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Methods for the assessment of PTCA success

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Summary: Numerous criteria for the assessment of the immediate and late results of percutaneous transluminal coronary angioplasty (PTCA) are currently in use. Here, the values and limitations of the transstenotic gradient (TG), visual qualitative angiogram assessment, quantitative coronary angiography and the coronary flow reserve (CFR) will be discussed.

Although measurement of the TG may be clinically useful, current data suggest that it does not accurately reflect the "true" pressure-flow-resistance across coronary lesions. Furthermore, the widely applied method of visual interpretation of coronary angiograms is hampered by several serious shortcomings: large intra- and interobserver variabilities, and lack of correlation with pathologic as well as intraoperative findings. In contradistinction, CFR and minimal luminal cross-sectional area (MLCA) appear to be more reliable parameters for judging the physiologic importance of (residual) coronary obstructions. In fact, given the curvilinear relation between CFR and MLCA (r=0.92), the available evidence suggests that at the moment quantitative coronary angiography – with measurement of the MLCA immediately after PTCA – is the method of choice in assessing the efficacy of coronary angioplasty.

Key words: percutaneous transluminal coronary angioplasty; transstenotic gradient; coronary flow reserve

Hemodynamic criteria

Initially, reduction or disappearance of the transstenotic pressure drop measured by the dilatation catheter during the angioplasty procedure played a major role in the evaluation of the result of a coronary dilatation. However, the value of these measurements in assessing the physiologic significance of residual coronary stenoses, even those obtained with the smallest catheters, must be questioned. First of all, the arterial translesional pressure gradient is affected by phasic changes in blood flow (Fig. 1): the maximal pressure gradient across a coronary stenosis occurs in early diastole (20, 75), which is consistent with the finding that the pressure drop increases in a curvilinear fashion with increasing flow (12, 22). Thus, within a narrowed segment, blood velocity increases and pressure decreases in accordance with Bernoulli's law. Secondly, recent progressive miniaturization of the balloon catheter has led some to question the reliability of pressure recording in this sense, since a reduced catheter diameter results in less accurate hydraulic pressure transmission necessary for this kind of measurement (16, 65). Thirdly, due to the physical presence of the dilatation catheter across the stenotic cross section, the remaining vessel luminal area is further reduced and, as a result, blood flow through the obstruction is impeded (20, 60). In fact, the measured pressure drop overestimates the "true" pressure difference across the stenosis in a predictable manner, which is dependent on the ratio of the diameter of the angioplasty catheter over the stenosis diameter (20, 36, 60). Recently, comparison of balloon catheter measurements with high fidelity (HiFi) ultra-miniature tip-transducer measurements in seven patients, showed that the HiFi transstenotic pressure drop values obtained were markedly lower both before and after angioplasty (65). Essentially, this difference is the result of using a catheter with a smaller shaft diameter (0.7 mm as opposed to about 1.0 to 1.2 mm for conventional balloon catheters).

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INCREASE IN CORONARY FLOW VELOCITY & PRESSURE GRADIENT AFTER PAPAVERINE I.C.

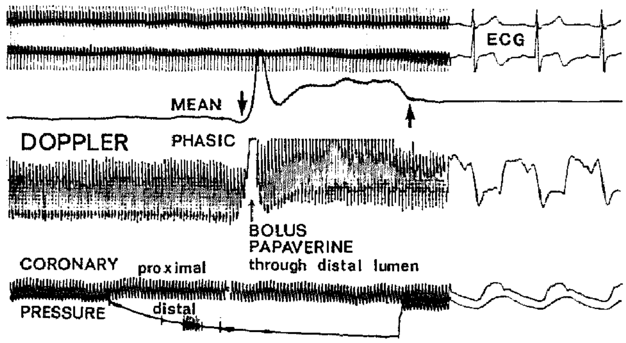

Fig. 1. Relation of the translesional pressure gradient and the intracoronary Doppler blood flow velocity before and after 4 mg of intracoronary papaverine, administered distal to the stenotic lesion through the dilatation catheter lumen. It can be observed on the right hand side of the tracing that the measured pressure gradient increases with increasing flow as a result of vasodilatation by papaverine. The changes in the tracings between the two arrows are artifactual, as a result of injection of papaverine.

Whereas the pressure distal to a coronary artery obstruction is mainly dependent on the severity of the stenosis and the amount of collateral flow to the corresponding myocardial region, it is entirely determined by the extent of this collateral circulation if anterograde flow is eliminated by an angioplasty catheter which totally obstructs the native vessel (48). Finally, the systolic translesional gradient – defined as the difference between the proximal systolic pressure (measured by the guiding catheter) and the distal systolic pressure (measured by the dilatation catheter) – decreases significantly as the angiographically quantified extent of the collateral circulation increases, and vice versa. At the same time, patients with clearly visible collaterals before PTCA show a significantly higher lesion recurrence rate relative to patients without angiographic evidence of collateral circulation (52% vs 28%, $p < 0.05$) (48).

To summarize, current data suggest that the absolute value of the transstenotic pressure difference measured with a balloon catheter during catheterization, does not accurately reflect the "true" pressure-flow-resistance characteristics across coronary lesions (60, 65). These problems notwithstanding, measurement of the pressure distal to a coronary stenosis by means of a dilatation catheter during the PTCA procedure can still be clinically useful, given the strong relationship between the final transstenotic pressure drop and consequent restenosis rates: the restenosis rate of patients with a residual gradient ≤ 15 mm Hg immediately post-PTCA is significantly lower in comparison with residual gradients > 15 mm Hg (37).

Angiographic criteria

In view of the above, coronary angiography has emerged as the most reliable method of judging the immediate and late results of a dilatation. However, there is the possible problem of inaccuracy of luminal diameter measurements immediately after angioplasty, due to the frequent appearance of inhomogeneous arterial filling with contrast at the dilatation site as a result of the passage of contrast material into split areas of the vessel intima and/or media (see Figs. 2 and 3) (4, 11, 13, 44, 57, 66). Particularly, the presence of dissection can result in irregular vascular wall outlines on the post-PTCA arteriogram (45).

Visual qualitative angiogram assessment

Attempts to correlate closely the anatomy of a coronary stenosis and its physiologic significance by visual interpretation of cineangiograms, are hampered be several serious shortcomings. The large intra-and inter-observer variabilities (9, 10, 43, 78), and lack of correlation with pathologic (1) and intraoperative (75) findings of visually interpreted coronary cineangiograms are well recognized. Furthermore, the reproducibility of visual lesion assessment is influenced by the severity of the coronary stenosis. In general, lesions between 20% to 80% diameter obstruction ("moderate lesions") have a wider range of intra-and inter-observer variabilities than stenoses less than 20% or more than 80% (62). The limitation that visual le-

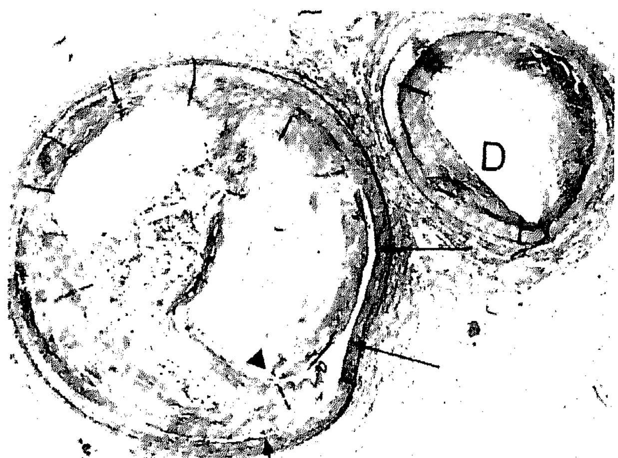

Fig. 2. Cross-section through the proximal part of the left anterior descending artery and adjacent diagonal branch (D), from a 65-year-old woman who died in an accident immediately after PTCA. The atherosclerotic plaque shows disruption and splitting (arrowhead), and is dissected and lifted from the media (arrows). A hemorrhagic area within the plaque opposite the split has an appearance which suggests that its occurrence predates the angioplasty procedure. Apart from an atherosclerotic narrowing of the lumen, the diagonal branch (D) does not show other changes. From Soward et al (66), with permission.

Fig. 3. (A) Histologic section through a stenotic lesion in the left anterior descending artery successfully dilated 5 months prior to the death of the patient. Extensive disruption of the medial layer (asterisk) is present, which had led to medial dissection. A proliferation of fibrocellular tissue (FC) fills the false channel and almost totally occludes the pre-existent lumen. A split in the pre-existent atherosclerotic plaque (AS) can be readily identified.

Fig. 3. (B) A slightly more distal segment of the same artery shows dehiscence of the plaque from the underlying media (closed arrows). The media shows a localized total interruption (open arrowhead), with only the elastic lamellae of the adventitia left intact.
From Essed et al (13), with permission.

sion assessment of coronary cineangiograms is not sufficiently accurate for measuring small luminal changes in moderate lesions, is compounded by the fact that these "minor" changes have major hemodynamic consequences. While resting coronary blood flow is not altered until an obstruction of at least 85% of the diameter is present, maximal coronary flow is already diminished by obstructions as small as 30%, and marked impairment of coronary flow reserve (CFR) occurs with progressive diameter stenosis from 65% to 95% (23). Also, with standard visual analysis of angiograms, underestimation of lesion severity occurs in 95% of vessels with >60% diameter stenosis, while both overestimation and underestimation of lesions with <60% stenosis are common (72). Finally, accurate determination of the degree of stenosis can usually only be made after radiographic processing of cineangiograms, preventing use of this information during interventional catheterization. However, practical semi-automated methods for measuring percent diameter stenosis from digital angiograms have been described (30, 34, 69). Thus, in contrast to conventional "off-line" cineangiograms, digital acquisition of coronary angiograms allows immediate (on-line) quantitative or visual analysis of stenoses during catheterization. Despite all the above, it is felt that the mean of visual stenosis measurements using several projections represents the best widely available method for assessing the anatomic-geometric severity of a coronary artery (re)stenosis (43). In fact, most studies to date regarding recurrent stenosis have used this approach.

Quantitative coronary angiography

Since visual interpretation of the coronary angiogram is a poor means of predicting the physiologic importance of obstructive coronary artery disease (72), various other systems have been introduced in recent years aimed at enhancing objectivity and reproducibility in the assessment of coronary artery dimensions. The systems used to date in the quantification of coronary cineangiograms vary a great deal: manual procedure that implement a vernier caliper or comparable device (14, 21, 39, 49), computerized manual edge-tracing procedures (5), and methods that make use of computer edge-detection algorithms (33, 51, 55, 68). Also, densitometric procedures are used by various investigators, in an attempt to derive cross-sectional area measurements from single-view coronary cineangiograms (32, 47, 50, 56, 67). An example of a quantiative method for assessing the severity of a coronary lesion, which applies a minimal cost algorithm for automatic vessel contour detection is shown in Fig. 4 (33, 51) and Table 1.

In general, a quantitative computer-based analysis method enhances objectivity, while it reduces the problems of high intra-and inter-observer var-

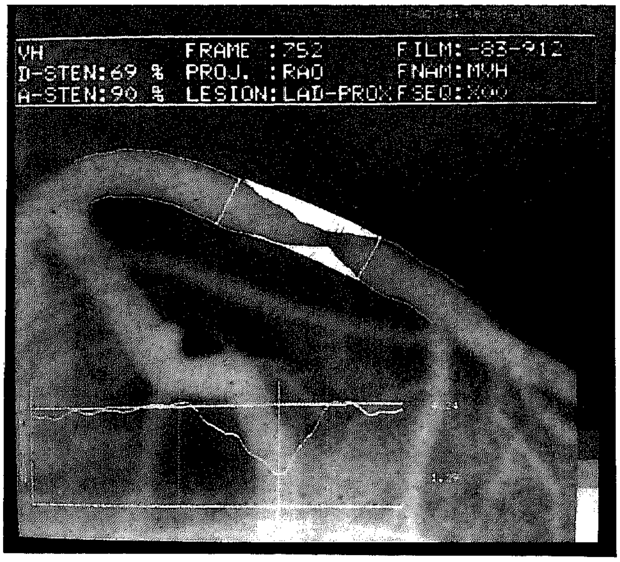

Fig. 4. (A) The detected contours together with the proximal and distal obstruction boundaries for a proximal lesion in the left anterior descending artery are shown. The interpolated percentage diameter stenosis - computed from the minimal diameter value at the obstruction (see diameter function graph in the lower portion of the illustration) and the corresponding value of the reference diameter - is 69%. The difference in area (mm^2) between the estimated outer contours and the detected luminal contours at the site of the obstruction, is a measure of the "atherosclerotic plaque" (shaded area).

Table 1. Quantitative data for LAD-prox lesion

Segmental location of obstruction	: 604
Extent obstruction	: 11.89 mm
Reference diameter	: 4.12 mm
Obstruction diameter	: 1.29 mm
Reference area	: 13.36 mm^2
Obstruction area	: 1.31 mm^2
Area plaque	: 16.79 mm^2
Symmetry measure	: 0.89
Diameter-stenosis	: 69%
Area-stenosis	: 90%
Transstenotic pressure gradient at mean flow of 2 ml/s	: 17.6 mmHg

iability inherent in visual interpretation of the coronary angiogram (51, 78); at the same time, this method allows for the calculation of the hemodynamic consequences of a coronary artery lesion. On the basis of the available quantitative data of a coronary obstruction, the following hemodynamic parameters can be computed: Poiseuille resistance, turbulent resistance, and the resulting pressure gradients (Table 2) (6, 24, 31, 42, 52, 64).

These derived hemodynamic parameters have been shown to correlate with the transstenotic pressure difference, and with exercise thallium-201 perfusion scintigraphy (59, 77). Furthermore, in theory resistance is a more relevant index of the physiologic severity of the arterial stenosis (5).

In fact, previous studies on the hemodynamic effects of an arterial stenosis have demonstrated that the minimal luminal cross-sectional area is a

Table 2. Computation of various hemodynamic parameters following quantitative analysis of a coronary obstruction

$$Rp = C1 \cdot \frac{\text{obstruction length}}{\text{obstruction area}^2}$$

Where: $C1 = 8 \cdot \pi \cdot (\text{blood viscosity})$
Blood viscosity = 0.03 (g/cm·s)

$$Rt = C2 \cdot \left(\frac{1}{\text{obstruction area}} - \frac{1}{\text{normal vessel area}}\right)$$

where: $C2 = \frac{\text{blood density}}{0.266}$
Blood density = 1.0 (g/cm^3)

$$Pgrad = Q \cdot (Rp + Q \cdot Rt)$$

where: Q = mean coronary blood flow (ml/s)

Formulae:
Pgrad = derived theoretical pressure gradient across the stenosis;
Rp = Poiseuille resistance;
Rt = turbulent resistance.

critical determinant of the lesion's severity (7, 25, 38, 41). Estimates of percent diameter stenosis and minimal luminal cross-sectional area obtained by the Brown-Dodge computer-assisted quantitative coronary angiography method have been compared with a physiologic parameter of lesion severity, the reactive hyperemic response obtained during cardiac surgery by means of a pulsed Doppler velocity probe (25). It was shown that while the percent diameter stenosis did not accurately predict the hemodynamic significance of a coronary stenosis, the minimal cross-sectional area could distinguish between a normal and an abnormal reactive hyperemic response, and thus may be useful in evaluating the hemodynamic significance of a (residual) stenosis. Although quantitative computer-based methods of analysis have enhanced objectivity, some pitfalls still exist. For one, the presence of overlapping branches interferes with quantitative analysis of lesion severity from coronary angiograms. Also, various sources of variation in the angiographic data acquisition can be distinguished:

1. Differences in the angles and height levels of the X-ray gantry with respect to the patient at the time of repeat angiography, versus those used at the time of the (pre-)intervention study;

2. Differences in vasomotor tone of the coronary arteries (pharmacologically induced or "spontaneous");

3. Variations in the quality of mixing of the contrast agent with the blood (53). Furthermore, quantification of the percentage area stenosis from diameter measurements obtained from a single angiographic view assumes a symmetric circular cross-section, an assumption which will not always be true. In a previous study in which 120 lesions were analyzed in several orthogonal projections, asymmetric lesions were seen in more than half of the cases (76). So , atherosclerotic disease

does not always involve the entire circumference of the vessel but, instead, frequently results in an asymmetric or eccentric lesion. In fact, it has been estimated that approximately 70% of coronary artery stenoses are eccentric rather than concentric in nature (18). In addition, a previous study of our own has suggested that changes in the luminal area of an artery, produced by the mechanical disruption of its internal wall as a result of angioplasty, cannot be assessed accurately from the detected contours of the vessel from a single plane angiographic view (59). The diagnostic value of this type of measurement is restricted by the fact that dilatation frequently results in irregular angiographic vascular wall outlines, so that the cross-sectional area derived from the detected contours of the vessel will overestimate the true luminal cross-sectional area. To overcome this limitation, the use of densitometry to compute cross-sectional areas is advocated, in the event that only single views are available immediately after the dilatation procedure.

In conclusion, when the efficacy of angioplasty is to be assessed by quantitative diameter measurements, the available evidence suggests that the severity of the (re)stenosis should be quantified from multiple angiographic views - orthogonal if possible - and then averaged.

Coronary flow reserve

In view of the shortcomings of visual interpretation of the coronary angiogram, and because the functional significance of a coronary artery stenosis derives from the effect of the lesion on regional coronary blood flow, some investigators consider the assessment of the myocardial hyperemic response (coronary flow reserve) a useful method of quantifying the early and late results of angioplasty (45). Various investigators have found that the hyperemia to baseline flow ratio accurately reflects coronary flow reserve (CFR) (17, 27, 70), when defining the hyperemic myocardial contrast appearance time as the time from onset of injection to maximal incremental appearance of contrast in a given myocardial region (in the case of PTCA the myocardial perfusion bed distal to the stenosis dilated). While a linear relation exists between translesional pressure drop and the CFR ($r=0.87$, $p<0.0001$) (45), there is an inverse relation between percent diameter stenosis and CFR ($r=-0.66$) (35). Previous work on CFR at our own laboratory, as assessed by the coronary vasodilatory response after 10 mg of intracoronary papaverine, has shown the following. Both percentage area stenosis ($r=0.92$) and the minimal luminal cross-sectional area ($r=0.92$) are curvilinearly related to the CFR (79). In addition, an area stenosis in excess of 51% is associated with a diminished CFR, while a critical coronary stenosis, defined as a coronary artery with a CFR$\leq$1, exists when the area stenosis is greater than 90%. Although coronary flow reserve in the myocardial region supplied by the dilated vessel increases substantially after the angioplasty procedure, it has not been found to be restored to normal immediately after dilatation (3, 25, 26, 29, 45, 63, 74). There are several potential explanations for this phenomenon.

1. Since coronary flow reserve is a ratio between resting flow and maximal coronary blood flow, any increase in resting flow results in a decrease of this ratio. However, several authors using the thermodilution technique in the coronary sinus or the great cardiac vein have reported comparable resting volume flows before and after angioplasty (15, 19, 54, 58, 61).

2. Metabolic, humoral or myogenic factors could potentially play a role in limiting coronary flow reserve after angioplasty (40). The metabolic derangements (lactate, hypoxanthine, potassium) due to the dilatation seem quickly reversible (58, 61, 71), and are therefore not likely to be of major significance in this regard some time after the procedure.

Although humoral factors - such as thromboxane release by platelets (8), and diminished local vessel wall generation of prostacyclin (PGI_2) after balloon injury of the atherosclerotic arterial segment (8) - may play a role in a specific subgroup of patients with complicated angioplasty, so far no scientific evidence has been presented of persisting humoral derangement of the vasoactive regulation after angioplasty. Furthermore. a longstanding reduction in perfusion pressure distal to the stenotic lesion may induce alterations in the complex mechanism of autonomic coronary blood flow autoregulation (2). A prolonged period of time might be needed before these abnormalities subside (74). Finally, Bates et al postulate

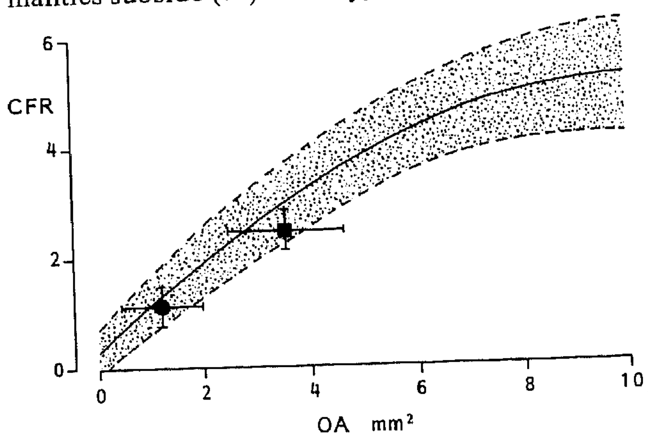

Fig. 5. Relationship between coronary flow reserve (CFR) and minimal obstruction area (OA) as previously reported (reference 79). The solid line is the best fit curve and the shaded area corresponds to the 95% confidence limits. The mean value and standard deviation of the coronary flow reserve and obstruction area before (•) and after (■) angioplasty are plotted.

that the difference in coronary flow reserve in men with normal arteries and those who underwent revascularization is inherent to the atherosclerotic disease process, which affects the microvascular reactivity (2).

3. In contradistinction, the impaired coronary flow reserve could very well be directly related to the severity of the residual stenosis. The cross-sectional area quantitatively measured immediately after angioplasty generally increases approximately threefold as a result of the procedure, but remains grossly abnormal and is still generally less than half the diameter of the inflated dilating balloon (28). In a previous study our laboratory has established the relationship between cross-sectional area and coronary flow reserve (79). A measured cross-sectional area of 3.0 to 3.5 mm^2 after angioplasty would correspond to an average coronary flow reserve of 2.5 to 3.0 (see Fig. 5).

Therefore, the persisting reduced cross-sectional area usually found immediately after PTCA is in itself a sufficient explanation for the limited restoration of coronary flow reserve, but does not exlude other contributing pathophysiologic mechanisms.

In conclusion, when the efficacy of angioplasty is to be assessed, the available evidence suggests that, for the moment, quantitative coronary angiography – with measurement of the minimal luminal cross-sectional area immediately post-PTCA – is still the method of choice.

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