Assessing the Hemodynamic Significance of Coronary Artery Stenoses: Analysis of Translesional Pressure–Flow Velocity Relations in Patients

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Objectives. The purpose of this study was to examine the relation among the angiographic severity of coronary artery lesions, coronary flow velocity and translesional pressure gradients.

Background. Determination of the clinical and hemodynamic significance of coronary artery stenoses is often difficult and inexact. Angiography has been shown to be an imperfect tool for determining the physiologic significance of eccentric or irregular coronary lumen narrowing.

Methods. Using a 0.018-in. (0.046 cm) intracoronary Doppler-tipped angioplasty guide wire, spectral flow velocity data both proximal and distal to coronary stenoses were compared with translesional pressure gradient measurements and angiographic data obtained during cardiac catheterization in 101 patients. There were 17 patients with normal angiographic findings and 84 with coronary artery disease, with lesions ranging from 28% to 99% diameter narrowing. Patients with coronary disease were assigned to two groups on the basis of translesional gradients at rest. Group A (n = 56) had gradients <20 mm Hg, and Group B (n = 28) had gradients ≥20 mm Hg.

Results. Proximal average peak velocity, diastolic velocity integral and total velocity integral were slightly but statistically lower in Group A; however, the distal average peak velocity and diastolic and total velocity integrals were all markedly (all p < 0.01) decreased in patients with gradients ≥20 mm Hg (Group B).

Angiography is an imperfect method for determining the physiologic significance of a variety of coronary artery lumen narrowing (1–6). Decisions concerning the need for intracoronary intervention should be based on either lesion hemodynamics or objective evidence of lesion significance with ischemic stress testing, such as thallium perfusion scintigraphy (7–9). In animal models, studies of coronary blood flow, coronary flow reserve and regional perfusion have demonstrated predictable relations between anatomic and physiologic variables (10,11); however, similar studies in patients do not demonstrate clinically reliable physiologic relations among quantitative angiography (6,12), myocardial perfusion scintigraphy (13,14), coronary flow reserve (13–16) or translesional gradients (17–20). This disparity of results is due in part to the technical limitations in assessing both the intraluminal accumulation of atherosclerotic material and translesional hemodynamics. Translesional gradients were historically used in determining the hemodynamic signifi-
cance of a coronary stenosis. This method had the technical limitations inherent in a procedure that requires introduction of a catheter into the coronary artery, and results were difficult to obtain on a routine basis (17-20). Directly measured intracoronary blood flow velocity information and determination of coronary flow reserve have also been of limited value (21,22) because these measurements were obtained only proximal to the lesions in question, with flow responses dependent on lesion resistance, prelesional vessel branching (directing flow away or around the lesion) and distal myocardial hyperemic capacity. Moreover, because the branching of proximal coronary arteries may provide nearly normal flow velocity in a portion of the proximal vessel despite severe or total occlusions, and because measurement of high jet lesion velocities is difficult, the continuity equation cannot easily be used to gauge lesion severity (23). In addition, data on proximally measured flow velocity have not been predictive of blood flow distal to coronary stenoses (24). Directly measured distal coronary blood flow velocity can now easily be obtained using a Doppler-tipped angioplasty guide wire system with spectral velocity analysis capabilities (25-27). We therefore hypothesized that differences in flow velocities proximal and distal to intracoronary lesions would reflect transluminal hemodynamics and prove useful in characterizing the hemodynamic significance of coronary lesions, especially those of angiographic intermediate or indeterminate severity.

Methods

Study patients. Patients who were referred for diagnostic coronary angiography for typical clinical indications, including evaluation of chest pain, exertional angina, postinfarction angina or angioplasty follow-up were considered eligible for the study. Patients with unstable angina, acute myocardial infarction (<4 days), valvular disease, renal failure or congestive heart failure were excluded. Angiographic exclusions included collateral supply to the vessel under study, left main coronary artery narrowing (>40% diameter stenosis on visual assessment) or lesions that were inaccessible to the Doppler coronary guide wire. Anti-ischemic medications (nitrates, beta-adrenergic blocking agents and calcium channel antagonists) and antiplatelet agents were continued as clinically indicated. All patients received intravenous diazepam (2 to 4 mg) and intravenous diphenhydramine (25 mg) before the study. The study was approved by the Human Subjects Committee of the Institutional Review Board. Consent was obtained orally and in writing before the study.

Of 103 patients studied, 2 were excluded because adequate proximal and distal flow velocity signals could not be obtained, leaving a final study group of 101 patients. Eighty-four patients had coronary artery lesions ranging from 28% to 99% reduction in lumen diameter of the studied vessel. The other 17 patients with normal coronary angiograms were studied as a control group.

Coronary angiography. Coronary angiography was performed from the femoral approach with 6F or 8F Judkins catheters in a routine manner after intracoronary (200 µg) or sublingual nitroglycerin (0.4 mg) was administered. When possible, orthogonal views of the lesion in question were obtained. Left ventriculography was performed in the 30° right anterior oblique projection. All patients received 3,000 to 5,000 U of intravenous heparin before the Doppler angioplasty guide wire was introduced and coronary flow velocity measurements were made.

Coronary flow velocity measurements. Doppler guide wire. Subselective flow velocity was measured with a 0.018-in. (0.046-cm) Doppler angioplasty guide wire (Flowire, Cardiometrics). As described and validated by Doucette et al. (25), the Doppler angioplasty guide wire is a 175-cm long, 0.018-in. (0.046 cm) diameter, flexible, steerable guide wire with a 12-MHz piezoelectric ultrasound transducer integrated into the tip. The forward-directed ultrasound beam diverges in a 27° arc from the long axis (measured to the −6 dB round-trip points of the ultrasound beam pattern). The pulse repetition frequency of >40 kHz, pulse duration of +0.83 ms and sampling delay of 6.5 ms are standard for clinical usage. The system is coupled to a real-time spectrum analyzer, videocassette recorder and video page printer. The quadrature/Doppler audio signals are processed by the spectrum analyzer using on-line fast Fourier transformation to provide a scrolling gray scale spectral display. The frequency response of the system calculates ~90 spectra/s. Simultaneous electrocardiographic (ECG) and arterial pressure are also input to the video display. The Doppler guide wire velocity demonstrated excellent correlation with electromagnetic flow velocity and volumetric flow in straight and curved tubed models, as well as in vivo testing using a canine left circumflex coronary artery. The Doppler guide wire measures phasic flow velocity patterns and tracks linearly with flow rates in most small, straight coronary arteries (25-27).

Transluminal velocity measurements. After diagnostic angiography, the Doppler guide wire was loaded into a 2.2F infusion catheter (Tracker 18, Target Therapeutics), and the assembly was passed through a standard angioplasty Y-connector attached to either a 6F or an 8F guiding catheter. The guide wire was then advanced into the artery. Baseline flow velocity data were obtained at least 1 cm proximal to the lesion. The wire was then advanced past the stenosis by at least 5 artery diameter lengths, avoiding placement in any side branches, and distal flow velocity data were obtained. Continuous flow velocity profiles, along with simultaneous ECG and aortic pressure, were displayed on the video monitor.

Transluminal pressure gradient measurements. After the flow velocity data were recorded, the 2.2F infusion catheter was advanced beyond the stenosis into the distal portion of the coronary artery. The guide wire was removed and the guiding and infusion catheters were flushed. Phasic and mean pressures in the distal arterial segment were recorded.
simultaneously, with aortic pressure measured at the ostium of the guiding catheter using fluid-filled tubing and standard transducers (Namic, Inc.). The infusion catheter was then withdrawn to the proximal location while pressure was continuously recorded to observe the intrinsic pressure difference between the diagnostic and infusion catheters. In general, the intrinsic gradients of this catheter system were <5 mm Hg. The translesional pressure gradient was defined as (Mean proximal diagnostic catheter pressure – Mean distal coronary artery pressure) – Intrinsic gradient. The patients with normal angiograms did not undergo intracoronary pressure measurements.

**Coronary flow reserve.** Proximal and distal coronary flow reserve measurements were determined in 29 of the patients arbitrarily chosen to cover a wide range of angiographic stenoses and translesional gradients (range 0 to 80 mm Hg) and in the 17 normal patients. After baseline proximal flow velocity data were obtained, intracoronary adenosine was administered (6 to 8 μg in the right coronary artery and 12 to 18 μg in the left coronary artery) (28), and a second set of velocity indexes were obtained at peak hyperemia. The Doppler guide wire was then advanced into the distal vessel, and the sequence was repeated. Coronary flow reserve was computed as the quotient of hyperemic/branch average peak velocity (21).

**Angiographic data analysis.** Quantitative angiography of the lesion or lesions of interest was performed by quantitative caliper or digital analysis using the Philips DCI or ImageCom systems (Systems Inc.) (29). The 6F or 8F guiding catheter was used as a reference standard. The lesion severity was then determined as percent diameter stenosis of the angiographically normal adjacent reference segment. In lesions where orthogonal views could not be obtained, the view with the most severe diameter narrowing was used.

**Coronary flow velocity data analysis.** Flow velocity data were printed on an integrated video page printer that provided computerized variables of intracoronary flow velocity, including peak and mean diastolic and systolic velocities, diastolic and systolic velocity integrals (obtained by planimetry of the total area under the peak instantaneous velocity profile), average peak velocities and the total velocity integral. These automatic variables were validated using a custom software program and manual tracing of the spectral peak Doppler velocity signal on a digital computer bit pad (26,27).

**Statistical analysis.** Statistical correlations for the angiographic, Doppler and hemodynamic variables were made using simple linear regressions. Comparison between discrete variables for groups with pressure gradients <20 mm Hg (Group A) and ≥20 mm Hg (Group B) were made using the unpaired Student t test. The patients with normal angiograms and no intracoronary pressure measurements were not included in the comparison between the two groups. A second grouping for statistical analysis was made by organizing the patients into six subgroups on the basis of translesional pressure gradients. These were Group I, normal arteries; Group II, gradient 0 to 9 mm Hg; Group III, 10 to 19 mm Hg; Group IV, 20 to 39 mm Hg; Group V, 31 to 50 mm Hg; Group VI, ≥51 mm Hg. Comparisons were made among these groups using the unpaired Student t test with the Bonferroni correction for multiple comparisons. Proximal and distal flow velocity variables within groups were compared using the paired Student t test. Statistical significance was accepted when the probability value was < 0.05.

Data are presented as mean values ± 1 SD, unless otherwise indicated.

### Results

The clinical characteristics of the study group are shown in Table 1. There were no significant differences in any of the clinical variables or medical regimens. Figures 1 and 2 illustrate data from representative patients from Groups A and B, respectively. The patient from Group A has no decrease in distal flow velocity and no rest translesional gradient, whereas the patient from Group B has a significant decrease in distal flow velocity, correlating with a high translesional pressure gradient.

### Statistical analysis

Statistical correlations for the angiographic, Doppler and hemodynamic variables were made using simple linear regressions. Comparison between discrete variables for groups with pressure gradients <20 mm Hg (Group A) and ≥20 mm Hg (Group B) were made using the unpaired Student t test. The patients with normal angiograms and no intracoronary pressure measurements were not included in the comparison between the two groups. A second grouping for statistical analysis was made by organizing the patients into six subgroups on the basis of translesional pressure gradients. These were Group I, normal arteries; Group II, gradient 0 to 9 mm Hg; Group III, 10 to 19 mm Hg; Group IV, 20 to 39 mm Hg; Group V, 31 to 50 mm Hg; Group VI, ≥51 mm Hg. Comparisons were made among these groups using the unpaired Student t test with the Bonferroni correction for multiple comparisons. Proximal and distal flow velocity variables within groups were compared using the paired Student t test. Statistical significance was accepted when the probability value was < 0.05.

Data are presented as mean values ± 1 SD, unless otherwise indicated.

### Table 1. Clinical Characteristics of the Study Patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group A (n = 56)</th>
<th>Group B (n = 28)</th>
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<tbody>
<tr>
<td>Male (%)</td>
<td>82</td>
<td>74</td>
</tr>
<tr>
<td>Mean age; range (yr)</td>
<td>57; 28–78</td>
<td>59; 31–80</td>
</tr>
<tr>
<td>History of MI (%)</td>
<td>26</td>
<td>18</td>
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<tr>
<td>History of prior CABG (%)</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>History of prior PTCA (%)</td>
<td>29</td>
<td>37</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>23</td>
<td>39</td>
</tr>
<tr>
<td>Smoking (%)</td>
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<td>53</td>
</tr>
<tr>
<td>Hypertension (%)</td>
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<td>53</td>
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<tr>
<td>Medications (% of pts receiving)</td>
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<td></td>
</tr>
<tr>
<td>Calcium channel blocker</td>
<td>83</td>
<td>91</td>
</tr>
<tr>
<td>Nitrates</td>
<td>61</td>
<td>44</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>35</td>
<td>35</td>
</tr>
</tbody>
</table>

*Seventeen patients with angiographically normal arteries were not included. p = NS for all clinical variables and medical regimens. CABG = coronary artery bypass graft surgery; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty; pts = patients.*

### Quantitative angiography and translesional gradients

Measurements were made in the left anterior descending coronary artery in 45 cases, the right coronary artery in 28 and the left circumflex in 28. There was a moderate degree of correlation between angiographic percent diameter stenosis and their corresponding gradients (r = 0.6, p < 0.001) (Fig. 3). In the angiographically intermediate group (Fig. 4), arbitrarily limited to 50% to 70% stenoses, there was poor correlation between percent stenosis and translesional gradient, with r = 0.2 (p = NS) (Fig. 4).

### Coronary flow velocity and translesional gradient

When patients were classified into two groups on the basis of
Figure 1. A, Angiographic views of eccentric lesion in the left anterior descending coronary artery in a 59-year old man with atypical chest pain. The lesion is severe (>70%) in the left anterior oblique (LAO) view, and moderate (<50%) in the right anterior oblique (RAO) view. Lower panels show the sites at which flow velocity and gradient data were obtained (the smaller arrow indicates the lesion, the larger arrow shows the guide wire position, proximally and distally). B, Flow velocity spectra (top panels) and translesional gradients (lower panels) at rest and during maximal hyperemia with intracoronary (IC) adenosine (12 µg). Proximal and distal flow velocity are nearly identical, with a ratio of 1.05. The rest gradient is zero. With adenosine, distal flow increases 2.5 × baseline, and the hyperemic gradient is 10 mm Hg. A thallium scintigraphic exercise study showed a minimal apical defect, and no angiplasty was performed. The patient's symptoms abated spontaneously, and he was well at 8-month follow-up. Ao = aortic; COR = distal coronary artery pressure (mm Hg); ECG = electrocardiogram.

a translesional gradient <20 mm Hg (Group A) and ≥20 mm Hg (Group B), the intracoronary flow velocity values obtained proximal to the area of stenosis in Group A were lower than those in Group B (Table 2). In contrast, the flow velocities measured distal to the stenosis were significantly greater in Group A than in Group B (Table 2). Diastolic velocity integral, average peak velocity and total velocity integral were all significantly decreased in Group B.
A ratio of proximal to distal flow velocity indexes was then generated to normalize for absolute differences in flow velocity. A ratio of 1.0 represents equivalent intracoronary flow velocity distal to a stenosis, with an increasing ratio indicative of reduced distal flow velocity. This flow ratio demonstrated highly significant differences between the groups, ranging from 1.1 ± 0.3 for Group A to ranges of 2.4 ± 0.9 to 2.5 ± 1.2 for Group B with regard to diastolic and total velocity integrals and average peak velocity (all p < 0.001 vs. Group A) (Table 2).

As noted in an earlier study (26), the diastolic/systolic velocity ratio is altered distal to significant stenoses. Proximal diastolic/systolic velocity ratios were not different between the two groups (1.7 ± 0.06 and 1.6 ± 0.8), but distal diastolic/systolic velocity ratios decreased in Group B (1.1 ± 0.3 vs. 1.9 ± 0.5, p < 0.001) as the normal intracoronary diastolic predominant flow pattern was altered.

Individual data for the correlation between translesional gradient and the ratio of proximal to distal total flow velocity integrals are shown in Figures 3 and 4. There is a higher correlation between translesional gradient and intracoronary flow velocity ratios (r=0.8) than between gradient and angiographic percent stenosis (r=0.6) (Fig. 3). Only two patients with flow ratios <1.7 had translesional gradients >30 mm Hg. These two patients are discussed later.

In angiographically intermediate stenoses (50% to 70%, Fig. 4), the correlation between flow velocity ratios and translesional gradients remained high (r = 0.8, p < 0.001) in contrast to the poor correlation in this difficult and select group between gradients and angiographic percent stenosis (r = 0.2, p = N.s.).

Gradient subgroup analysis. Patients were classified into six subgroups on the basis of severity of translesional gradients (Group I, normal arteries; Group II, gradient 0 to 9 mm Hg; Group III, 10 to 19 mm Hg; Group IV, 20 to 30 mm Hg; Group V, 30 to 50 mm Hg; Group VI, ≥51 mm Hg) to identify a range at which a translesional gradient will significantly attenuate distal intracoronary blood flow velocity at rest (Fig. 5). Comparing absolute proximal flow velocities among the groups with coronary artery disease (Groups II to VI) revealed a gradual increase in flow velocity indexes with increasing translesional gradients (Table 3). There were no significant differences in absolute distal flow velocity among the groups; however, by normalizing each patient's distal flow velocities by his or her...
Figure 3. Top, Correlation between angiography (percent diameter stenosis) and translesional pressure gradients (mm Hg). Bottom, Correlation between the ratio of proximal to distal total velocity integral (Ratio PV,) and translesional pressure gradients (mm Hg). The two solid squares represent the proximal right coronary artery stenoses occurring before any branch points (see text for discussion).

Individual proximal flow velocities and creating proximal/distal flow ratios, significant differences emerged. Groups II to IV (gradients ≤30 mm Hg) had similar proximal/distal ratios (1.1 ± 0.2 to 1.4 ± 0.5), whereas Groups V and VI had significantly higher ratios (2.4 ± 0.7 to 2.9 ± 1.6, \( p < 0.001 \)) (Table 3). Absolute flow velocity values were not able to segregate stenoses by translesional gradients, but ratios of proximal to distal flow velocities clearly separated stenoses into those with gradients ≤30 mm Hg and those with gradients >30 mm Hg under rest conditions.

In the subjects with angiographically normal arteries and in Groups II and III, the proximal and distal flow velocity indexes were nearly equal within each group (Fig. 5). The distal total velocity integral and average peak velocity in Group II (0 to 9 mm Hg) reached a low level of statistical significance when compared with proximal velocities, despite small absolute differences. Group IV (20 to 30 mm Hg) showed a significant difference between proximal and distal total velocity integral and a trend in both diastolic velocity integral and average peak velocity (Table 4). Groups V and VI showed a markedly significant decline in all three distal flow velocity variables.

Angiographic data. Angiographically determined proximal and distal cross-sectional areas of the normal group and normal reference arterial segments in the diseased group demonstrated a nonsignificant trend toward larger sizes in the proximal cross-sectional area in the normal group (Group I) compared with all others. There were no statistical differences in distal cross-sectional area or minimal lumen diameter (Table 3).

Flow velocity in nonbranching right coronary arteries. Only two patients had flow velocity ratios <1.7 with translesional gradients >30 mm Hg. In these two patients (highlighted in Fig. 3), the flow velocity proximal and distal to the stenosis was unchanged despite angiographic and hemodynamic evidence of significant lesions. Both of these lesions were located in the proximal right coronary artery before any branch points in the proximal and midartery. The similar proximal and distal flow velocity responses in these specialized cases are in accordance with the continuity equation for an unbranching tube model. All other lesions occurred in arteries after branch points, although the vessels were small (<1 mm). Removal of these two patients from the data analysis, so that only stenoses involving branching vessels are examined, improves the correlation between translesional gradient and flow velocity ratio (\( r = 0.9, p < 0.0001 \)), with no change in the correlation between gradient and angiographic percent stenosis (\( r = 0.6, p < 0.001 \)).

Coronary hyperemia and flow reserve. Proximal and distal coronary flow reserve (hyperemic/basal average peak velocity) was measured in the 17 normal patients as well as in 29 patients with angiographic percent stenoses ranging from 50% to 85% and translesional gradients from 0 to
strated that gradients >30 mm Hg were nearly always a ratio, significant differences emerged that reliably demonstrate the hemodynamic severity of a given lesion. However, by normalizing distal flow using a proximal/distal flow ratio, significant differences emerged that reliably demonstrated that gradients >30 mm Hg were nearly always associated with a significant decline in distal flow velocity, with an increased ratio of >1.7:1. The flow velocity ratio has particular utility in identifying the hemodynamic significance of stenoses of angiographically intermediate severity (50% to 70%). Flow velocity data obtained in hemodynamically significant lesions before coronary angioplasty (26,27) demonstrate that clinically important stenoses can be characterized by three findings: increased proximal/distal flow ratios, loss of diastolic/systolic velocity ratio (per beat) and impaired distal (not proximal) hyperemic responses to maximal vasodilators. In the current study with many angiographically intermediate lesions, the most reliable finding associated with a translesional gradient >30 mm Hg was an increased proximal/distal flow velocity ratio. We hypothesize that the flow velocity gradient results from normal arterial inflow proximal to the stenosis, which is then distributed and diverted to other lower resistance regions through proximal branches. Flow velocity distally, beyond the stenosis, is thus diminished. This finding is consistent with classical hydrodynamic physical laws of flow resistance (24). It is also, with rare exception, in distinction to the continuity equation (23,30), which states that, when the cross-sectional area of the proximal and distal segments is the same, flow velocity should be equal both proximal and distal to a stenosis provided that there is no alternative outlet (blood) is carried through the tube. In this study, all lesions except the two proximal right coronary artery stenoses occurred after major branch points. No specific analysis was performed to determine the effect of the degree of branching (number of branches, size) on postlesional flow velocities.

### Table 2. Flow Velocity Data

<table>
<thead>
<tr>
<th>Group</th>
<th>Proximal</th>
<th>Distal</th>
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<tbody>
<tr>
<td>(gradient &lt;20 mm Hg)</td>
<td>(gradient ≥30 mm Hg)</td>
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</tr>
<tr>
<td>DVI (U)</td>
<td>20.6 ± 11.3</td>
<td>28.2 ± 16.6</td>
</tr>
<tr>
<td>TVI (U)</td>
<td>28.2 ± 15.5</td>
<td>37.4 ± 20.8</td>
</tr>
<tr>
<td>APV (cm/s)</td>
<td>31.9 ± 14.9</td>
<td>42.4 ± 19.7</td>
</tr>
<tr>
<td>DSVR</td>
<td>1.7 ± 0.6</td>
<td>1.6 ± 0.8</td>
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</table>

### Discussion

This study shows that the presence of a rest translesional gradient ≥30 mm Hg can be determined by utilizing a ratio of proximal to distal flow velocities in branching epicardial vessels. Groups were generated using a 20-mm Hg gradient cutoff for historical comparison, but subgroup analysis demonstrated that it is at a gradient of ≥30 mm Hg that distal coronary flow velocities begin to decline to a significant degree compared with proximal values. Absolute flow velocities measured either proximal or distal to a coronary stenosis were not able, in and of themselves, to reliably predict the hemodynamic severity of a given lesion. However, by normalizing distal flow using a proximal/distal flow ratio, significant differences emerged that reliably demonstrated that gradients >30 mm Hg were nearly always associated with a significant decline in distal flow velocity, with an increased ratio of >1.7:1. The flow velocity ratio has particular utility in identifying the hemodynamic significance of stenoses of angiographically intermediate severity (50% to 70%). Flow velocity data obtained in hemodynamically significant lesions before coronary angioplasty (26,27) demonstrate that clinically important stenoses can be characterized by three findings: increased proximal/distal flow ratios, loss of diastolic/systolic velocity ratio (per beat) and impaired distal (not proximal) hyperemic responses to maximal vasodilators. In the current study with many angiographically intermediate lesions, the most reliable finding associated with a translesional gradient >30 mm Hg was an increased proximal/distal flow velocity ratio. We hypothesize that the flow velocity gradient results from normal arterial inflow proximal to the stenosis, which is then distributed and diverted to other lower resistance regions through proximal branches. Flow velocity distally, beyond the stenosis, is thus diminished. This finding is consistent with classical hydrodynamic physical laws of flow resistance (24). It is also, with rare exception, in distinction to the continuity equation (23,30), which states that, when the cross-sectional area of the proximal and distal segments is the same, flow velocity should be equal both proximal and distal to a stenosis provided that there is no alternative outlet of flow (i.e., no branching) and that the same volume of fluid (blood) is carried through the tube. In this study, all lesions except the two proximal right coronary artery stenoses occurred after major branch points. No specific analysis was performed to determine the effect of the degree of branching (number of branches, size) on postlesional flow velocities.

![Figure 5. Top, Subgroup analysis comparing proximal and distal diastolic velocity integral (DVI). Bottom, Subgroup analysis comparing proximal and distal total velocity integral (TVI). See text for definition of gradient groups.](image-url)
Table 3. Flow Velocity Data by Hemodynamic Subgroup

<table>
<thead>
<tr>
<th>Gradient (mm Hg)</th>
<th>Group I (normal arteries)</th>
<th>Group II (0 to 9)</th>
<th>Group III (10 to 19)</th>
<th>Group IV (20 to 30)</th>
<th>Group V (31 to 50)</th>
<th>Group VI (≥51)</th>
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<tr>
<td>Stenosis (%)</td>
<td>54.7 ± 13.7</td>
<td>55.7 ± 9.2</td>
<td>57.3 ± 18.4</td>
<td>70.1 ± 14.7</td>
<td>76.8 ± 13.8</td>
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<tr>
<td>Gradient (mm Hg)</td>
<td>5.1 ± 3.1</td>
<td>14.2 ± 3.3</td>
<td>23.7 ± 4.6</td>
<td>41.5 ± 5.9</td>
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<td>Proximal</td>
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<tr>
<td>DVI (U)</td>
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<td>21.3 ± 11.4</td>
<td>21.0 ± 5.6</td>
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<td>32.7 ± 20.2</td>
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<tr>
<td>TVI (U)</td>
<td>17.3 ± 6.8</td>
<td>24.1 ± 13.0</td>
<td>32.4 ± 16.9</td>
<td>29.8 ± 6.8</td>
<td>36.4 ± 19.1</td>
<td>42.1 ± 26.1</td>
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<tr>
<td>APV (cm/s)</td>
<td>22.6 ± 8.1</td>
<td>27.3 ± 11.3</td>
<td>36.7 ± 16.9</td>
<td>36.1 ± 8.0</td>
<td>40.4 ± 19.1</td>
<td>47.0 ± 24.1</td>
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<td>Distal</td>
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<tr>
<td>DVI (U)</td>
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<td>17.2 ± 11.5</td>
<td>21.7 ± 11.5</td>
<td>16.7 ± 5.8</td>
<td>11.0 ± 7.8</td>
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<tr>
<td>TVI (U)</td>
<td>16.5 ± 7.2</td>
<td>21.9 ± 13.6</td>
<td>28.6 ± 16.1</td>
<td>22.6 ± 6.3</td>
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<td>APV (cm/s)</td>
<td>19.9 ± 6.6</td>
<td>25.0 ± 11.6</td>
<td>33.7 ± 14.7</td>
<td>28.2 ± 9.1</td>
<td>16.4 ± 9.3</td>
<td>17.8 ± 8.7</td>
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<td>Ratio (proximal/distal)</td>
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<td>2.9 ± 1.6</td>
<td>2.8 ± 1.0</td>
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<td>Angiographic data</td>
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<td>Proximal area (mm²)</td>
<td>11.7 ± 3.5</td>
<td>8.3 ± 2.3</td>
<td>8.5 ± 2.3</td>
<td>8.8 ± 4.7</td>
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<td>7.9 ± 4.6</td>
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<tr>
<td>Distal area (mm²)</td>
<td>5.7 ± 2.2</td>
<td>5.1 ± 2.4</td>
<td>5.2 ± 2.9</td>
<td>4.9 ± 2.1</td>
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<td>5.1 ± 2.8</td>
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<tr>
<td>Minimal lumen diameter (mm)</td>
<td>1.4 ± 0.3</td>
<td>1.4 ± 0.5</td>
<td>1.1 ± 0.3</td>
<td>1.1 ± 0.3</td>
<td>1.1 ± 0.4</td>
<td>1.1 ± 0.3</td>
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*p < 0.01 versus normal arteries. tp < 0.05 versus gradient of 20 to 30 mm Hg. tp < 0.001 versus normal arteries and gradients of 0 to 9 and 10 to 19 mm Hg.

Abbreviations as in Table 2.

The continuity equation appears to apply in the two patients with severe right coronary artery stenoses occurring before any branch points in which equal proximal and distal flow velocities were measured despite gradients >30 mm Hg. Values for the proximal and distal coronary flow reserve, measured in one of these patients, were found to be blunted (1.6 proximal and 1.5 distal).

Clinically significant translesional gradients. The selection of what constitutes a significant translesional gradient was arbitrarily determined from the historical review of coronary hemodynamics obtained at the time of angioplasty with the use of relatively large (4.5F)-diameter double-lumen catheters (17-20). Satisfactory early and late results after dilation were associated with rest residual gradients <20 mm Hg and final angiographic diameter stenosis <30% (17,19). Gradients <20 mm Hg were associated with reduced late restenosis rates and lower postprocedural abrupt closures (17,19). One study demonstrated correlation between residual gradient after percutaneous transluminal coronary angioplasty and subsequent restenosis, with a cutoff gradient value of 15 mm Hg (17). In contrast to animal studies (31), there are scant data in patients to confirm what rest translesional gradient is correlated with provokable ischemia. Although it is desirable to have no translesional gradients within the coronary artery tree, some lesions may create gradients without demonstrable evidence of exercise-induced myocardial ischemia (18,32).

In our analysis, gradients between 20 and 30 mm Hg...
Translesional gradients and angiography. In this and other studies (17–20), angiographically severe (>70%) lesions generally had significant gradients; however, the limitations of angiography are well known. Quantitative cineangiography has improved image interpretation but remains imprecise in the intermediate range of stenosis severity. When studies reporting stenosis severity are reviewed, often a single “worst case” view is selected, reported and used in clinical decision making. An eccentric lesion with one view showing >80% stenosis and one view showing <40% stenosis may not be associated with a translesional gradient. Conversely, an angiographically moderate lesion can be associated with a significant translesional gradient, but the technical difficulties of pressure measurements and the potential for complications currently make this technique undesirable. The quality and ease of obtaining velocity data suggest that the flow velocity technique is superior to translesional pressure gradient measurements. The high incidence of discordant results between radionuclide stress testing and angiography is a well known confounding factor (35). Further complicating the decision process about whether to perform angioplasty on eccentric or angiographically moderate stenoses. The sequence of angiography and subsequent radionuclide stress testing could be eliminated by accurate assessment of the lesion by flow velocity guide wire during diagnostic catheterization and before any planned intracoronary intervention.

As shown in Figure 5, there is considerable hemodynamic variability of the gradient data in the 50% to 70% diameter stenosis range. This is the area where angiography is the least helpful in determining lesion significance (1–6,36). Intracoronary flow velocity measurements have an excellent correlation with predicting severe translesional gradients and thus provide more physiologically useful information, even in this difficult set of coronary stenoses.

Study limitations. When manipulating a guide wire tip distal to a coronary stenosis, it may on rare occasions be difficult to find the maximal distal velocity signals; thus in this situation, it is possible to falsely conclude that a significant flow velocity dropoff is present. For this reason, we always directed the distal tip in several different orientations in all patients to identify the maximal and most intense spectral flow velocity tracing with a complete Doppler envelope. In tortuous segments, stable distal signals were usually obtainable; however, it often required more wire manipulation to find the maximal spectral velocity signal. Despite these efforts, however, some distal flow velocities may have been underestimated. Conversely, a guide wire positioned to sample a high velocity jet in a more distal lesion might produce a falsely elevated distal flow velocity and near-normalized flow ratio, indicating an insignificant lesion. All patients with serial lesions of at least a moderate degree were excluded for this reason. Retrograde collateral flow (37) may also confound distal flow velocity interpretation, and all patients with angiographic or Doppler evidence of collateral flow were excluded.

The accuracy of translesional flow and pressure gradients for intermediate stenoses may be affected by a tracking catheter or guide wire across the narrowing; however, the small size of the cross-sectional area of the guide wire (0.16 mm²) is <10% of the residual cross-sectional area of a 2.5-mm–diameter vessel that has a 60% stenosis. Only significantly stenotic lesions with minimal lumen areas approaching 0.75 mm² would be affected by the 2.2F tracking catheter. Guiding catheter obstruction at the ostium of the coronary artery interfering with artery flow was minimized in most instances by using 6F guiding catheters with outside tip diameters of 0.050 in. (0.127 cm).

Rest gradients may not reflect ischemia-producing conditions, such as exercise or emotional stimuli associated with coronary vasospastic and exacerbation of significant lesions or increased myocardial blood flow demands (38,39). Preliminary data in our laboratory (33) indicate that most gradients will be increased when a corresponding distal hyperemic response remains intact. In those vessels with more severe gradients at rest, the distal vasodilative response is impaired, and there is little or no augmentation of the translesional gradient with provocative hyperemic stimuli such as intracoronary adenosine. The contribution of intact hyperemia to coincident exacerbation of adverse hemodynamic responses remains under study.

This study did not address the correlation with ischemic testing for lesion significance. The relationships among ischemic testing (thallium scintigraphy), quantitative angiography, translesional pressure gradient and coronary blood flow velocity will provide a comparative basis for characterizing the physiologic significance of a particular coronary stenosis and are currently under study (32–34). In light of the reported incidence of false positive ischemic testing for the diagnosis of significant epicardial disease in specific patient subgroups (15,35), the logical approach to lesions of questionable significance would be direct translesional assessment, as described here.

Safety of guide wire instrumentation in normal and mildly diseased arteries. Of 50 patients who underwent guide wire instrumentation but did not have angioplasty, none had a complication of wire insertion early (<48 h) or on late follow-up (6 months) as assessed by new ischemia or intervention (40). Two patients underwent repeat catheterization for symptoms, but neither had lesions of sufficient angiographic or hemodynamic severity to warrant intervention.

Clinical significance. The accepted angiographic and non-invasive methods of coronary lesion characterization, especially with regard to lesions of intermediate severity, should
be reconsidered in the context of directly measured lesional hemodynamics and pressure-flow relations. This study suggests that there is a more accurate method, at least compared with angiography, that is both easy and safe to perform. Translesional flow velocity could be used to assess coronary lesions at the time of catheterization and to assist in more accurately selecting patients whose lesions require intracoronary intervention.

References