Measurement of transstenotic pressure gradient during percutaneous transluminal coronary angioplasty

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ABSTRACT Obstruction to blood flow is accompanied by a pressure gradient across the obstructed site. In certain clinical settings, magnitude of pressure gradient has been used to judge severity of obstruction, and gradient reduction to judge success of an interventional procedure. In percutaneous transluminal coronary angioplasty (PTCA) the relationships between transstenotic pressure gradient, diameter stenosis, and lesion length are imprecisely known. We therefore examined 4263 sets of measurements in patients who underwent PTCA on single, discrete coronary arterial lesions. Multivariate regression analysis demonstrated that pressure gradient was artifically elevated by about 12 mm Hg at low values of diameter stenosis but increased by the 4th power of stenosis as expected from fluid dynamics models. Pressure gradient was dampened and relatively constant at values of diameter stenosis of 60% or higher, probably because of total or near-total occlusion of the artery. Lesion length was not found to influence pressure gradient. Reductions in diameter stenosis (∆D) and pressure gradient (∆G) were related nonlinearly, with ∆D proportional to the square root of ∆G, suggesting that a reduction in gradient is directly proportional to an increase in cross-sectional area of the stenosis. The predictive value of final post-PTCA pressure gradients was found: a final gradient of 15 mm Hg or less predicted a final post-PTCA diameter stenosis of 30% or less, with 75% sensitivity and 29% specificity (p < .01). The results of this study suggest that (1) pressure gradient as currently measured during PTCA is related to diameter stenosis but not to lesion length (2) reductions in pressure gradient and diameter stenosis are nonlinearly related, and (3) reductions in pressure gradient and final post-PTCA pressure gradient are useful indicators of initial angiographic outcome.

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THE FUNDAMENTAL aim of percutaneous transluminal coronary angioplasty (PTCA) is to enlarge a coronary artery lumen at a site of discrete, atheromatous obstruction.1–3 By reducing obstruction, coronary blood flow is increased and, in particular, coronary flow reserve is increased.4–7 Assessing enlargement of a coronary artery lumen during the course of a dilatation procedure is often difficult. Fluoroscopy with high-resolution video imaging can outline an arterial lumen but is suboptimal for quantitative analysis. Caliper or other quantitative methods for measuring a stenosis can be applied to cineangiographic film8 but are unavailable during the procedure.

Obstruction to blood flow is accompanied by a pressure drop, or gradient, across the obstructed site.9–12 Gradients have been used to quantify degree of obstruction in peripheral arteries13, 14 and valvular heart disease.12, 15 Elimination of pressure gradient has also been used to judge the success of interventions to relieve obstruction.13, 16, 17 A balloon dilatation catheter positioned at the site of a coronary arterial obstruction can be used to measure pressure distal to the obstruction and permits calculation of the transstenotic pressure gradient.1, 18 It is well known that standard dilatation catheters contribute to coronary obstruction and magnify the true pressure gradient.18–21 However, since catheter size is constant, a fall in measured pressure gradient should reflect lessening of obstruction if the heart rate and blood pressure remain relatively unchanged.18 Furthermore, the gradient at the termination of the PTCA procedure should help predict the later cineangiographic measurements. The precise relationship between these two markers of initial success has not been well defined.
We undertook this study to determine first, the relationship between transstenotic pressure gradient, diameter stenosis, and lesion length in patients who underwent single lesion PTCA and, second, the reliability of changes in pressure gradient in predicting changes in diameter stenosis induced by dilatation.

**Methods**

**Patient selection.** From July 14, 1980, through May 15, 1985, 4845 PTCA procedures were performed at Emory University hospitals. Angioplasty was conducted with standard dilatation catheters that facilitated measurement of the transstenotic pressure gradient during the procedure.18 Excluded from this study were 215 patients who had dilatation of bypass grafts. The remaining 4630 patients underwent PTCA on single or multiple lesions in one or more native coronary arteries. From this group, data on 4263 single discrete lesions were available for analysis.

**Data collection.** Methods used to collect angiographic and pressure gradient data have been previously reported in detail.22 Briefly, severity of a coronary arterial lesion was determined angiographically as percent diameter stenosis. Cineangiograms were measured before and after PTCA with a programmable digital caliper system. The mean value of two or three available projections was recorded as a whole number in percent. Decline in diameter stenosis as a result of PTCA was defined as ΔD (diameter stenosis before PTCA minus diameter stenosis after PTCA). Thus the decline in diameter stenosis, ΔD, was recorded as a positive whole number of percentage points.

Caliper measurements of lesion length were made from the same cineangiogram frames from which percent diameter stenosis measurements were taken. A calibrated scale permitted translation of measurements into millimeters. The longest of the several measurements made from different views was recorded.

Pressures were obtained with saline-filled tubing and strain-gauge transducers. Distal coronary arterial pressure was recorded from the central lumen of the angioplasty catheter while it was positioned across a stenosis. The difference between mean aortic and mean distal coronary arterial pressures was recorded as transstenotic pressure gradient. Reduction in pressure gradient as a result of PTCA was defined as ΔG (pressure gradient before PTCA minus pressure gradient after PTCA). Thus reduction in pressure gradient, ΔG, was recorded as a positive whole number in millimeters of mercury.

**Statistical analysis.** All continuous variables are shown as mean ± SD. For illustration only, variables were grouped by narrow ranges and frequency distributions were made. Stepwise multiple regression analysis was performed with transstenotic pressure gradient as the dependent variable and diameter stenosis and lesion length as independent variables. Therefore both diameter stenosis and lesion length were evaluated simultaneously, rather than separately, for influence on pressure gradient. All available values of diameter stenosis and transstenotic pressure gradient, both before and after PTCA, were used in the regression analysis. Multivariable regression was also performed with ΔD as the dependent variable and ΔG and lesion length as the independent variables. Predictions of post-PTCA diameter stenosis were made by constructing a contingency table. The sensitivity, specificity, predictive accuracy-positive, predictive-accuracy negative, and chi-square test of significance were calculated. A p value < .05 was considered significant.

**Results**

**Diameter stenosis (figure 1).** Pre-PTCA diameter stenosis was recorded for 4257 of 4263 lesions (99.9%). Four percent were total obstructions, 63% had diameter stenosis greater than 70%, and 96% had stenosis of 50% or greater. Mean diameter stenosis before PTCA was 74 ± 14%.

Post-PTCA diameter stenosis was recorded for 4133 of 4263 lesions (97%). Sixty-three percent had diameter stenosis under 30% and 93% had stenosis under 50%. Mean diameter stenosis after PTCA was 27 ± 18%.

Reduction in diameter stenosis (ΔD) could be calculated for 4133 of 4263 lesions (97%). Ninety-three percent had a ΔD of 20% or more and 68% had a ΔD of 40% or more. Mean ΔD was 46 ± 20%.

**Transstenotic pressure gradient (figure 2).** Pre-PTCA pressure gradient was recorded for 3749 of 4263 lesions (88%). Twelve percent had gradients of 70 mm Hg or greater, 55% had gradients of 50 mm Hg or greater, and 95% had gradients of 30 mm Hg or greater. Mean transstenotic pressure gradient before PTCA was 51 ± 15 mm Hg.

Post-PTCA pressure gradient was recorded for 3490 of 4263 lesions (82%). Thirteen percent had gradients under 5 mm Hg, 68% had gradients under 15 mm Hg, and 93% had gradients under 25 mm Hg. Mean transstenotic pressure gradient after PTCA was 12 ± 8 mm Hg.
 Twenty-two percent had a transstenotic pressure gradient exhibited a magnitude of more than 50 mm Hg and 74% had a ΔG of more than 30 mm Hg. Only 2% had a ΔG under 10 mm Hg. Mean ΔG was 38 ± 15 mm Hg.

Lesion length (figure 3). Lesion length was recorded for 4106 of 4263 lesions (96%). Of these, 82% were under 10 mm in length. Only 1.5% were greater than 20 mm in length. Mean lesion length was 6 ± 4 mm.

Pressure gradient, diameter stenosis, and lesion length (figure 4). When pre-PTCA and post-PTCA values were plotted by decile and half-decile of diameter stenosis, with all values of lesion length included, mean transstenotic pressure gradient exhibited a sigmoid-shaped relationship to diameter stenosis (figure 4, top). The relationship was essentially flat both for diameter stenosis under 30% to 40% and over 60% to 70%. Even for minimal post-PTCA arterial narrowings (diameter stenosis less than 10%), the mean pressure gradient remained elevated (11 ± 7 mm Hg). Mean pressure gradient began to rise from an almost flat non-zero baseline at diameter stenoses of approximately 30% to 40%. Mean pressure gradient began to level off at diameter stenosis of approximately 60% to 70%.

Multivariate regression analysis for two intervals of diameter stenosis, 0 to 60% and 61% to 100%, is shown in figure 4, bottom. In the diameter stenosis range from 0 to 60%, the transstenotic pressure gradient was found to be a function of the 4th power of the diameter stenosis measurement. The regression equation was $y = 12 + (3.1 \times 10^{-6}) x^4$, SEE = 11, $r = 0.8$, $n = 4098$, $p < .001$. In the diameter stenosis range from 61% to 100%, the transstenotic pressure gradient was found to be constant. The regression
equation was \( y = 52, \) \( \text{SEE} = 15, r = .06, n = 3052, \) \( p < .05. \) Lesion length was not found to influence the pressure gradient in either diameter stenosis range.

\( \Delta D, \Delta G, \) and lesion length (figure 5). Values of \( \Delta D \) were plotted by decile and half-decile of \( \Delta G, \) with all values of lesion length included. Mean reduction in diameter stenosis exhibited a nonlinear relationship to \( \Delta G \) (figure 5, top). Multivariate regression analysis revealed that \( \Delta D \) was primarily a function of the square root of \( \Delta G \) (figure 5, bottom). The regression equation was \( y = 19 + 6.3 \sqrt{x} - (0.03) (\sqrt{x})^3, \) \( \text{SEE} = 16, r \) \( = .24, n = 3420, p < .05. \) The dominant terms in this equation were \( 19 + 6.3 \sqrt{x}. \) The final term, \( (0.03) (\sqrt{x})^3, \) served to flatten out the relationship for large values of \( \Delta G, \) e.g., greater than 50 mm Hg. Lesion length was not found to be a determinant of \( \Delta D. \)

**Predictive value of post-PTCA pressure gradient.** The predictive values of post-PTCA pressure gradient equal to or less than 15 mm Hg for three levels of post-PTCA diameter stenoses are shown in table 1.

<table>
<thead>
<tr>
<th>Post-PTCA gradient (mm Hg)</th>
<th>Post-PTCA diameter stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 15 (2557)</td>
<td>(2510) (2335) (1807)</td>
</tr>
<tr>
<td>&gt; 15 (923)</td>
<td>(882) (808) (610)</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>74% 74% 75%</td>
</tr>
<tr>
<td>Specificity</td>
<td>47% 34% 29%</td>
</tr>
<tr>
<td>Predictive accuracy-positive</td>
<td>98% 91% 71%</td>
</tr>
<tr>
<td>Predictive accuracy-negative</td>
<td>4% 13% 34%</td>
</tr>
<tr>
<td>p value</td>
<td>&lt;.001 &lt;.001 &lt;.01</td>
</tr>
</tbody>
</table>

Data in parentheses are number of measurements.

Achieving a final gradient of 15 mm Hg or less was a reasonably sensitive but nonspecific predictor of a satisfactory arteriographic outcome. A final gradient of 15 mm Hg or less was 98% accurate for predicting that post-PTCA diameter stenosis was under 50% (predictive accuracy-positive), 91% accurate for predicting that final diameter stenosis was under 40%, and 71% accurate for predicting final diameter stenosis under 30%.

Final gradients greater than 15 mm Hg were found in large numbers of patients with excellent final diameter stenosis measurements. Of 923 post-PTCA gradients greater than 15 mm Hg, 882 (96%) had diameter stenosis measurements under 50%, 808 (87%) had diameter stenosis measurements under 40%, and 610 (66%) had diameter stenosis measurements under 30%. This excellent angiographic outcome, in spite of a high final gradient, reduced the specificity of a suboptimal gradient response.

**Discussion**

Reduction in angiographic severity of a coronary arterial stenosis is the sine qua non of successful PTCA. The final diameter stenosis measurement is usually not available until cineangiograms are processed, generally minutes to hours after conclusion of the PTCA procedure. The transstenotic pressure gradient can be measured before balloon dilatation is performed and after each successive inflation/deflation cycle. The values for initial (pre-PTCA) gradient, final (post-PTCA) gradient, and magnitude of gradient reduction are available at the conclusion of the procedure, before catheters are withdrawn and before cineangiograms are processed for later review. Our study suggests that these pressure gradient measurements can be a useful indicator of the final diameter stenosis.
measurement and the magnitude of reduction of diameter stenosis.

**Arterial stenosis.** This study suggests that the relationship between diameter stenosis and transtenotic pressure gradient, in single discrete coronary arterial lesions, is governed by theoretical and experimental fluid dynamics models. Use of an angioplasty catheter for transtenotic measurement of distal coronary arterial pressure introduces artifacts into these relationships. Pressure gradient is artifically elevated at low diameter stenosis values and dampened at high diameter stenosis values.

Theoretical considerations, confirmed by experimental data, give the relationship between severity of an arterial narrowing, length of the narrowing, and pressure drop across the narrowing the following form:

\[ G = f_1(\text{As}^2, L) \cdot Q + f_2(\text{As}^2, \text{An}^2) \cdot Q^2 \]

In this formulation G is the pressure gradient, \( f_1 \) is a function of the square of cross-sectional area of the stenosis (As) and stenosis length (L), and \( f_2 \) is a function of the squares of cross-sectional areas of the stenosis (As) and the normal artery (An). The symbol Q refers to mass blood flow through the artery. With a small change in coefficients but no change in form of the relationship, absolute flow (Q) could be replaced by flow velocity. Although there are limiting considerations, this formulation appears to be reasonably accurate.

The practical importance of this formulation is that for the usual resting state or mildly hyperemic conditions found at PTCA, the pressure gradient across a stenosis is mainly a function of the relative cross-sectional area of the stenosis, which can be approximated by the 4th power of the relative diameter stenosis measurement. The pressure gradient should be zero for small degrees of stenosis and should rise in proportion to the 4th power of diameter stenosis until reduction of flow begins, at which time the pressure gradient levels off to its maximum.

The points where the gradient begins to rise and where flow reduction begins are not precisely known. Both theory and experimental results suggest that a gradient begins to develop for diameter stenosis values between 50% and 60% and that by 80% to 90% flow reduction has begun. Flow reduction then proceeds rapidly for any further obstruction.

Data from our patients (figure 4) agree with these theoretical and experimental findings. For diameter stenoses less than 60% the transtenotic pressure gradient was a function of the 4th power of the stenosis. The non-zero gradient of approximately 12 mm Hg found at low values of diameter stenosis probably reflects the presence of the angioplasty catheter within the stenosis. These minimal stenoses, which should not have had a pressure gradient associated with them, did in fact have a pressure drop from the proximal to distal sides. Furthermore, the rapid rise in pressure gradient in our patients, although proportional to the 4th power of the stenosis, began at 25% to 30% diameter stenosis rather than at 50% to 60% as expected. This again might reflect the fact that the catheter contributed to the stenosis and, from the standpoint of pressure gradient, made the stenosis appear more severe. At diameter stenoses greater than 60%, the additional obstruction created by the catheter produced severe flow reduction and essentially a total occlusion. Measured distal coronary arterial pressure fell to low constant values.

**Lesion length.** The hemodynamic significance of the length of a coronary arterial obstruction continues to be an enigma. Theoretically, the length should influence the pressure drop across a stenosis because length is present in the viscous resistance term of the model. Practical significance of lesion length is unclear. Some studies have demonstrated the importance of lesion length, whereas others have not found length to be important.

Our data did not confirm a relationship between transtenotic pressure gradient and lesion length. This was true for both regions of diameter stenoses analyzed, 0 to 60% and 61% to 100%. Practically, only stenoses in the range from 0 to 60% could reflect the influence of lesion length because, in that region, pressure gradient appears to follow the theoretic model. For stenoses in the range from 61% to 100% the gradient is relatively constant because the artery is almost totally occluded, and lesion length probably would not matter in those cases.

Failure to find a relationship between gradient and lesion length in our data may also have been an artifact of the transtenotic method of pressure measurement. Most experimental preparations use two pressure probes. One probe is placed proximal to a stenosis and the second is placed distal. The actual narrowing is not disturbed or altered by this method. The transtenotic method, placing a catheter through the stenosis to measure pressure distally, does disturb the narrowing. Specifically, the effects of lesion length on the pressure gradient may be reduced or negated by this method.

One experimental study of the transtenotic method of pressure gradient measurement found that lesion length had minor effects on the gradient. Thus lesion...
length may indeed be an important factor in magnitude of pressure gradient across an arterial stenosis, but its effects may be masked by the transtenotic method of pressure measurement.

**Decline in pressure gradient.** PTCA decreases high values of both diameter stenosis and pressure gradient. In our patients this was best described by a nonlinear relationship, with ∆D proportional to the square root of ∆G. A corrective term was also found that served to decrease expected gains in the reduction of stenosis for large declines in ∆G. If one accepts that the square of the diameter stenosis measurement can be an approximation of cross-sectional area, this relationship implies that the decline in pressure gradient is proportional to the increase in cross-sectional area of the stenosis.

**Usefulness of pressure gradient measurements.** Low pressure gradients at the conclusion of PTCA may have long-term implications. The PTCA Registry of the National Heart, Lung, and Blood Institute identified patients with post-PTCA gradients of 20 mm Hg or greater to be at higher risk of restenosis.\(^{30}\) Another study found patients with post-PTCA gradients of 18 mm Hg or greater to be at higher risk of restenosis.\(^ {31}\) Data from our institution suggested that post-PTCA gradients of 15 mm Hg or greater were associated with higher risk of restenosis.\(^ {32, 33}\)

The final diameter stenosis measurement at the conclusion of the PTCA procedure is also very important for long-term success. Determining whether the final gradient measurement could help predict this later angiographic measurement was one of our purposes. Some studies have suggested that a final diameter stenosis measurement of 30% or higher is a significant predictor of risk for restenosis.\(^ {32, 34}\) In our patients, the lowest pressure gradient known to be associated with risk for restenosis, 15 mm Hg, was significantly sensitive and accurate for determining that the final diameter stenosis measurement was 30% or less (table 1). Slightly higher levels of final diameter stenosis, 40% and 50%, were detected with equal sensitivity but higher predictive accuracy.

Although this level of 15 mm Hg was sensitive and had excellent predictive value when it was achieved (predictive accuracy-positive), the converse was not true. Post-PTCA pressure gradients over 15 mm Hg were also associated with low final diameter stenosis measurements in many cases. Thus low specificity and low predictive accuracy-negative were found. In this regard, a final gradient of 15 mm Hg or less was meaningful when it was achieved. However, failure to achieve this value did not necessarily imply angiographic failure. In other words, much meaningful information was conveyed when the final gradient was less than 15 mm Hg, but when it was greater than 15 mm Hg uncertainty still existed.

**Limitations.** The regression formulas outlined in figures 4 and 5 probably have very little direct application to individual patients, although the forms of the relationships are important. For an individual stenosis, knowledge of the absolute cross-sectional areas of the normal artery and the stenosis, as well as flow or flow velocity, would be necessary. Our data, derived from several thousand measurements, represent a pool of numerous artery sizes, stenosis sizes, and flows. We did not specifically record artery size or stenosis size in any manner other than relative diameter stenosis in percent. The degree to which this angiographic measure represents true functional severity of an obstruction is still incompletely known.\(^ {28, 35}\) Furthermore, the square and 4th power of diameter stenosis can only be crude approximations of cross-sectional area and its square.

A great deal of variation in pressure gradient for any given degree of stenosis was observed in our patients (figure 4, top). Other studies using much smaller catheters for pressure measurement have also documented a wide variation in gradient among angiographically similar stenoses.\(^ {19-21}\) Some of this variation represents inaccuracies of an angiographic measure of severity. Variations in total flow and the velocity of flow occur. Numerous technical factors may also play a role. The tip of the angioplasty catheter may lodge against an irregularly shaped wall of an atheromatous coronary artery, thereby prohibiting accurate determination of distal coronary arterial pressure. This particularly would be the case in tortuous or sharply curved arteries. Inflation and deflation of the angioplasty balloon causes alternate bulging and collapse of the septum separating the guidewire-pressure channel from the balloon inflation channel. A variable degree of impingement of the septum on the guidewire may distort transmission of pressure from the catheter tip. Although shaft diameters of our dilatation catheters were constant, balloon diameters varied. Even in the collapsed state, larger diameter balloons may have obstructed flow more than smaller diameter balloons. Finally, presence of variable amounts of collateral flow to the distal coronary arterial bed affects distal pressure.\(^ {36}\)

Some of these factors may explain the low specificity of final pressure gradient for final diameter stenosis (table 1). A high gradient at the conclusion of PTCA implies a low distal coronary arterial pressure. This may not entirely represent a severe residual stenosis.
but may instead represent dampened transmission of true distal pressure by the catheter. A lodged catheter tip, bulging septum, or incompletely collapsed balloon may inhibit accurate recording of distal pressure. Slight repositioning of the catheter tip, manipulation of the guidewire, further collapse of the balloon, or flushing of the guidewire-pressure channel of the catheter may remove obstacles to accurate determination of distal pressure. As mentioned previously, a low gradient at the conclusion of PTCA conveys useful information about the distal coronary arterial pressure. A high gradient at the conclusion of PTCA, especially if fluoroscopy suggests adequate reduction in stenosis, should prompt a search for artifactual dampening of the distal pressure measurement.

Conclusions. In spite of random measurement error and artifacts caused by the dilatation catheter, transstenotic pressure gradient measurements follow relationships derived from fluid dynamics and are useful in assessing immediate outcome of PTCA. Gradients are artifactualy elevated by approximately 12 mm Hg at low values of diameter stenosis because the catheter occludes the artery further. At diameter stenosis values greater than approximately 60%, gradients are dampened and virtually constant because the artery is essentially totally occluded. Lesion length does not appear to influence pressure gradient, but this may also be an artifact of the transstenotic method of pressure measurement. Reductions in diameter stenosis and pressure gradient are correlated in a nonlinear fashion based on changes in cross-sectional area of the stenosis. Low pressure gradient values at the conclusion of PTCA have previously been shown to be associated with better chances of long-term success. In this study, a low final gradient (<15 mm Hg) was found to be sensitive and accurate for determining final diameter stenosis at three different values: 30%, 40%, and 50%. Reduction in pressure gradient to a low final value implies reduction in diameter stenosis to a low final value. Measurements of reduction in pressure gradient and final gradient value, which are available at the conclusion of the PTCA procedure, can therefore be useful indicators of initial angiographic outcome.

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