute Registry. N Engl J Med 1988;318:265–70.
2. Parisi AF, Folland ED, Hartigan P. A comparison of angioplasty with medical therapy in the treatment of single vessel coronary artery disease. Veterans Affairs ACME Investigators. N Engl J Med 1992;326:10–6.
3. King SB III, Schlumpf M. Ten-year completed follow-up of percutaneous transluminal coronary angioplasty: the early Zurich experience. J Am Coll Cardiol 1993;22:353–60.
4. Talley JD, Hurst JW, King SB III, et al. Clinical outcome 5 years after

attempted percutaneous transluminal coronary angioplasty in 427 patients. Circulation 1988;77:820-9.

5. Weintraub WS, Ghazzal ZM, Cohen CL, et al. Clinical implications of late proven patency after successful coronary angioplasty. Circulation 1991;84:572-82.
6. Ellis SG, Fisher L, Dushman-Ellis S, et al. Comparison of coronary angioplasty with medical treatment for single- and double-vessel coronary disease with left anterior descending coronary involvement: long-term outcome based on an Emory-CASS registry study. Am Heart J 1989;118:208-20.
7. Rogers WJ, Coggin CJ, Gersh BJ, et al., for CASS investigators. Ten-year follow-up of quality of life in patients randomized to receive medical therapy or coronary artery bypass graft surgery (CASS). Circulation 1990;82:1647-58.
8. Peduzzi P, Hultgren H, Thomsen J, Detre K. Ten-year effect of medical and surgical therapy on quality of life: Veterans Administration Cooperative Study of coronary artery surgery. Am J Cardiol 1987;59:1017-23.
9. Laird-Meeter K, ten Katen HJ, Brower RW, et al. Angina pectoris, one to 10 years after aortocoronary bypass surgery. Eur Heart J 1983;4:678-86.
10. Fitzgibbon GM, Leach AJ, Kafka HP, Keon WJ. Coronary bypass graft fate: long-term angiographic study. J Am Coll Cardiol 1991;17:1075-80.
11. Loop FT, Lytle BW, Cosgrove DM, et al. Influence of the internal mammary artery graft on 10-year survival and other cardiac events. N Engl J Med 1986;314:1-6.
12. Foster ED, Fisher LD, Kaiser GC, Myers WO, CASS principal investigators. Comparison of operative mortality and morbidity for initial and repeat coronary artery bypass grafting: the Coronary Artery Surgery Study (CASS) registry experience. Ann Thorac Surg 1984;38:563-70.
13. Laird-Meeter K, van den Brand MJ, Serruys PW, et al. Reoperation after aortocoronary bypass procedure. Results in 53 patients in a group of 1041 with consecutive first operations. Br Heart J 1983;50:157-62.
14. Williams DO, Gruentzig AR, Kent KM, Detre KM, Kelsey SF, To T. Efficacy of repeat percutaneous transluminal coronary angioplasty for coronary restenosis. Am J Cardiol 1984;53:32C-5C.
15. Reeder GS, Krishan I, Nobrega FT, et al. Is percutaneous coronary angioplasty less expensive than bypass surgery? N Engl J Med 1984;311:1157-62.
16. Kelly ME, Taylor GJ, Moses HW, et al. Comparative cost of myocardial revascularization: percutaneous transluminal angioplasty and coronary artery bypass surgery. J Am Coll Cardiol 1985;5:16-20.
17. Hlatky MA, Lipscomb J, Nelson C, et al. Resource use and cost of initial coronary revascularization: coronary angioplasty versus coronary bypass surgery. Circulation 1990;82 Suppl IV:IV-208-13.
18. Thompson RC, Holmes DR, Gersh BJ, Bailey KR. Predicting early and intermediate-term outcome of coronary angioplasty in the elderly. Circulation 1993;88:1579-87.
19. Elayda MA, Hall RJ, Gray AG, Mathur VS, Cooley DA. Coronary revascularization in the elderly patient. J Am Coll Cardiol 1984;3:398-402.
20. Montague NT III, Kouchoukos NT, Wilson TAS, et al. Morbidity and mortality of coronary bypass grafting in patients 70 years of age and older. Ann Thorac Surg 1985;39:552-7.
21. Nobuyoshi M, Kimura T, Nosaka H, et al. Restenosis after successful percutaneous transluminal coronary angioplasty: serial angiographic follow-up of 229 patients. J Am Coll Cardiol 1988;12:616-23.
22. Austen WG, Edwards GE, Frye RL, et al. A reporting system on patients evaluated for coronary artery disease. Report of the ad hoc committee for grading of coronary artery disease, Council on Cardiovascular Surgery, American Heart Association. Circulation 1975;51:7-40.
23. van Domburg RT, Sanders WJ, Hoare MR, Zeelenberg C. CLINT, a software package for acquiring and processing multiple choice and numeric data for clinical trials. Computers in Cardiology. Long Beach (CA): IEEE Computer Society, 1984:301-4.
24. Alderman EL, Bourassa MG, Cohen LS, et al., for CASS investigators. Ten-year follow-up of survival and myocardial infarction in the randomized Coronary Artery Surgery Study. Circulation 1990;82:1629-46.