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Intracoronary Blood Flow Velocity and Transstenotic Pressure Gradient Using Sensor-Tip Pressure and Doppler Guidewires: A New Technology for the Assessment of Stenosis Severity in the Catheterization Laboratory

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In a patient undergoing percutaneous balloon angioplasty of a stenotic proximal right coronary artery the transstenotic pressure gradient was measured using a 0.018″ guidewire with a distal optical microsensor. Blood flow velocity was measured proximal to the stenosis using a 0.018″ Doppler guidewire. Transstenotic pressure gradient and blood flow velocity were measured in baseline conditions and after intracoronary injection of 12.5 mg of papaverine. Coronary blood flow was calculated from the measured blood flow velocity and the corresponding cross-sectional area. The measured pressure gradients were compared with the values derived from the stenosis geometry assessed with quantitative coronary angiography (automated edge detection measurements in two orthogonal views, assuming an elliptical cross-sectional area).

The measured transstenotic pressure gradient was 15 mm Hg in baseline conditions and 42 mm Hg at the peak effect of the papaverine injection. A 50% flow velocity increase was observed at peak hyperemia (time-averaged maximal flow velocity = 30 cm/s before and 45 cm/s after papaverine). The transstenotic pressure gradient calculated from the measured stenosis geometry was 20 mm Hg and 42 mm Hg in baseline and hyperemic conditions, respectively.

The combined use of a pressure and a Doppler guidewire provides a complete assessment of the transstenotic pressure/coronary flow velocity relation at rest and after pharmacologically induced hyperemia and allows the characterization of stenosis hemodynamics and functional severity.

Key words: quantitative coronary angiography, coronary blood flow, intravascular ultrasound

INTRODUCTION

A 58 year-old man was referred to our Hospital because of disabling effort angina and presence during a maximal bicycle stress test of horizontal ST-segment depression at 125 Watts in the infero-lateral leads despite a tailored maximal medical therapy. Selective coronary angiography of the native coronary arteries showed a severe proximal stenosis of the right coronary artery without visible collateral circulation from the left coronary artery which was free from significant narrowings. Left ventricular function was normal. An 8F soft-tip Judkins guiding catheter was used to selectively cannulate the right coronary artery. Two coronary angiograms were performed after intracoronary injection of 3 mg of isosorbide dinitrate in a 30° RAO view and a 60° LAO view. The catheter was filmed not filled with contrast medium in the same projections for calibration [1] and cineangiography was performed at 25 frames/s with a 5″ field of view. A previously described and validated [2–4] computer-assisted automatic quantitative coronary angiographic analysis system (CAAS) was used for the analysis of the selected end-diastolic cineframe using a geometric technique (Fig. 1A,B). The automatic mea-

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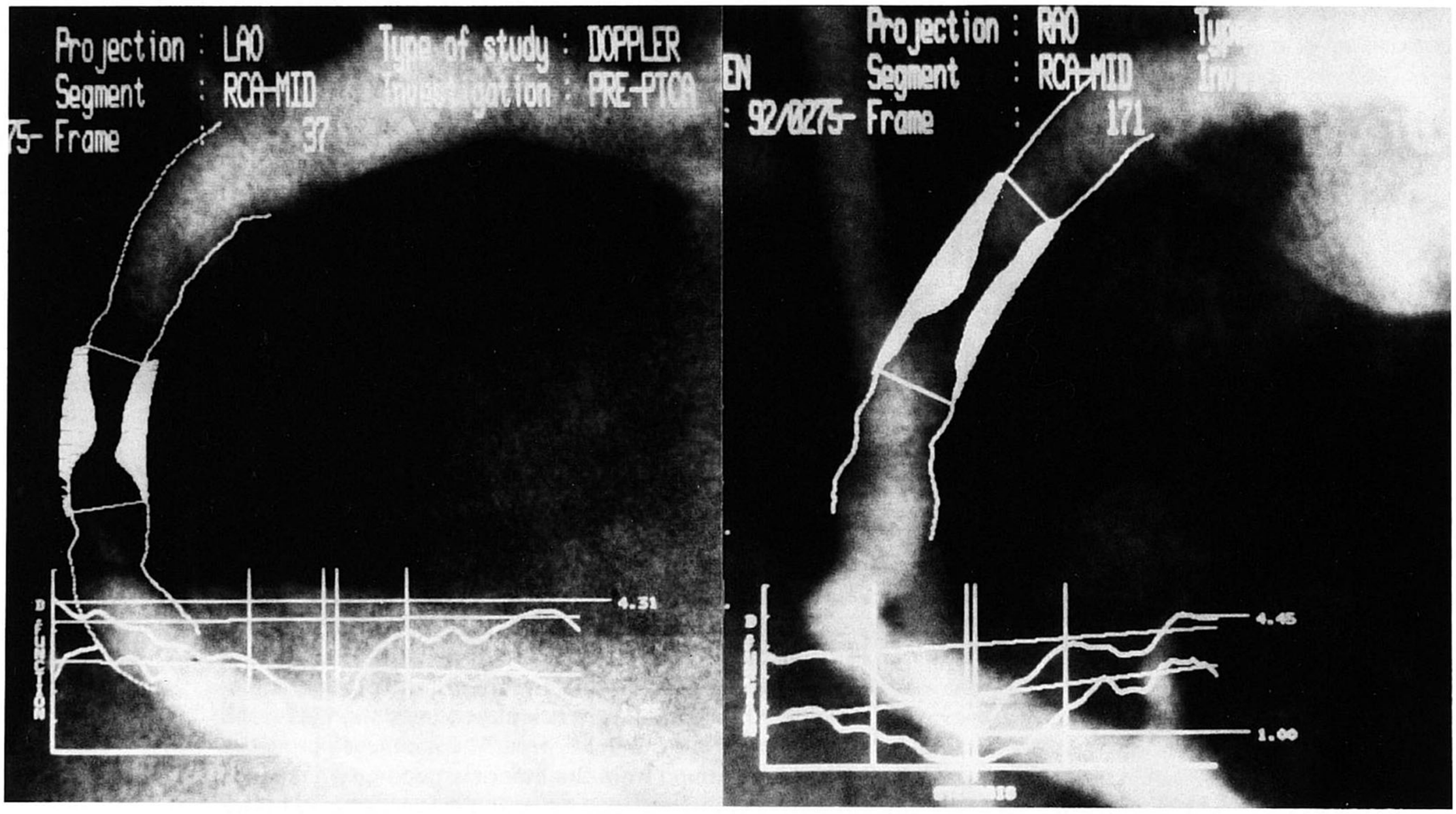

Fig. 1. Biplane orthogonal cineangiograms (A: LAO, B: RAO) of a right coronary artery showing the presence of a significant concentric stenosis of the middle segment. The magnified image has been digitized into a 512 × 512 pixel matrix corresponding to < 0.1 mm/pixel with the 5″ field of view of the image intensifier used. The diagram shows the measured diameter of the examined segment after automatic contour detection and the filled white areas outside the stenosis lumen represent the automatically reconstructed (interpolated technique) original lumen profile where the diameter of the reference segment is measured.

surement of the reference diameter was performed with an interpolated technique and was used for the calculation of percent diameter and cross-sectional area (CSA) stenosis. Based on the measured stenosis geometry the hemodynamic parameters were calculated according to Appendix A.

After intravenous injection of heparin 10,000 I.U. and acetylsalicylic acid 250 mg a 12 MHz 0.018″ (diameter = 0.46 mm) Doppler guidewire [5] (Cardiometrics, Mountain View, CA, USA) was introduced into the proximal right coronary artery and blood flow velocity (BFV) was measured in the first segment of the right coronary artery (arrow in Fig. 2A). No major side-branches were interposed between Doppler measurement site and the stenosis. Cineangiography (LAO 60°, Fig. 2A) was repeated with the Doppler guidewire in place in order to measure the vascular diameter at the site of the Doppler sample volume (5.2 mm distance from the guidewire tip). A constant CSA was assumed throughout the procedure as a result of the pretreatment with intracoronary nitrates [6]. From the time-averaged maximal BFV, automatically calculated for two consecutive beats from the spectral Doppler envelope (Fig. 3), mean BFV was calculated as described in Appendix B. Coronary blood flow was then calculated as the product of CSA at the site of the Doppler measurement times mean BFV. A 0.018″ (diameter 0.46 mm) guidewire with a fiber optic pressure microsensor 3 cm from its tip (RadiMedical Systems, Uppsala, Sweden) was calibrated immediately before insertion and subsequently introduced into the proximal right coronary artery [7]. After recording of the proximal intracoronary pressure for comparison with the measurements obtained in the same position through the guiding catheter (Fig. 2C) the pressure guidewire was advanced across the stenosis (Fig. 2B) and the transstenotic pressure gradient was measured (Fig. 2D). The signals received simultaneously from the control unit of the fiber optic pressure sensor and from a Statham-Gould pressure transducer connected to the guiding catheter were transmitted to a computer-assisted central work station. Systolic, diastolic, mean pressures, and mean pressure gradient were automatically measured from 4 sinus beats selected from a continuous recording of 16 s [8] (Fig. 2C,D).

After intracoronary injection of 12.5 mg of papaverine through the guiding catheter, the transstenotic pressure gradient and BFV were continuously measured up to the

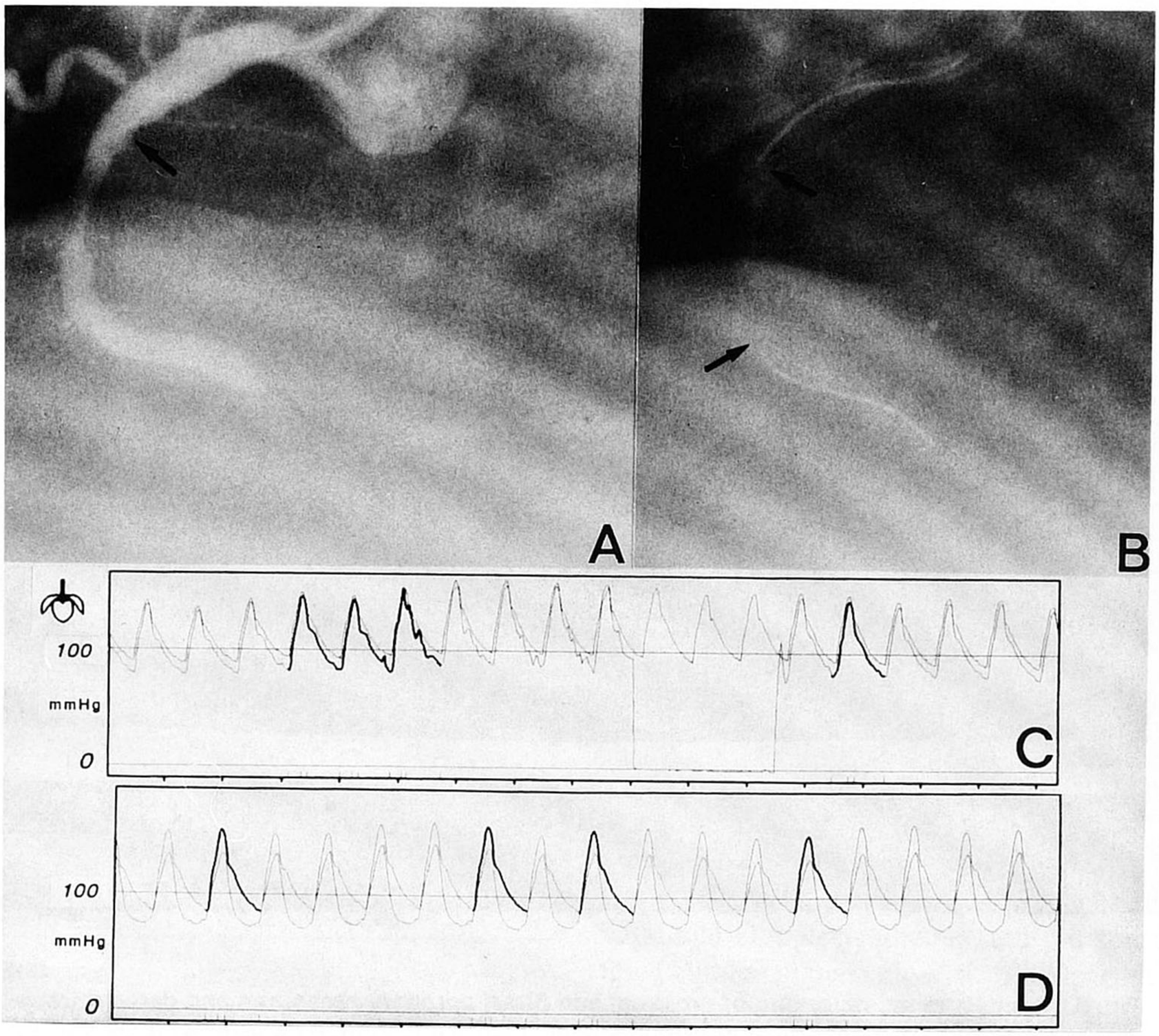

Fig. 2. A: Cineangiogram of the right coronary artery showing the position of the Doppler guidewire, proximal to the stenosis (arrow). The position of the pressure sensor, at the junction between more radioopaque floppy distal tip and body of the guidewire, is better appreciated in the image without contrast (B, arrow). In C and D the almost complete superimposition of proximal and distal coronary pressures with the pressure transducer proximal to the stenosis (C) can be compared with the moderate pressure gradient observed in baseline conditions when the guidewire was advanced distal to the stenosis (D).

end of the papaverine effect (return to baseline around 3 min after injection). An off-line beat-to-beat program of analysis of the pressure signal was used to measure proximal and post-stenotic coronary pressures corresponding to the video-recorded on-line measurements during the pharmacologically induced hyperemic reaction [8] (Fig. 3). Thirty-five minutes was necessary for the complete acquisition of the pressure and BFV signals and the quantitative angiographic procedure. The patient subsequently underwent successful coronary balloon angioplasty.

ANALYSIS OF THE RESULTS

The results of the QCA, Doppler, and pressure measurements and derived parameters in baseline conditions and at the peak effect of the papaverine injection are summarized in Table I. Table II compares the transstenotic pressure gradient measured with the micromachined pressure optical sensor and the pressure gradient estimated from the QCA geometric measurements and the measured BFV. For this last calculation the CSA of the pressure guidewire (0.17 mm^2) was subtracted from the CSA of the reference segment and of the stenosis.

The injection of papaverine 12.5 mg induced a prolonged increase of BFV and transstenotic pressure gradient (maximal values reported in Table I and shown in Fig. 3). In Figure 4 the proximal and post-stenotic coronary pressures recorded following the injection of papaverine (peak effect-restoration of baseline conditions) are plotted against the corresponding BFVs (measurement of two consecutive beats every 8 s).

In Figure 5 the distal coronary pressure measurements after papaverine injection are plotted against the measured coronary flow, shown as a ratio to baseline flow at rest according to the method proposed by Kirkeeide et al. [9]. With this method coronary blood flow is normally cal-

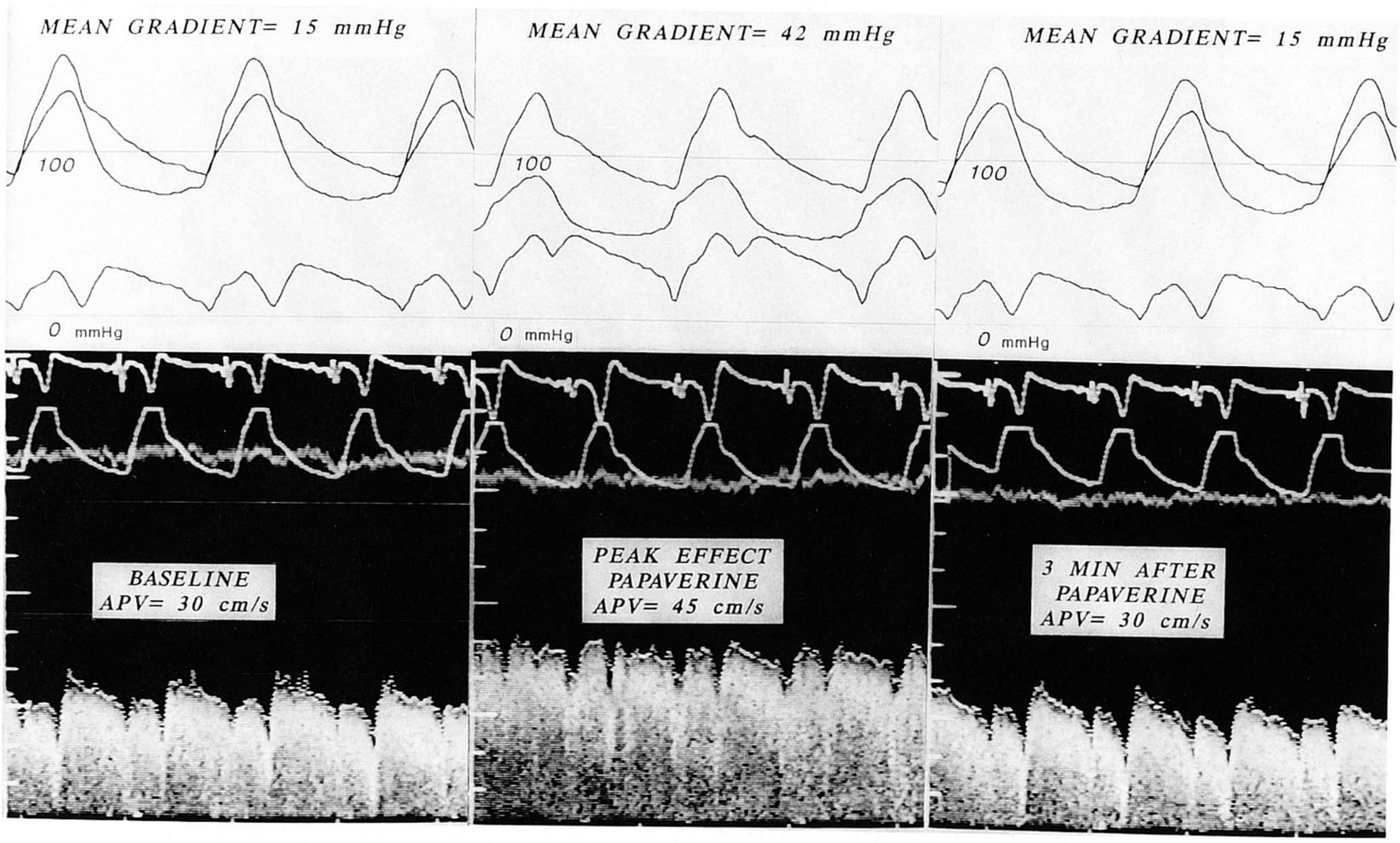

Fig. 3. Simultaneous recording of proximal and distal coronary pressures and derived transstenotic pressure gradient (lower line) immediately before injection of papaverine (baseline, on the left), at peak hyperemia (middle), and 3 min after restoration of baseline conditions (on the right). The corresponding Doppler tracings are shown in the lower images. Note the automatic detection of the maximal BFV (dotted line tracking the Doppler envelope obtained from the spectral analysis of the signal). The indicated time averaged maximal BFV (APV, cm/s) is automatically calculated in the last 2 displayed beats.

culated assuming a mean BFV at rest of 15 cm/s, a value exactly coincident with the measured mean BFV in this patient, and the pressure gradient is calculated from the stenosis geometry assuming a fixed mean proximal coronary blood pressure of 100 mm Hg modified in this case to 110 mm Hg to use a value closer to the true measurement. The lower continuous line plots the relation between coronary perfusion pressure and coronary flow under conditions of maximal vasodilatation. A coronary closing pressure of 10 mm Hg and a coronary flow reserve of 5.5 were assumed [10]. Note that the point of maximal measured flow reserve increase (1.50 times baseline flow) is not aligned on the theoretical relation distal coronary pressure/coronary flow at maximal vasodilatation so that a second line can be drawn to describe the measured pressure/flow relation at maximal vasodilation.

DISCUSSION

An example of simultaneous measurement of BFV and transstenotic pressure gradient was previously reported by our group using a combined Doppler-balloon catheter after PTCA [11–12]. The obstruction to flow due to the relatively large diameter of the balloon catheter (0.64 mm^2) precluded the application of this method to the evaluation of a severe coronary stenosis before coronary interventions. In a recent multicenter trial [13] quantitative analysis of 636 stenoses before coronary angioplasty showed a minimal CSA of 0.82 ± 0.11 mm^2. In moderate or intermediate stenosis and after coronary angioplasty the measurement of the transstenotic gradient can be obtained with conventional fluid-filled catheters with a less severe obstruction to flow. Also in these conditions, however, when the measured transstenotic gradient is essential in the decision-making process, the higher accuracy of the measurements allowed by the use of smaller high-fidelity pressure transducers is desirable.

The introduction of miniaturized pressure transducers mounted at the tip of a flexible soft-tip guidewire of 0.17 mm^2 of CSA potentially allows the direct measurement of the pressure gradient with a minor further reduction of the stenosis CSA [14]. The use of miniaturized Doppler

TABLE I. Angiographic and Hemodynamic Parameters

Quantitative coronary angiography	LAO	RAO	MEAN
Length stenosis (mm)	1.55	1.10	1.32
Reference diameter (interpolated technique) (mm)	3.75	3.58	3.66
Minimal lumen diameter (mm)	1.23	1.00	1.11
Diameter at the site of the Doppler sampling volume (mm)	3.92	*[a]	3.92
Percent diameter stenosis (%)	67%	72%	70%
Reference cross-sectional area (mm^2)	11.07	10.08	10.57
Minimal cross-sectional area (mm^2)	1.20	0.79	0.97[b]
CSA at the site of the Doppler sampling volume (mm^2)	12.10	*[a]	12.10
Percent cross-sectional area stenosis (%)	89%	94%	91%

Doppler blood flow velocity (cm/s)	BAS	PAP
Average peak blood flow velocity	30	45
Mean blood flow velocity	15	22.5

Coronary blood flow (ml/s)	BAS	PAP
Mean coronary blood flow	1.81	2.72

Pressure Measurements (mm Hg)	BAS	PAP
Proximal systolic coronary blood pressure	157	143
Proximal diastolic coronary blood pressure	87	82
Proximal mean coronary blood pressure	112	106
Post-stenotic systolic coronary blood pressure	137	89
Post-stenotic diastolic coronary blood pressure	73	51
Post-stenotic mean coronary blood pressure	97	64
Transstenotic mean pressure gradient	15	42

[a]Not measured because of significant foreshortening.
[b]Calculated from the minimal lumen diameter in the two orthogonal projections assuming an elliptical model.

TABLE II. Measured and Estimated Mean Predicted Transstenotic Pressure Gradients (mm Hg)

Baseline			Papaverine		
Measured	Estimated (QCA)	% diff	Measured	Estimated (QCA)	% diff
15	20	+33	42	42	0

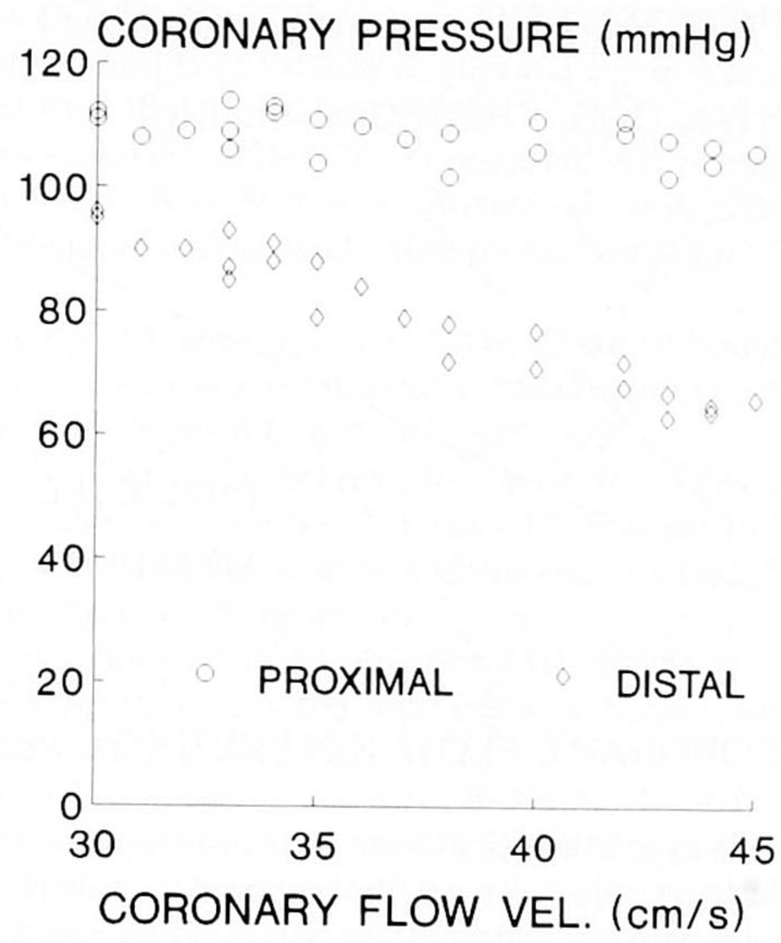

Fig. 4. Plotting of the measured proximal and distal coronary mean pressures vs. the simultaneous coronary BFV during the effect of the papaverine injection. The data-points indicate simultaneous measurements over two cardiac cycles every 8 s.

transducers with a larger sample volume than the conventional Doppler catheters and the spectral analysis of the Doppler signal allow a reliable BFV measurement without any further obstruction to flow if the velocity probe is positioned proximal to the stenosis. The pressure and BFV measurements are complementary parameters in the characterization of stenosis hemodynamics. A low increase in BFV may occur in a variety of conditions including modifications of basal flow or impairment of the vasodilatory mechanisms of the distal vasculature [15]. The simultaneous measurement of a major increase of transstenotic pressure gradient confirms that the flow limiting factor is the high resistance across the stenosis. Conversely, the measurement of a rapidly increasing transstenotic pressure gradient during vasodilatation does not fully define the functional severity of a stenosis if the level of flow increase is not simultaneously measured. In the model of Kirkeeide et al. [9] it is assumed for the purpose of the assessment of the hemodynamic effects of the stenosis that the vasodilatory capacity of the distal bed is intact and that collateral circulation is absent. These reasons may explain why the measured coronary flow reserve was lower and the post-stenotic coronary pressure higher than predicted from the assumed theoretical model. The coronary distal pressure and blood flow at maximal hyperemia are ultimately determined by factors unrelated to the stenosis geometry such as the vasodilatory capacity of the distal coronary arteries and the resistance in parallel to the stenosis resistance offered by the collateral vessels.

The trajectory of the distal pressure/BFV curve, how-

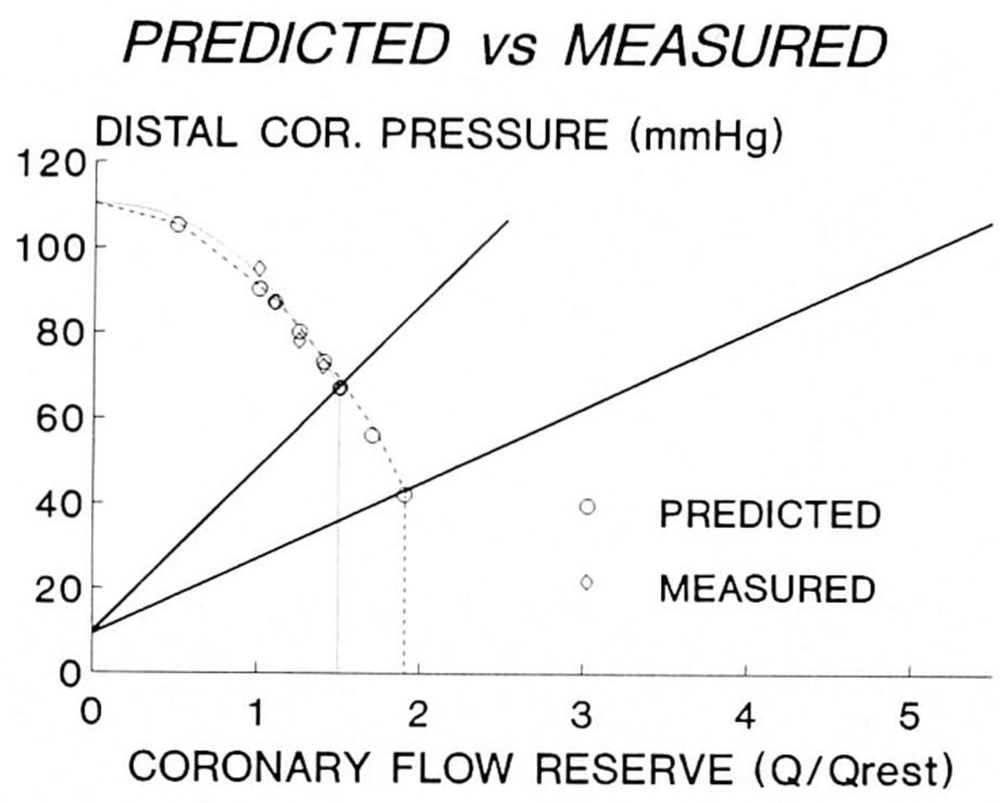

Fig. 5. Plotting of distal post-stenotic coronary mean pressure after papaverine injection vs. the ratio to baseline coronary flow, as proposed by Kirkeeide et al. [9]. Five measured data points (diamond-shaped markers) are shown to indicate the trend of the relation from baseline flow (ratio = 1) to maximal hyperemia (ratio = 1.50). The calculation of mean coronary distal pressure was performed assuming a fixed aortic pressure of 110 mm Hg and over a wider range of coronary flow, from a value corresponding to a ratio to baseline flow of 0.5 to the maximal predicted coronary flow (ratio to baseline = 1.91), corresponding to the point in which the calculated distal pressure intercepts the theoretical relation coronary flow/distal coronary pressure (lower continuous line) [10]. The trajectories of the two curves (dashed line = predicted, dotted line = measured) are almost superimposed. Note that the maximal increase in coronary flow is less than predicted from the theoretical relation coronary flow/distal coronary pressure and is consistent with a shift to the left of this relation (upper continuous line).

ever, is characteristic of the stenosis geometry and the slope of this relation is an index of stenosis severity independent of the values reached at maximal vasodilatation. The prediction of the pressure gradient under different regimens of flow is routinely provided by many systems of computer-assisted quantitative analysis based on the measurements of stenosis geometry [3,9,10,16]. The calculation of the transstenotic pressure gradients based on coronary blood flows calculated from BFV and CSA at the site of the Doppler measurement overestimated the measured values in baseline conditions while, during maximal hyperemia, the predicted pressure gradient and the measured pressure gradient were identical. Inaccuracies in the measurement of stenosis geometry or in the calculation of coronary flow as well as modifications of stenosis geometry in different flow conditions can explain the small differences observed.

A possible limitation of this case-report is the recording of the BFV proximal instead than distal to the lesion. This approach, used in order to avoid the obstruction to flow induced by the passage of two separate guidewires across the stenosis precludes the possibility of the assessment of alterations of the flow velocity pattern distal to the stenosis such as a decrease of the diastolic/systolic velocity ratio [28]. A solution to this problem and a great advantage in terms of practical applicability would be the incorporation of both the Doppler and the pressure sensors in a single guidewire system.

In conclusion, this first report of the combined use of miniaturized coronary pressure and Doppler probes shows that the characterization of stenosis severity can be obtained using a direct simultaneous measurement of the transstenotic pressure gradient and BFV in baseline and in hyperemic conditions. With this approach, the relation between transstenotic pressure gradient/distal coronary pressure and coronary flow reserve can be fully ascertained, allowing a complete assessment of stenosis hemodynamics and the validation of the models proposed for the estimation of these parameters based on QCA measurements of stenosis geometry. The usefulness of this approach in the detection of the functional significance of individual coronary stenoses, however, must be studied in comparison with standard objective tests of myocardial ischemia in a large series of stenoses of different angiographic severity.

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APPENDIX A

Computation of Hemodynamic Parameters From Quantitative Coronary Angiography

The effects of changes in stenosis geometry on transstenotic pressure losses were extensively studied by Young et al. [17–20] using models of stenosis of different length, shape, and percent diameter reduction, under conditions of steady and pulsatile flow. The equation validated by these authors, based on classic Newtonian fluid dynamics, was adapted for tapering stenosis and X-ray analysis by Brown et al. [16]. The algorithm implemented in the software package of the CAAS system uses the following formula:

$$\Delta P = \frac{8\pi\mu L}{1.33\ A_s^2} Q + \frac{\rho}{0.266}\left(\frac{1}{A_s} - \frac{1}{A_n}\right)^2 Q^2 \quad (1)$$

where ΔP is the transstenotic pressure gradient in mm Hg, μ is dynamic blood viscosity in Poise (assumed equal to 0.03), L is the length of the stenosis in mm, A_n is the CSA of the reference normal segment in mm^2, A_s is the minimal CSA of the stenotic segment in mm^2, Q is the mean coronary blood flow in ml/s, and ρ is the blood density in g/ml (assumed equal to 1.05).

This equation assumes that at the exit of the stenosis flow completely separates from the streamline contours so that large eddies develop in the divergent segment distal to the stenosis. An exit half-angle of 15° has been shown to be sufficient to induce a complete separation of flow and this condition seems fulfilled in the examined artery in which exit angles of 31° and 34° were measured with quantitative angiography from the diameter profile

in the LAO and RAO projections. The calculated pressure gradient, therefore, is described as the sum of the losses due to viscous components and the losses due to separation of flow at the exit of the stenosis and can be written in the simplified form

$$\Delta P = K_p Q + K_s Q^2 \quad (2)$$

where K_P and K_S are the coefficient of pressure losses due to, respectively, viscous friction and separation of flow. In the hemodynamic report of the quantitative angiographic analysis using the CAAS system the pressure gradients are calculated for volume flow ranging from 1 to 3 ml/s. In this case the volume flow was derived from the mean Doppler BFV (see Appendix B) and the CSA at the site of the Doppler measurement, calculated from the angiographic diameter assuming a circular cross-section.

APPENDIX B

Doppler Measurements of Coronary Blood Flow Velocity

The measurement of the mean BFV requires an adequate sampling of the Doppler signal:

1. The ultrasound beam probe must be aligned with the centerline of flow; the guidewire has the piezoelectric crystal mounted at the tip so that a partial malalignment of the probe would minimally affect the velocity recording (underestimation of flow of 6% in the presence of an angle of 30° with the velocity vector).
2. The entire flow profile or at least a large part of it including the maximal velocity must be included in the Doppler sample volume; the ultrasound beam opens at 15° from each side from the transducer so that even in the presence of a non-ideal position of the Doppler guidewire (eccentric, off-axis) a large part of the velocity profile will be examined.
3. The presence of the Doppler probe must not modify the velocity profile at the site of the sample volume. In in vitro models Tadaoka et al. [21] has shown a complete restoration of the flow profile at a distance equal to 10 times the diameter of the Doppler probe (the diameter of the Doppler probe is 0.46 mm and the distance of the sample volume was kept constant at 5.2 mm).
4. A spectral analysis of the Doppler frequency must be performed to identify all the different velocities in the sample volume, including the maximal velocity [22]. The frequency spectrum can then be easily converted in the velocity spectrum based only on the knowledge of the ultrasound frequency and the velocity of sound in blood. Theoretically, mean BFV can be measured from the weighted average of the velocity spectrum. This method, however, requires a complete insonification of the velocity profile of the examined vessel and is influenced by the presence of non-flow related signals [23] such as the high intensity-low velocity signals from vessel wall movements during the cardiac cycle (wall thumps). The final measurement, therefore, is critically dependent on the modalities of signal processing. Also the weighing factors for the different velocities cannot be reliably determined as signal intensity is modified by several unknown parameters such as rouleaux formation [24,25].

A different approach is based on the use of the maximal BFV which is less sensitive to the presence of noise and is more easily included in the sample volume based on the above-described characteristics of the Doppler system. Mean BFV can be estimated from the maximal BFV assuming Poiseuille flow using the equation describing the velocity of a laminar flow field:

$$V_x = \frac{\Delta P}{4\mu L}(a^2 - x^2) \quad (1)$$

in which V_x is the velocity of the flow lamina x, ΔP is the pressure gradient in the vascular segment of length L, is blood flow viscosity, a is the radius L is the length in mm of the considered segment. X is the distance of the lamina x from the vessel centerline. This last value is 0 for the centerline of flow so that equation 1 can be rewritten:

$$V_{max} = \frac{\Delta P}{4\mu L} a^2 \quad (2)$$

Under the assumed conditions and if mean velocity times CSA (A) equals blood flow (Q), from the Poiseuille equation follows that

$$V_{mean} = \frac{Q}{A} = \frac{\frac{(\Delta P \pi a^4)}{8\mu L}}{A} \quad (3)$$

with $A = \pi r^2$, equation 3 can be simplified using (2) to

$$V_{mean} = \frac{\Delta P a^2}{8\mu L} = \frac{V_{max}}{2} \quad (4)$$

An important limitation to the applicability of this formula is that the velocity profile is assumed to be parabolic and fully developed. The distance L necessary to allow the full development of a parabolic flow profile is defined by the equation [26]

$$L = (0.03\ R_e)\ d$$

where R_e is the Reynolds number and d the diameter of

the conduit. Consequently, the velocity measurement should be taken not too close to the origin of the vessel because a vascular segment of a length of 4–6 times the vessel diameter is necessary for a complete development of the velocity profile at the Reynolds numbers present in normal epicardial coronary arteries (150–200). The same problem must be considered sampling distal to major bifurcations of the vessel and, more importantly, in the presence of changes of the vascular diameter so that the measurement of mean BFV from maximal BFV can be misleading across short stenotic segments. Also the non-Newtonian characteristics of blood will induce a flatter velocity profile than expected based on the vascular diameter and mean blood viscosity so that an underestimation of the mean BFV can be expected deriving this parameter from the maximal BFV [27]. These considerations underline the difficulties to obtain reliable volume flow measurements based on BFV measurements despite the recent progress in Doppler probe technology and signal analysis. Nevertheless, recent validation studies have shown a high correlation between flow measured with an electromagnetic flowmeter and flow derived from Doppler measurements obtained with the probe used in this study both in vitro and in vivo [5].