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# Can Restenosis After Coronary Angioplasty Be Predicted From Clinical Variables?

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*Objectives.* The purpose of this study was to determine whether variables shown to correlate with restenosis in one group (learning group) could be shown to predict recurrent stenosis in a second group (validation group).

*Background.* Restenosis remains a critical limitation after percutaneous transluminal coronary angioplasty. Although several clinical variables have been shown to correlate with restenosis, there are few data concerning attempts to predict recurrent stenosis.

*Methods.* The source of data was the clinical data base at Emory University. Patients who had had previous coronary surgery and patients who underwent coronary angioplasty in the setting of acute myocardial infarction were excluded. A total of 4,006 patients with angiographic restudy after successful angioplasty were identified. They were classified into a learning group of 2,500 patients and a validation group of 1,506 patients. The correlates of restenosis in the learning group were determined by stepwise logistic regression, and a model was developed to predict the probability of restenosis and was tested in the validation group. By using various cut points for the predicted probability of restenosis, a receiver operating characteristic curve was created. Goodness of fit of the model was evaluated by comparing average predicted probabilities with average observed probabilities within subgroups on the basis of risk level determined by linear regression analysis.

*Results.* In the learning group 1,145 patients had restenosis and 1,355 did not. Correlates of restenosis were severe angina, severe diameter stenosis before angioplasty, left anterior descending coronary artery dilation, diabetes, greater diameter stenosis after angioplasty, hypertension, absence of an intimal tear, eccentric morphology and older patient age. The model derived from the learning group was used to predict restenosis in the validation group. By varying the cut point for the predicted probability of restenosis above which restenosis is diagnosed and below which it is not, a receiver operating characteristic curve was created. The curve was close to the line of identity, reflecting a poor predictive ability. However, the model was shown to fit well with the predicted probability of restenosis correlating well with the observed probability ($r = 0.98$, $p = 0.0001$).

*Conclusions.* Clinical variables provide limited ability to predict definitively whether a particular patient will have restenosis. However, the current model may be used to predict the probability of restenosis, with some uncertainty, at least in well characterized patients who have already had angioplasty.

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Restenosis remains a major limitation of percutaneous coronary angioplasty (1–4). The ability to successfully predict which patients will develop restenosis may be useful in selecting cases for angioplasty. Although extensive published data have defined the risk factors for restenosis (3,4), there are few data on the ability of clinical variables to predict restenosis. It was the purpose of this study to determine the clinical variables predicting restenosis, develop a prediction model from these variables and then test this model in a validation data set.

## Methods

**Study patients.** From June 1980 through June 1991, 9,058 patients without prior percutaneous transluminal coronary angioplasty or coronary surgery had elective coronary angioplasty performed successfully without complications at Emory University or Crawford W. Long Hospitals. Included in this analysis were patients who had the procedure performed electively for stable or unstable angina pectoris or after several days' stabilization after acute myocardial infarction. Those who had the procedure performed in the acute stage of myocardial infarction or after cardiopulmonary resuscitation for cardiac arrest were excluded. All patients who underwent an angiographic restudy were identified. A total of 4,006 patients (44%) fulfilled the following criteria: 1) angiographically successful angioplasty proce-

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dure; 2) no in-hospital complications (death, Q wave myocardial infarction or coronary bypass surgery); and 3) angiographic restudy within 12 months after angioplasty. These 4,006 patients form the basis of this study. They returned for restudy after angioplasty either because of recurrent symptoms or to determine whether restenosis had occurred.

**Definitions.** We used the following definitions:

*Single-vessel disease* = ≥50% lumen diameter narrowing in either the left anterior descending, left circumflex or right coronary artery or a major branch or branches.

*Multivessel disease* = the presence of ≥50% lumen diameter narrowing in more than one of these major epicardial vessel systems.

*Angiographically successful coronary angioplasty* = a procedure in which all lesions with attempted dilation had a >20% reduction in diameter stenosis and had <50% residual diameter stenosis.

*Restenosis* (defined per patient) = recurrent diameter narrowing >50% at the first site dilated. Although percent diameter stenosis is a continuous variable, a cut point must be selected to make a diagnosis of restenosis. An alternative definition of restenosis, loss of 50% of the gain in diameter narrowing, was also considered.

**Data collection.** Baseline and restudy demographic, clinical, angiographic and procedural data including complications were recorded prospectively by physicians on standardized forms and entered into a computerized data base. The diameter narrowing and lesion length manifested on angiograms obtained before and immediately after angioplasty and on restudy were measured with validated digital electronic calipers (Sandhill Scientific) (5) by experienced angiographers other than the primary operator. The narrowing of each coronary artery lesion was expressed as the percent diameter narrowing of the abnormal segment compared with measurements in the normal adjacent arterial regions. The diameter stenosis recorded was the mean value determined in two near orthogonal views.

**Coronary angioplasty technique and angiographic restudy.** All angioplasty procedures were performed with previously described standard techniques (6). All patients received aspirin (325 mg) and most of them received a calcium channel blocking agent (nifedipine, 10 mg three times daily, or diltiazem, 30 to 60 mg four times daily) orally before angioplasty unless a prior history of an adverse or hypersensitivity reaction was present. Before attempted balloon dilation, diazepam (5 to 10 mg), atropine (0.6 to 1.0 mg) and heparin (10,000 to 15,000 U) were given intravenously.

Restudy angiography was performed after coronary angioplasty under the guidance of the primary angioplasty operator. Although the entire coronary tree was visualized, special attention was directed at the original dilation sites. The severity of obstruction of these sites was specifically assessed and recorded.

**Statistical analyses.** The patients were randomly classified into a 2,500-patient learning group and a 1,506-patient test group. All data are displayed as mean value ± SD or as a proportion. Differences between patients with and without restenosis were compared for categoric variables with the chi-square test and for continuous variables with the Student *t* test. Correlates of restenosis were determined by stepwise logistic regression analysis. The relation between the probability of restenosis P(R) and the correlates of restenosis was modeled as

$$P(R) = \frac{e^{(b_0 + \Sigma b_i x_i)}}{1 + e^{(b_0 + \Sigma b_i x_i)}} \quad [1]$$

where e is the natural log base, $b_0$ is the constant term and the $b_i$ are the coefficients for each variable. For each categoric variable, the value of each $x_i$ is 0 if the variable is absent and 1 if present. The $x_i$ for a continuous variable was its respective integer value. The restudy rate may affect the observed restenosis rate. Assuming that the covariates do not affect the restudy rate, the constant term may be adjusted for any presumed underlying restenosis rate by the following equation adapted from Cain and Breslow (7):

$$b_* = b_0 - \log \frac{P(R)}{1 - P(R)} + \log \frac{P(R)_*}{1 - P(R)_*} \quad [2]$$

where $b_*$ is the calculated constant term, P(R) is the observed rate of restenosis in the learning group and $P(R)_*$ is an assumed underlying restenosis rate. The standard error of the constant term was not corrected because with a large sample size the correction to the standard error would be minimal. The delta technique was used to assess the 95% confidence intervals of P(R) with consideration of the covariances between the coefficients (8).

The predicted probability of restenosis was determined for each patient in the validation group with the model derived from the learning group (9). By selecting a cut point for predicted probability above which restenosis is predicted to occur and below which it is predicted to be absent, a sensitivity and specificity may be determined as in a diagnostic test. As this cut point is raised from a low level, the sensitivity falls and the specificity rises. This interrelation between the sensitivity and specificity was displayed as a receiver operating characteristic curve (ROC) (10). The ability of the model to predict restenosis was further defined by the overlap index ($O_I$) (11). The overlap index is related to the area under the ROC curve ($ROC_A$): $ROC_A = 1 - O_I/2$. An overlap of 0 means no overlap in the predicted probability of restenosis in the validation group between those who do and those who do not have restenosis. An overlap of 1 means that the median predicted probability of restenosis is the same in those with and without restenosis. The Mann-Whitney test was used to assess whether the $O_I$ was significantly different from 1. An area under an ROC curve of 0.5 means that there is no ability of the model to predict restenosis, whereas an area of 1.0 means that the model can absolutely separate patients with and without restenosis.

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Table 1. Learning Group: Clinical Characteristics of Patients With and Without Restenosis

| | Total (n = 2,500) | No Restenosis (n = 1,355) | Restenosis (n = 1,145) | p Value |
|---|---|---|---|---|
| Age (yr) | 57 ± 10 | 57 ± 10 | 58 ± 11 | 0.015 |
| Age ≥60 yr | 1,103 (44.1) | 578 (42.7) | 525 (45.9) | 0.11 |
| Male | 1,926 (77.0) | 1,032 (76.2) | 894 (78.1) | NS |
| Hypertension | 1,046 (41.8) | 537 (39.6) | 509 (44.5) | 0.015 |
| Diabetes | 322 (12.9) | 150 (11.1) | 172 (15.0) | 0.0033 |
| Class III to IV angina | 1,342 (57.6) (n = 2,329) | 655 (52.5) (n = 1,247) | 678 (63.5) (n = 1,082) | <0.0001 |
| Congestive heart failure | 48 (2.0) (n = 2,415) | 32 (2.4) (n = 1,309) | 16 (1.4) (n = 1,106) | 0.080 |
| Prior myocardial infarction | 778 (31.3) | 422 (31.1) | 356 (31.1) | NS |

Data are presented as mean value ± SD or number (%) of patients in group.

The validation group was also classified into patients with varying predicted probability of restenosis from 0 to 100 in steps of 10. The mean predicted probability of restenosis in each decile was compared by linear regression to the proportion observed to have restenosis.

## Results

**Clinical characteristics of the study patients.** The clinical characteristics of the 2,500 patients in the learning group are displayed in Table 1. There were 1,145 patients with restenosis at the first site dilated, with 1,355 patients with a patent artery at that site. As a check on this definition of restenosis, the concordance of the 50% diameter stenosis at restudy was compared with loss of 50% of the gain. There was concordance in 2,335 patients (94.5%) and discordance in 136 (5.5%). The patients in the group with restenosis were slightly older. There was no difference in gender between groups. Hypertension was present in just over 40% and was more frequent in the group with restenosis. Diabetes was present in 11% of patients without restenosis and in 15% of patients with restenosis ($p = 0.0033$). Class III or IV angina at the time of coronary angioplasty was present in 52% of patients without restenosis and 63.5% of patients with restenosis ($p < 0.0001$). Congestive heart failure was uncommon and there was a trend to less failure in the group with restenosis. There was no difference in the prevalence of prior myocardial infarction.

**Angiographic and procedural characteristics.** These data are displayed in Table 2. There was no difference in the prevalence of multivessel disease or in the ejection fraction. Multisite dilations were performed in just over 20% of cases in both groups. The proximal left anterior descending coronary artery was the site of dilation in 49% of the group with restenosis and 40% of the group without restenosis. The distributions of diameter stenosis before and after coronary angioplasty were higher in the group with restenosis. Lesion calcium did not correlate with restenosis. Eccentric lesions were more common in the group with restenosis. Intimal tears were more common in the group without restenosis. Lesion length did not correlate with restenosis. The time to restudy was shorter and the diameter stenosis was much greater in the group with restenosis.

**Model for predicting restenosis.** The significant variables from Tables 1 and 2 were used to create a model to predict the occurrence of restenosis (Table 3). The continuous variables (diameter before and after angioplasty and patient age) are categorized in the table but enter the model in their continuous forms. The variables with the strongest univariate relative risks were class III to IV angina (relative risk 1.28), severe stenosis before angioplasty (relative risk up to 1.41 for total occlusions), proximal left anterior descending coronary artery dilations (relative risk 1.22), diabetes mellitus (relative risk 1.19) and a suboptimal result (relative risk 1.13). Of the 2,500 patients, complete data for the logistic regression were available in 2,271 (91%). Each of the univariate correlates was also a multivariate correlate of restenosis. Multivariate odds ratios are displayed for the categoric and continuous variables. Odds ratios for categoric variables are the odds of restenosis at particular levels of the covariate compared with the odds of restenosis at the base level of that covariate. Odds ratios for continuous variables are the odds associated with a 1-unit increase in the covariate value. The correlates with the stronger univariate relative risks also had the higher odds ratios. The observed restenosis rate of 46% may be inaccurate because of the incomplete restudy rate. By using equation 2, the constant term may be corrected to −3.99 for an underlying restenosis rate of 25%, −3.74 for 30%, −3.51 for 35% and −3.29 for 40%.

The logistic model shown in Table 3 was used to estimate the probability of restenosis in each patient in the validation group. For the 1,506 patients in the validation group, group data permitting the validation to be performed were available in 1,375 (91%). The probability of restenosis was calculated by using equation 1. The predicted probabilities of restenosis in patients with and without restenosis are displayed in Figure 1. Note that the distribution of predicted probabilities is higher in the group with restenosis ($p < 0.0001$) but with a large overlap (the overlap index was 0.76). Cut points of

**Table 2.** Learning Group: Angiographic and Procedural Characteristics of Patients With and Without Restenosis

| | Total (n = 2,500) | No Restenosis (n = 1,355) | Restenosis (n = 1,145) | p Value |
|---|---|---|---|---|
| Multivessel disease | 679 (27.2) | 356 (26.5) | 320 (27.9) | NS |
| Ejection fraction (%) | 59 ± 11 | 59 ± 11 | 58 ± 12 | NS |
| Ejection fraction <50% | 254 (16.5) | 121 (15.4) | 133 (17.6) | NS |
| | (n = 1,542) | (n = 786) | (n = 756) | |
| Multisite | 556 (22.2) | 294 (21.7) | 262 (22.9) | NS |
| Proximal LAD dilation | 1,388 (44.5) | 809 (40.3) | 579 (49.4) | <0.0001 |
| Diameter before PTCA (%) | 75 ± 14 | 73 ± 14 | 76 ± 13 | <0.0001 |
| Diameter before PTCA ≥70% | 1,578 (63.2) | 794 (58.7) | 784 (68.6) | <0.0001 |
| | (n = 2,496) | (n = 1,353) | (n = 1,143) | |
| Diameter after PTCA (%) | 24 ± 11 | 23 ± 10 | 24 ± 11 | 0.0037 |
| Diameter after PTCA ≥30% | 765 (30.9) | 383 (28.6) | 382 (33.7) | 0.0067 |
| | (n = 2,472) | (n = 1,338) | (n = 1,134) | |
| Lesion calcium | 165 (6.6) | 85 (6.3) | 80 (7.0) | NS |
| | (n = 2,494) | (n = 1,353) | (n = 1,141) | |
| Eccentric lesion | 1,172 (52.4) | 659 (50.6) | 513 (54.6) | 0.052 |
| | (n = 2,464) | (n = 1,335) | (n = 1,129) | |
| Lesion tear | 716 (28.6) | 411 (30.3) | 305 (26.6) | 0.042 |
| Lesion length (mm) | 6.8 ± 4.8 | 6.8 ± 5.2 | 6.9 ± 4.4 | NS |
| Lesion length ≥10 mm | 482 (20.2) | 265 (20.3) | 217 (20.1) | NS |
| | (n = 2,388) | (n = 1,306) | (n = 1,082) | |
| Time from PTCA (days) | 166 ± 74 | 182 ± 72 | 147 ± 72 | <0.0001 |
| Diameter stenosis on restudy (%) | 48 ± 27 | 26 ± 12 | 74 ± 15 | <0.0001 |

Data are presented as number (%) of patients in group or mean value ± SD. LAD = left anterior descending coronary artery; PTCA = percutaneous transluminal coronary angioplasty.

calculated probability from 10 to 90 were chosen. This allowed the calculation of sensitivity and specificity at each cut point, generating a receiver operating characteristic curve (Fig. 2). The farther the curve is from the line of identity, the better a diagnostic test. The points in this curve are shown in Table 4. Note that the accuracy peaked at 59% at a cut point of 50. The area under the receiver operating characteristic curve was 0.62.

The validation group was then classified according to the predicted probability of restenosis from the logistic model (Table 5). Within each 10-point range of probabilities, the mean predicted probability was determined. In addition, the total number of patients within that range in the validation group, the number of patients with restenosis and the observed rate of restenosis were calculated. The predicted and observed restenosis rates, averaged within subgroups, were compared by linear regression analysis (Fig. 3).

**Comparison of patients with and without restudy.** The observed restenosis rate may be affected by the 44% restudy rate, and the correlates of restenosis may be affected if these correlates are used to determine the need for restudy. Thus, the 4,006 patients undergoing restudy were compared with the 5,052 patients not undergoing restudy. In Table 6, data for all variables from Tables 1 and 2 that correlated with the restudy rate are presented. Dilation of the proximal left anterior descending coronary artery was the strongest correlate of restudy, with a restudy rate of 48.8% in patients with proximal left anterior descending dilation versus 41.2% in patients without such dilation ($p < 0.0001$). The small p values may reflect the large sample size, because there was only a slight effect of the covariates on the restudy rate. All of the univariate correlates were also multivariate correlates of restudy except for diabetes and diameter stenosis before angioplasty.

## Discussion

In this study a model to predict the probability of restenosis was developed. In a learning group of 2,500 patients the multivariate correlates of restenosis were angina class, diameter stenosis before angioplasty, proximal left anterior descending artery occlusion, diabetes mellitus, diameter stenosis after angioplasty, hypertension, absence of an intimal tear, eccentric morphology and older patient age. Although the correlation between average predicted and observed restenosis rates within subgroups in the validation group (Fig. 3) confirmed goodness of fit of the model, it was not possible to predict the presence or absence of restenosis in individual patients in the validation group with much accuracy. The relatively high overlap index of 0.76, which is the same as a relatively low area under the receiver operating characteristic curve of 0.64, confirmed this observation. This limited ability to predict restenosis for an individual patient is not surprising because the relative risks are all low; the strongest relative risk is only 1.28 for patients with class III to IV angina. This finding is not likely to be due to the

**Table 3.** Correlates of Restenosis in the Learning Group

| | Univariate | | | | Multivariate | | | |
|---|---|---|---|---|---|---|---|---|
| | n | Rate | RR | p | p | Coefficient | SE | Odds Ratio |
| Angina class | | | | | | | | |
| I–II | 987 | 40.0 | 1 | <0.0001 | <0.001 | 0.42092 | 0.08861 | 1.0 |
| III–IV | 1,342 | 51.1 | 1.28 | | | | | 1.52 (CI 1.28–1.81) |
| Diameter Pre | | | | | | | | |
| <70% | 918 | 39.1 | 1 | <0.0001 | <0.001 | 0.020233 | 0.003337 | 1.020 (CI 1.014–1.027) |
| 70% to 89% | 1,212 | 48.8 | 1.24 | | | | | |
| 90% to 99% | 230 | 50.9 | 1.30 | | | | | |
| 100% | 136 | 55.1 | 1.41 | | | | | |
| Proximal LAD lesion | | | | | | | | |
| No | 1,388 | 41.7 | 1 | <0.0001 | <0.001 | 0.55578 | 0.08897 | 1.0 |
| Yes | 1,112 | 50.9 | 1.22 | | | | | 1.74 (CI 1.46–2.08) |
| Diabetes | | | | | | | | |
| No | 2,178 | 44.7 | 1 | 0.0033 | 0.036 | 0.26813 | 0.1286 | 1.0 |
| Yes | 322 | 53.4 | 1.19 | | | | | 1.31 (CI 1.02–1.68) |
| Diameter Post | | | | | | | | |
| <30% | 1,707 | 44.1 | 1.0 | 0.0037 | 0.004 | 0.012081 | 0.004173 | 1.012 (CI 1.004–1.021) |
| ≥30% | 765 | 49.9 | 1.13 | | | | | |
| Hypertension | | | | | | | | |
| No | 1,454 | 43.7 | 1 | 0.015 | 0.005 | 0.20798 | 0.08913 | 1.0 |
| Yes | 1,046 | 48.7 | 1.11 | | | | | 1.23 (CI 1.03–1.47) |
| Intimal tear | | | | | | | | |
| No | 1,784 | 47.1 | 1.11 | 0.042 | 0.005 | −0.30454 | 0.09694 | 1.36 (CI 1.12–1.64) |
| Yes | 716 | 42.6 | 1 | | | | | 1.0 |
| Eccentric lesion | | | | | | | | |
| No | 1,172 | 43.8 | 1 | 0.052 | 0.099 | 0.14396 | 0.08724 | 1.0 |
| Yes | 1,292 | 47.7 | 1.09 | | | | | 1.15 (CI 0.97–1.37) |
| Age | | | | | | | | |
| <60 yr | 1,397 | 44.4 | 1 | 0.015 | 0.016 | 0.008911 | 0.004253 | 1.009 (CI 1.001–1.017) |
| ≥60 yr | 1,103 | 47.6 | 1.07 | | | | | |
| Constant | | | | | | −3.0565 | 0.3771 | |

CI = 95% confidence interval; LAD = left anterior descending coronary artery; Post = after angioplasty; Pre = before angioplasty; RR = relative risk.

definition of restenosis because the other most commonly used definition of restenosis, loss of 50% of the gain, was strongly concordant with this definition.

The model may also be used to estimate the probability of restenosis in an individual patient, as indicated in the following examples: 1) In a 50-year old patient without diabetes or hypertension, presenting with class II angina, a smooth lesion (65% occlusion) in the right coronary artery is suc-

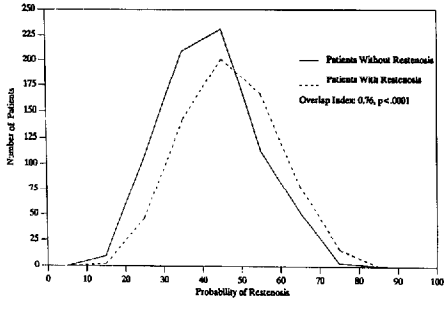


**Figure 1.** Distribution of the probability of restenosis calculated from the logistic model in patients with and without restenosis.

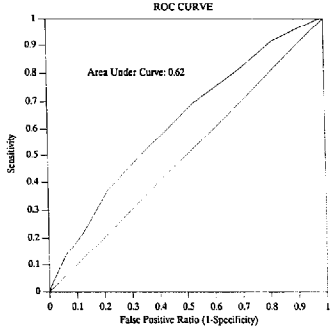


**Figure 2.** Receiver operating characteristic (ROC) curve comparing the sensitivity with the specificity from the logistic model to predict the presence of restenosis in the validation group.

cessfully dilated to 20% occlusion in association with a slight intimal tear. The probability of recurrent stenosis is 19%, with a 95% confidence interval of 14% to 23%. By using the model to correct to an underlying probability of restenosis of, for instance, 30%, the probability of restenosis in this patient drops to 13%, with a 95% confidence interval of 10% to 16%. In contrast, in a 75-year old patient with severe angina, hypertension and diabetes, dilation of an irregular lesion in the proximal left anterior descending artery reduces diameter stenosis from 85% to 35% without an intimal tear. The probability of recurrent stenosis is 79%, with a 95% confidence interval of 73% to 85%. By correcting to a 30% underlying restenosis rate, the probability of restenosis drops to 71%, with a 95% confidence interval of 63% to 79%.

**Comparison with previous studies.** All of the correlates of restenosis noted in this study have been noted previously.

**Table 4.** Sensitivity and Specificity of the Model to Predict Restenosis

| Cut Point | Sensitivity | Specificity | Accuracy |
|---|---|---|---|
| 10 | 0 | 100 | 47.3 |
| 20 | 2.3 | 99.7 | 48.4 |
| 25 | 7.5 | 97.2 | 49.9 |
| 30 | 18.9 | 91.4 | 53.3 |
| 35 | 30.7 | 81.3 | 54.6 |
| 40 | 47.8 | 69.3 | 58.0 |
| 45 | 63.7 | 53.0 | 58.6 |
| 50 | 78.7 | 36.9 | 59.0 |
| 55 | 87.8 | 21.7 | 56.6 |
| 60 | 94.1 | 13.4 | 55.8 |
| 70 | 99.6 | 1.8 | 53.3 |
| 10 | 100 | 0 | 52.7 |

**Table 5.** Comparison of Predicted and Observed Restenosis Rates in the Validation Group

| Predicted Range (%) | Mean Predicted Rate (%) | Dilation Sites | | Observed Rate (%) |
|---|---|---|---|---|
| | | Total No. | No. With Restenosis | |
| 10–19 | 15.5 ± 2.3 | 12 | 2 | 16.7 |
| 20–29 | 25.6 ± 2.5 | 152 | 46 | 30.3 |
| 30–39 | 35.0 ± 2.6 | 351 | 142 | 40.5 |
| 40–49 | 44.5 ± 2.4 | 432 | 201 | 46.5 |
| 50–59 | 53.9 ± 2.6 | 279 | 166 | 59.5 |
| 60–69 | 63.5 ± 2.4 | 130 | 78 | 60.0 |
| 70–79 | 73.5 ± 2.6 | 19 | 16 | 84.2 |

Although a recent meta-analysis (12) showed that male gender, continued smoking after angioplasty, diabetes, absence of a previous myocardial infarction and unstable angina are risk factors, a review of individual studies shows considerable variation in risk factors and how they are defined. Severe or recent onset angina and diabetes have been found to be risk factors with consistency (1,2,13–20) and were the most powerful clinical risk factors in this study. Hypertension was recorded as a definite risk factor in one preliminary study (21) and tended to be a risk factor in one report (14). More severe stenosis before or a less satisfactory angiographic result, or both, was a risk factor in multiple studies (1,2,13–15,18–23). The presence of spasm superimposed on a fixed lesion was a suggested risk factor in smaller studies (24–26). Total occlusions are specifically recognized to result in increased risk (27–29). The importance of the left anterior descending coronary artery, most often the proxi-

**Figure 3.** Observed probability of restenosis in the validation group at incremental levels of probability of restenosis predicted by the logistic model. The **points** are the average predicted and observed restenosis rates for each subgroup. The **dashed line** is the linear regression of these points, which is close to the **solid line** of identity (slope 1.05, intercept 1.60, r = 0.98, p = 0.0001).

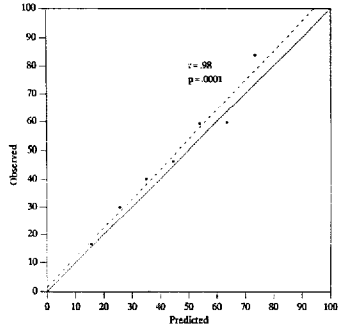

Table 6. Correlates of Angiographic Restudy

| | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|
| | Patients Restudied (no.) | Rate (%) | p Value | p Value | Coefficient | SE |
| Proximal LAD lesion | | | | | | |
| Yes | 1,768/3,625 | 48.8 | <0.0001 | <0.001 | 0.28123 | 0.04739 |
| No | 2,238/5,432 | 41.2 | | | | |
| Patient age | | | | | | |
| <60 yr | 2,358/5,005 | 47.1 | <0.0001 | <0.001 | 0.010226 | 0.002259 |
| ≥60 yr | 1,648/3,946 | 41.8 | | | | |
| Prior MI | | | | | | |
| No | 2,748/5,870 | 46.8 | <0.0001 | <0.001 | 0.26003 | 0.04974 |
| Yes | 1,257/3,105 | 40.5 | | | | |
| Gender | | | | | | |
| Female | 935/2,352 | 39.8 | <0.0001 | <0.001 | −0.18021 | 0.05455 |
| Male | 3,071/6,703 | 45.8 | | | | |
| Sites dilated | | | | | | |
| Single | 3,1197,183 | 43.4 | 0.0026 | 0.005 | −0.16155 | 0.05737 |
| Multiple | 887/1,875 | 47.3 | | | | |
| Angina class | | | | | | |
| 0 to II | 1,544/3,255 | 47.4 | <0.0001 | 0.015 | 0.11551 | 0.04820 |
| III to IV | 2,189/5,188 | 42.2 | | | | |
| Lesion length | | | | | | |
| <10 mm | 3,060/6,897 | 44.4 | 0.072 | 0.048 | −0.010541 | 0.005073 |
| ≥10 mm | 757/1,616 | 46.8 | | | | |
| Eccentric lesion | | | | | | |
| No | 1,861/4,088 | 45.5 | 0.049 | 0.093 | 0.077907 | 0.04687 |
| Yes | 2,091/4,813 | 43.4 | | | | |
| Lesion diameter Pre | | | | | | |
| <70% | 1,417/3,025 | 46.8 | 0.0001 | NS | | |
| 70 to 89% | 1,998/4,566 | 43.8 | | | | |
| 90 to 99% | 365/943 | 38.7 | | | | |
| 100% | 222/509 | 43.6 | | | | |
| Diabetes | | | | | | |
| No | 3,507/7,814 | 44.9 | 0.0763 | NS | | |
| Yes | 498/1,182 | 42.1 | | | | |

MI = myocardial infarction; other abbreviations as in Table 3.

mal portion, has been reported frequently (2,13,15–17,22). Older patient age and absence of an intimal tear were previously reported to be risk factors in studies from Emory (2,15,23). Absence of an intimal tear was also previously noted as a risk factor in a study from another institution (13), as was lesion eccentricity (11,21,30). Other risk factors not found to be significant in this study, such as male gender (1,16,18), absence of a previous myocardial infarction (1,14,18), smoking status (20), abnormalities in blood lipids (14,18,20,31), lesion calcium (19,22,30) and longer lesions (16) have been reported as risk factors only inconsistently. Several risk factors for restenosis that require more detailed angiographic review, such a lesion tortuosity or bend point lesions (15), were available in far too few patients to be incorporated into this study. The incorporation of other morphologic criteria might have slightly improved the ability to predict restenosis. Reports of risk factors with relative risks >1.5 are unusual. With varying definitions, study groups and study designs examining relatively weak risk factors, it is not surprising that variation is noted in published studies. The problem is that each of the clinical variables is a correlate without a clear relation to the underlying pathophysiologic process. Until the process of myointimal proliferation is sufficiently well understood that a biochemical marker becomes available, predicting restenosis is likely to remain uncertain.

**Limitations of the study.** As noted, there are several limitations to this study. 1) The definition of restenosis used in this study was a per person definition, based on the first lesion dilated, that allowed incorporation of clinical, angiographic and site descriptors into one model. However, this definition limits the direct mathematic application of the model to patients in whom the concern is not limited to the first lesion. 2) The restudy rate was incomplete. The relative risks and correlation coefficients for restenosis would be the same if these risk factors did not influence the decision to perform restudy cardiac catheterization. The probability of restenosis for any patient would be lower than that calcu-

lated from the model if the underlying rate of restenosis was, for instance, 30% instead of the 46% in this study. The model may be corrected to other baseline restenosis values by adjusting the constant term with equation 2.

3) The choice of covariates examined is another limitation. Although the clinical variables examined in this study (and many others) are common and readily available, other prognostic variables may prove to be of greater importance in the future. Although the covariates did actually vary with the restudy rate, for most variables the differences were minimal, even when statistically significant. The restudy rate was higher in patients with less severe angina, a factor that might have slightly increased the observed relative risk. It was also higher with left anterior descending artery occlusion, a factor that might have decreased the observed relative risk. If the restudy rate in patients without left anterior descending dilations increased from 41.2% to that in patients with left anterior descending dilations of 48.8% and if the underlying restenosis rate in these patients is assumed to be 30%, then the relative risk would increase from 1.22% to 1.28%.

The initial decision to perform angioplasty may also be affected by these covariates. If one correlate is used to determine the need for angioplasty or if there is no interaction among several correlates affecting the decision to perform angioplasty, then the univariate relative risks will not be affected, but the multivariate model will be affected by changing the composition of patients in the study group. For instance, if patients with proximal left anterior descending artery disease are selected not to undergo angioplasty because of the higher risk of restenosis, then the proportion of patients in the angioplasty group with proximal left anterior descending artery disease would decrease without affecting the relative risk of restenosis, whereas the importance of left anterior descending artery disease in the multivariate model would decline. If there is more than one correlate affecting the decision to perform angioplasty, then the changes in observed results will be more complicated. Thus, if patients with more severely stenotic proximal left anterior descending artery disease are selectively treated with coronary surgery rather than angioplasty, then the univariate relative risks of both proximal left anterior descending artery disease and severe stenoses will decrease and the multivariate model will be affected as well. It is not possible to estimate the effect of this distortion on the relative risks and the multivariate model without knowledge of the total group from which patients were originally selected for angioplasty. Even then, the multiple correlates noted in this study would make such estimates quite complicated. This issue is not as obscure as it might appear at first glance because it is, perhaps, in the patient in whom angioplasty is being considered that estimation of the risk of restenosis is most relevant. Thus, there is a complex effect on the ability to predict restenosis from clinical variables if these same variables are also used to guide the decision to perform angioplasty.

4) The issue of selection of patients for angioplasty relates to the final limitation, the nature of the validation group. The validation group and learning group were selected at random. The model developed here could also be tested in patients from another institution.

**Conclusions.** The fundamental points of this study remain: 1) It is not possible in any one patient to predict reliably whether restenosis will definitely occur; and 2) it is possible to predict the probability of restenosis, with some uncertainty, at least in well characterized patients who have already had angioplasty.

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