Relation Between Lesion Characteristics and Risk With Percutaneous Intervention in the Stent and Glycoprotein IIb/IIIa Era

An Analysis of Results From 10 907 Lesions and Proposal for New Classification Scheme

Stephen G. Ellis, MD; Victor Guetta, MD; Dave Miller, MS; Patrick L. Whitlow, MD; Eric J. Topol, MD

Background—The currently used American College of Cardiology/American Heart Association lesion classification scheme dates from an era when balloon angioplasty was the only percutaneous treatment available and major complications occurred in ≈7% of patients. Major advances in treatment options would suggest that this scheme may be outmoded, but the schemes that have been suggested to update lesion classification have not been widely accepted.

Methods and Results—Four thousand one hundred eighty-one consecutive patients (6676 lesions) formed a training set and 2146 patients (4231 lesions) formed a validation set treated from 1995 to 1997 at a single center used by 3 hospital groups. Twenty-seven pretreatment candidate variables were analyzed with the use of stepwise proportional logistic regression, and 9 (nonchronic total occlusion with TIMI flow 0, degenerated vein graft, vein graft age >10 years, lesion length ≥10 mm, severe calcium, lesion irregularity, large filling defect, angulated ≥45 degrees plus calcium, and eccentricity) were independently correlated (P<0.05) with ranked adverse outcome (death, Q-wave or creatine kinase ≥3 times normal myocardial infarction, or emergency coronary artery bypass grafting) or possibly related to non–Q-wave myocardial infarction or no complication). A scheme based on these findings and the old American College of Cardiology/American Heart Association scheme were found to have c-statistics in the validation set of 0.672 and 0.620 (P=0.010 vs old scheme), respectively.

Conclusions—Appreciation of these contemporary risk factors for complications of coronary intervention may assist in patient selection and in risk adjustment for comparison of outcomes between providers. (Circulation. 1999;100:1971-1976.)

Key Words: angioplasty ■ stents ■ platelet aggregation inhibitors ■ risk factors ■ angiography

The American College of Cardiology/American Heart Association (ACC/AHA) lesion classification scheme was proposed in 1986 and modified in 1990. It is still widely used to assess risk of patients and lesions undergoing percutaneous intervention and serves as a risk adjustment parameter in “scorecarding” individual operators and hospitals. Dramatic changes have occurred in the approach to percutaneous intervention since that time, allowing treatment of more complex lesions and lower overall risk. It would be reasonable to suspect that the ACC/AHA scheme would need to be revised, but several schemes that have been suggested have not been widely adapted.

Our purpose was to develop a new predictive model for adverse outcomes with the use of contemporary data and to compare its performance in a validation sample against that of the current modified ACC/AHA scheme.

Methods

Patients

Data from 6327 consecutively treated patients undergoing coronary intervention from January 1, 1995, until December 31, 1997, treated by physician operators from 1 of 3 cardiology groups (full-time Cleveland Clinic staff, Ohio Permanente Medical Group staff, part-time associate staff) were analyzed. Baseline clinical data were entered prospectively into an established database, and in-hospital clinical outcomes were evaluated by a cadre of trained personnel independent from the physician operators. ECGs were routinely obtained before and immediately after the procedure, the morning after the procedure, and in the event of suspected ischemia. Creatine kinase (CK) levels were routinely assayed 6 to 8 hours after the procedure, and
TABLE 1. Angiographic Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Definitions and Conventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bifurcation lesion</td>
<td>Branch &gt;1.5 mm emanating from within the shoulders of the lesion</td>
</tr>
<tr>
<td>Calcification in the target lesion/subdivided into</td>
<td>1 = Mild: requiring cardiac motion to see; 2 = moderate: obvious without cardiac motion; 3 = severe</td>
</tr>
<tr>
<td>Calcification in target vessel</td>
<td>Any angiographically apparent calcium in the target vessel</td>
</tr>
<tr>
<td>Calcified (≥ grade 2) and angulated (&gt;45°) lesion</td>
<td>See separate definitions</td>
</tr>
<tr>
<td>Chronic total occlusion</td>
<td>Total occlusion (TIMI 0 and 1) with either: (1) known duration ≥3 mo, or (2) bridging collaterals</td>
</tr>
<tr>
<td>Degenerated saphenous vein graft</td>
<td>SVG with ≥50% of the length of the graft with luminal irregularity, filling defect, gross irregularity, or staining</td>
</tr>
<tr>
<td>Filling defect</td>
<td>An angiographic lucency, usually globular, with contrast surrounding at least 3 sides (or equivalent), divided into 3 grades: 1 = haziness alone, 2 = defect 1–2 mm, 3 = defect &gt; 2 mm in diameter</td>
</tr>
<tr>
<td>Left ventricular ejection fraction</td>
<td>Degrees at end diastole in nonforeshortened view subtended by a 15-mm treatment device</td>
</tr>
<tr>
<td>Lesion angle</td>
<td>Assessed by angiography, echo, or gated nuclear scan</td>
</tr>
<tr>
<td>Lesion ectasia</td>
<td>Irregularly shaped or “sawtooth” lumen edges (cannot be coded as present simultaneously with thrombus, which takes precedence if both are present)</td>
</tr>
<tr>
<td>Lesion irregularity</td>
<td>Irregularly shaped or “sawtooth” lumen edges (cannot be coded as present simultaneously with thrombus, which takes precedence if both are present)</td>
</tr>
<tr>
<td>Lesion length</td>
<td>Measured shoulder to shoulder</td>
</tr>
<tr>
<td>Modified ACC/AHA lesion score</td>
<td>See Reference 2</td>
</tr>
<tr>
<td>Nonchronic total occlusion</td>
<td>Total occlusion not meeting criteria for chronicity (qv)</td>
</tr>
<tr>
<td>Normal reference diameter</td>
<td>Diameter of normal-appearing lumen within the same coronary segment (may require averaging proximal and distal to lesion); if no normal area in the same segment, may be measured from adjacent segment providing no side branch ≥1.5 mm is interposed</td>
</tr>
<tr>
<td>Number of diseased vessels</td>
<td>Number of coronary arteries with ≥50% diameter stenosis (left anterior descending, circumflex, or right coronary arteries; or bypassable branches thereof)</td>
</tr>
<tr>
<td>Number of lesions</td>
<td>≥50% Diameter stenosis in the target vessel</td>
</tr>
<tr>
<td>Ostial location</td>
<td>Within 3 mm of the aorta or major vessel</td>
</tr>
<tr>
<td>Plaque mass estimate</td>
<td>Lesion length ≥50%×%diameter stenosis×normal reference diameter</td>
</tr>
<tr>
<td>Proximal tortuosity (old definition)</td>
<td>Moderate = 2≤60° or 1 ≈90° bend, severe = 2 or more &gt;90° bends</td>
</tr>
<tr>
<td>Proximal tortuosity (trial definition)</td>
<td>Sum of degrees in all bends ≥60° proximal to target lesion</td>
</tr>
<tr>
<td>Restenotic lesion</td>
<td>Lesion previously treated with percutaneous coronary intervention</td>
</tr>
<tr>
<td>Saphenous vein graft luminal irregularity</td>
<td>Measured as a percentage of graft length</td>
</tr>
<tr>
<td>Saphenous vein graft number of major plaques</td>
<td>Number of ≥50% stenosis in saphenous vein graft</td>
</tr>
<tr>
<td>Saphenous vein graft filling defect</td>
<td>Thrombus or filling defect in a saphenous vein graft</td>
</tr>
<tr>
<td>Saphenous vein graft staining</td>
<td>Staining without an apparent thrombus or filling defect in a saphenous vein graft</td>
</tr>
<tr>
<td>Saphenous vein graft ectasia</td>
<td>Ectasia (qv) in a saphenous vein graft</td>
</tr>
<tr>
<td>Thrombus with staining</td>
<td>Contrast “hangup” in an area of apparent thrombus</td>
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</table>

**Variables and Definitions**

**Baseline Clinical Variables**

Acute MI (<24 hours), age, cardiogenic shock, current smoking, diabetes mellitus (insulin-dependent and non-insulin-dependent), gender, hypercholesteremia (total cholesterol ≥240 mg%, LDL cholesterol ≥130 mg%, or HDL cholesterol <35 mg%), hypertension, New York Heart Association congestive heart failure class, prior remote MI (>2 weeks), recent MI (1 to 14 days), saphenous vein graft age (years), and surgically inoperable, unstable angina. Except for vein graft age (analogous to “chronic” total occlusion in the ACC/AHA scheme in that it relates a time duration with a morphological or locating variable), these variables were used for descriptive purposes only.

**Angiographic Variables**

See Table 1 for variables assessed and their definitions. Angiographic variables were analyzed by 1 of 2 independent observers blinded to clinical outcome in the training set analysis and by 1 of 12 clinical interventionists overread by the Cleveland Clinic Core Angiographic Laboratory in the validation set analysis.

**Treatment Variables**

Treatment variables were abciximab and primary treatment device (balloon, directional atherectomy, laser, Rotablator, stent, and transluminal extraction catheter [TEC]).

**Outcome Variables**

Outcome variables were cardiac death, emergency bypass surgery (with acute ischemia or for the prevention of acute ischemia within 24 hours of the procedure), and MI [Q-wave and non–Q-wave/subcategorized by CK level (ECG changes or enzyme elevations consequent to an acute MI at the patient’s presentation are excluded)].

**Statistical Analysis**

Continuous data are presented as mean ± 1 SD if normally distributed and as median and interquartile range if skewed. Categorical data are presented as a percentage. Cases for the training set analysis were composed of all patients treated during 1995 to 1996 with any ischemic complication and a
randomly selected cohort of patients without complications (3:1 patients with no complications:patients with complications). This cohort was termed the enriched training set. This approach allowed us to study characteristics not routinely evaluated without having to review thousands of cineangiograms. However, if characteristics were relatively infrequent in this sample (n<50) and recorded routinely in our database, the entire 1995 to 1996 data set was used to ascertain their relation to clinical outcome. Secondary analyses of the population without the most predictive variables was performed to improve identification of intermediate-risk lesion morphologies. Cases for the validation set analysis were composed of all patients treated during 1997.

Adverse outcomes were characterized as most severe: cardiac death, Q-wave MI, non-Q-wave MI with CK ≥5x upper limit of normal and positive cardiac isoenzymes, or emergency bypass surgery; severe: non-Q-wave MI with CK elevation 3 to 5x upper limit of normal in the presence of abnormal cardiac isoenzymes; moderate: non-Q-wave MI with CK elevation 2 to 3x upper limit of normal with positive cardiac isoenzymes; uncertain: the presence of non–Q-wave MI, possibly associated with the lesion evaluated (this typically occurred when multiple lesions were treated and there was no obvious angiographic complication); and no complication associated with lesion treatment. Because of the small number of lesions associated with the severe category in the test population, the most severe and severe categories were subsequently collapsed for the purposes of all analyses subsequent to our preliminary investigation.

Stepwise proportional odds logistic regression analysis was performed to identify independent correlates of adverse ischemic outcomes in the training sample. This, in contradistinction to standard multiple logistic regression, allows for simultaneous fitting of a model to a ranked ordinal outcome.

On the basis of their relation to graded adverse outcome, variables were classified as strongly or moderately correlated. With the use of the training sample, a scheme to optimize the true-positive, false-negative relation was developed. The presence of any strong correlate qualified the lesion as highest risk (class IV). The presence of any strong correlate and 1 to 2 moderate characteristics qualified the lesion as highest risk (class IV). The presence of any strong correlate and 3 characteristics qualified the lesion as highest risk (class IV). The presence of any strong correlate and 4 characteristics qualified the lesion as highest risk (class IV).

The predictive capability of the new scheme and the current ACC/AHA scheme were then tested in the 1997 validation population. Comparison of their predictive capacities were performed with the use of the methods of Hanley and McNeil. Subgroup analyses were also performed in the 1997 stent-plus-abciximab–treated population.

All statistical analyses were performed with SYSTAT (SYSTAT version 7.0, SPSS Inc) or SAS/STAT (SAS Institute Inc, version 6.1).

**Results**

**Patient Population**

Baseline patient demographics for the training, validation, and total population studied are provided in Table 2. Six thousand three hundred twenty-seven patients and 10 907 lesions in total were analyzed. Patients were typically male and middle-aged. Sixty-two percent had unstable angina. Twenty-nine percent had prior bypass surgery. Devices and drug utilization frequency for the 1995 to 1996 population were as follows: stents, 40.7% (planned in 36.9% and bailout in 3.8%); abciximab, 26.2% (planned in 24.0% and bailout in 2.2%); Rotablator, 18.9%; directional coronary atherectomy, 0.9%; excimer laser coronary angioplasty, 0.2%; and TEC, 0.2%. The figures for the 1997 population were as follows: stent, 64.2% (62.6% planned and 1.6% bailout); abciximab, 41.1% (38.4% planned, 2.7% bailout); Rotablator, 17.7%; directional coronary atherectomy, 0.6%; excimer laser angioplasty, 0.5%; and TEC, 0.1%. No significant differences were observed between the training and validation samples except for the use of stents and abciximab.

**Clinical Outcomes**

For the training and validation cohorts together, technical success achieved at ≥1 target sites was achieved in 95.8% of patients, and major complications (death, Q-wave MI, or emergency bypass surgery) occurred in 1.9% of patients (Table 3). There was no significant difference between the training and validation sets for any major outcome.

**Training Sample Evaluation**

In the enriched training sample, there were 85 lesions associated with “most severe” complications, 11 lesions associated with “severe” complications, 93 lesions associated with “moderately severe” complications, and 57 lesions associated with “uncertain” complications.
associated with “possible” complications (a total of 246 adverse event–related lesions). This number increased to 257 in the full evaluation consequent to our inability to retrieve cineangiograms on 7 patients (11 lesions) associated with complications during the analysis of the enriched training sample.

As can be seen in Table 4, 10 variables were identified as independent correlates of graded adverse outcome. Detailed clinical outcomes for the 2 most important correlates in the entire 1995 to 1997 cohort were for nonchronic total occlusion: death, 4.5%; Q-wave infarction, 0.1%; emergency bypass surgery, 2.8%; non–Q-wave infarction, 5.2% (CK >5× 0.6%, CK 3 to 5× 3.9%, CK 2 to 3× 0.7%); for degenerated saphenous vein grafts: death, 1.1%; Q-wave infarction, 2.8%; emergency bypass surgery, 0.4%; non–Q-wave infarction, 12.7% (CK >5× 1.5%, CK 3 to 5× 8.8%, CK 2 to 3× 2.4%). The proposed schema derived from this analysis is presented in Figure 1 (the 2 lesion length variables were combined). The c-statistic evaluating the predictive value of the new model for complications in the training set was 0.701.

**Validation Sample Evaluation**

Performance of the new model in the 1997 validation sample is shown in Table 5 and Figure 2. The calibration coefficient ($r$) for the relation between risk in the training and validation samples for each risk group (Figure 2) is 0.971. The c-statistic for the new model was 0.672 (the c-statistic for the ACC/AHA scheme was 0.620, $P=0.010$). The new model had its predictive accuracy maintained in the prespecified stent+abiciiximab subset (c-statistic = 0.663), whereas by the ACC/AHA scheme, the c-statistic was only 0.589.

**Discussion**

The ACC/AHA lesion risk classification schema has been criticized because of its subjectivity and because it emanates...
from an era when stents and glycoprotein IIb/IIIa inhibitors in particular were not available. Nonetheless, in the hands of core angiographic laboratories and in those practitioners who are both objective and well versed in its meaning, this system has been demonstrated repeatedly to have predictive power in the assessment of risk for populations of patients.14–16

Our comprehensive reevaluation of the relation between lesion morphology and short-term outcome with percutaneous intervention was undertaken with several goals and considerations. First, we wanted to develop and validate a better predictive instrument suitable for the current era of intervention. We expected that changes in treatment and outcome might attenuate the correlation of some previously important lesion characteristics with outcome. We intended to make use of inferences from observations with the use of intracoronary ultrasound and angioscopy17–19 to postulate new or modified angiographic characteristics to evaluate. We recognized, however, that prediction of risk generally becomes more difficult as overall risk diminishes (as it has in the decade since the modified ACC/AHA scheme was developed). Second, we hoped to more objectively characterize certain angiographic risk factors to lessen the subjectivity of the risk assessment. Third, we wanted for the first time to certain characteristics and outcome in this setting, although some-

in device profile and trackability, as well as the capacity for diminish the sole predictive capability of lesion morphology. In the end, any measure of the relation between lesion characteristics and outcome in this setting, although some-

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References


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