Current, the success of coronary angioplasty is defined by anatomic criteria. Because of the known limitations of coronary arteriography, the translesional pressure gradient and coronary vasodilatory reserve were studied in 15 patients undergoing coronary angioplasty with the intent of defining a physiologically successful result. Coronary vasodilatory reserve was measured by a digital radiographic technique that has been previously validated against directly measured coronary sinus flow ($r = 0.90, \ p < 0.0001$).

A significant reduction in luminal stenosis from 71 ± 12 to 34 ± 11% ($p < 0.001$) was accompanied by a reduction in translesional gradient from 47 ± 19 to 21 ± 12 mm Hg ($p < 0.001$) and an increase in coronary vasodilatory reserve from 1.03 ± 0.15 to 1.29 ± 0.13 ($p < 0.001$). There was a significant correlation between changes in luminal stenosis and changes in translesional gradient ($r = 0.61, \ p < 0.05$), although a change of 20% or less in luminal diameter was accompanied by no change in pressure gradient. A more significant relation between changes in gradient and in coronary hyperemic reserve existed ($r = 0.77, \ p < 0.005$). The relation was accurate even for small changes in gradient.

Because saphenous vein bypass grafts have been shown to increase coronary vasodilatory reserve to at least 1.20, it is proposed that this physiologic criterion be used to define the success of revascularization by angioplasty. In patients in whom this value was achieved, translesional gradient was invariably 25% or less of ostial pressure and 20 mm Hg or less. Either coronary vasodilatory reserve or translesional gradient, which can be measured at the time of angioplasty, offers distinct advantages over previous arteriographic standards.

Assessment of Coronary Angioplasty

Currently, the accepted standard for successful angioplasty is a 20% increase in luminal diameter measured by coronary arteriography (2). This measurement has several serious shortcomings. The reproducibility (6), interobserver variability (7) and lack of correlation with pathologic (8) and intraoperative (9) findings of the arteriogram are well recognized. Additionally, the most profound changes in coronary hemodynamics occur with lesions greater than 60% of luminal diameter (10). Beyond that degree of stenosis, marked changes in blood flow or pressure gradient can occur with very little change in luminal area. Thus, the most marked change in coronary hemodynamics occurs at the highest degree of stenosis, where changes are the most difficult to measure accurately. Finally accurate determination of degree of stenosis can be made only after radiographic processing of cineangiograms, preventing use of this information in the catheterization laboratory during the procedure itself.
Need for other methods. For these reasons, other methods of quantitating the results of angioplasty are necessary. Previous investigators (10-14) have demonstrated that myocardial hyperemic response (coronary vasodilatory reserve) is a sensitive and accurate method of assessing the physiologic consequence of epicardial artery stenosis. Using digital subtraction and image enhancement of selective coronary arteriograms, we recently developed a method of determining regional coronary vasodilatory reserve in patients (15). We were able to determine the coronary ostia to myocardial transit time (the myocardial contrast appearance time) of a contrast bolus (15,16). Using a prior contrast injection, we were also able to quantitate contrast hyperemic flow using this technique. We and others (15,17,18) have found that hyperemia/baseline flow ratio accurately reflects coronary vasodilatory reserve.

Aim of study. The purpose of this study was threefold. First, we wished to study the changes in coronary vasodilatory reserve that accompany the lessening of hemodynamic severity of an individual coronary artery stenosis. Second, by correlating the physiologic changes occurring with decreasing arterial stenosis, we wished to define a useful method of determining a successful angioplasty. Finally, by examining the relation between physiologic changes and pressure gradient, we attempted to determine a minimal translesional pressure gradient that would be accepted as a criterion for a successful procedure.

Methods

Patient selection. Fifteen patients undergoing clinically indicated percutaneous transluminal coronary angioplasty at University Hospital and the Veterans Administration Medical Center, Ann Arbor, were studied. Patients were chosen on the basis of severe refractory angina and appropriate location and geometry of arterial stenosis. Patients were required to cease respiration for 15 seconds so that appropriate arteriograms could be obtained. Informed consent was given by each patient.

Angioplasty protocol. Before the procedure, patients were treated with nifedipine, 20 mg three times daily, aspirin, 325 mg daily, and dipyridamole, 75 mg three times daily. Patients were premedicated with meperidine hydrochloride, 75 to 100 mg, and secobarbital, 25 to 50 mg, administered intramuscularly. At the initiation of the procedure, low molecular weight dextran, 10% in 500 ml dextrose solution, was infused intravenously. Heparin sodium, 10,000 units, was administered intravenously. Systemic nitrate administration sufficient to cause a 10% decrease in systolic blood pressure was maintained throughout the procedure, either with intravenous nitroglycerin infusion or with sublingual isosorbide dinitrate administration.

On initiation of the procedure, a pulmonary artery catheter and a bipolar right atrial pacing catheter wire were placed through antecubital or femoral veins. Standard selective coronary arteriograms were obtained using the Judkins technique and preformed coronary catheters. Arteriograms for digital processing were obtained before and after angioplasty, as described later.

A 9 French femoral artery sheath was then placed, and an 8 or 9 French USCI Myler guiding catheter (USCI, C.R. Bard Inc.) was placed in the right or left coronary ostia. Catheters were manipulated to assure that ostial reflux of contrast agent occurred and that arterial waveforms were not ventricularized. In this manner, reliable mean coronary ostial pressures could be determined.

A USCI Gruentzig Dilaca balloon dilation catheter (USCI, C.R. Bard Inc.) was then advanced under fluoroscopic and hemodynamic monitoring. Proper catheter position was determined by repeat hand contrast injections and determination of translesional pressure gradients. With the catheter properly positioned, repeat balloon inflations employing 4 to 10 atm pressure were performed. Inflations ceased after lack of sequential decrease in pressure gradient occurred.

Gradient determination. Coronary ostia-distal coronary pressure gradients were determined using saline-flushed guiding and dilation catheters and Statham PD-23 (Statham Gould Company) transducers. Waveforms were examined with the balloon catheter in the guiding catheter before and after placement into the coronary artery to assure close correspondence of waveforms. Mean arterial pressures proximal and distal to the coronary stenosis were subsequently determined. Gradients were determined when stabilization of gradients had occurred after balloon deflation.

Coronary arteriography. To obtain images for digital image processing, the following technique was employed. Selective coronary arteriography was performed using a Phillips or Siemens cineangiographic unit. No table panning was allowed. To eliminate thoracic motion, patients were instructed to cease respiration at end-inspiration for 15 seconds. Cineangiography, performed with 35 mm cine film (Kodak Corporation), was initiated at least one cycle before contrast injection. To obtain fixed parameter cineangiography, the Phillips cineangiographic unit was programmed to override the automatic brightness control after five, 1 ms pulse width exposures. The Siemens cineangiographic unit is equipped with a manual override of the automatic brightness control that is activated 1 second after filming is initiated. In this manner, fixed kV, mA and pulse width X-ray exposure at 30 frames/s are obtained.

Arterial opacification was initially accomplished with hand injection of sodium-meglumine diatrizoate (Quibb and Sons, Inc., Renografin-76). Six to 8 cc were used in the left coronary artery and 4 to 6 cc in the right coronary artery. Injection was synchronized to the electrocardiographic R wave and lasted for two cardiac cycles. To more accurately synchronize injections, our laboratory now uses electrocardiographic-synchronized power injection of contrast me-
mum. For this purpose, a Medrad power injector IV (Medrad Corporation, mark IV) is used. An injection rate of 5 cc/s (total 7 cc) is used in the left coronary artery and 4 cc/s (total 5 cc) is used in the right coronary artery. A pressure limit of 350 psi is used.

Filming of both right and left coronary arteries was performed in the left anterior oblique projection. This view allows for maximal myocardial opacification and best separates the myocardial segments served by left anterior descending, diagonal and circumflex vessels. To obtain arteriograms at basal state, at least 3 minutes was allowed to elapse after previous contrast injections. To obtain arteriograms at hyperemic state, an initial dose of 4 to 6 cc of contrast medium was injected. Ten seconds was allowed to elapse, and fixed parameter radiography was performed again with repeat contrast injection for arterial opacification.

In the present study fixed parameter radiography at basal and hyperemic states was performed before coronary angioplasty. Once angioplasty was completed and the patient was in a clinically stable condition, filming at basal and hyperemic states was performed again using the standard Judkins catheter.

**Arteriographic estimate of stenosis.** Cineangiograms were analyzed without knowledge of luminal area or myocardial transit appearance time. Each stenosis was examined in multiple projections, including cranial and caudal angulation. The projection in which the stenosis appeared most severe was used. Caliper determination of percent diameter reduction was obtained by one investigator (W.O.). This procedure was performed in the same projection before and after dilation. This method of determination of lesion severity was the same as that used by centers involved in the National Heart, Lung, and Blood Institute registry.

**Digital image processing.** Image processing was performed as previously described (15). Selective arteriograms were displayed on a projector (Vanguard Corporation, XR-35) equipped with a primary beam splitter coupled to a fixed-gain video camera. The first six consecutive end-diastolic frames of the arteriogram were digitized. A 256 × 256 eight-bit (256 gray scale) matrix was employed. A video digitizer (Colorado Video Model 274) was employed using eight-frame averaging. Video images were stored and processed on a PDP 11/34 minicomputer (Digital Equipment Corporation).

Image enhancement was accomplished by serial subtraction of each end-diastolic frame from the previous frame, a technique known as gated interval differencing (15). A functional image was generated with appearance time for each pixel defined as the maximal incremental increase in radiographic density between cycles for that pixel. Images were color-coded to denote contrast within the five cardiac cycles after contrast injection in a red, yellow, white, green and blue sequence. From this functional image, the contrast medium appearance picture and myocardial contrast appearance time could be calculated. The myocardial contrast appearance time for a myocardial region was determined by histogramic analysis of that area of interest and is calculated as the mean myocardial contrast appearance time of the pixels in that area of interest. The contrast medium appearance picture color-coded image allows for visual interpretation of the data and can be used as a quality control measure for the computer-generated myocardial contrast appearance time. Myocardial contrast appearance time is defined as the time from onset of injection to maximal incremental appearance of contrast in a given myocardial region. Coronary vasodilatory reserve was measured as the ratio of the rest to hyperemic myocardial contrast appearance time of the myocardial perfusion bed distal to the stenosis undergoing dilation.

We have previously demonstrated (15,16) that the myocardial contrast appearance time accurately reflects relative regional coronary blood flow when compared with coronary sinus thermodilution technique. When paired myocardial contrast appearance time determinations were performed (15), a variability of 12% was found to exist. In large part, this variability is related to the timing of hand contrast medium injections.

To determine the variability of the coronary vasodilatory reserve ratios, base and hyperemic myocardial contrast appearance times were obtained in four separate myocardial regions. Twelve paired coronary vasodilatory reserve values were obtained. A variability of 6% was found to exist for these paired values. This value was the mean absolute difference of the paired values divided by their means and expressed as percent. Therefore, in our laboratory, we consider statistically significant alterations of coronary vasodilatory reserve to occur if there is a greater than 12% alteration in reserve.

**Statistical analysis.** Least square linear regression analysis and Student’s t test were used in statistical analysis.

**Results**

**Clinical findings.** Of the 15 patients enrolled in this study, 12 had physiologic, arteriographic and hemodynamic variables measured before and after angioplasty (Table I). Among the remaining three patients, a reliable post angioplasty gradient could not be obtained on one and gradient and coronary flow data could not be collected in two patients who had severe coronary spasm after angioplasty. Canadian Heart Association angina class in the 15 patients decreased after angioplasty from $3.0 \pm 0.8$ to $1.8 \pm 0.4$ (probability $p < 0.01$). Diameter stenosis decreased from $71 \pm 12$ to $34 \pm 11\%$ ($p < 0.001$) and translesional gradient decreased from $47 \pm 19$ to $21 \pm 12$ mm Hg ($p < 0.001$).

**Alteration in coronary vasodilatory reserve after angioplasty.** Figure 1 shows the angiograms after a successful left anterior descending coronary artery angioplasty. Al-
Table 1. Clinical Results

<table>
<thead>
<tr>
<th>Case</th>
<th>Coronary Artery Dilated</th>
<th>Angina Class</th>
<th>GRAD/MAP Pre</th>
<th>Post</th>
<th>Percent Stenosis Pre</th>
<th>Post</th>
<th>Percent Gradient Pre</th>
<th>Post</th>
<th>MCAT Ratio Pre</th>
<th>Post</th>
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<tbody>
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<td>1</td>
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<td>III I</td>
<td>45/87</td>
<td>7/89</td>
<td>0.74</td>
<td>0.33</td>
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<tr>
<td>2</td>
<td>LAD</td>
<td>III I</td>
<td>29/55</td>
<td>3/53</td>
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<td>0.30</td>
<td>0.52</td>
<td>0.06</td>
<td>1.01</td>
<td>1.48</td>
</tr>
<tr>
<td>3</td>
<td>RCA</td>
<td>II I</td>
<td>36/65</td>
<td>13/58</td>
<td>0.79</td>
<td>0.25</td>
<td>0.55</td>
<td>0.22</td>
<td>0.78</td>
<td>1.28</td>
</tr>
<tr>
<td>4*</td>
<td>LAD</td>
<td>IV</td>
<td>48/74</td>
<td>—</td>
<td>0.80</td>
<td>—</td>
<td>0.65</td>
<td>—</td>
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<td>—</td>
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<td>5†</td>
<td>LAD</td>
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<td>18/88</td>
<td>0.72</td>
<td>0.50</td>
<td>0.37</td>
<td>0.20</td>
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<td>23/73</td>
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<td>0.58</td>
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<td>0.96</td>
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<td>—</td>
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<td>LAD</td>
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<td>24/77</td>
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<td>0.56</td>
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<td>LAD</td>
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<td>1.04</td>
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<td>11</td>
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<td>IV II</td>
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<td>3/53</td>
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<td>0.25</td>
<td>0.70</td>
<td>0.06</td>
<td>1.01</td>
<td>1.34</td>
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<tr>
<td>13</td>
<td>LAD</td>
<td>IV I</td>
<td>60/100</td>
<td>35/85</td>
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<td>0.25</td>
<td>0.60</td>
<td>0.37</td>
<td>1.08</td>
<td>1.21</td>
</tr>
<tr>
<td>14</td>
<td>LAD</td>
<td>II I</td>
<td>15/60</td>
<td>3/55</td>
<td>0.70</td>
<td>0.42</td>
<td>0.25</td>
<td>0.05</td>
<td>1.36</td>
<td>1.50</td>
</tr>
<tr>
<td>15</td>
<td>RCA</td>
<td>III</td>
<td>50/100</td>
<td>—</td>
<td>0.75</td>
<td>—</td>
<td>0.50</td>
<td>—</td>
<td>0.97</td>
<td>—</td>
</tr>
</tbody>
</table>

*Patient with acute occlusion after coronary spasm, requiring emergency bypass; †reliable translesional gradient not obtained; ‡coronary spasm after angioplasty. Angina Class = Canadian Heart Association class; GRAD = gradient (mm Hg); LAD = left anterior descending; MAP = mean arterial pressure (mm Hg); MCAT = myocardial contrast appearance time; Post = after angioplasty; Pre = before angioplasty; RCA = right coronary artery.

Discussion

Because of the known limitations of coronary arteriography, we attempted to develop an alternative method for evaluating the results of coronary angioplasty. The physiologic and hemodynamic changes occurring with coronary angioplasty in 15 patients were evaluated. Other than the ability to remain motionless, with sustained inspiration, no preselection bias existed in this consecutive group of patients from our two institutions. Patients were chosen for coronary angioplasty on the basis of criteria defined from the National Heart, Lung, and Blood Institute registry. Symptom dura-
tion (9.3 ± 9 months), Canadian Heart Association angina class (3.0 ± 0.8) and lesion severity before angioplasty were all comparable with those in registry patients (2). Angioplasty was arteriographically successful in 12 of the 15 initial patients (Table 1) because a 20% or greater decrease in lesion severity occurred. The changes in arteriographic lesion severity, gradient and coronary vasodilatory reserve were thus measured in patients with arteriographically successful coronary angioplasty.

**Limitations of arteriographic assessment of angioplasty (Fig. 3 and 4).** The present study demonstrates the limitations that exist when arteriographic measurements are performed. Correlation is poor between changes in gradient and in percent stenosis (Fig. 3). Additionally, the y intercept of Figure 3 is at 20% stenosis change, suggesting that either changes of 20% or less in stenosis severity do not significantly alter translesional gradients or that a bias of 20% exists in the measurement of postangioplasty arteriograms.
The latter possibility is more likely because a true 20% reduction in lesion severity should markedly reduce the resistance of a highly stenotic vessel.

Although overall a significant correlation exists between gradient and percent stenosis, no correlation is present for lesions of intermediate severity (20 to 70% stenosis) (Fig. 4). As an example, a 50% stenosis could be associated with a gradient between 20 and 60% of mean arterial pressure. The poor correlation for lesions of intermediate severity is a crucial shortcoming because these lesions are precisely those in which greatest difficulty in assessing lesion severity exists (20). This lack of correlation is due, in part, to our inability to accurately measure these lesions. It also reflects the dependence of gradient on the level of coronary flow. To accurately predict gradients, knowledge of absolute regional coronary flow is required (11); however, to date, this has not been possible in human beings.

Advantages and limitations of translesional pressure measurements. These measurements have been used to determine a successful procedure (21) and may overcome some limitations of arteriography. Busch et al. (22) demonstrated that mean gradients can be reliably measured through angioplasty catheters. A limitation of use of gradients in assessing lesion severity is the dependence of the gradient on the level of coronary flow (11), a dependence that is especially important for high grade lesions. In addition, distortion of actual gradient may be induced by the catheter itself, again particularly with high-grade lesions. The main limitation is that no data exist correlating the translesional gradient with the physiologic significance of a lesion. Despite these limitations, much useful information can be de-
Coronary vasodilatory reserve was correlated with coronary vasodilatory reserve values, a significant relation was found. Lesions with a gradient of 25% or less of mean arterial pressure have coronary vasodilatory reserve values significantly above values for highly stenotic vessels (15) and above the lower limit for successful coronary bypass surgery (19). Lesions with a gradient greater than 40% of mean arterial pressure have complete loss of coronary vasodilatory reserve, suggesting a critical coronary stenosis. To assure a result comparable with coronary bypass surgery, we believe that a gradient of 25% or less of mean arterial pressure should be achieved. Gradients between 25 and 40% of mean arterial pressure are of intermediate severity, and their functional severity, in large part, will depend on the demands of each individual patient.

Limitations of the digital technique. As with other digital subtraction methods, motion artifact is the overriding limitation of the digital technique used. With patient coaching in breath-holding, this can usually be overcome. Markedly irregular cardiac rhythms are a limitation to the gating process and can, in part, be overcome by atrial pacing. The timing of contrast injection is also crucial and can be optimized by electrocardiogram-gated power injection. In our laboratory, contrast medium is used as a hyperemia-inducing stimulus. Although contrast medium is not the most potent coronary vasodilator, its safety and short-lived effects allow for repeated myocardial contrast appearance time determinations at basal or hyperemic flow states. Methods that are...
sensitive to regional myocardial flow (18) have demonstrated a clear separation for contrast hyperemic flow values between normal and highly stenotic arteries. A variability of 12% is within the range of variability of other methods of measuring regional coronary vasodilatory reserve (25).

Because this measurement is a relative technique, absolute coronary blood flow cannot be measured. Hyperemic changes in contrast velocity (which reflects arterial resistance) are measured. The coronary vasodilatory reserve value for normal arteries is lower than that measured by flowmeter in canine arteries (10). This, in part, is related to the fact that we are measuring mean contrast velocity while the flowmeter measures peak blood flow.

Advantages of technique. With these limitations in mind, relative changes in regional coronary blood flow can be accurately measured by this digital technique (15,16). This allows us to reliably measure coronary vasodilatory reserve and assess the physiologic severity of a lesion. We demonstrated the close relation between hemodynamic and physiologic lesion severity (Fig. 5). The relation is accurate for lesions of intermediate severity. This technique, therefore, has great promise in allowing the severity of intermediate lesions to be determined. No bias can be introduced because computer analysis of the data is performed. As demonstrated in Figure 6, small changes in gradient can be shown to cause small changes in coronary vasodilatory reserve. The ability to predict translesional gradient using coronary vasodilatory reserve may have a significant impact on both preoperative assessment of complex coronary anatomy and assessment of the results of angioplasty.

Implications. The present study demonstrates that coronary angioplasty can immediately and significantly improve both translesional gradients and coronary vasodilatory reserve. Although successful angioplasty reduces gradients into the normal range, it does not return values to normal. The seven lesions with gradients of 25% or less of mean arterial pressure had mean coronary vasodilatory reserve values comparable with those of bypass grafts (1.49 ± 0.35 versus 1.37 ± 0.11), but significantly below values for normal coronary arteries (1.80 ± 0.11, p < 0.001). This finding will require further study as its clinical significance is unknown because all seven patients studied were asymptomatic at follow-up (Table 1). One explanation for the low coronary vasodilatory reserve values after angioplasty may be the drug regimen employed. Both nitrates (26) and calcium channel blocking agents (27,28) have been shown to significantly alter coronary blood flow at rest. We continued these medications for clinical reasons.

References


