Quantitative Coronary Angiography: Measurement of the "Critical" Stenosis in Patients with Unstable Angina and Single-Vessel Disease Without Collaterals

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SUMMARY  Quantitative angiographic assessment of proximal coronary artery stenosis was performed in 15 patients with consecutive presentations in two categories defined by clinical and angiographic criteria. Group 1 consisted of 10 patients who had new onset of refractory rest angina and ischemic ST-T changes, but no infarction, single-vessel coronary disease without collateralization, and normal left ventricular (LV) angiograms. Group 2 consisted of five patients who were similar to patients in group 1, but had subendocardial infarction (SEI). Quantitative coronary arteriography, using paired perpendicular angiographic views and digital computation, yielded statistically different lesion dimensions and hemodynamic predictions for the two groups. Minimum stenosis diameters were 0.88 ± 0.14 (SD) and 0.64 ± 0.08 mm, respectively, for groups 1 and 2. This corresponded to 72% and 78% diameter reduction and 92% and 95% cross-sectional area reduction for the two groups. These small dimensional differences among lesions in the two groups resulted in large differences in their hemodynamic impact as predicted from classic fluid mechanics theory. We conclude that there are characteristic lesion dimensions for the isolated "critical" stenosis in these selected patients with rest angina. Further small increases in lesion severity result in SEI. Certain practical applications and limitations of these observations are discussed.

THE TERM "CRITICAL LESION" is commonly used but poorly defined in human disease. Are there, in fact, identifiable characteristics of the "critical" human coronary stenosis? A critical lesion may be defined clinically as one that results in ischemic symptoms at rest, or physiologically as one that permits only marginally sufficient levels of myocardial perfusion in the basal state. Various clinical and experimental reports have contributed to our understanding of the degree of coronary constriction necessary to impair normal basal myocardial perfusion.1-18 In spite of this information, the relationship between symptoms of coronary disease and the magnitude of stenosis is widely known to be inconsistent.19-21 For example, patients with total obstruction of a large coronary branch sometimes have enough collateral development to preserve both ventricular function and the asymptomatic state. Conversely, patients with variant angina22 may have only minimal atherosclerosis.23 Thus, one might anticipate similar inconsistencies in...
attempts to characterize the coronary lesion responsible for ischemia at rest. One experiment of nature does occur relatively rarely to provide us with a clinical model that resembles the isolated experimental coronary constriction. This is the patient with recent onset of exertional angina that rapidly progresses to refractory intermittent rest pain who, on angiography, has proximal single-vessel stenosis, an apparently normal left ventricular contractile pattern, and no evidence of collateral development.

This report describes the analysis of lesions in such patients using a computer-based technique. To avoid variability and error associated with visual interpretation of the coronary angiogram, we have developed a method that generates a true-scale, three-dimensional representation of a diseased coronary segment with \( \pm 150 \mu \) dimensional accuracy and \( \pm 4\% \) variability on estimates of percent stenosis. By this technique, the isolated stenosis in patients with rest angina, no infarction, and no collateral development has been shown to have consistent dimensional characteristics. And in a group of similar patients with associated subendocardial myocardial infarction, a slightly but significantly greater stenosis has been identified.

**Methods**

**Quantitative Angiography**

Fifteen patients presented clinically with angina at rest, refractory to medical therapy. Each had single-vessel disease. The 15 stenotic arterial segments were analyzed using a newly developed, digital computer method. We obtained coronary cineangiograms in routine fashion using Judkins technique in multiple projections, including cranial angulation projections. For each left anterior oblique (LAO) projection, we filmed a perpendicular right anterior oblique (RAO) projection. For example, a perpendicular pair might be a \( 60^\circ \) LAO and a \( 30^\circ \) RAO. Our radiographic equipment is the General Electric Fluoricon system, operating at less than 7 msec/frame, 70–120 kV maximum. Individually adjusted film processing results in high-contrast images, as shown in figure 1. Cine frames were selected from the perpendicular pair of projections that showed the lesion most clearly. For each of the two views, frames were selected at end-systole, end-diastole and midcycle. These frames were projected at about fivefold arterial magnification onto a large screen marked off in \( x, y \) coordinates.

Three trained observers separately traced the out-

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**Figure 1.** Examples of highly magnified areas from angiographic frames showing the diseased arterial segments analyzed. Considerable image clarity was lost in preparing this illustration. A) Example of a lesion from a patient in group 1 (unstable angina) selected because its calculated dimensions were closest to the group 1 average. On the left is the magnified lesion image; on the right is the computer representation of the lesion. B) Example of the average group 2 lesion (subendocardial infarct) and its digital representation. Kodak 2474 35-mm cine film was used. All images are at the same scale, or given. RAO = right anterior oblique; LAO = left anterior oblique.
line of the magnified, projected lesion image from the
selected frame pairs. The diseased arterial segment
was traced from the “normal” proximal to the “nor-
mal” distal portion. A traced section of the catheter
tip, of known dimensions, provided a scaling factor.
These traced images were transmitted, using a
digitizer, to a PDP 11/45 computer. The computer
program reduces the lesion image to true scale by
compensating for pin cushion distortion, x-ray beam
divergence and magnification. These true-scale images
from the two perpendicular projections were then
matched along their center lines. This combination of
data from the perpendicular projections allowed a
three-dimensional characterization of the diseased
arterial segment. Figure 2 shows the hard-copy com-
puter printout of a typical processed lesion. The
segments are displayed as they would appear in true
scale in each of the two perpendicular projections,
LAO and RAO. Matched portions of the two views
are mathematically stretched out to true length in
the center panels. The computer determines the length
of the lesion as the distance between the two points which
are 10% reduced in cross-sectional area from the
normal proximal and distal areas. From these data, the
computer calculates and prints vessel diameter and
cross-sectional area (assuming an elliptical cross sec-
tion) in the “normal” proximal and distal portions,
and at the point of maximum narrowing. Percent
diameter and area stenosis are calculated according to
the formulas of figure 3. More complex geometric
functions of the lesion are estimated, including
atheroma mass and flow resistance. Resistance is es-
imated assuming fully developed flow in the converg-
ing portion of the lesion and turbulent flow in the
diverging portion. A pressure drop across the lesion
may be predicted by multiplying the estimated resis-
tance by a selected flow value.

Since the lesions from each of these patients were
traced by three independent observers at three
different points in the cardiac cycle, each lesion
dimension represents an average of nine repeated
measurements. The variability of repeated mea-
surements for a given lesion was small. For example,
the average standard deviation of the minimum
diameter estimate among the 15 lesions was 103 μ.

Patients

Fifteen patients who underwent cardiac catheteriza-
tion for symptomatic coronary artery disease
presented with one of two clinical syndromes: 1) un-
stable angina with medically refractory rest pain, or

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**Figure 2.** Example of the hard-copy computer printout of the lesion analysis of a typical group 1 (unstable angina) patient. Diameters of approximately 3 mm were measured in the normal portions of the vessel. In the left anterior oblique (LAO) projection, the minimum lumen diameter (dmin) in the stenosis is 1 mm, a 67% reduction from its averaged normal diameters (%DS). The minimum cross-sectional lumen area (Amin) is 0.71 mm², a 90% reduction from the averaged normal areas (%AS). Lesion length is 10.2 mm. The Poiseuille resistance (Rpo) is 2.4 mm Hg/ml/sec. The turbulent (orifice) resistance (Ror) is calculated for a range of flow values. The predicted pressure drop across the stenosis is thus 9.8 mm Hg for 1 ml/sec flow, 34 mm Hg for 2 ml/sec flow, and so on. RAO = right anterior oblique.
2) subendocardial myocardial infarction (SEI) with persistent refractory rest angina. Patients with ST-segment elevations on the ECG during rest pain were excluded from both groups. All patients were male veterans. None had had previous bypass surgery. Patients with each of the above clinical presentations who also fit the angiographic criteria described below represent consecutive cases of each syndrome studied in the Wadsworth VA Hospital’s cardiovascular diagnostic laboratory during the periods given. Group 1 consisted of 10 patients who underwent catheterization between October 1972 and November 1977 (mean age 52 years; range 38–61 years) with 1) recent onset of exertional angina whose severity had progressed rapidly to refractory rest pain unresponsive to medical therapy, with localizing ischemic ST-T changes on the ECG and no evidence of a previous myocardial infarction. The average interval between onset of angina and arteriography was 3 weeks; 2) single-vessel coronary artery disease without collateral development; 3) apparent normal wall motion on left ventricular (LV) angiograms. Group 2, who underwent catheterization between March 1974 and December 1977, consisted of five patients (mean age 51 years; range 42–60 years) similar to patients in group 1, but who had ECG or enzymatic evidence of a subendocardial infarction (i.e., persistent T-wave inversion for longer than 72 hours without new q waves and/or CPK elevation > 111 IU/ml (upper limit of normal for our laboratory), but < 360 IU/ml. Three of these five patients had very mild segmental hypokinesis in the LV angiogram. All 15 patients of groups 1 and 2 were studied during their clinical syndrome of intermittent rest pain.

In group 1, eight patients had left anterior descending (LAD) lesions, one patient had a dominant left circumflex, and one had a right coronary artery (RCA) lesion. In group 2, four patients had LAD lesions and one patient had an RCA lesion.

Results

Figure 2 presents typical values for group 1 patients. Table 1 summarizes the data for both groups, and presents the statistical comparison. Figure 3 shows the mean minimum lumen diameter ($d_{\text{min}}$), percent diameter stenosis (%DS), minimum cross-sectional lumen area ($A_{\text{min}}$), percent area stenosis (%AS), and length of lesions in both groups. The mean local diameter was averaged from the two perpendicular views. Table 1 shows that there were significant differences in $d_{\text{min}}$ between the two groups ($p < 0.01$). There were also significant differences in %DS. In group 1 patients, the mean $d_{\text{min}}$ was 0.88 ± 0.14 mm (sd), a 72% diameter reduction. Group 2 patients had a mean $d_{\text{min}}$ of 0.64 ± 0.08 mm, a 78% diameter reduction. The mean lesion length in group 1 was 14.4 ± 5.5 mm; in group 2 it was 15.3 ± 3.1 mm.

Average local cross-sectional area is calculated assuming that the vessel is elliptical in cross section. The local diameters determined from the two angiographic views were used as the major and minor axes of the ellipse. As shown in table 1, there were significant differences in $A_{\text{min}}$ between the two groups. The mean $A_{\text{min}}$ was 0.63 ± 0.19 mm² (sd) in group 1, and 0.35 ± 0.11 mm² in group 2. There were also significant differences in %AS.

Resistance to flow through the stenosis was calculated according to classic theory for steady flow.
TABLE 1. Averaged Determinations of Lesion Geometry and Derived Resistance and Pressure Functions for Each of the Patient Groups

<table>
<thead>
<tr>
<th></th>
<th>Geometric determinations</th>
<th>Derived functions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$D_{ma}$ (mm)</td>
<td>$A_{ma}$ (mm²)</td>
</tr>
<tr>
<td>Group 1</td>
<td>0.88 ± 0.14</td>
<td>0.63 ± 0.19</td>
</tr>
<tr>
<td>$n = 10$</td>
<td>(0.69-1.07)</td>
<td>(0.99-0.94)</td>
</tr>
<tr>
<td>Group 2</td>
<td>0.64 ± 0.08</td>
<td>0.35 ± 0.11</td>
</tr>
<tr>
<td>$n = 5$</td>
<td>(0.53-0.73)</td>
<td>(0.22-0.51)</td>
</tr>
</tbody>
</table>

Statistical comparison

(group 1 vs group 2) † * † † NS NS NS *

Values are given as mean ± sd. Values in parentheses represent the range.

$^*P < 0.05.$

$^\dagger P < 0.01.$

$^\ddagger$ NS

Abbreviations: $D_{ma}$ = minimum lumen diameter; $A_{ma}$ = percent diameter stenosis; $A_{ma}$ = minimum cross-sectional lumen area; $A_{AS}$ = percent area stenosis; $R_p$ = Poiseuille resistance; $R_t$ = turbulent resistance; $\Delta P$ (Q = 1) = estimated stenosis pressure based on hypothetical stenosis flow of 1 ml/sec.

Discussion

We have attempted to identify quantitatively the features of the isolated "critical" coronary stenosis in a well-defined subset of patients, with coronary disease. From the autoregulatory perspective, a critical stenosis may be defined as one resulting in a segmental myocardial perfusion of less than 30% of basal flow. From the physiologic perspective, a critical stenosis is one that results in a myocardial perfusion that is not well-defined. myocardial perfusion limitation include other narrowing of the stenosis (and other collateral factors) appear at about 50% of basal flow. Factors that determine collateral flow are: coronary flow reserve, autoregulation, and the capacity of myocardial flow limitation. Inadequate collateral blood flow reduction is not a well-defined factor.

For example, May et al. produced uniform stenoses 10 mm long in canine lumen arteries and showed that the myocardial blood flow reduction in animals with normal coronary arteries was not well-defined. The myocardial blood flow reduction in these animals was less than 50% of basal flow. The myocardial blood flow reduction in animals with critical coronary stenosis was greater than 50% of basal flow. The myocardial blood flow reduction in animals with critical coronary stenosis was greater than 50% of basal flow. The myocardial blood flow reduction in animals with critical coronary stenosis was greater than 50% of basal flow.
diameter reduction resulted in a “critical” decrease in coronary blood flow, and that “significant” but less severe lesions (50–90%) had normal flows. This study was subject to the reported difficulties with the $^{85}$Kr technique and to the subjective tendency to overestimate the severity of the stenosis from the angiogram (see below). Our group 1 category was defined to select patients with “critical” stenosis. In these patients with medically refractory unstable angina and proximal single-vessel disease without infarction or evident collateralization, the lesion under consideration threatened the total flow available to a defined, fully viable segment of the left ventricle. It appears that the stenosis necessary to produce this syndrome is 0.9 mm in minimum diameter and 0.6 mm² in minimum area, with an overall length of 14 mm. This represents a 72% reduction in diameter and 92% area reduction. Further increased narrowing of the coronary artery was associated in five cases with subendocardial infarction.

The characteristic lesion parameters in our patients with symptomatic single-vessel disease show considerably less variability than the results of Rafflenbeul et al., who reported coronary stenctions ranging from 30–80% diameter reduction in “symptomatic” patients with single-vessel disease. However, the clinical symptoms of their patients were not defined. For example, in variant angina, a relatively mild coronary stenosis may be associated with ischemic symptoms, and this clinical presentation was excluded from our analysis. Furthermore, while these investigators used an objective, “morphometric” technique, they analyzed only a single angiographic projection. This can result in a considerable error in measuring the degree of stenosis, as lesions are often narrower in one projection than in others.

Interpretation of the finding of characteristic lesion dimensions in these two coronary syndromes requires certain qualification. The minimum lumen diameter necessary to cause arterial flow reduction depends in part on the mass, and thus the metabolic requirements, of myocardium distal to the stenosis. Although a 0.9-mm lumen diameter in the proximal LAD or dominant RCA may cause unstable angina, it is a nearly normal measurement in a small diagonal or marginal branch, and yet it may be incompatible with life in the left main coronary artery. Thus, arteries with different flow loads will have different dimensions of critical stenosis or, more appropriately, different critical resistances. Our stenosis dimensions show little variability in these two coronary syndromes because, in part, these diseased LAD and dominant RCAs perfused approximately similar myocardial beds.

Despite the general unavailability of computer-based systems for quantitative angiography, there is certain clinical utility in the above information. First, quantitative methods may become more widely available. Our telephone link to the Seattle PDP 11/45 computer by means of a video terminal and digitizer is accurate, relatively inexpensive (about
results in a clinical progression from ischemia to sub-endocardial infarction. Even more severe coronary narrowing is found in association with transmural infarction. Various other etiologies of unstable angina have been proposed, such as platelet emboli, arterial spasm, or hemorrhage into an ulcerated plaque. Our measurements do not exclude these mechanisms; they suggest, however, that in the patient with atherosclerotic heart disease and lacking collaterals, the major determinant of the severity of ischemia is the degree of luminal narrowing. Other factors such as coronary arterial constriction, transient microthrombus formation, or increased inotropic or chronotropic state could induce small perturbations in the oxygen supply-demand balance. In the setting of severe stenosis these would result in intermittent clinical manifestations of ischemia.

These measurements were purposely restricted to a highly specific subset of patients. Attempts to extrapolate these results to the broad spectrum of patients with ischemic heart disease are to be undertaken with caution, except as discussed above. The "typical" patient with coronary disease may have multiple stenoses, collateral development, previous myocardial necrosis, and compensatory myocardial hypertrophy, all of which can alter dramatically the relationship between lesion severity and the clinical manifestations of ischemia.

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