Digital Angiographic Assessment of the Physiological Changes to the Regional Microcirculation Induced by Successful Coronary Angioplasty

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Background: Impulse response analysis of digital coronary angiographic images calculates a parameter known as the mean transit time of the microcirculation (T_{micro}). This has been shown to accurately assess the regional microcirculatory response to proximal stenosis in relation to flow. Our goal was to apply impulse response analysis to patients undergoing successful angioplasty and to quantify the induced physiological changes with respect to quantitative angiographic measurements of stenosis dimensions.

Methods and Results: We studied 24 patients before and after successful single-vessel percutaneous transluminal coronary angioplasty (PTCA). Minimal luminal stenosis area was increased from 0.2±0.6 before PTCA to 4.1±1.3 mm² after PTCA (P<.0001). In all patients this was accompanied by an increase in the inverse of T_{micro} (T_{micro}⁻¹), from 8.5±3.0 to 26.5±9.0 min⁻¹ (P<.0001) with a linear correlation between T_{micro}⁻¹ and minimal luminal stenosis area (r=.73; SEE=7.74). Stenosis flow reserve, estimated by integration of stenosis dimensions, increased in all patients from 1.8±1.0 to 4.5±0.4 after PTCA (P<.01). A comparison of T_{micro}⁻¹ with stenosis flow reserve revealed a nonlinear relation. In 16 patients undergoing PTCA of the left anterior descending or circumflex artery, contrast injections into the left main stem allowed simultaneous measurements of T_{micro}⁻¹ in the adjacent, nonstenotic artery. Adjacent artery T_{micro}⁻¹ did not change after PTCA (25.8±6.2 compared with 25.6±6.8 min⁻¹ before PTCA; P=NS); moreover, T_{micro}⁻¹ of the dilated artery measured after PTCA was equivalent to the nonstenotic adjacent artery, indicating normalization of microcirculatory responses.

Conclusions: These data suggest that T_{micro}⁻¹ determined by digital angiographic impulse response analysis of a single contrast injection under resting flow conditions may be a practical method to assess the regional microcirculatory response to changes in stenosis severity effected by coronary angioplasty. (Circulation. 1994;90:163-171.)

Key Words: digital angiography • myocardial perfusion • percutaneous transluminal coronary angioplasty

Visual assessment of angiographic coronary artery dimensions does not reliably permit accurate evaluation of the hemodynamic significance of coronary stenoses.1-4 A practical angiographic method to measure regulatory changes in regional microcirculatory vasodilation would be additional new information for diagnosis and for guiding strategy during the course of percutaneous transluminal coronary angioplasty (PTCA). Several methods to describe radiographic contrast material kinetics have reported accurate measurement of myocardial perfusion or coronary flow reserve.5 These approaches have focused on the phase of contrast appearance6-10 or washout,6,7,11 area under the time-density curve,7 and total transit time.12 A major limitation of these methods is that they require further interventions to achieve accurate and reproducible results, i.e., power coronary injection to standardize the injection bolus,8,12 atrial pacing for ECG-gated acquisition,9,12 hyperemic stimuli,9,10,12,13 and repeated injections and measurements.5,9,10,12 These limitations have prevented these methods from widespread use.5 We have developed a method called impulse response analysis that accurately measures the regional microcirculatory response to proximal stenosis and overcomes many of the technical limitations of other digital angiographic methods.14-16 It can be performed with a single hand injection under resting flow conditions, and it is insensitive to moderate variations in heart rate or arterial blood pressure.17 Impulse response analysis mathematically models the arterial and microcirculatory portions of the coronary circulation as two compartments. In canine validation studies the inverse of the regional mean transit time for the microcirculatory compartment (T_{micro}⁻¹) measured under resting flow conditions correlated closely with maximal hyperemic flow and coronary flow reserve derived from direct flow measurements. This method reliably differentiated normal arteries from moderately stenotic vessels where resting flow was not impaired or from vessels with critical stenosis with a diminished resting flow.14-16

The purpose of this study was to apply digital angiographic impulse response analysis in the human coro-
nary circulation to categorize the regional microcirculatory response to successful single-vessel PTCA.

Methods

Patient Population

Twenty-four consecutive patients undergoing proximal single-vehicle coronary angioplasty were included in this study. This group consisted of 22 men and 2 women, aged 44 to 75 years (mean±SD, 57±8). All patients had evidence of myocardial ischemia, either at rest (8 patients) or during stress testing (16 patients). Ten patients had no history of previous myocardial infarction, 11 had non-Q-wave myocardial infarction between 1 and 10 months before the intervention, and 3 had Q-wave infarction 1 to 7 months before the intervention. In all patients with myocardial infarction, PTCA was performed on the infarct-related vessel. Five patients with a history of systemic hypertension had evidence of left ventricular hypertrophy by ECG and angiographic criteria. Twenty patients had single-vessel disease; 4, all with stenoses of the right coronary artery, had additional moderate stenoses of the distal left circumflex artery (LCx; patients 8, 11, and 14) or of a small first diagonal branch (patient 17). Before PTCA, collaterals to the vessel undergoing treatment had been visualized in 4 patients; however, the small extent of collateral filling suggested only low collateral flow.18

Angioplasty Protocol

All patients were pretreated with aspirin. Before the procedure, a continuous infusion of low molecular weight dextran was started, and 12 000 U heparin sodium were administered. Guiding and PTCA balloon catheter types and sizes and inflation pressures were at the discretion of the operator. Biplane angiographic projections were carefully chosen to minimize the overlap between the myocardial perfusion territories of major branches (ie, LCx and left anterior descending artery [LAD] territories) or contrast material exiting the coronary sinus. To correct for X-ray scatter and veiling glare,19 a 3×3×2-mm lead blocker was positioned in both planes between the X-ray tube and the patient to project within the cardiac silhouette. The baseline angiogram (pre-PTCA) for impulse response analysis was performed 2 minutes after intracoronary administration of 0.2 mg nitroglycerin. Two seconds after starting image acquisition, a 6- to 8-mL bolus of nonionic contrast material (Ultravist, Schering AG, Berlin, Germany) was hand injected during held inspiration. Exposure was continued until decreasing density of contrast material washout was visible in the coronary sinus. Two minutes later the baseline coronary angiogram for stenosis quantification was performed. Biplane projections were chosen, which optimally visualized the stenotic segment positioned near the isocenter and avoided overlap of arteries. The angioplasty procedure was performed by standard techniques and was concluded when there was less than 50% residual diameter stenosis and TIMI grade 3 distal runoff.20 Throughout the procedure, a continuous infusion of heparin (250 U/min) was maintained via the guiding catheter; further supplementary intracoronary administrations of nitroglycerin were allowed. After conclusion of the procedure and withdrawal of the guide wire, the two post-PTCA angiograms were performed analogous to the pre-PTCA studies. If additional nitroglycerin had not been given during the procedure, these angiograms were preceded by a second bolus of nitroglycerin.

Image Acquisition and Videodensitometric Processing

Digital angiographic imaging was performed with a simultaneous biplane multiradial isocentric image processing system coupled to an image processing computer (Siemens Beta 1 and Digifan 3, Erlangen, Germany). Angiograms for densitometric analysis were acquired using a linear, fixed-gain exposure protocol at 12 frames per second per plane in a (512)2-pixel, 256-bit gray-level format. Digitized images were viewed in a cine-loop format while rectangular regions of interest (ROI) were positioned for time-density curve extraction. A ROI density curve extraction. A ROI density curve was placed over the proximal coronary artery just distal to the tip of the guiding catheter (input ROI) and a second over the lead blocker. Two or three larger ROIs (approximately 1000 pixels) were positioned consecutively over the distal myocardium supplied by the PTCA-related coronary artery. Care was taken to avoid regions containing noncontiguous walls by placing these ROIs over the myocardial blush near the outer border of the heart and to avoid overlap with major coronary branches, coronary venous structures, or the right atrium. When left coronary PTCA was performed, additional myocardial ROIs were placed over the territories supplied by the adjacent, non-PTCA–related and nonstenotic main branch of the left coronary artery (LAD or LCx).

The mean digitized density within each ROI was determined as a function of time. The curves were corrected for scatter and veiling glare by subtracting the intensity over the lead blocker frame by frame from the input and output ROI.19 The resultant curves were logarithmically transformed to correct for exponential attenuation of radiation, subtracted from preinjection background, and smoothed for high frequency variations due to cardiac motion by unweighted time domain filtration over two cardiac cycles. A least-squares fitted monoeponential decay function replaced the terminal portion of the input curve to compensate for the late artifact produced by contrast material overlap from coronary venous return. This method of performing logarithmic transformation after correcting for scatter and veiling glare has been validated previously and typically yields absolute densitometric errors of +0.1% to +1.1%.19

Impulse Response Analysis

The system impulse response function describes the transit of contrast material from the proximal coronary artery (the input) to the distal myocardial microcirculation (the output). The impulse response algorithm uses a two-compartment lagged normal density function to model indicator dispersion in the coronary circulation.21–26 The input and output signals are the regional time-density curves, which are proportional to the relative concentration of contrast material. Previous experiments have shown that the two compartments accurately characterize flow and indicator distribution volume of the epicardial coronary artery (first compartment) and the myocardial microcirculation (second compartment).14–16 These concepts are further illustrated in Fig 1. The epicardial coronary arteries are modeled as a simple conduit where dispersion is symmetrical about a mean transit time (Tm). The highly branched myocardial microcirculation is modeled as a well-stirred mixing chamber, which produces nonsymmetrical dispersion. This is described by a monoeponential decay function with a mean transit time (Tm). The lagged normal density function is generated by convolution of the two compartmental functions. The compartmental transit times were determined by iterative convolution of the model (expressed as a difference equation) with the actual input function, using a fast Fourier transform algorithm and serially adjusting the parameters (Tm, Tm, Tm, and σ) by a gradient descending method until the best χ2 fit with the output curve was obtained.

The microcirculatory compartment is defined by its Tm value, which is equal to its distribution volume divided by the flow. In previous work, Tm was shown to best correlate with the microcirculatory regulation of flow, whereas the arterial mean transit time was related to coronary artery length (ie, the distance of the myocardial ROI from the input ROI) and cross-sectional dimensions.24 In this study the microcirculatory mean transit times are reported as their inverse (Tm), expressed in min−1), and the values given are the mean of the
four to six output regions of interest (two or three output curves per plane of projection).

The method of videodensitometric impulse response analysis used to quantify the response of regional myocardial microcirculation has been previously described and validated in the intact canine coronary circulation.\textsuperscript{4-10} In these studies, impulse response analysis after hand-injected coronary angiograms performed with or without a hyperemic stimulus parallelled regional coronary flow reserve and maximal hyperemic flow in response to increasing severity of proximal stenosis of the LAD and LCx coronary arteries. The method was not affected by the complexity of the shape of the hand-injected contrast bolus, the type of contrast material used, the length or volume of the conduit arteries, moderate changes of heart rate or blood pressure, or the presence of angiographically visible collaterals. As long as angiographic projections are carefully obtained to minimize overlap of myocardium supplied by the LAD and the LCx coronary arteries, there is no appreciable interobserver and intraobserver variation related to the location of ROI placement within a given vessel’s myocardial territory.

**Quantitative Coronary Arteriography**

Thirty-five millimeter cinefilm biplane end-diastolic frames were optically magnified 2.5 times and digitized in a (512)\(^2\)-pixel matrix with an eight-bit gray scale (Mipron I, Kontron, Electronics, Eching, Germany). Automatic edge detection of the coronary borders was performed using an empirically determined first and second derivation algorithm, allowing absolute measurements of stenosis dimensions (luminal diameters of the stenotic and the proximal normal segment, stenosis length). Minimal cross-sectional stenosis luminal area was calculated from an elliptical approximation based on biplane data. The accuracy, precision, and reproducibility of this technique have been established in previous studies.\textsuperscript{27,28} In case of visible coronary dissection after PTCA, the dimensions of the inner lumen were chosen for analysis.

Stenosis dimensions were used to calculate an integrated measure of stenosis severity to estimate stenosis flow reserve as described previously by Kirkeeide et al.\textsuperscript{29} Brown et al.,\textsuperscript{30} and Gould and coworkers.\textsuperscript{31,32} This approach couples equations characterizing fluid flow through an idealized stenotic segment and assumed distal coronary pressure-flow relations. Stenosis flow reserve was calculated by the following quadratic equation:

\[
-\rho \frac{Q^2}{2} \left[ \frac{1}{A_s} - \frac{1}{A_c} \right] \text{SFR}^2 + \left( \frac{(\text{MAP} - P_c)}{\text{SFR}_o + 8\pi\mu L} \right) \text{SFR} + (\text{MAP} - P_c) = 0
\]

where \(A_c\) indicates cross-sectional area of the normal segment, \(A_s\) is cross-sectional area of the stenotic segment, \(L\) is stenosis length, MAP is mean arterial pressure (assumed to be 100 mm Hg), \(P_c\) is effective coronary back pressure (assumed to be 10 mm Hg), \(Q\) is flow, \(\rho\) is blood density (assumed to be 1.05 g/cm\(^3\)), \(\mu\) is blood viscosity (assumed to be 0.023 g/cm/s), SFR\(_o\) is stenosis flow reserve of a normal artery (assumed to be 5.0\textsuperscript{29}), and \(Q\) is coronary flow calculated as a product of \(A_c\) and the assumed resting flow velocity of 15 cm/s.\textsuperscript{29}

**Statistical Analysis**

Data are expressed as mean±SD. Statistical comparison of pre- and post-PTCA groups was by paired two-tailed Student’s \(t\) test. Subgroup analysis was evaluated by unpaired two-tailed \(t\) tests. Intermethod comparisons were made by linear regression analysis. Statistical significance was assumed for \(P<.05\).
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Mean±SD 69±13 70±11 94±19 90±13* 0.9±0.6 4.1±1.3† 1.6±1.0 4.5±0.4‡ 8.5±3.0 26.5±9.0†

Previous MI indicates previous myocardial infarction; T_{micro}⁻¹, inverse of the mean transit time for microcirculation; RCA, right coronary artery; LAD, left anterior descending coronary artery; LCx, left circumflex artery; Q, Q-wave infarction; Non-Q, non-Q-wave infarction; --, absent; and +, present.

*P<.05.
†P<.001.
‡P<.001.

### Results

The demographic, anatomic, and physiological characteristics of the 24 patients are listed in Table 1. On average, heart rate remained stable; individual changes were 10% or less. Mean arterial pressure decreased slightly but significantly from 94±19 before PTCA to 90±13 mm Hg after (P<.05). A change of more than 10% was observed in 7 patients. Successful PTCA was associated with a significant increase of stenotic area from 0.9±0.6 to 4.1±1.3 mm² (P<.0001) and calculated stenosis flow reserve increased 2.5-fold, from 1.8±1.0 to 4.5±0.4 (P<.001).

Impulse response measurements of regional perfusion showed that T_{micro}⁻¹ increased in each patient after PTCA, with an overall threefold increase from 8.5±3.0 to 26.5±9.0 min⁻¹ after PTCA (P<.0001). Values for T_{micro}⁻¹ before and after PTCA were not dependent on heart rate or mean arterial blood pressure (r=0.22 and r=0.22, respectively). Fig 2 shows that there was a linear correlation (r=.73) between the absolute values of T_{micro}⁻¹ with the corresponding minimal luminal area over the wide range of stenosis dimensions encountered before and after PTCA. There was no apparent correlation within the subgroups limited to just the pre- or post-PTCA values. Moreover, every patient demonstrated an improvement in stenotic dimensions and in the microcirculatory response to successful PTCA.

Fig 3 illustrates the relation of T_{micro}⁻¹ to stenosis flow reserve. Both parameters discriminate well between pre- and post-PTCA states. The data suggest a dichotomous, nonlinear relation. There was a complete concordance between an improvement in stenosis flow reserve and T_{micro}⁻¹.

Five patients with left ventricular hypertrophy had a history of treated systemic hypertension. Hemodynamic and angiographic measurements did not differ significantly from the other 19 patients.
Eight patients with unstable angina were on continuous intravenous nitrate therapy at the time of the study. Because of this vasodilator therapy, mean arterial pressure was significantly lower (84±19 mm Hg before PTCA and 82±10 mm Hg after) compared with patients with stable angina (99±17 and 94±13 mm Hg, respectively; P<.01 for both comparisons). Pre- and post-PTCA T\textsubscript{micro}^{-1} and angiographic geometric data did not differ significantly from stable patients.

Fourteen patients had a history of previous myocardial infarction. These patients had a significantly lower mean arterial pressure both before PTCA (86±15 compared with 106±18 mm Hg for patients without infarction; P=.01) and after (84±11 compared with 98±12 mm Hg; P<.01). There were no other significant differences in hemodynamic, angiographic, or impulse response data in comparison to patients without infarction. Before angioplasty, however, there was tendency for a lower stenosis flow reserve (1.7±0.9 compared with 1.9±1.2 for patients without infarction; P=NS) and T\textsubscript{micro}^{-1} (8.0±2.4 compared with 9.3±3.6 min\textsuperscript{-1}; P=NS), although minimal stenosis luminal area was roughly identical (0.9±0.6 compared with 0.9±0.6 mm\textsuperscript{2}; P=NS).

Fourteen patients underwent PTCA of the LAD, 2 of the LCx, and 8 of the right coronary artery. These groups did not differ with respect to hemodynamic or stenosis geometry parameters, and there were no significant differences for T\textsubscript{micro}^{-1} between pre-PTCA (LAD, 8.4±2.8 min\textsuperscript{-1}; LCx, 7.7±6 min\textsuperscript{-1}; right coronary artery, 8.9±3.7 min\textsuperscript{-1}) and post-PTCA measurements (28.1±8.3 min\textsuperscript{-1}, 25.2±3 min\textsuperscript{-1}, and 24.1±11.2 min\textsuperscript{-1}, respectively).

**Fig 2.** Graph showing the relation of the inverse of the mean transit time of the microcirculation (T\textsubscript{micro}^{-1}) with minimal luminal area (mm\textsuperscript{2}) determined by biplane coronary angiography. The thin lines connect the individual responses; the line of regression is solid bold. △ and ▽, before and after percutaneous transluminal coronary angioplasty.

**Fig 3.** Graph showing the relation of the inverse of the mean transit time of the microcirculation (T\textsubscript{micro}^{-1}) with stenosis flow reserve determined by integration of angiographic geometric data. △ and ▽, before and after, percutaneous transluminal coronary angioplasty.

**Fig 4.** Measurements of the inverse of the mean transit time of the microcirculation (T\textsubscript{micro}^{-1}) before (pre-) and after (post-) percutaneous transluminal coronary angioplasty (PTCA) of patients with stenosis of the left anterior descending or left circumflex arteries. A, data for the dilated artery. B, data for the adjacent nonstenotic artery.
Fig 4 illustrates the impulse response data for the 16 patients with PTCA of the LAD or LCx. In these patients, analysis of the adjacent nonstenotic artery was possible from the same nonselective contrast injections into the left main coronary artery. Fig 4A shows the results for the dilated artery and Fig 4B the corresponding data for the adjacent nonstenotic artery. Adjacent $T_{\text{micro}}^{-1}$ was $25.6 \pm 6.8$ min$^{-1}$ before PTCA and remained constant after PTCA ($25.8 \pm 6.2$ min$^{-1}$; $P=\text{NS}$). $T_{\text{micro}}^{-1}$ of the dilated artery after PTCA was nearly equivalent to values of the normal adjacent artery ($27.6 \pm 7.9$ min$^{-1}$; $P=\text{NS}$). For comparison of paired impulse response data of the dilated and adjacent arteries, Fig 5 illustrates the ratio of $T_{\text{micro}}^{-1}$ of the dilated artery to the adjacent artery in each patient. This ratio normalizes from $0.35 \pm 0.10$ before PTCA to $1.07 \pm 0.14$ after.

**Discussion**

The present study extends the use of digital angiographic impulse response analysis to assess regional microcirculation after PTCA of proximal single stenosis in each of the three major coronary arteries in the human coronary circulation. The results show that changes in $T_{\text{micro}}^{-1}$ are concordant with changes in geometric measurements of stenosis severity, including minimal stenotic area and stenosis flow reserve. Successful PTCA was associated with an in average greater than threefold increase in $T_{\text{micro}}^{-1}$, which completely normalized in comparison with adjacent myocardial regions supplied by a normal coronary artery. The absolute values of $T_{\text{micro}}^{-1}$ before and after PTCA were similar in normal but ischemic compared with partially infarcted or moderately hypertherphied myocardium and conformed to the range of values previously reported in the intact canine coronary circulation.$^{14,16}$ These data suggest that this angiographic method may provide new information about the acute physiological vasodilation responses of the regional microcirculation after PTCA.

**Quantification of Changes in Flow Reserve Induced by PTCA**

Reports of other densitometric methods to assess PTCA have described a 1.3- to 2.5-fold improvement after successful angioplasty.$^{34-38}$ There are only a few reports of normalization that was not consistently seen in all patients.$^{36,37}$ $T_{\text{micro}}^{-1}$, however, demonstrated a threefold increase and normalization in all patients. Doppler catheter measurements of coronary flow reserve have also reported inconsistent results. Whereas some patients demonstrate immediate normalization, others show only marginal improvement.$^{39-41}$ These inconsistencies may be partially caused by the recognized limitations of these methods, which require resting and hyperemic measurements of flow or velocity to calculate flow reserve. Inaccuracies will occur if resting flow increases after PTCA$^{42,43}$ or if maximal hyperemic response is blunted.$^{44}$ One potential advantage of our method is that $T_{\text{micro}}$ might be less sensitive to these influences because there are important conceptual differences between $T_{\text{micro}}$ and conventional measurements of coronary flow reserve: $T_{\text{micro}}$ itself is a ratio of volume and flow (Fig 6). Previous studies have shown that the microcirculatory intravascular volume changes inversely with small vessel resistance.$^{45,46}$ Small vessel resistance is the main determinant of the regulation of blood flow and is thus reciprocally related to the severity of a proximal stenosis. With increasing stenosis severity, resting flow is maintained by a gradual vasodilation and therefore an expansion of distribution volume; this will result in a decrease of $T_{\text{micro}}^{-1}$. Once volume is maximized, a further worsening of stenosis will diminish resting flow and further reduce $T_{\text{micro}}^{-1}$. If there is hyperemia after successful PTCA, it will presumably be secondary to a parallel increase of flow and distribution volume, keeping the ratio similar to a normal resting state.

In the present study we compared impulse response analysis with the method of integrated dimensional estimation of stenosis flow reserve described by Kirkcide et al.$^{29}$ Although both methods have been shown to have a linear correlation with coronary flow reserve under ideal conditions in animal models$^{16,29}$ and they independently predicted the states before and after angioplasty in our present study, their interrelation was nonlinear. There are several potential reasons for this. Starting with the pre-PTCA state, geometric measurements are more variable and tend to overestimate luminal area for vessels less than 1 mm in diameter if circular in cross section and even more so in highly eccentric stenoses.$^{13,47}$ Also, stenosis measurements do not reflect the contribution to flow provided by collaterals, whereas impulse response analysis measurements have been shown to reflect the measured collateral flow supplying or drafted away from a regional myocardial.
bed. For the post-PTCA conditions, the calculated stenosis dimensions may overestimate or underestimate cross-sectional area depending on the correct identification of vascular borders, the presence of intraluminal flaps, and extraluminal dissection. Moreover, the value of stenosis flow reserve is artificially bounded by the assumption that the maximum achievable hyperemic flow is five times the resting flow. A further assumption for the calculation of stenosis flow reserve is that poststenotic and microcirculatory perfusion pressures are equal. Although necessary to solve the initial theoretical equation, this assumption is valid only for single stenoses but not for multiple consecutive stenoses or diffuse disease. We did not specifically select patients with short and discrete stenoses, and eight patients had longer or consecutive lesions. On the other hand, T\textsubscript{\text{micro}}\textsuperscript{-1} measurements are more variable in normal vessels or successfully dilated arteries in part because the fixed precision of the measurement is relatively greater when a shorter transit time is expressed as an inverse.

**Limitations**

Prolonged breath holding is required during image acquisition to minimize densitometric artifacts. Peak contrast density over a myocardial region of interest distal of a tight stenosis may not occur until 10 seconds. Although excellent patient cooperation is necessary, we did not routinely train patients in breath holding before the procedure, and no study had to be rejected because of respiratory or motion artifacts.

Radiographic contrast material is not a purely intravascular indicator. Time-density curves are affected by a systematic error caused by diffusion of contrast material into extravascular space. This effect is inversely related to flow and introduces a nonlinear error with an overestimation of mean transit times especially with slow coronary flow. The magnitude of this error is probably small and did not affect earlier low flow validation studies.

Densitometric analysis from planar images of three-dimensional objects is limited by the superimposition of overlaying structures. For example, in left anterior oblique projection, measurements in the LAD territory may include parts of the left ventricular free wall as well as the septum, whereas in right anterior oblique projection the corresponding region of interest will include parts of the anterior free wall measured tangentially. Therefore, different regions of interest will relate to different myocardial volumes or perfusion territories of major branches, which may affect the calculated mean transit time. These effects may be reduced by adjusting the projections and placement of ROIs to minimize the overlap of different vascular territories and by averaging the results of biplane measurements. The striking difference of T\textsubscript{\text{micro}}\textsuperscript{-1} between the ischemic and nonischemic regions before PTCA comparing LAD and LCx territories and the near equivalency for the measurements after PTCA (Fig 4) suggest that the superimposition of different microcirculation perfusion beds can be effectively minimized. Moreover, we have shown that placement of ROIs can be varied along the long axis of the heart from apex to base without a systematic effect on T\textsubscript{\text{micro}}\textsuperscript{-1}. However, a tomographic imaging technique would further eliminate overlap and allow categorization of epicardial and subendocardial microcirculatory responses.

We had observed a small decrease in mean aortic pressure after PTCA. Data from our studies in dogs indicate that within the range of mean aortic pressure observed in this study, T\textsubscript{\text{micro}}\textsuperscript{-1} and coronary flow reserve remain constant. However, care must be taken because below a mean aortic pressure of 60 mm Hg, T\textsubscript{\text{micro}}\textsuperscript{-1} and coronary flow reserve decrease progressively.

The clinical definition of successful PTCA used in this study was based on coronary dimensions and visual assessment of flow. It is well known that it does not necessarily ensure that coronary hemodynamics have normalized.

Finally, more widespread application of myocardial densitometric impulse response analysis requires further validation in the situation where angioplasty results are unsuccessful by angiographic criteria or as determined by an independent method such as intravascular ultrasound.

In conclusion, impulse response analysis predicts changes in myocardial microcirculation associated with clinically and angiographically successful balloon angio-
plasty. The technique is simple, requiring a single hand-injected bolus of contrast material without any pharmacological interventions. Although our study showed concordance between impulse response analysis and two geometric parameters of stenosis severity, we are not implying an equivalency. The two approaches measure fundamentally different but interrelated parameters. Impulse response analysis describes the microcirculatory response to PTCA in relation to flow; ie, it measures a physiological phenomenon, not anatomic changes. As such, impulse response analysis may provide data that supplements and augments geometric quantification of stenosis severity.

References


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Circulation. 1994;90:163-171
doi: 10.1161/01.CIR.90.1.163

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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