Assessment of Immediate and Long-term Functional Results of Percutaneous Transluminal Coronary Angioplasty

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Assessment of the functional significance of coronary artery lesions during cardiac catheterization has recently become possible by calculating coronary flow reserve from both myocardial contrast appearance time and density in the resting and hyperemic states determined from digitized coronary cineangiograms. However, the interobserver and intraobserver variabilities, as well as the short-, medium-, and long-term variabilities of the coronary flow reserve measurements, have to be established before this technique becomes an acceptable means of assessing the immediate and long-term functional results of revascularization procedures such as percutaneous transluminal coronary angioplasty (PTCA). Variability was defined as the mean difference and standard deviation of the difference between duplicate determinations of coronary flow reserve. The intraobserver variability (mean difference ± SD) in the measurement of coronary flow reserve was -0.01 ± 0.07. Interobserver variability by two observers was $+0.08 \pm 0.52$. Short-term variability based on the analysis of two coronary cineangiograms taken 5 minutes apart was -0.02 ± 0.26. Medium-term variability (coronary cineangiographies repeated 1–3 hours apart) was found to be -0.06 ± 0.52. Long-term variability (coronary cineangiographies repeated 3–5 months apart) was 0.11 ± 0.63. Having established the reproducibility of this radiographic method, we studied the prospective changes in coronary flow reserve in 25 patients undergoing PTCA for single vessel coronary artery disease. Coronary flow reserve measurements and quantitative coronary cineangiography were performed before, immediately after, and 3–5 months after PTCA. PTCA resulted in an immediate increase in coronary flow reserve from 1 ± 0.3 to 2.3 ± 0.6 with a concomitant increase in obstruction area from 0.9 ± 0.3 to 3.3 ± 0.7 mm^2. Nine of the 25 patients developed restenosis defined as a diameter stenosis greater than 50% at follow-up. The other 16 patients had a coronary flow reserve of 3.3 ± 0.6, which was measured 3–5 months after PTCA. Coronary flow reserve measurement from digitized coronary cineangiograms is a reproducible method for the assessment of the physiological importance of coronary artery obstructions. Short-, medium-, and long-term investigations of the functional results of interventions such as pharmacological therapy or revascularization can be performed reliably with this technique. (*Circulation* 1988;78:15–24)

Since the introduction of percutaneous transluminal coronary angioplasty (PTCA) in 1977,[1] this procedure has gained increasing importance in the treatment of coronary artery obstructions. The immediate and long-term results of PTCA are usually assessed by visual interpretation of coronary angiograms. However, the visual interpretation of the coronary angiogram provides inadequate information about the physiological importance of obstructive coronary artery disease,[2] and is prone to interobserver and intraobserver variations. Although computer-based quantitative analyses have reduced the high interobserver and intraobserver variabilities[3,4] in the assessment of percent diameter stenosis and have provided absolute data on the stenosis geometry,[5] the physiological importance of a coronary stenosis cannot be inferred from geometrical data alone.[6,7] Recently, measurement of the

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coronary flow reserve has been proposed as a better method to evaluate the hemodynamic repercussions of a coronary stenosis.[7,8] Three techniques have been developed that allow the measurement of regional coronary flow reserve during cardiac catheterization. The first is a pulsed-Doppler coronary artery catheter that can measure intracoronary blood flow velocity.[9,10] The second technique is an indicator dilution technique with a platinum-tipped angioplasty guidewire with hydrogen as the indicator.[11] The third technique is based on the radiographic assessment of myocardial perfusion with contrast medium.[6,12–16] The major advantage of this technique is that guide wires and other hardware need not be introduced into the coronary artery, so this method can be used during routine cardiac catheterization. Although the technique is computer based, a crucial component of the analysis procedure is the user-dependent selection of the boundaries of the regions of interest, making intraobserver and interobserver variability potential pitfalls. Knowledge about the short-, medium-, and long-term variabilities in the measurements of coronary flow reserve is an essential prerequisite if this radiographic technique is to be used for the determination of the immediate and long-term functional results of pharmacological therapy or revascularization procedures such as PTCA. The aims of this investigation were to determine the interobserver and intraobserver variabilities as well as the short-, medium-, and long-term variabilities in coronary flow reserve measurements from digitized coronary cineangiograms and then to assess the immediate and long-term functional result of PTCA and its relation to quantitatively determined coronary stenosis geometry.

Patients and Methods

Patient Selection

Twenty-five patients underwent PTCA for disabling angina pectoris despite optimal pharmacological therapy. The right coronary artery was dilated in five patients, the circumflex artery in five patients, and the left anterior descending artery in 15 patients. Their age (mean ± SD) was 54 ± 9 years. Twenty-four patients were men. Recatheterization was performed 3–5 months later as part of an ongoing study on restenosis after PTCA. Informed consent was obtained for the additional investigations. Patients were selected on the basis of the following criteria: primary successful PTCA for one-vessel coronary artery disease (residual diameter stenosis less than 50%), normal blood pressure (mean aortic pressure ranging from 85 to 105 mm Hg), normal left ventricular wall motion with an ejection fraction of more than 55%, normal left ventricular end-diastolic pressure, and no angiographic evidence of collateral circulation, cardiac hypertrophy, anemia, polycythemia, documented previous myocardial infarction, and valvular heart disease.

TABLE 1. Variability in X-ray Gantry Settings and Voltage and Current of the X-ray Generator With Repeated Cineangiographic Studies

	Overall mean value	Mean	*p* value	SD difference
LAO (degrees)	53	0.1	NS	0.2
IID (cm)	23.6	−0.1	NS	2.0
FID (cm)	72.3	0	NS	0.1
OID (cm)	5.4	0	NS	0.1
Voltage (kV)	71.2	0.1	NS	2.9
Current (mA)	717	−5.5	NS	16.1

Data from 20 patients.
LAO, left anterior oblique projection; IID, isocenter-image intensifier distance; FID, focus-isocenter distance; OID, object-isocenter distance; SD difference, standard deviation of the difference; NS, not significant.

Coronary Flow Reserve Measurements

The procedure for the coronary flow reserve measurement from digitized coronary cineangiograms recorded on 35-mm cinefilm has been established on the Cardiovascular Angiography Analysis System developed at our institution.[13] The film speed was 25 frames/sec with a pulse time of 4 msec. For the right coronary artery, a left or right anterior oblique projection was used; for the left coronary artery, a left anterior oblique projection was used. The x-ray gantry settings were standardized in the short- and medium-term variability studies. This resulted in a good reproducibility of isocenter-image intensifier distance, focus-isocenter distance, and object-isocenter distance (Table 1). Voltage (kV) and current (mA) of the x-ray generator are adjusted automatically in our catheterization laboratory during the first three or four cineframes of each cinerun by a microprocessor system.[17] The on-line recorded voltage and current are then held constant during the cinerun. This microprocessor-based technique provided results of good reproducibility in both voltage and current of the x-ray generator (Table 1). The heart was atrially paced at a rate just above the spontaneous heart rate, ranging from 70 to 90 beats/min. An electrocardiographic (ECG)-triggered injection into the coronary artery was performed with Iopamidol at 37° C through a Medrad Mark IV infusion pump (Pittsburgh, Pennsylvania). This nonionic contrast agent has a viscosity of 9.4 cP at 37° C, an osmolality of 0.796 osm/kg, and an iodine content of 370 mg/ml. The injection rate and volume of the contrast medium were judged to be adequate when back flow of contrast medium into the aorta occurred. The injection rate ranged from 3 to 6 ml/sec, and the injection volume ranged from 5 to 9 ml depending on the size of the coronary artery. The angiogram was repeated with identical patient position and x-ray gantry settings, 30 seconds after hyperemia induced by a bolus injection of 12.5 mg papaverine into the coronary artery.[12] Five or six end-diastolic cineframes were selected from succes-

sive cardiac cycles. Logarithmic nonmagnified mask-mode background subtraction was applied to the image subset to eliminate noncontrast medium densities. The last end-diastolic frame before contrast administration was chosen as the mask. From the sequence of background-subtracted images, a contrast arrival time image was determined with an empirically derived fixed-density threshold.[13] Each pixel was labeled with the sequence number of the cardiac cycle in which the pixel intensity level for the first time exceeded the threshold, starting from the beginning of the ECG-triggered contrast injection. In addition to the contrast arrival time image, a density image was computed with each pixel intensity value being representative for the maximal local contrast medium accumulation. The coronary flow reserve was defined as the ratio of the regional flow computed from a hyperemic image [Q(h)] divided by the regional flow of the corresponding baseline image [Q(b)]. Regional flow values were quantitatively determined from the relation in which regional blood flow equals regional vascular volume divided by the transit time.[13] Regional vascular volume was assessed from the logarithmic mask-mode subtraction images with the Lambert-Beer relation. Coronary flow reserve can then be calculated as

$$\text{CFR} = \frac{Q(h)}{Q(b)} = \frac{D(h)}{D(b)} : \frac{T(h)}{T(b)}$$

where CFR is coronary flow reserve, D is the mean contrast density, and T is the mean appearance time at baseline (b) and hyperemia (h). Mean contrast medium appearance time and density were computed within user-defined regions that were chosen in such a way that the epicardial coronary arteries visible on the angiogram, the coronary sinus, and the great cardiac vein were excluded from the analysis.[13] For each of the three major coronary arteries (right coronary artery, left anterior descending coronary artery, and circumflex artery), only one region was chosen and analyzed. Normal values for coronary flow reserve as measured with this technique in our laboratory have previously been established.[18] The mean coronary flow reserve of 24 angiographically normal coronary arteries was 5 ± 0.6. A normal coronary flow reserve is therefore greater than 3.4 (2 SD below 5). This is comparable to the values for normal coronary flow reserve measured with intracoronary Doppler catheters as reported by Wilson et al.[9,10]

Intraobserver Variability

Intraobserver variability was assessed by measuring the coronary flow reserve in 11 regions in six patients twice from the same cineangiograms by the same observer. In five patients, two regions in the myocardium supplied by the left coronary artery were analyzed, and in one patient, a region was analyzed in the myocardium supplied by the right coronary artery. Care was taken to ensure that the regions in the duplicate determinations were identical.

Interobserver Variability

Interobserver variability was assessed by measuring the coronary flow reserve in 12 regions in seven patients from the same coronary cineangiograms by two observers. In five patients, two regions in the myocardium supplied by the left coronary artery were analyzed, and in two patients, a region was analyzed in the myocardium supplied by the right coronary artery. The selected boundaries of the regions were unknown to the other observer.

Short-term Variability

Short-term variability was defined as the variation in coronary flow reserve measured from two coronary cineangiograms taken 5 minutes apart with identical position of patient, x-ray source, and image intensifier. Coronary flow reserve was measured in 13 regions in seven patients. In six patients, two regions in the myocardium supplied by the left coronary artery were analyzed, and in one patient, a region was analyzed in the myocardium supplied by the right coronary artery. Care was taken to ensure that the selected regions in the duplicate determinations were identical.

Medium-term Variability and Immediate Functional Results of PTCA

Coronary flow reserve was measured before and immediately after PTCA in 25 patients. In five patients, the right coronary artery was dilated. In 20 patients undergoing PTCA of the left anterior descending coronary artery or the circumflex artery, coronary flow reserve was measured in both myocardial regions. To calculate the medium-term variability (1–3 hours), regions ($n = 20$) were chosen in the myocardium supplied by the nondilated coronary arteries. To assess the immediate alterations in coronary flow reserve due to PTCA, regions ($n = 25$) were chosen in the myocardium supplied by the dilated coronary arteries. During PTCA, various vasoactive drugs were administered (nitrates and calcium antagonists) as clinically indicated, which probably resulted in changes in vasomotor tone. Care was taken to ensure that cineangiographic projection and x-ray gantry settings, as well as the analyzed regions, were identical before and after PTCA.

Long-term Variability and Long-term Functional Results of PTCA

During follow-up of coronary cineangiography 3–5 months (mean 4.2 months) after PTCA, coronary flow reserve was measured again in these 25 patients. To calculate the long-term variability, regions ($n = 20$) were chosen in the myocardium supplied by the nondilated coronary arteries. To assess the long-term alterations in coronary flow reserve after PTCA, regions ($n = 25$) were chosen in the myocardium supplied by the dilated coronary

arteries. The follow-up investigation was always performed in a second cineangiographic room with different x-ray equipment. There was no standardized protocol for the administration of vasoactive medication before data acquisition; therefore, vasomotor tone in both conditions was unknown and ignored. Care was taken to ensure that identical regions of interest were analyzed.

Quantitative Coronary Cineangiography

Coronary arterial dimensions were determined before PTCA, immediately after PTCA, and at follow-up with the computer-based Cardiovascular Angiography Analysis System.[5,19] The boundaries of selected coronary artery segments were detected automatically from optically magnified and video-digitized regions of a cineframe. Calibration of the diameters in absolute values (mm) was achieved by detecting the boundaries of a section of the contrast catheter and by comparing the mean diameter in pixels with the known size in millimeters. Pincushion distortion was corrected. A computer estimation of the original arterial dimensions at the site of obstruction was used to define the reference region. The interpolated percent diameter stenosis and the minimal cross-sectional area (mm^2) at the site of obstruction were calculated by averaging the values from at least two orthogonal projections, preferably.

Statistical Analysis

Results from the various studies were analyzed for significant differences with Student's t test for paired observations (level of significance, $p = 0.05$). Least-squares linear regression analyses were used to describe the relations between coronary flow reserve and the quantitatively determined coronary artery dimensions.

Results

Intraobserver Variability

Figure 1 shows the results of measuring twice the coronary flow reserve in 11 regions in six patients by the same observer from the same coronary

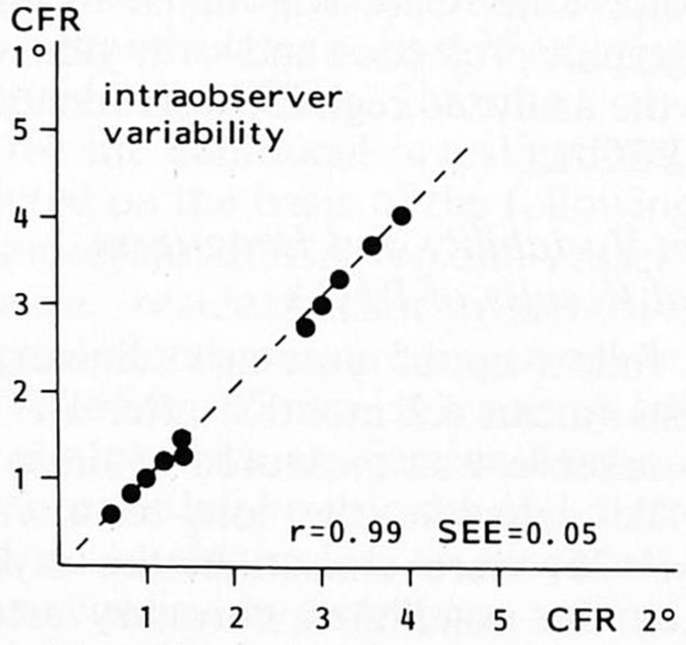

FIGURE 1. *Plot of intraobserver variability. CFR 1°, first determination of coronary flow reserve; CFR 2°, second determination of coronary flow reserve.*

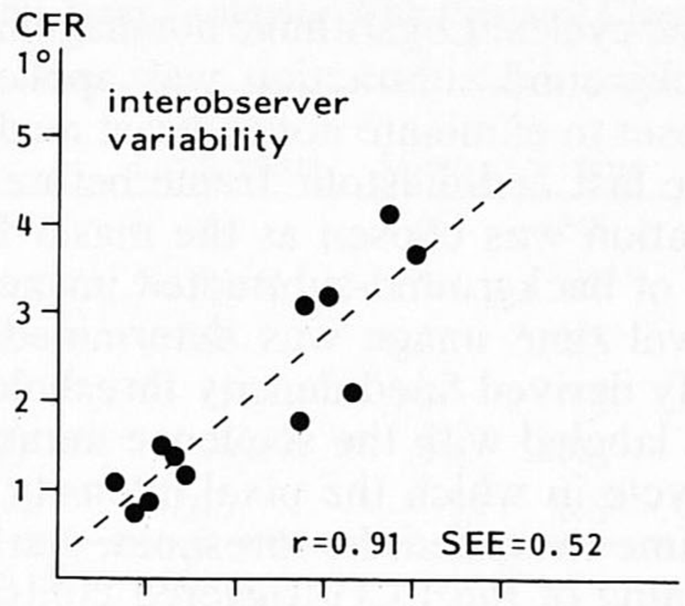

FIGURE 2. *Plot of interobserver variability. CFR 1°, first determination of coronary flow reserve; CFR 2°, second determination of coronary flow reserve.*

cineangiograms. There is no significant difference between the first and second measurements.

Interobserver Variability

With the same coronary cineangiograms in 12 regions in seven patients, coronary flow reserve measurements are shown for two observers without the knowledge of each other's selected regions (Figure 2). There is no significant difference in the measurements between the two observers.

Short-term Variability

Figure 3 shows the coronary flow reserve as measured from repeated acquisition and analysis of coronary cineangiograms taken 5 minutes apart in 13 regions in seven patients. No significant differences between the two measurements were found. The hemodynamic data are shown in Table 2.

Medium-term Variability

Figure 4 shows the coronary flow reserve measurements for a myocardial region supplied by a cornary artery not involved in dilatation in 20 patients immediately before and after (1–3 hours) angioplasty. No significant differences were found between the measurements obtained before and after the angioplasty. The hemodynamic data are shown in Table 2.

FIGURE 3. *Plot of short-term variability. CFR 1°, first determination of coronary flow reserve; CFR 2°, second determination of coronary flow reserve.*

TABLE 2. Hemodynamic Data of Short-, Medium-, and Long-term Variability Studies

Variability	1°	2°	Difference	Significance
Short-term ($n=7$)				
P_{ao}	97±10	98±9	1±3	NS
HR	77±12	77±12	0±0	NS
Medium-term ($n=20$)				
P_{ao}	95±12	91±11	4±8	NS
HR	79±11	79±11	0±0	NS
Long-term ($n=20$)				
P_{ao}	91±11	97±15	6±13	NS
HR	79±11	81±13	2±8	NS

P_{ao}, mean aortic pressure (mm Hg); HR, heart rate (beats/min); NS, not significant.

Long-term Variability

Figure 5 shows the coronary flow reserve as measured in a myocardial region supplied by a nondilated coronary artery immediately after angioplasty as well as 3–5 months later in 20 patients. There is no significant difference between the two measurements. The hemodynamic data are shown in Table 2.

Immediate Functional and Anatomic Results of PTCA

Diameter stenosis decreased from 65±6% to 32±10%. The coronary flow reserves of the dilated coronary arteries increased from 1±0.3 to 2.3±0.6, and the cross-sectional area at the site of obstruction increased from 0.9±0.3 to 3.3±0.7 mm². The data of the individual patients are shown in Figures 6 and 7. Eighteen of the 25 patients (72%) had an increase of coronary flow reserve greater than 2 SD of the medium-term variability.

Long-term Functional and Anatomic Results of PTCA

Three to 5 months after PTCA, the mean percent diameter stenosis was 38±18%. The coronary flow

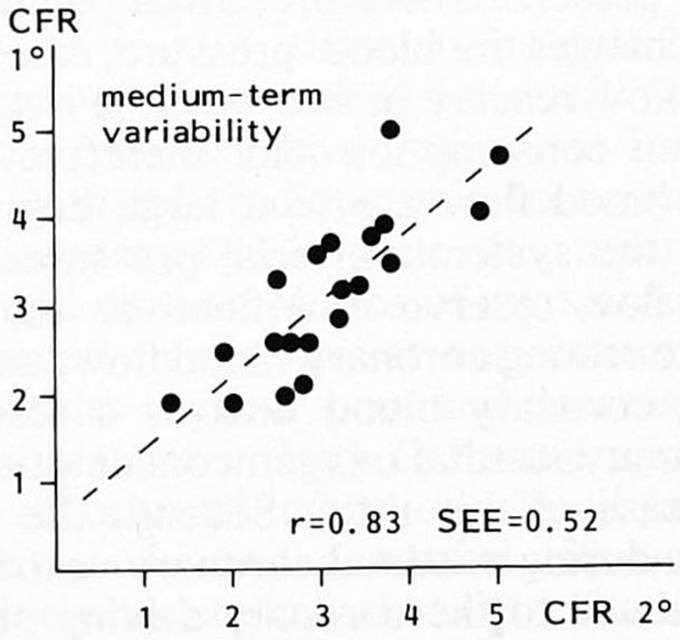

FIGURE 4. *Plot of medium-term variability. CFR 1°, first determination of coronary flow reserve; CFR 2°, second determination of coronary flow reserve.*

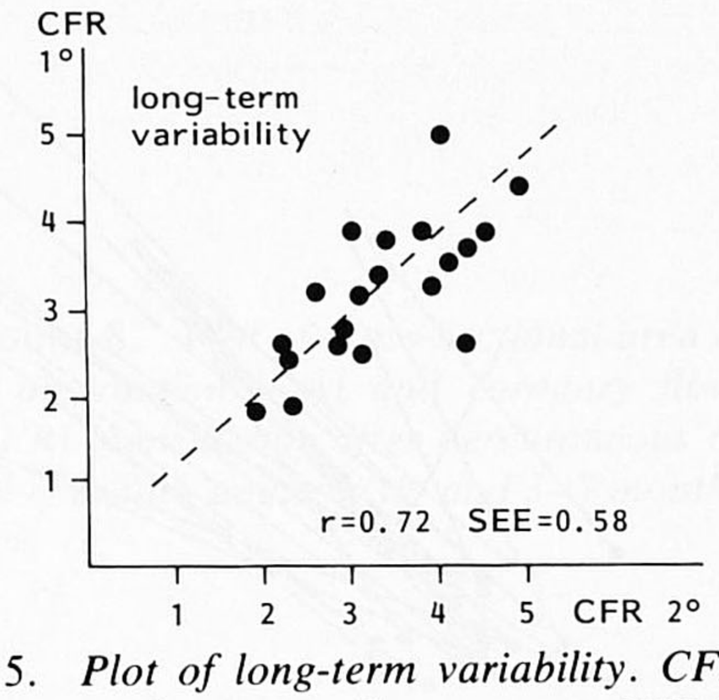

FIGURE 5. *Plot of long-term variability. CFR 1°, first determination of coronary flow reserve; CFR 2°, second determination of coronary flow reserve.*

reserve of the dilated coronary arteries was 2.6±1, and the cross-sectional area at the site of obstruction was 2.8±1.4 mm². The alterations in these two variables of the individual patients during the 3–5 months after PTCA are shown in Figures 8 and 9. Nine of the 25 patients (36%) had restenosis defined as diameter stenosis greater than 50% during follow-up angiography. These nine patients had an obstruction area mean±SD of 1.3±0.4 mm² and a coronary flow reserve of 1.5±0.4. The patients without restenosis had an obstruction area of 3.6±1 mm² and a coronary flow reserve of 3.3±0.6. Seven of the 25 patients (28%) had an increase of coronary flow reserve greater than 2 SD of the long-term variability, and four of the 25 patients (16%), all with restenosis, had a decrease of coronary flow reserve greater than 2 SD of the long-term variability.

Discussion

To understand the implications of coronary artery disease in a patient, the clinician must have information on anatomy as well as functional capacity of coronary arteries and of the left ventricle. Coronary flow reserve defined as the ratio of maximal to resting coronary blood flow has been introduced as a measure of the functional capacity of coronary arteries.[7,8] The relation between coronary artery anatomy and functional capacity/coronary flow reserve has been extensively studied in animal models.[20–22] Gould et al[22] produced varying degrees of coronary narrowing and showed that stenoses in excess of a diameter narrowing of 30–45% reduced coronary vasodilator responses in a predictable fashion. Although the reduction in coronary flow reserve can be predicted by quantification of stenosis geometry in selected patients with limited coronary artery disease,[10,13] the functional capacity of coronary arteries in many patients cannot be inferred from anatomic data alone. For instance, the functional capacity of a coronary artery with two or three obstructive lesions cannot be predicted by quantitative analysis of the coronary angiogram. This implies that accurate and reproducible means of measuring regional

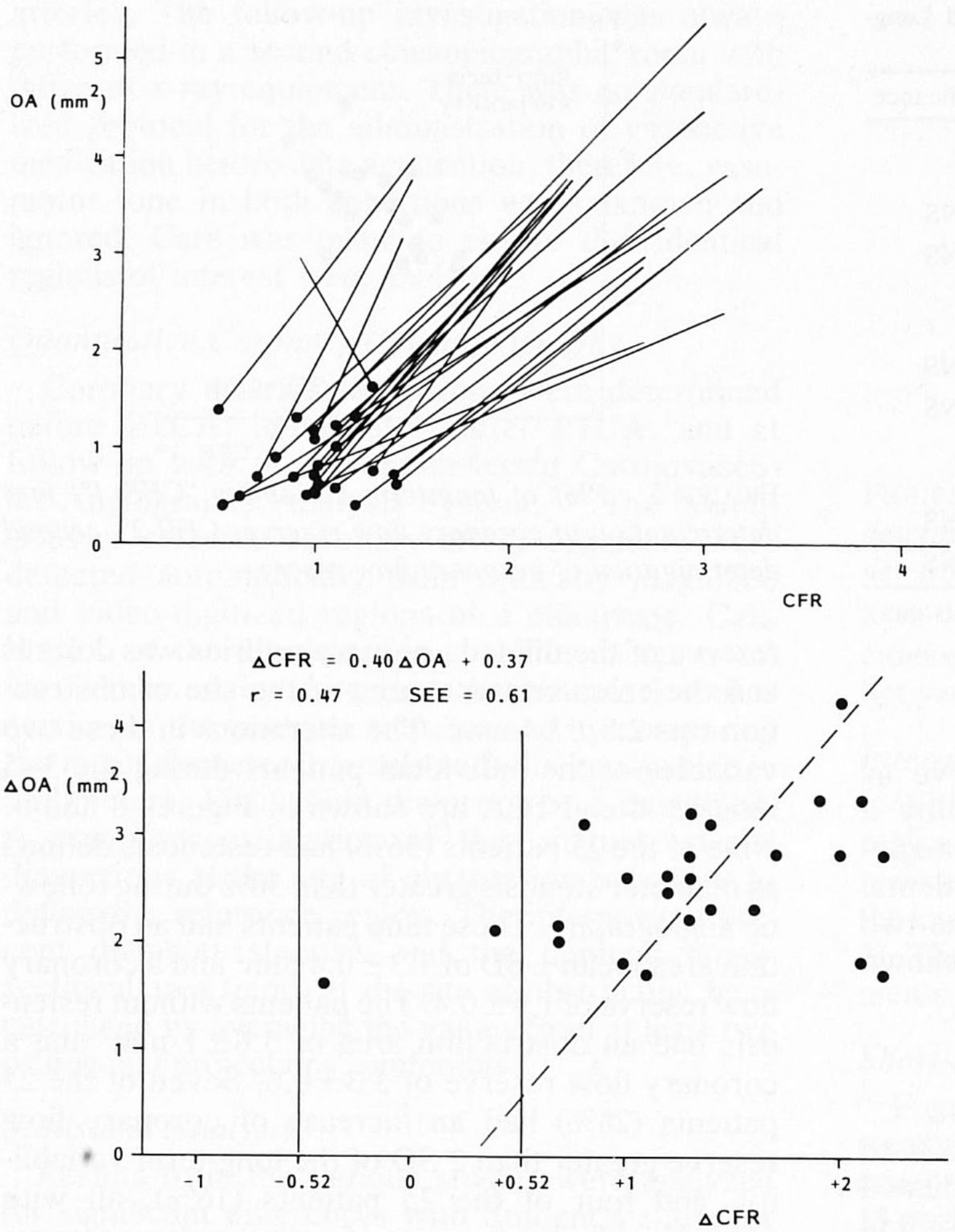

FIGURE 6. *Plot of cross-sectional area at the site of obstruction (OA) and coronary flow reserve (CFR) before and immediately after percutaneous transluminal coronary angioplasty.*

FIGURE 7. *Plot of relation between change in obstruction area (ΔOA) and change in coronary flow reserve (ΔCFR) as immediate result of percutaneous transluminal coronary angioplasty. Vertical lines mark 1 SD of the medium-term variability.*

coronary flow reserve are a necessary addition to quantitative coronary cineangiography.

The first aim of the present study was to determine interobserver and intraobserver, as well as short-, medium-, and long-term, variability in radiographic coronary flow reserve measurements. Various factors potentially contribute to these variabilities.

1) The x-ray gantry settings and voltage and current of the x-ray generator must be identical to permit a valid comparison of the myocardial contrast density measurements on both the baseline and hyperemic cineangiograms. This is also a prerequisite if a comparison of two or more coronary flow reserve measurements at different times is to be made. The radiographic equipment used in this study seems adequate in this regard (Table 1).

2) Cinefilm development must be very stable. In our laboratories, a 21-step (log 1.5 increment) sensitometric full-frame strip is generated on each cinefilm with a dummy camera before the angiographic investigation. This strip is developed with the angiographic data and is used to control the chemical process. Developer is replenished per meter of cinefilm instead of per unit of time and is therefore independent of the speed of the machine. Together with accurate temperature control and the use of a medium-grain developer, a reliable chemical process results that is characterized by a mean density of 0.82 and a gradient of 1.25.

3) Many patient-related factors are important determiners of the measured coronary flow reserve and contribute to the variability of this radiographic method. Changes in heart rate may influence the coronary flow reserve.[23,24] Furthermore, subtraction of the digitized selected end-diastolic cineframes is only possible when a strictly regular rhythm is present. Therefore, atrial pacing is mandatory. Changes in blood pressure can influence coronary flow reserve in two ways.[8] First, myocardial oxygen consumption and, therefore, baseline coronary blood flow are to a large degree determined by the systemic arterial pressure. Because coronary flow reserve is defined as the ratio of maximal to resting coronary blood flow, an increase in resting coronary blood flow as a result of an increase in myocardial oxygen consumption results in a decrease of this ratio. Second, the coronary blood flow during maximal coronary vasodilation is linearly related to the coronary driving pressure.[25] Cineangiograms that are used for the calculation of flow reserve during baseline and hyperemic conditions or for repeated radiographic coronary flow

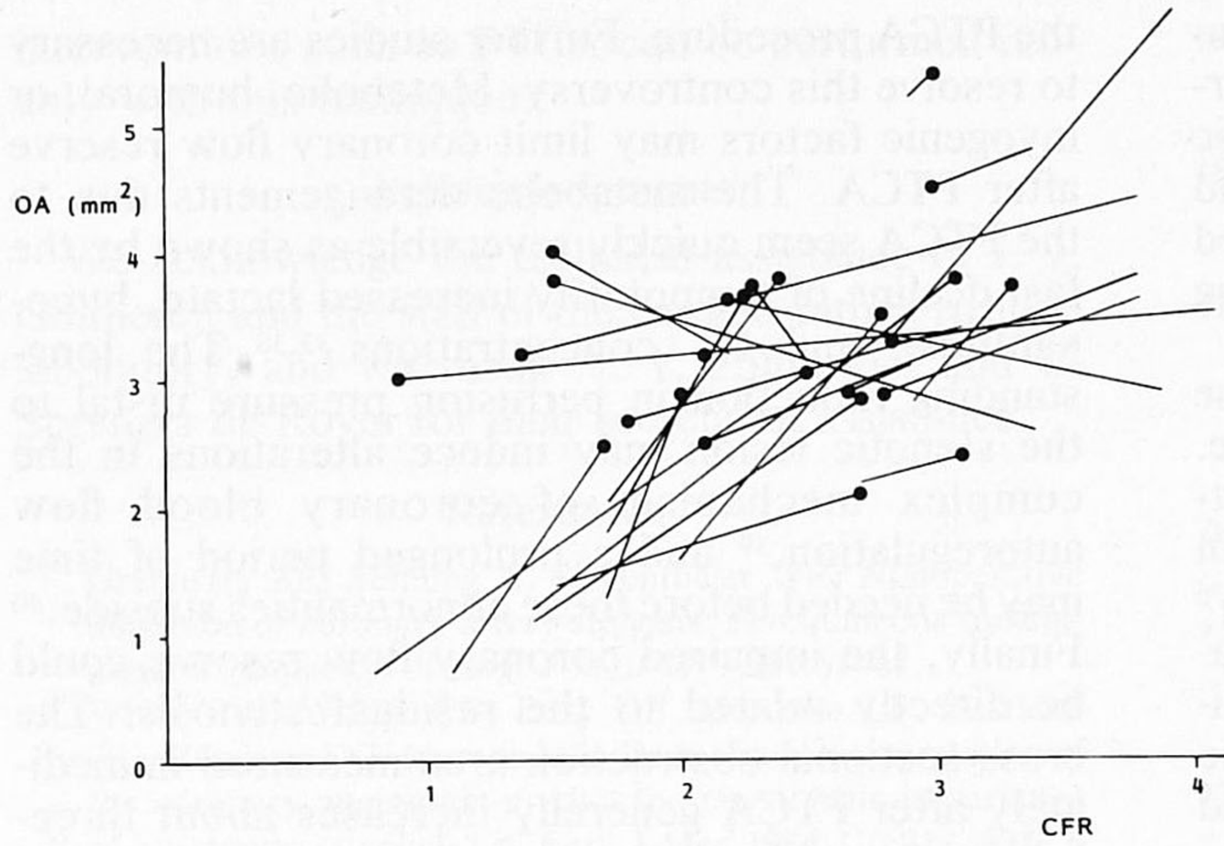

FIGURE 8. *Plot of cross-sectional area at the site of obstruction (OA) and coronary flow reserve (CFR) immediately after percutaneous transluminal coronary angioplasty and 3–5 months later.*

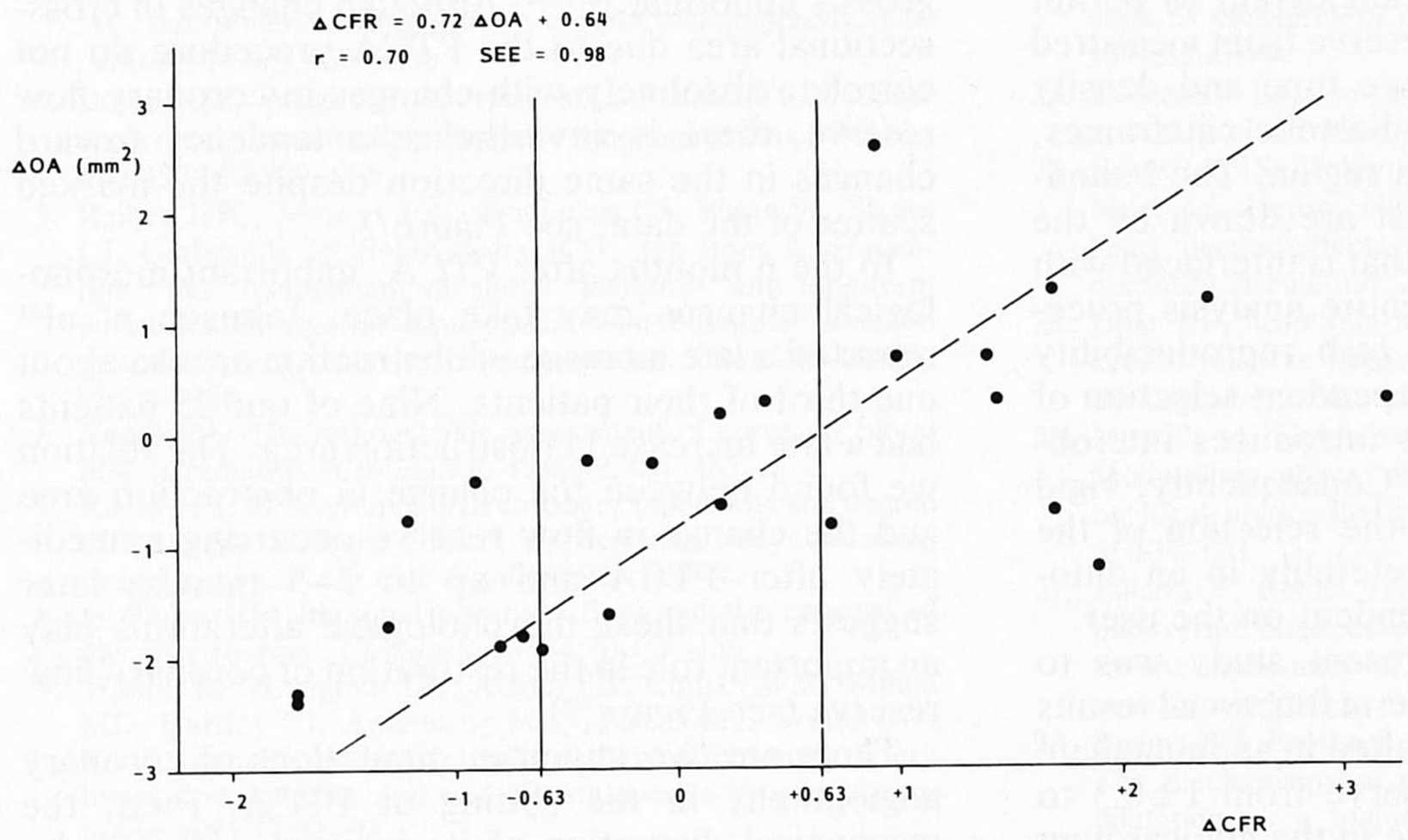

FIGURE 9. *Plot of relation between change in obstruction area (ΔOA) and change in coronary flow reserve (ΔCFR) occurring immediately after percutaneous transluminal coronary angioplasty and up to 3–5 months later. Vertical lines mark 1 SD of the long-term variability.*

reserve measurements should thus be obtained with the same blood pressure. As shown in Table 2, alterations in blood pressure or heart rate were negligible in this study. Coronary flow reserve measured in the animal model can be reduced by a large increase in left ventricular diastolic pressure[8] or by a marked change in contractility and systolic function.[26] At present, there are no data regarding the influence of abnormal systolic left ventricular function on coronary flow reserve in humans as measured with this radiographic technique, but a study on coronary flow reserve after reperfusion in the acute and chronic phases of myocardial infarction is currently underway at our institution. Preliminary results suggest a marked decrease in coronary flow reserve in both the acute and chronic phases of myocardial infarction. As all patients in the present study had a normal left ventricular function, it seems unlikely that these factors play a role in the variabilities described in this report. Medium- and long-term variabilities are certainly affected by changes in vasomotor tone.[27,28] Alterations in collateral channel filling patterns during and after angioplasty may also play a role. Although we excluded patients with angiographically visible collaterals, collateral vessels not visible by standard angiographic techniques are often present.[29] The long-term study might be influenced especially by changes in neurohumoral factors. Endothelium-derived relaxing factor has a physiological dilator role by acting as a local autocoid on subjacent smooth muscle and may be an important control in coronary flow and flow reserve.[30,31]

4) A prerequisite of this radiographic technique is the use of an ECG-triggered pump to inject a fixed volume at a fixed contrast injection rate.[6,15] Although injection of a radiographic contrast agent induces profound alterations in coronary blood flow,[32] the ratio of hyperemic coronary blood flow to baseline flow is unaffected by the contrast agent during the first 5 seconds after injection when injection rate and volume are identical in hyperemic and baseline conditions.[15,16] The injection rate and volume should be sufficient to ensure complete filling of the epicar-

dial coronary arteries with contrast during pharmacologically induced hyperemia.[6,15,16] The disturbance in coronary blood flow due to the radiographic contrast agent lasts for less than 20 seconds, and sequential injections of contrast agent in doses used in this investigation do not result in persisting changes in coronary blood flow.[32–34]

5) The method of induction of a hyperemic response in the coronary circulation should be reproducible. Intracoronary papaverine induces a strong and short-lasting hyperemia that is reasonably reproducible in magnitude as well as in timing.[35] Wilson and White[36] recently investigated the dose of intracoronary papaverine needed to produce maximal coronary vasodilation, and they reported a maximal hyperemic response after 8 mg in most coronary arteries and after 12 mg in all coronary arteries.

6) The analysis of the cineangiogram to permit calculation of coronary flow reserve from measured myocardial contrast appearance time and density involves the selection of end-diastolic cineframes, digitization, and selection of a region. The boundaries of the regions of interest are drawn by the observer with a writing tablet that is interfaced with the computer. Although the entire analysis procedure can be performed with high reproducibility (see Figure 1), the observer-dependent selection of the boundaries of the regions introduces interobserver variability (Figure 2). Consequently, rigid criteria should be applied to the selection of the boundaries of the regions, preferably in an automated manner that is not dependent on the user.

The second aim of the present study was to assess the immediate and long-term functional results of PTCA. Although PTCA resulted in an immediate increase of coronary flow reserve from 1 ± 0.3 to 2.3 ± 0.6, coronary flow reserve in the myocardium supplied by the dilated coronary artery immediately after PTCA was still substantially lower than the coronary flow reserve of 3.2 ± 0.9 in the myocardium supplied by nonsignificant, nondilated, and angiographically diseased coronary arteries (diameter stenosis <50%) (see Figure 4). During the 3–5-month follow-up, nine patients developed restenosis defined as a diameter stenosis greater than 50%. By 5 months after PTCA, the other 16 patients had a coronary flow reserve of 3.3 ± 0.6 in the dilated coronary arteries, which is comparable to the coronary flow reserve of adjacent myocardial regions supplied by nondilated coronary arteries of these same patients. There are several possible explanations for the limited restoration of coronary flow reserve immediately after PTCA. Because coronary flow reserve is a ratio between maximal and resting flows, an increase in resting flow results in a decrease of this ratio. Although several authors using the thermodilution technique have reported comparable volume flows before and after PTCA,[33,34] recent work performed in our laboratory[37] with intracoronary Doppler catheters suggests that resting coronary blood flow velocity increases during the PTCA procedure. Further studies are necessary to resolve this controversy. Metabolic, humoral, or myogenic factors may limit coronary flow reserve after PTCA. The metabolic derangements due to the PTCA seem quickly reversible as shown by the fast decline of temporarily increased lactate, hypoxanthine, and K^+ concentrations.[33,38] The long-standing reduction in perfusion pressure distal to the stenotic lesion may induce alterations in the complex mechanism of coronary blood flow autoregulation,[39] and a prolonged period of time may be needed before these abnormalities subside.[40] Finally, the impaired coronary flow reserve could be directly related to the residual stenosis. The cross-sectional obstruction area measured immediately after PTCA generally increases about threefold as a result of the procedure, but it remains grossly abnormal.[18,19,41] Although changes in cross-sectional area due to the PTCA procedure do not correlate absolutely with changes in coronary flow reserve, there is nevertheless a tendency toward changes in the same direction despite the marked scatter of the data, see Figure 7.

In the 6 months after PTCA, important morphological changes may take place. Johnson et al[41] reported a late increase in obstruction area in about one third of their patients. Nine of our 25 patients had a late increase in obstruction area. The relation we found between the change in obstruction area and the change in flow reserve occurring immediately after PTCA and up to 3–5 months later suggests that these morphological alterations play an important role in the restoration of coronary flow reserve (see Figure 9).

There are two important limitations of coronary angiography in the setting of PTCA. First, the mechanical disruption of its internal wall may be difficult to assess by angiographic means.[19,42] The irregular shape with intimal tears that fill with contrast medium to a variable extent will result in some overestimation of the true functional luminal size immediately after PTCA. Second, the extent of coronary atherosclerosis may be difficult to delineate angiographically. McPherson et al[43] documented that substantial intimal atherosclerosis resulting in diffuse obstructive disease that involves the entire length of an epicardial artery is often present, even when angiograms reveal only discrete lesions. This may explain why despite only minimal residual stenosis, our patients that had no restenosis had a coronary flow reserve of the dilated, as well as the nondilated coronary, arteries that was still somewhat lower than the normal values for coronary flow reserve as previously reported.[9,13,18]

Conclusion

Coronary flow reserve measurement from digitized coronary cineangiograms is a reproducible means that may be used to assess the functional capacity of coronary arteries. Short-, medium-, and long-term investigations of the functional results of

interventions such as PTCA can be performed reliably with this technique.

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