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P. W. Serruys, W. Wijns, J. H. C. Reiber, P. de Feyter, M. van den Brand, F. Piscione, P. G. Hugenholtz

Thoraxcenter and Erasmus University, Rotterdam, The Netherlands

Values and limitations of transstenotic pressure gradients measured during percutaneous coronary angioplasty

Summary

The pressure gradient across coronary stenoses is measured routinely during angioplasty. Due to the finite size of the angioplasty catheter within the stenotic cross section, the remaining luminal area is further reduced and the transstenotic gradient may be overestimating the "true" pressure drop. This "true" pressure gradient can be approximated from the mean coronary blood flow and the stenosis geometry from theoretical models. Goal of this study was to assess the values and limitations of the in vivo measurements of the pressure gradient versus the calculated values. Therefore, flow in the great cardiac vein was measured in 13 patients before and/or after angioplasty of a proximal left anterior descending stenosis, not filled by collaterals. The Poiseuille and turbulent contributions to flow resistance were determined from stenosis geometry assessed by quantitative coronary angiography. A fourfold increase in the luminal area (from 0.7 mm^2 pre- to 2.8 mm^2 post angioplasty) was associated with a fourfold decrease in the in vivo measured transstenotic gradient (from 59 mm Hg pre- to 13 mm Hg post angioplasty). The occlusion area and the measured gradient were linearly correlated: gradient = 69 − 17 · occlusion area (r = 0.76). However, as expected, the transstenotic gradient systematically overestimated the theoretical gradient calculated from the laws of fluid dynamics. A nonlinear relation was found between the calculated gradient P and the occlusion area A_s: $P = 15 \cdot A_s^{-2}$ (r = 0.87).
Conclusion: The present study shows clearly that the absolute value of the transstenotic gradients obtained during angioplasty do not reflect accurately the flow resistance.

Zusammenfassung: Wertigkeit der Messung des transstenotischen Druckgradienten während perkutaner transluminaler Koronarangioplastie (PTCA)

Der Druckgradient im Bereich einer Koronarstenose wird routinemäßig während der Angioplastie gemessen, indem man bei über der Stenose liegendem Dilatationskatheter den durch das zentrale Lumen gemessenen Druck distal der Stenose vom proximalen Koronararteriendruck, gemessen an der Spitze des Führungskatheters, subtrahiert. Dieser Druckgradient wird als wichtiges Kriterium für die hämodynamische Wirksamkeit einer Koronarstenose angesehen. Allerdings ist hierbei zu berücksichtigen, daß durch den im bereits stenosierten Lumen liegenden Angioplastiekatheter (mit definierter Größe) eine weitere Reduktion des Lumens erfolgt, wodurch der „wahre" Druckabfall überschätzt werden kann. Dieser wahre Druckabfall kann unter Zuhilfenahme theoretischer Modelle der Flußgesetze aus dem mittleren Koronarblutfluß und der Geometrie der Stenose abgeschätzt werden. Ziel dieser Studie war, Wert bzw. Einschränkung von In-vivo-Messungen des Druckgradienten gegen errechnete Werte zu ermitteln. Zu diesem Zweck wurde bei 13 Patienten vor und nach perkutaner transluminaler Koronarangioplastie (PTCA) einer Stenose des proximalen Ramus interventricularis anterior (LAD) ohne Kollateraldurchblutung der Fluß in der großen Herzvene gemessen (Thermodilutionstechnik).
Aus der durch quantitative Koronarangiographie erhaltenen Geometrie der Stenose wurde der Einfluß auf den Flußwiderstand abgeleitet. Ein vierfacher Zuwachs der Lumenfläche (von 0,7 mm^2 vor PTCA zu 2,8 mm nach PTCA) war verbunden mit einem vierfachen Abfall des in vivo gemessenen transstenotischen Druckgradienten (von 59 mm Hg vor PTCA auf 13 mm Hg nach PTCA). Die Stenosefläche und der gemessene Gradient zeigten eine lineare Korrelation: Gradient = 69 − 17 · Stenosefläche (r = 0,76). Allerdings wurde, wie erwartet, der gemessene transstenotische Gradient im Vergleich zum theoretischen Gradienten, errechnet aus Flußgesetzen, überschätzt. Zwischen errechnetem Gradienten (P) und Stenosefläche (A_s) wurde eine nichtlineare Relation gefunden: $P = 15 \cdot A_s^{-2}$ (r = 0,87). Ein starker Anstieg des Gradienten ergab sich, wenn eine kritische Stenosefläche von 1 mm unterschritten wurde.

With the technical assistance of P. van Eldik-Helleman and C.J. Kooyman, MSc.

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Die vorliegende Untersuchung zeigt somit eindeutig, daß der absolute Wert des transstenotischen Druckgradienten, gemessen während PTCA, nicht exakt auf den Flußwiderstand, also die hämodynamische Wirksamkeit, schließen läßt. Dennoch erscheint die Reduktion des Druckgradienten von großer klinischer Bedeutung sowohl für die Beurteilung der Effektivität einer PTCA als auch hinsichtlich der Vorhersage einer möglichen Restenosierung.

Since the introduction of percutaneous coronary angioplasty (PTCA), the pressure distal to the stenosis is measured routinely through the central lumen of the dilatation catheter [5]. Subtracting this pressure from the proximal coronary pressure recorded from the guiding catheter tip yields the transstenotic pressure gradient. This gradient represents the loss of energy as blood traverses the stenosis and is an important determinant of ischemia. However, the accuracy of the absolute value of the transstenotic gradients measured during PTCA must be questioned as the presence of the dilatation catheter further reduces the luminal area.

Leiboff et al. [8] have shown in canine femoral arteries that the transstenotic gradient overestimated the "true" gradient in a predictable manner, which is dependent on the ratio of the diameter of the angioplasty catheter diameter to the stenosis diameter. In order to further characterize this relation in the coronary artery bed of humans, we compared the transstenotic gradient with the theoretical pressure drop calculated from fluid mechanic equations for steady flow of an incompressible fluid in rigid tubes. Therefore, the stenosis geometry was analyzed by quantitative coronary cineangiography and the mean myocardial blood flow was measured by the thermodilution technique in a selected group of patients with proximal left anterior descending coronary artery disease.

Patients and methods

13 patients with exertional angina pectoris were studied; all were candidates for PTCA of an isolated proximal left anterior descending stenosis. The distal part of the vessel was not filled by collaterals, as judged from angiography.

The subjects gave informed consent and no complications resulted from the study. Details regarding the PTCA technique used in our laboratory have been previously described [12, 15].

The mean transstenotic pressure gradient was measured with the dilatation catheters and calculated on line after a data acquisition period of 20 seconds [2].

The flow in the great cardiac vein, which must be known for the calculation of the theoretical gradient (see below), was obtained with a Baim catheter using the thermodilution technique [1, 14]. The position of the catheter was confirmed by dye injection before and after PTCA. Measurements were included only if selective sampling from the anterior vein was possible. Such selective great cardiac vein flows were available before PTCA in three patients, after PTCA in three patients, and before and after in seven patients. Thus, 20 data points were available for comparison. The coronary cineangiograms were analyzed by CAAS, our computer-assisted Coronary Angiography Analysis System, which has been described extensively elsewhere [10, 11, 13]. Briefly, this system allows an objective and reproducible quantitation of coronary stenosis. A region in a 35 mm cineframe encompassing the selected arterial segment is optically magnified and converted into video format by means of a specially constructed cine-video converter and digitized for subsequent analysis by computer. Contours of the arterial segment are detected automatically on the basis of first and second derivative functions: contour positions are corrected for pincushion distortion from the image intensifiers. The dimensions of the minimal obstruction area and normal reference area are presented in mm^2. The calibration factor is derived from a computer processed segment of the contrast catheters. From the arterial contour data, a diameter-function (D-function) is computed. The minimal obstruction diameter and a reference diameter, approximated by the interpolated diameter technique [10, 11, 13], are expressed in mm (Figures 1a and 1b). Assuming circular cross sections at the obstructive and reference positions, corresponding luminal areas (mm^2) are calculated. The length of the stenotic segment was determined from the diameter function on the basis of curvature analysis of the D-function and expressed in mm.

The same angiographic projection was used before and after PTCA, except for two post-PTCA lesions where the mean value from two orthogonal projections was used. An example of a coronary arterial analysis is shown in Figures 1a and 1b, as well as a schematic representation of the measured parameters (Figure

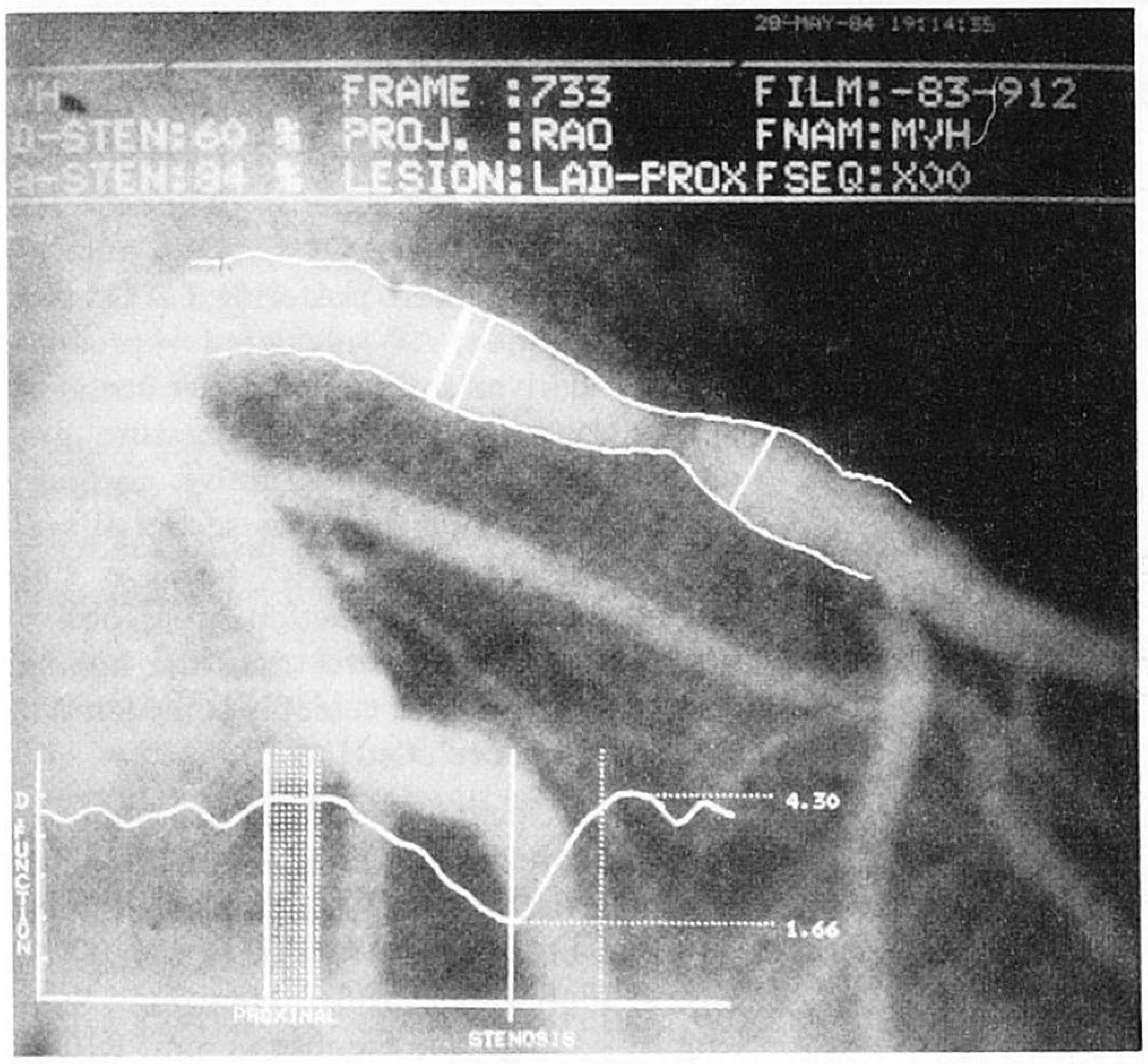

Figure 1a – Abbildung 1a

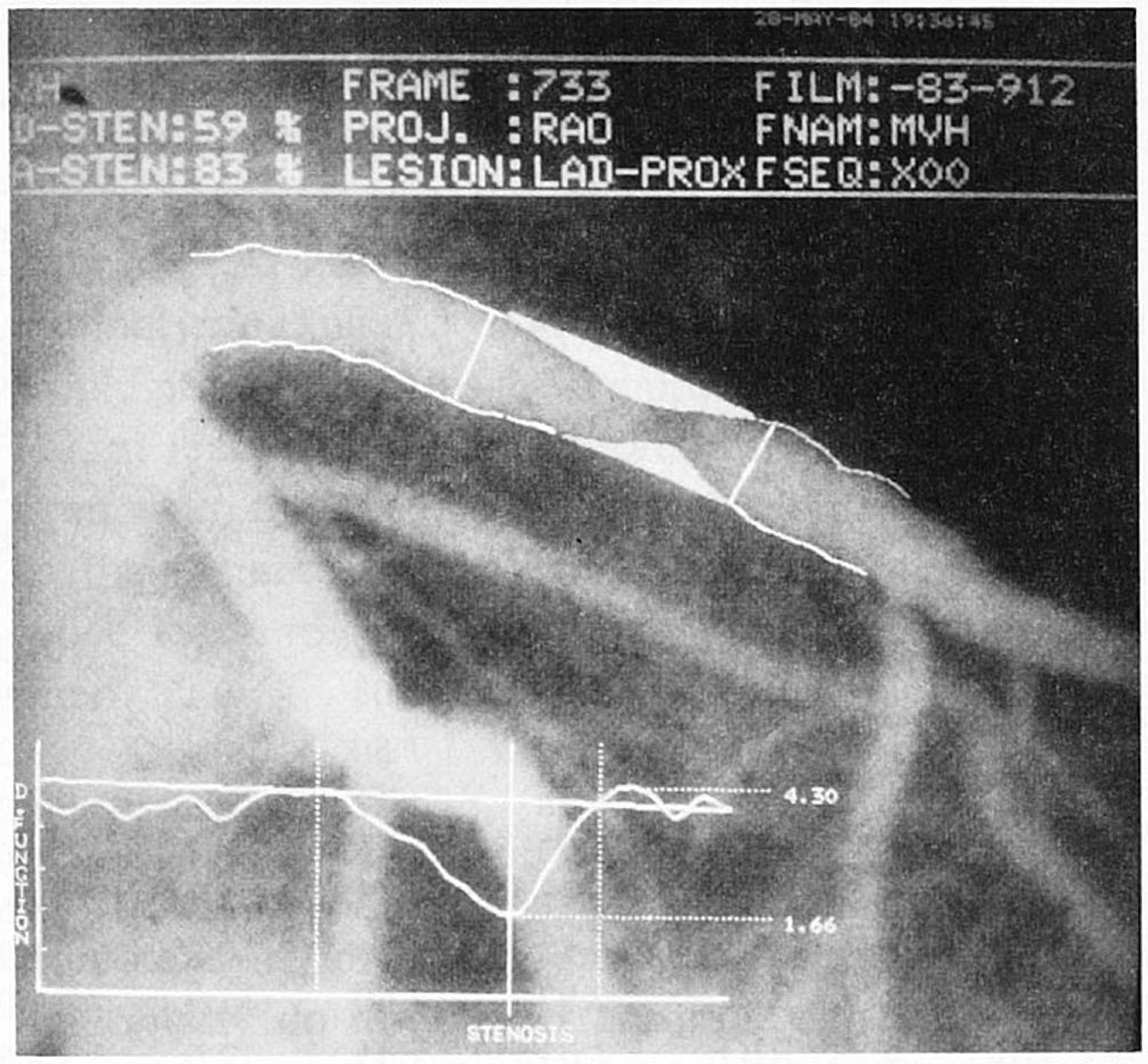

Figure 1b – Abbildung 1b

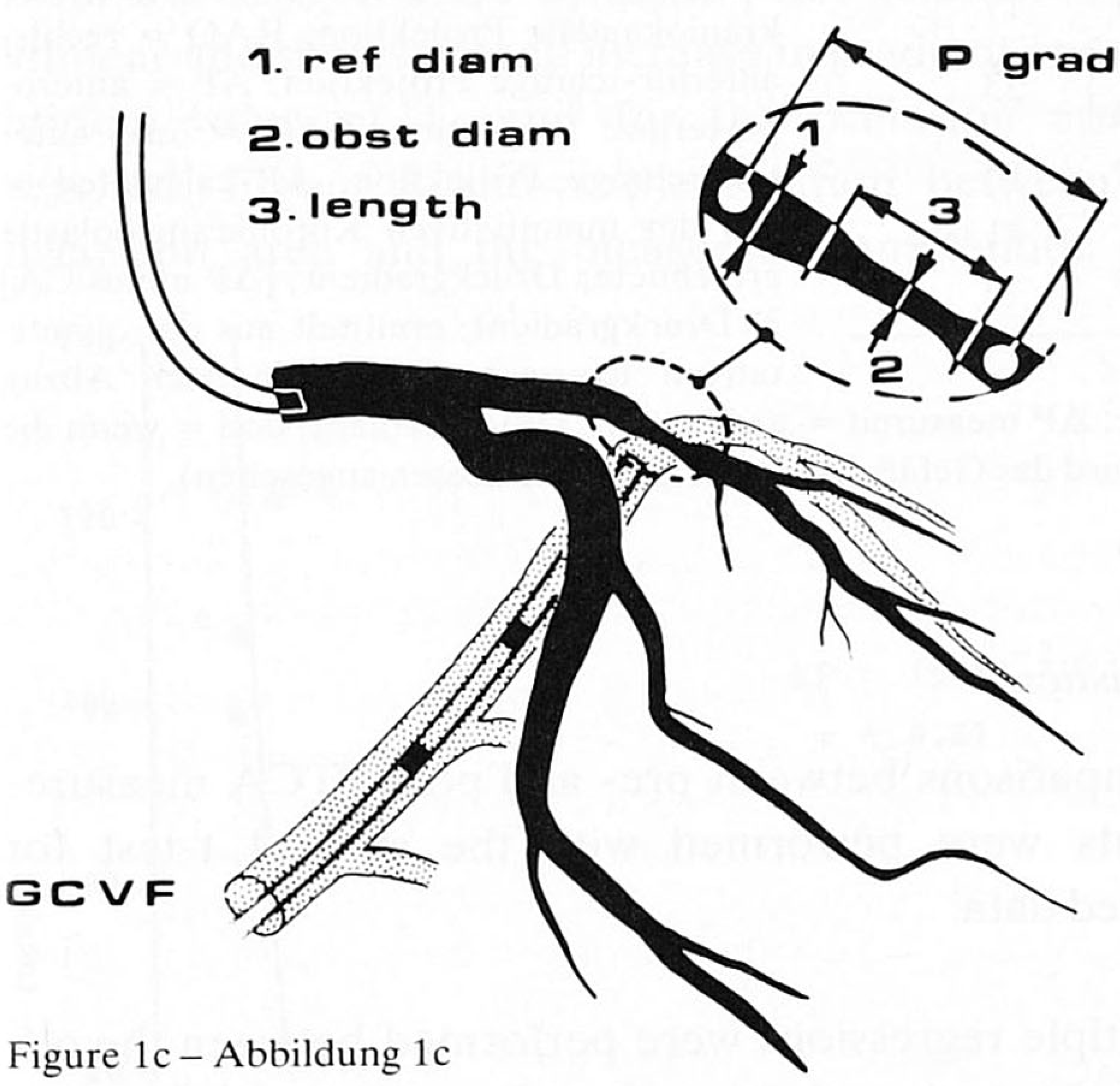

Figure 1c – Abbildung 1c

Figures 1a to 1c. Detected contours for a representative left anterior descending coronary artery stenosis superimposed on the original video image. The diameter function is shown on the bottom. – a) The reference diameter (or area) was selected proximal to the stenosis. The calibrated diameter values in mm are plotted along the ordinate strating from the proximal to the distal part of the analyzed segment along the abscissa. A percent area stenosis of 84% results. – b) The normal size of the artery over the obstruction has been estimated by the interpolated method. The resulting reference contours are shown and the difference in area between this boundary and the detected contours is a measure of the atherosclerotic plaque (shaded area). A percent stenosis of 83% results. – c) Schematic representation of the coronary artery with the guiding catheter in the ostium (top left), the thermodilution catheter in the coronary sinus (bottom left) measuring the great cardiac vein flow (GCVF). The inset (top right) shows how the transstenotic pressure gradient was measured (between the white dots). The theoretical pressure drop was calculated from 1. the reference diameter (or area) shown proximal to the stenosis for the seek of clarity; 2. the obstruction diameter (or area) and 3. the length of the stenosis.

Abbildungen 1a bis 1c. Ermittelte Umrisse für eine repräsentative Stenose des Ramus interventricularis anterior (LAD) in Projektion auf das Originalvideobild. Unten die graphische Darstellung (Diameterfunktion). – a) Der Referenzdurchmesser (bzw. -fläche) wurde proximal der Stenose gewählt. Auf der Ordinate finden sich die ermittelten Diameterwerte entsprechend der auf der Abszisse aufgetragenen Lokalisation vom proximalen bis zum distalen Teil des analysierten Segments. Es resultiert eine prozentuale Flächenreduktion von 84%. – b) Durch Interpolation ist die normale Weite der Arterie im Bereich der Obstruktion abgeschätzt worden. Die resultierenden Referenzkonturen sind aufgetragen; die Differenz zwischen dieser Umgrenzung und den angiographisch ermittelten Konturen wird durch atherosklerotische Plaques verursacht (schraffierter Bereich). Es resultiert eine 83%ige Stenose (Flächenreduktion). – c) Schematische Darstellung einer Koronararterie mit Führungskatheter im Ostium (oben links) und Thermodilutionskatheter im Koronarsinus (unten links) zur Messung des Flusses in der großen Herzvene (GCVF). Der Ausschnitt oben rechts zeigt, wie der transstenotische Druckgradient gemessen wurde (zwischen den weißen Markierungen). Der theoretische Druckabfall wurde errechnet unter Berücksichtigung des Referenzdiameters (bzw. Fläche) proximal der Stenose, des Stenosedurchmessers (bzw. Fläche) und der Länge der Stenose.

1c). From an extensive validation study of the analysis procedure it has been shown that the variability (standard deviation of the differences) of repeated coronary acquisition and computer analysis is less than 0.22 mm for absolute arterial dimensions in a well-controlled study [11].

The theoretical pressure gradient was calculated according to the well-known formulas described in the literature [3, 6]:

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

where Pgrad is the theoretical pressure drop (mm Hg)

No.	Patient name		Angio view	Occlusion area (mm^2)	GCV flow (ml/s^{-1})	Sten. length (mm)	ΔP calculated	(−AC)	ΔP measured
1	PO	b	RIO	0.96	2.13	7.0	18.9	–	80 occl
			LSO	0.79		9.9	52.2	–	
2	VY	b	RAO	1.19	1.20	12.0	13.5	39.5	59
		a	CRA	2.43	1.52	7.3	1.9	3.9	5
		a	RAO	4.26		11.9	0.8	1.2	
3	MA	b	RIO	1.52	1.40	7.9	5.5	18	59
		a	RIO	3.84	1.62	6.8	0.8	1.3	12
4	BO	b	LSO	1.47	1.02	7.5	3.5	12.3	69
5	ME	b	RAO	0.34	1.42	10.0	107.2	–	62 occl
		a	RIO	2.64	2.08	9.1	1.9	4.6	28
6	BE	a	LSO	1.87	1.50	6.4	3.2	8.3	4
7	HE	b	CRA	0.48	1.27	8.8	8.2	–	71 occl
		a	CRA	1.93	1.45	8.7	4.6	9.1	18
8	BA	b	RAO	0.57	1.23	14.3	55.6	–	56 occl
		b	RIO	0.53	1.23	10.8	51.9	–	52 occl
		a	RIO	2.97	1.50	11.3	1.0	2.8	11
9	GR	a	RIO	1.63	1.45	12.0	8.5	19.6	13
10	MA	b	RAO	2.38	1.68	6.9	2.3	5	48
		a	AP	3.41	1.85	10.5	0.9	2.1	17
11	PI	a	RIO	2.06	1.63	8.9	4.2	7.9	23
		a	LAO	3.08		4.1	0.8	1.4	
12	EC	a	RAO	2.88	1.33	13.1	1.5	3.2	13
13	VE	b	RAO	0.32	1.23	8.5	122.5	–	41 occl
		a	RAO	2.04	1.67	6.6	3.3	3.8	5

Table 1. Measured versus calculated gradient (b = before angioplasty; a = after angioplasty; angio = angiographic; GCV = great cardiac vein; RIO = right inferior oblique; LSO = left superior oblique; CRA = cranio-caudal; RAO = right anterior oblique; AP = antero posterior; LAO = left anterior oblique; ΔP calculated = pressure gradient derived from quantitative coronary angiography; [ΔP − CA] = pressure gradient derived from quantitative coronary angiography, when the cross sectional area of the angioplasty catheter [AC] is subtracted from the obstruction area; occl = when AC area is greater than the luminal obstruction area, the vessel is considered to be completely occluded [occl]).

Tabelle 1. Gegenüberstellung der gemessenen und errechneten Gradienten (b = vor Angioplastie; a = nach Angioplastie; angio view = angiographische Projektion; GVC flow = Fluß in der großen Herzvene; Sten. length = Länge der Stenose in mm; RIO = rechts-inferior-schräge Projektion; LSO = links-superior-schräge Projektion; CRA = kraniokaudale Projektion; RAO = rechts-anterior-schräge Projektion; AP = antero-posteriore Projektion; LAO = links-anterior-schräge Projektion; ΔP calculated = aus der quantitativen Koronarangioplastie errechneter Druckgradient; [ΔP minus CA] = Druckgradient, ermittelt aus der quantitativen Koronarangiographie nach Abzug der Querschnittsfläche des Angioplastiekatheters [AC] von der Stenosefläche; ΔP measured = gemessener Druckgradient; occl = wenn die Querschnittsfläche des Angioplastiekatheters größer als die Stenosefläche ist, wird das Gefäß als vollständig verschlossen angesehen).

over the stenosis, Q the mean coronary blood flow (ml/s), Rp the Poiseuille resistance and Rt the turbulent resistance. These resistances have been defined as follows:

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

where C1 = 8 · (blood viscosity) with

blood viscosity = 0.03 (g/cm · s)

$$Rt = C2 \left(\frac{1}{\text{obstruction area}} - \frac{1}{\text{normal distal area}}\right)^2$$

$$\text{where } C2 = \frac{\text{blood density}}{0.266} \text{ with}$$

blood density = 1.0 (g/cm^3).

In the formulas given above, the obstruction area calculated from the coronary cineangiograms must be corrected for by the cross-sectional area of the dilatation catheter; for this catheter area the value of 0.64 mm^2 was used.

Statistics

Comparisons between pre- and post-PTCA measurements were performed with the student t-test for paired data.

Multiple regressions were performed between the obstruction area and either the measured or the theoretical gradient until the best fit was obtained. The individual data are tabulated in Table 1.

Results

The median values and the ranges for the obstruction area, the measured gradient and the theoretical gradient are shown in Table 2. A fourfold increase in the luminal area was associated with a fourfold decrease in the measured gradient; however, the absolute values for the transstenotic gradient were consistently larger than the theoretical gradient. No changes in the reference area or in the length of the stenosis were observed. The resting blood flow increased slightly but not significantly from 1.3 to 1.6 ml/s. The relation

	GCVQ (ml/s)	Obstruction area (mm²)	ΔP (mmHg)	GRAD (mmHg)
Before	1.3 (1.0–2.1)	0.7 (0.3–2.4)	44 (2–122)	59 (41–80)
		*	*	*
After	1.6 (1.3–2.1)	2.8 (1.9–3.8)	2 (1–5)	13 (4–28)

* = $p<0.005$.

Table 2. Hemodynamic and angiographic measurements before and after PTCA. – The medium value and the range are given. (GCVQ = great cardiac vein flow; ΔP = theoretical or calculated pressure drop; GRAD = measured or transstenotic gradient.)

Tabelle 2. Hämodynamische und angiographische Messungen vor und nach PTCA (Mittelwerte und Abweichungsbereich). (GCVQ = flow in der großen Herzvene; ΔP = theoretischer oder kalkulierter Druckabfall; GRAD = gemessener transstenotischer Gradient.)

between the occlusion area and the theoretical pressure drop (Figure 2) was best fitted by the equation: $P = a \cdot (\text{occlusion area})^b$; where P = theoretical gradient, a = 15 and b = −2 (r = 0.87). As expected from the laws of fluid dynamics, this relation is curvilinear and shows a steep increase in gradient once the critical value of 1 mm² for the occlusion area is reached. Figure 3 shows the relation between the occlusion area and the measured transstenotic gradient, which was best fitted by the linear equation: GRAD = a − b occlusion area, where GRAD = measured gradient, a = 69 and b = 17 (r = 0.76). According to this relation, the average gradient measured after PTCA, i.e. 13 mm Hg, would correspond to a luminal area of 3.3 mm². The theoretical relation would predict with this area, a pressure drop of 1.4 mm Hg, at least within the observed range of flow. Thus, even when the lumen of the vessel is large as compared to the diameter of the angioplasty catheter, its presence leads to an overestimation of the "true" gradient.

Discussion

The present study shows that the absolute value of the transstenotic pressure gradients obtained during angioplasty do not reflect accurately the flow resistances. As suggested by others [4, 8], this is related to the presence of the angioplasty catheter across the stenosis, further reducing its minimal luminal area. These findings are not surprising, but were until recently [16] never demonstrated in human coronary arteries. The data also show that calculation of

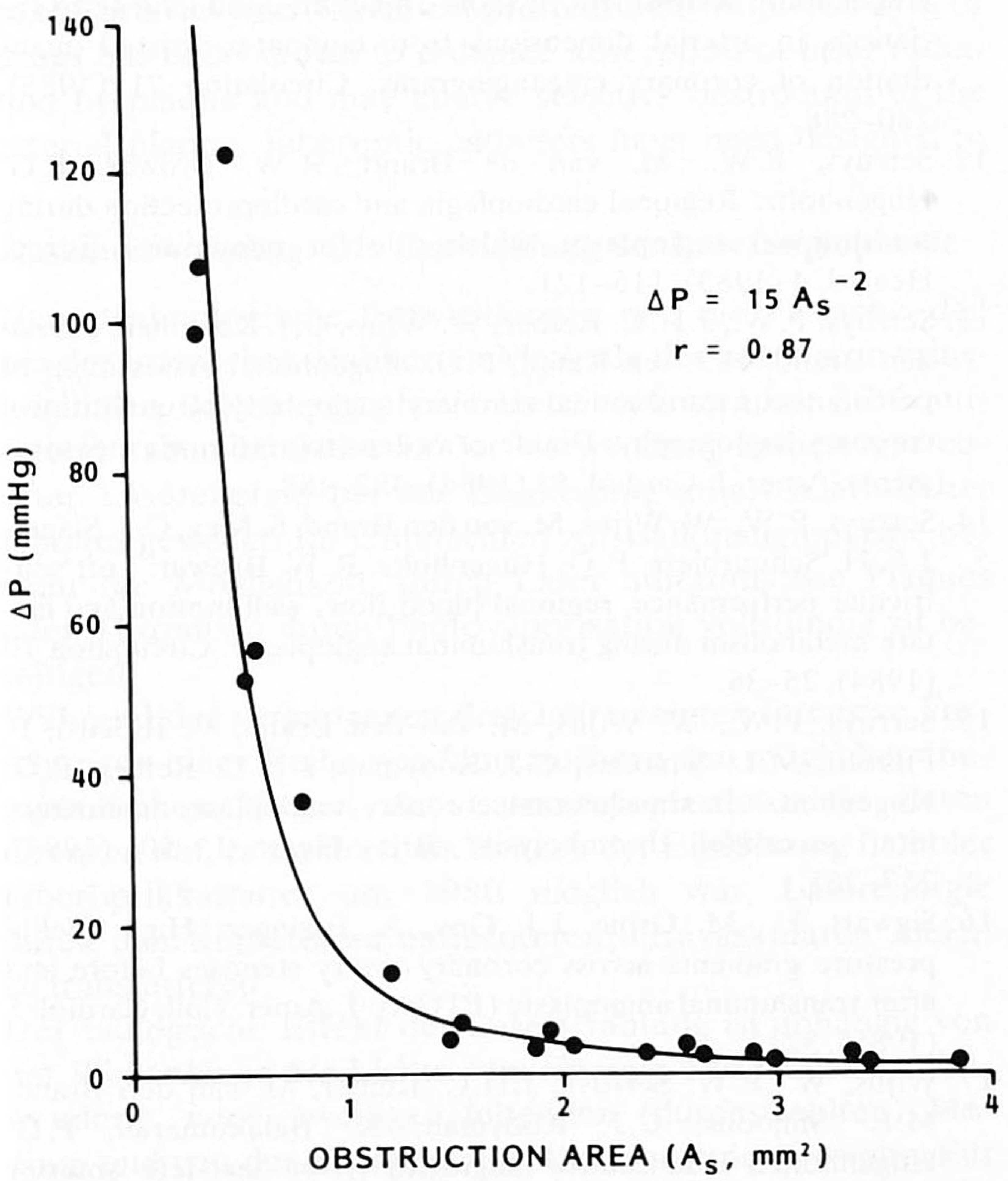

Figure 2. Curvilinear relationship between the obstruction area (A_s) and the theoretical pressure gradient (ΔP). The relation is best fitted (r = 0.87) by the equation: $P = 15 \cdot A_s^{-2}$.

Abbildung 2. Kurvolineares Verhältnis zwischen Stenosefläche (A_s) und theoretischem Druckgradienten (ΔP); die Relation ist am besten wiedergegeben (r = 0,87) durch die Gleichung $P = 15 \cdot A_s^{-2}$.

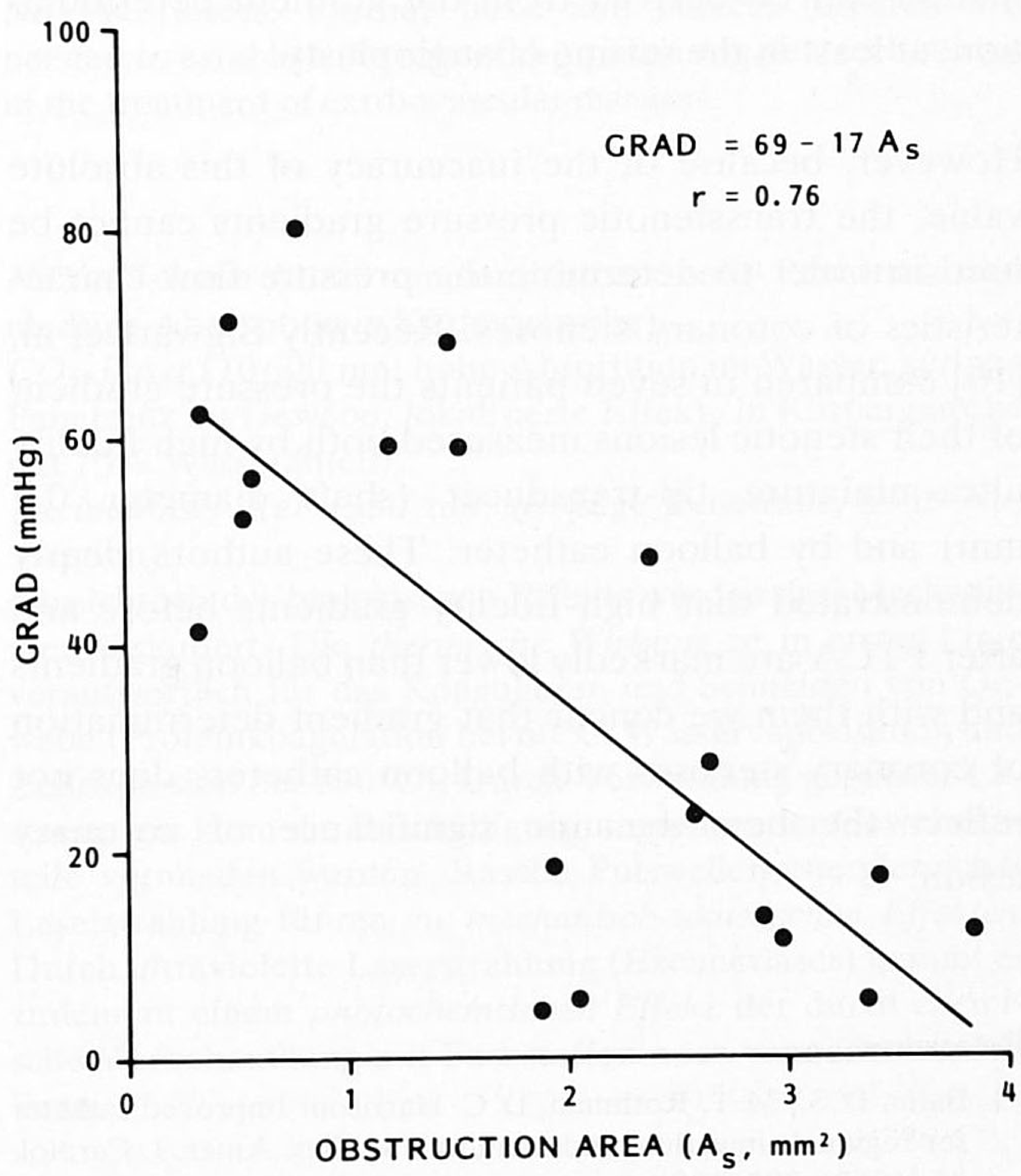

Figure 3. Linear relation between the obstruction area (A_s) and the transstenotically measured gradient (GRAD): GRAD = 69 − 17 · A_s (r = 0.76).

Abbildung 3. Lineares Verhältnis zwischen Stenosefläche (A_s) und dem transstenotisch gemessenen Druckgradienten (GRAD): GRAD = 69 − 17 · A_s (r = 0,76).

theoretical pressure gradients on the basis of an hypothetical coronary blood flow could result in inaccurate numbers as the range of flows that we measured was rather large, even at rest (from 1.02 to 2.13 ml/s).

These findings may seem, at first glance, contradictory to previous reports, including ours. Many investigators indeed have shown good correlations between the transstenotic pressure gradient and other estimates of the physiologic significance of a lesion, such as clinical symptoms [4], results of thallium scintigraphy [7] or measurements of the coronary flow reserve [9]. Very often, relatively poor correlations were found with the angiographically defined degree of stenosis. However, these studies were using visual analysis of angiograms. Using an objective and accurate quantitation of the angiograms, we found good correlations both for the angiographic and hemodynamic measures of the physiological significance of the stenosis [17].

The reduction of the gradient after dilatation as well as the predictive value of the residual gradient for later restenosis (A.R. Grüntzig, personal communication) are of great clinical value. This shows that useful information can be derived from the gradient determination, at least in the setting of angioplasty.

However, because of the inaccuracy of this absolute value, the transstenotic pressure gradients cannot be used in order to determine the pressure flow characteristics of coronary stenoses. Recently Sigwart et al. [16] compared in seven patients the pressure gradient of their stenotic lesions measured both by high fidelity ultra-miniature tip-transducer (shaft diameter 0.7 mm) and by balloon catheter. These authors clearly demonstrated that high fidelity gradients before and after PTCA are markedly lower than balloon gradients and with them we concur that gradient determination of coronary stenoses with balloon catheters does not reflect the hemodynamic significance of coronary lesion.

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Address all correspondence to: Patrick W. Serruys, M.D., Catheterization Laboratory, Thoraxcenter, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands.