Automated Quantitation of Indexes of Coronary Lesion Complexity

Comparison Between Patients With Stable and Unstable Angina

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Analysis of lesion morphology is becoming increasingly important in the study of coronary artery disease. Lesion irregularity has been shown to be one of the most important predictive features for development of myocardial infarction. Most studies to date have used only qualitative assessments of morphology and are thus subject to variability and lack of standardization inherent in subjective visual inspection. We describe a new approach that allows quantitation of lesion morphology. Fifty-nine patients with unstable angina and 17 patients with stable angina were compared. Five morphometric parameters were tested (peaks per centimeter, summed maximum error per centimeter, integrated error per centimeter, number of major features per centimeter, and scaled edge length ratio), four of which were significantly different between the two groups and indicated greater lesion complexity in unstable compared with stable angina patients. No correlation was found between the parameters tested and the degree of luminal narrowing, showing the method's independence from traditional assessments of lesion severity. Excellent intraobserver and interobserver reproducibility was found for all of the parameters. This technique provides a more rigorous approach for analysis of lesion morphology than has previously been available, may provide a method for premorbid detection of high-risk lesions amenable to interventional therapy, and is especially well suited to detect subtle changes in lesion morphology after therapeutic interventions because the parameters are derived on a continuous scale and are not categorical. (Circulation 1990;82:439–447)

Traditional methods of coronary artery disease description such as percent stenosis, number of diseased vessels, and lesion distribution have not been found to vary significantly between different ischemic cardiac syndromes and are only weak predictors of cardiac events. Coronary lesion morphology, however, varies between stable and unstable patients; complex lesions that have rough or irregular borders are more often found in clinically unstable situations. Increased roughness also predicts the development of myocardial infarction: A recent study by Ellis et al showed that irregular lesions were associated with a more than fourfold increased risk for development of myocardial infarc-

tion for any degree of percent stenosis. The same study ranked lesion roughness as the most predictive feature for development of myocardial infarction, ahead of percent stenosis. Another study, by Freeman et al., found that complex coronary morphology, evidence of coronary thrombus, and the presence of multivessel disease were predictive of inhospital cardiac events. Thus, lesion morphology may be the most important angiographically detectable feature of a coronary stenosis that is associated with clinical manifestations.

Complex lesions are usually defined qualitatively by irregular or hazy borders, outpouchings within a narrowed segment (presumed ulcerated plaque), intraluminal lucencies (indicating thrombus formation), and sharp leading or trailing edges associated with a lesion. Evidence that angiography can differentiate between complex and simple stenoses has been demonstrated with postmortem angiographic analysis. Most studies to date have used only qualitative assessments of morphology, which are subject to interobserver and intraobserver variability inherent in visual

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The present study describes a new method for objectively and reproducibly quantitating lesion morphology with computer analysis of coronary lesions. The program used is an extension of a previously validated process for quantitatively evaluating coronary stenosis. Mathematical techniques for describing the complexity of continuous curves with vector and fractal analyses were applied to the study of arterial edge morphology. The morphometric parameters derived were compared between groups of patients with stable or unstable angina to demonstrate their usefulness in distinguishing between these syndromes and to examine their potential prognostic significance.

**Methods**

**Patient Characteristics**

Patients (n = 80) were selected from previous studies coordinated at the Ann Arbor Veterans Administration Medical Center. Two groups of patients were analyzed—those with chronic stable angina and those with unstable angina. All patients met the study criteria defined below and had undergone cardiac catheterization soon after characterization of their anginal syndrome. The first group comprised 63 patients obtained in a prospective fashion from four different centers in a study evaluating the effects of tissue-type plasminogen activator (rt-PA) on unstable angina. All patients had unstable angina defined by resting chest pain with reversible electrocardiographic changes within 7 days of study entry. Exclusion criteria included recent myocardial infarction (<2 weeks prior), defined by chest pain of more than 30 minutes' duration, development of Q waves, creatine phosphokinase values of more than threefold that of normal or T wave inversion for more than 24 hours), contraindications to thrombolytic therapy (history of stroke or arteriovenous malformation, history of bleeding diathesis, major surgery within the previous 2 weeks, poorly controlled hypertension [blood pressure, >180/110 mm Hg], platelet count of less than 100,000, or history of gastrointestinal or genitourinary bleeding within the past month, central nervous system or spinal trauma within 3 months, or age of more than 75 years). All patients underwent cardiac catheterization within 1 week of study entry. Four centers participated in the study, and patients were enrolled consecutively at each center. Angiographers at each site determined from clinical, electrocardiographic, and angiographic evidence the lesion responsible for the unstable angina. The angiograms and culpable lesions were analyzed at the Ann Arbor Veterans Administration Medical Center. Only baseline, pre–rt-PA infusion angiograms were used in this study. Four patients from this group were found to have 100% stenosis of the angina-producing artery and were excluded from this analysis.

The stable angina cohort was selected from previous studies comparing the use of 5F, 6F, and 8F catheters at this institution. Seventeen patients with chronic stable angina were studied. Exclusion criteria included unstable angina symptoms (e.g., rest pain, new onset angina, or change in anginal pattern), more than 50% left main coronary stenosis, all three major coronary vessels with more than 70% stenosis, significant heart failure, presence of diabetes mellitus, or serum creatine level of more than 1.5. One patient angiogram was of too poor quality to be analyzed for this study; 16 patients and 20 lesions were evaluated. The lesions analyzed were the same as those used for the previous studies evaluating the effect of various catheter sizes on image quality and were not selected with any knowledge that they would be used for lesion morphology analysis. Review of patient catheterization reports and cine films showed that the lesions used were representative of the severity of coronary artery disease. Eighty percent of all stenoses (20 of 25) were analyzed, and in all patients these lesions were either the most severe (excluding total obstructions) or were the only lesions technically suitable for analysis. The use of representative lesions from stable angina patients chosen without any a priori knowledge that they would be used in a study evaluating lesion morphology helped to minimize any potential selection bias.

All angiograms were projected on a cine viewer (Vanguard Instruments, model XR-15, Melville, N.Y.) optically coupled to a video camera. At 2.4:1 optical magnification, the video signal was digitized at 512×512×8 bit resolution onto a digital angiographic computer (ADAC Laboratories, model DPS-4100C, Milpitas, Calif.). Images were magnified two-fold with bilinear interpolation. The operator determined the lesion of interest from preselected cine frames by placing a variable sized circle around the appropriate segment of the artery. Every effort was made to minimize the amount of normal artery included in the portion analyzed because inclusion of variable amounts of normal artery could bias results and increase variability. The automatic edge detection portion of the program, previously described, was enhanced by the addition of a sequential edge linking technique that provides spatial sampling of sufficient density to characterize complex arterial borders. The sequential edge linking algorithm uses the known, undersampled edge points as a template to generate very detailed contiguous pixel edges all along the magnified arterial border. These additional edge points are selected based on their expected
pixel intensities and locations interpolated from the known edge points surrounding them. After detailed edge detection was completed, each border of a given lesion was analyzed individually with vector and fractal analysis techniques described below.

Image and film quality were determined by the standards of the center performing the catheterization. So as not to limit the applicability of this method, no unusual restrictions were placed on the method of image acquisition or film processing. To be eligible for analysis, however, it was required that the image show the entire lesion without overlap of other vessels and that a straight portion of the shaft of the angiographic catheter was within the field of view. To account for variations in image noise and quality, a portion of the angiographic catheter was analyzed as described below.

Curvature of a circle is defined as the inverse of the radius of that circle; as the radius decreases, the curvature value increases. Any point along a continuous curve may be thought of as lying on the perimeter of a circle, and its curvature may be calculated with vector analysis by standard Frenet-Serret formulas.20,21 These formulas show that curvature is directly proportional to the rate of change of the tangent vector to the curve with respect to the arc length of the curve. Tight bends are associated with high curvature values and a straight line has a curvature value of zero. Arterial borders may be treated as continuous curves and their shape may be described by plotting the curvature value at each point along the edge ("curvature signature"). The angiographic catheter is assumed to have smooth, straight borders; therefore, its edges should have curvature values of zero. Deviations from zero are assumed to reflect all factors contributing to image noise. Therefore, to account for image noise and difference in image quality, the curvature signature of the arterial edge was divided by the standard deviation (SD) of the curvature of the catheter edges to yield a normalized curvature signature. Curvature peaks of arterial edges were only considered significant when values were more than 2 SDs of the catheter curvature values. Such peaks were considered to represent true irregularities of the arterial border.

Morphometric Parameters

Five morphometric parameters were calculated—four derived from the normalized curvature signature and one based on the concept of fractal analysis (Figures 1 and 2).22 Parameters were determined individually for each border of an arterial lesion segment. The use of these parameters as shape descriptors was previously validated by substituting various mathematical functions for arterial borders.19

Peaks per centimeter: number of curvature peaks outside ±2 SDs per centimeter of lesion length.

Summed maximum errors per centimeter: sum of the maximum normalized curvature value occurring at each significant peak, corrected for lesion length.

Integrated error per centimeter: the summation of areas under the curvature signature for each significant peak, corrected for lesion length.

Number of major features per centimeter: determined using pattern recognition when examining the curvature signature of a border. A "feature" was defined as a bulge or indentation along the edge of a lesion that corresponds to groupings of three curvature peaks (a "triplet") of alternating sign along the curvature signa-

FIGURE 1. Panel A: Curvature signature of an arterial border demonstrating peaks per centimeter. Standard deviations of curvature are plotted on ordinate, with a cutoff of ±2 SDs (shaded area). Peaks in curvature signature beyond ±2 SD "normal" range are considered significant (labeled 1–4). In all panels, x axis represents lesion length. Panel B: Analysis of curvature signature showing summed maximum error. Maximum values at each curvature peak (arrows) are added together to obtain this parameter. Panel C: Integrated curvature error is calculated by finding all regions of the curvature signature that extend beyond the ±2 SD lines, integrating under curve in these regions, and summing these values (shaded areas). Panel D: Number of major features is extracted from analysis of triplet patterns of significant positive-negative-positive or negative-positive-negative curvature peaks. Two features are found in this curvature signature, ABC and BCD.

FIGURE 2. Scaled edge length ratio is ratio of two measured lengths of same arterial border (L1/L2) using different ruler sizes. L1 is determined using a ruler length of 2 pixels, and L2 is calculated with a ruler length of one half arterial diameter of normal segment.
ture (i.e., from positive to negative to positive or from negative to positive to negative [Figure 1]). The number of features is obtained by summing the number of triplets thus defined and correcting for lesion length.

**Scaled edge length ratio:** calculated with a simplification of fractal analysis (Figure 2). True fractal analysis uses multiple ruler sizes to measure the length of the same border and takes the slope of the line resulting from the plot of the logarithm of the measured length versus the logarithm of the ruler length as a descriptor of border roughness. The scaled edge length ratio parameter used in this study equals the ratio of two measured lengths of the same arterial border using different ruler sizes. The two lengths were chosen empirically for this study. The first length (L1) was measured using a ruler length of 2 pixels on the digitized angiogram. The second length (L2) was measured using a ruler length of one half the maximum diameter of the normal arterial segment. For irregular borders, L1 is greater than L2 because a smaller ruler is able to measure more of the edge detail. The scaled edge length ratio equals L1 divided by L2. As lesion roughness increases, L1 increases out of proportion to L2; therefore, the scaled edge length ratio also increases.

An example of the finalized borders from the automatic edge detection program and curvature signature for the edges is shown in Figure 3. Note that one edge is relatively smooth but the other is quite complex with a number of significant curvature peaks.

The five morphometric parameters described were calculated for each edge of each lesion segment for...
between stable and unstable angina. Because the parameters (for either stable or unstable or both populations) were not normally distributed, a Mann-Whitney nonparametric test was used for statistical comparison between the two groups. The groups were compared by assigning each lesion the average of the parameter values for the two edges of that lesion. The cohorts were also compared by traditional methods of coronary artery disease description, including percent diameter stenosis, minimum luminal diameter, and lesion distribution. Each of the morphometric parameters was compared with percent stenosis and minimum luminal diameter using least-squares linear regression analysis to determine whether there was any dependence of these morphometric parameters on measures of luminal narrowing. Reproducibility was assessed by examining interobserver variability between two independent operators in 10 patients selected at random from a list of patient cine numbers. Three had stable and seven had unstable angina. Intraobserver variability for one of these operators was determined in the same 10 patients. Variability analysis was performed using the same preselected cine frames for each observation. The assessment of reproducibility was performed by using linear regression analysis and comparing the mean differences versus 0.0 by a t test. Each lesion was also assigned to one of the Ambrose morphology classifications, and the results in the two groups were compared with χ² testing. Finally, a cutoff value to differentiate between stable and unstable lesions was determined for each parameter. This value was chosen as the one that maximized the concordance with the diagnosis of the clinical syndrome while attempting to keep the sensitivity and specificity within 10% of one another. For this analysis, the following definitions were used. "Sensitivity" was defined as the number of unstable angina patients with a parameter value equal to or more than the cutoff divided by the total number of unstable patients. "Specificity" was defined as the number of stable angina patients with a parameter value less than the cutoff divided by the total number of stable patients. "Concordance" was defined as the number of stable and unstable angina patients correctly identified by the quantitative parameter divided by the total number of patients.

### Results

Four of the five morphometric parameters were found to be significantly different between the unstable and stable angina patients (Table 1). There were approximately one and one half the number of significant peaks per centimeter between the unstable and stable angina patients (4.29±2.19 vs 2.69±2.36, p=0.0056). Roughly twice the mean value for summed maximum errors per centimeter was found in the unstable cohort (15.42±10.57 vs 8.43±8.91, p=0.0018), as was the case for integrated errors per centimeter (112.5±94.8 vs 51.7±61.9, p=0.0008). Also significantly different were the number of major features per centimeter (bulges and indentations) detected (unsable angina, 0.82±0.83; stable, 0.37±0.62; p=0.0069). The scaled edge length ratio was not different between the two groups (stable angina, 1.089±0.039; stable angina, 1.068±0.0021, p=0.0841). Collectively, these data indicate quantifiably greater lesion complexity in the unstable angina population.

The quantitative analysis used in this study was found to be highly reproducible for all of the parameters (Table 2). The correlation coefficients for both

### Table 1. Morphometric Differences Between Stable and Unstable Angina

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Unstable angina (n=59)</th>
<th>Stable angina (n=20)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peaks/cm</td>
<td>4.29±2.19</td>
<td>2.69±2.36</td>
<td>0.0056</td>
</tr>
<tr>
<td>Summed maximum error/cm</td>
<td>15.42±10.57</td>
<td>8.43±8.91</td>
<td>0.0018</td>
</tr>
<tr>
<td>Integrated error/cm</td>
<td>112.5±94.8</td>
<td>51.7±61.9</td>
<td>0.0008</td>
</tr>
<tr>
<td>Number of features/cm</td>
<td>0.82±0.83</td>
<td>0.37±0.62</td>
<td>0.0069</td>
</tr>
<tr>
<td>Scaled edge length ratio</td>
<td>1.089±0.039</td>
<td>1.068±0.021</td>
<td>0.0841</td>
</tr>
</tbody>
</table>

Values are given as mean±SD. Each lesion was evaluated by taking the average of the parameters calculated from its two edges.

*p*Mann-Whitney test.

### Table 2. Intraobserver and Interobserver Variability of Morphometric Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>r</th>
<th>Mean difference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intraobserver variability</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peaks/cm</td>
<td>0.93</td>
<td>0.44±0.90</td>
</tr>
<tr>
<td>Summed maximum error/cm</td>
<td>0.96</td>
<td>1.37±2.59</td>
</tr>
<tr>
<td>Integrated error/cm</td>
<td>0.98</td>
<td>−7.6±16.1</td>
</tr>
<tr>
<td>Number of features/cm</td>
<td>0.83</td>
<td>0.07±0.55</td>
</tr>
<tr>
<td>Scaled edge length ratio</td>
<td>0.90</td>
<td>0.002±0.014</td>
</tr>
<tr>
<td><strong>Interobserver variability</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peaks/cm</td>
<td>0.94</td>
<td>0.55±0.88</td>
</tr>
<tr>
<td>Summed maximum error/cm</td>
<td>0.93</td>
<td>1.56±3.46</td>
</tr>
<tr>
<td>Integrated error/cm</td>
<td>0.94</td>
<td>10.4±25.6</td>
</tr>
<tr>
<td>Number of features/cm</td>
<td>0.79</td>
<td>0.0±0.71</td>
</tr>
<tr>
<td>Scaled edge length ratio</td>
<td>0.86</td>
<td>0.009±0.016</td>
</tr>
</tbody>
</table>

Mean difference is given as mean±SD. All p values are >0.05 for mean difference versus 0.0.
TABLE 3. Comparison of Percent Diameter Stenosis, Minimum Diameter, Lesion Distribution, and Qualitative Morphology for Unstable and Stable Angina Cohorts

<table>
<thead>
<tr>
<th>Lesion Site</th>
<th>Unstable Angina (n=59)</th>
<th>Stable angina (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(76.2±13.7% stenosis*, 0.74±0.44 mm minimum diameter†)</td>
<td>(49.2±21.4% stenosis*, 1.79±0.78 mm minimum diameter†)</td>
</tr>
<tr>
<td>Code</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>26</td>
<td>44.1</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>16.9</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>3.4</td>
</tr>
<tr>
<td>5</td>
<td>16</td>
<td>27.1</td>
</tr>
</tbody>
</table>

*Statistically different from stable angina cohort at p<0.0001 by an unpaired Student's t test. ‡Distribution of morphology types not statistically different from stable angina cohort by χ² test, p=0.7239.

Lesion site codes: 1, left main coronary artery; 2, left anterior descending artery; 3, circumflex artery; 4, ramus intermedius; 5, right coronary artery; B, bypass graft.

Morphology codes: 0, concentric, smooth lesion; 1, asymmetric narrowing with convex intraluminal obstruction that is smooth and broad based; 2, asymmetric narrowing with convex intraluminal obstruction that has a narrow base or neck due to overhanging edges or borders that are very irregular or scalloped, including fractured plaques and dissections; 3, two or more serial lesions (qualitative morphology designations from Ambrose et al†).

The stable and unstable angina groups were also compared by traditional methods of coronary artery disease description, including lesion distribution, percent diameter stenosis, minimum diameter, and the qualitative morphology classification scheme defined by Ambrose et al† (Table 3). Unstable angina patients were found to have a significantly greater percent diameter stenosis (76.2±13.7% versus 49.2±21.4%, p<0.0001) and smaller minimum luminal diameter (0.74±0.44 versus 1.79±0.78 mm, p<0.0001). When the groups were compared by the Ambrose morphology classification scheme, no statistically significant difference was found by χ² analysis (p=0.7239), although the expected trend of more complex lesions in the unstable angina group was evident.

Each of the quantitative parameters was compared with both percent diameter stenosis and minimum diameter by linear regression analysis after combining the two cohorts (Table 4). No significant correlation was found between the morphometric parameters and these measures of luminal narrowing, showing the methods' independence from traditional assessments of lesion severity.

The two groups were compared graphically to determine the amount of overlap for each parameter between the stable and unstable angina patients (Figure 4). An analysis was performed to determine a cutoff value for differentiating stable from unstable lesions for each of the four parameters that were found to be significantly different between the two groups. The cutoff values were chosen to maximize the concordance while keeping sensitivity and specificity within 10% of one another (Table 5). For these four parameters, the cutoff values yielded sensitivities ranging from 71.2% to 79.7%, specificities ranging from 65.0% to 70.0%, and concordance rates ranging from 70.9% to 77.2%. The best results were obtained with the peaks per centimeter parameter (cutoff value 2.7: sensitivity, 79.7%; specificity, 70.0%; concordance, 77.2%) for differentiating unstable from stable angina lesions.

Discussion

We describe an automated computer program that analyzes digitized angiograms and extracts quantitative morphometric parameters. The approach used is different from previous attempts at morphology analysis and employs standard mathematical formulas from vector and fractal analysis known to be useful in shape description. The initial validation of this method was performed by substituting various mathematical functions for the arterial borders.19 This showed that the software was able to correctly identify features and measure sine wave amplitudes and curvature to within a fraction of a pixel. Because this method is quantitative and may be applied in a general fashion to all types of arterial borders, many of the problems of previous attempts at qualitative morphology description are avoided.

TABLE 4. Correlations With Traditional Methods of Coronary Artery Disease Description

<table>
<thead>
<tr>
<th>Parameter</th>
<th>r versus percent stenosis</th>
<th>r versus minimum diameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peaks/cm</td>
<td>0.0703</td>
<td>-0.0978</td>
</tr>
<tr>
<td>Summed maximum errors/cm</td>
<td>0.0524</td>
<td>-0.0556</td>
</tr>
<tr>
<td>Integrated errors/cm</td>
<td>0.0453</td>
<td>-0.0329</td>
</tr>
<tr>
<td>Number of features/cm</td>
<td>0.0730</td>
<td>-0.0373</td>
</tr>
<tr>
<td>Scaled edge length ratio</td>
<td>0.0995</td>
<td>-0.0946</td>
</tr>
</tbody>
</table>

n=79; analyses were performed after combining the two populations. All r values are associated with p values ≥0.39.
Major problems are associated with qualitative assessment of morphology due to the subjective nature of the process. There is a lack of standardization in interpretation between different laboratories, and no rigorous indexing system exists to grade lesions or detect subtle changes in response to therapy. Most previous studies using qualitative descriptions of morphology require that each lesion be assigned to a discrete morphology type.\(^4\)\(^{-10}\) The method described above allows all parameters of a lesion to be derived in continuous scale fashion and therefore avoids the problem of assigning a lesion to a predetermined category. Use of this method would allow uniformity in clinical trials and provide a rigorous and perhaps more sensitive system for grading change in lesion morphology. Another major problem with subjective visual inspection of coronary lesions is the inherent potential for interobserver and intraobserver variability.\(^14\)\(^,\)\(^15\) The program described showed excellent reproducibility as evidenced by low interobserver and intraobserver variability for all of the parameters.

Previous quantitative assessments of lesion morphology have been few in number. Wilson et al.\(^16\) used an “ulceration index” to describe lesion roughness. The method, however, is cumbersome, because it relies on hand tracing of arterial borders. In addition, the ulceration index was dependent on measurement of two separate luminal diameters within a lesion, a problem that was avoided in the present study because each edge is initially examined separately for individual shape characteristics. All parameters are, therefore, independent of lesion stenosis. Probably the most important difficulty with the Wilson approach is that it detects only complex lesions with areas of plaque ulceration within a narrowed segment. The current methodology is applicable to all lesion morphologies and does not require specific characteristics for analysis.

The importance of complicated stenoses (those with plaque rupture, ulceration, or hemorrhage) in the pathogenesis of acute thrombosis and myocardial infarction is well known. Pooled data from five necropsy studies showed that 292 episodes of acute thrombosis were associated with 265 complicated stenoses, a prevalence of 91%.\(^23\)\(^{-27}\) Postmortem angiography was found to have a sensitivity of 88% and specificity of 79% in defining complicated stenoses on the basis of an irregular border or intraluminal lucencies,\(^13\)\(^,\)\(^28\) suggesting that these lesions may be detected before the development of thrombosis and potentially modified to reduce the risk of future cardiac events. A recent study using qualitative morphology analysis to compare stable and unstable patients found that evidence of coronary thrombus had a sensitivity of only 42% and evidence of complex lesion morphology (defined as haziness, smudging, or irregular lesion margins) had a sensitivity of only 44% in detecting lesions from unstable angina patients.\(^29\) In

**Table 5. Cutoff Values to Differentiate Stable From Unstable Angina Lesions**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cutoff value</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Concordance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peaks/cm</td>
<td>≥2.7</td>
<td>79.7</td>
<td>70.0</td>
<td>77.2</td>
</tr>
<tr>
<td>Summed maximum error/cm</td>
<td>≥9.61</td>
<td>71.2</td>
<td>70.0</td>
<td>70.9</td>
</tr>
<tr>
<td>Integrated error/cm</td>
<td>≥55.0</td>
<td>74.6</td>
<td>70.0</td>
<td>73.4</td>
</tr>
<tr>
<td>Number of features/cm</td>
<td>≥0.32</td>
<td>74.6</td>
<td>65.0</td>
<td>72.2</td>
</tr>
</tbody>
</table>

**Figure 4.** Plots of cumulative frequencies at different values for parameters that distinguish between stable and unstable angina patients. y axis gives cumulative percentage of lesions in each group associated with an index value equal to or less than value on x axis. Cutoff or critical value (C.V.) is generally seen at value on the x axis where two curves are most divergent. SPEC, specificity; SENS, sensitivity; CONC, concordance.
our study, the quantitative parameters peaks per centimeter, summed maximum errors per centimeter, integrated errors per centimeter, and number of features per centimeter gave sensitivities of 71.2–79.7%, while maintaining specificities of 65.0±70.0%. This compares favorably to the above-mentioned study29 in which the combination of two criteria (intracoronary thrombus and complex morphology) yielded a sensitivity of 70% and a specificity of 79%.

In the present study, although four of the five quantitative morphometric parameters tested were found to be significantly different between stable and unstable angina populations, no statistically significant difference was found between the unstable and stable angina patients when the qualitative classification scheme of Ambrose et al was used even though a trend toward greater lesion complexity was noted in the unstable group. This may have resulted from the relatively small sample size of the stable angina group but serves to emphasize that this quantitative method appears to be more sensitive for detecting differences, even between small groups of patients. The method is also better suited for detecting subtle changes that might be induced by therapy with thrombolytic, antiplatelet, or lipid-lowering agents because the parameters are derived in a continuous, noncategorical fashion.

The one parameter that did not show a difference between the stable and unstable angina patient was the scaled edge length ratio. The calculation of this parameter was based on the concept of fractal analysis and was thus conceptually different from the other four parameters that were calculated using curvature analysis. The failure of this parameter to differentiate between the two groups of patients may have been due to not choosing the optimal ruler lengths to maximize differences in border measurements or to our inability to apply the more formal method of fractal analysis due to computer limitations. Hopefully, future refinements of this concept will also prove useful in defining complex lesion morphology.

In summary, this method provides an objective and quantitative description of morphology that differentiates stable from unstable angina patients. Major advantages include the ease and rapidity with which analysis may be performed, lack of reliance on expert users, excellent reproducibility, avoidance of subjective visual inspection, independence from traditional methods of coronary artery disease description such as percent stenosis, and ability to assess lesion morphology in a continuous scale fashion rather than assigning lesions to discrete categories. This type of analysis can give uniformity and power to trials studying the effects of interventions on coronary lesions in an attempt to alter patient prognosis. Given the importance of coronary morphology in predicting the clinical behavior of a lesion, a more rigorous and quantitative approach will probably be mandated in future clinical trials studying this aspect of coronary disease.

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References
18. Ellis SG, DeBoe SF, Sanz ML, Mancini GB: Accuracy and reproducibility of 5 fr catheter systems for outpatient use compared with 8 fr systems. Circulation 1987;76(suppl IV):IV-369

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