Maximal Blood Flow Velocity in Severe Coronary Stenoses Measured with a Doppler Guidewire

LIMITATIONS FOR THE APPLICATION OF THE CONTINUITY EQUATION IN THE ASSESSMENT OF STENOSIS SEVERITY

Carlo Di Mario, MD, Nicolas Meneveau, MD, Robert Gil, MD, Peter de Jaegere, MD, Pim J. de Feyter, MD, PhD, Cornelis J. Slager, PhD, Jos R. T. C. Roelandt, MD, PhD, and Patrick W. Serruys, MD, PhD

In vitro and animal experiments have shown that the severity of coronary stenoses can be assessed using the continuity equation if the maximal blood flow velocity of the stenotic jet is measured. The large diameter and the low range of velocities measurable without frequency aliasing with the conventional intracoronary Doppler catheters precluded the clinical application of this method for hemodynamically significant coronary stenoses in humans. This article reports the results obtained using a 12 MHz steerable angioplasty guidewire in a consecutive series of 52 patients undergoing percutaneous coronary angioplasty (61 coronary stenoses). The ratio between coronary flow velocity in a reference segment and in the stenosis was used to estimate the percent cross-sectional area stenosis. A Doppler recording suitable for quantization was obtained in the stenotic segment in only 10 of 61 arteries (16%). The time-averaged peak velocity increased from 15 ± 5 to 115 ± 26 cm/sec from the reference normal segment to the stenosis. Volumetric coronary flow calculated from the product of mean flow velocity and cross-sectional area was similar in the stenosis and in the reference segment (33.2 ± 14.9 vs 33.5 ± 17.0 mL/min, respectively, difference not significant). The percent cross-sectional area stenosis and minimal luminal cross-sectional area derived from the Doppler velocity measurements using the continuity equation and calculated with quantitative angiography were also similar (Doppler, 86.7 ± 5.1% and 1.00 ± 0.48 mm^2; quantitative angiography, 85.9 ± 7.9% and 1.02 ± 0.50 mm^2). A significant correlation was observed between Doppler-derived and angiographic measurements (percent cross-sectional area: r = 0.64, $p < 0.05$; minimal cross-sectional area: r = 0.69, $p < 0.05$). Although the percent cross-sectional area stenosis and minimal cross-sectional area derived from the Doppler measurements based on the continuity equation were significantly correlated with the corresponding quantitative angiographic measurements, this determination could be achieved in a minority of cases (16%), limiting the practical application of this approach for the assessment of coronary stenosis severity.

(Am J Cardiol 1993;71:54D–61D)

The principle of the continuity equation is largely applied for the calculation of cardiac valve areas from the integration of Doppler flow velocity measurements and 2-dimensional echocardiography.[1] Miniaturization of the Doppler probes, tip-mounted on flexible catheters 1 mm in diameter, has allowed the application of this equation for the assessment of the severity of coronary artery stenoses.[2] In vitro studies in hydraulic models of coronary stenoses have shown an excellent correlation between true cross-sectional area of the stenosis and stenosis area calculated from the ratio of the flow velocity in a normal segment and in the stenosis.[3] Similar results were obtained also in animal experiments[4] and, more recently, in humans for the assessment of moderate coronary stenoses (<50% diameter stenosis).[5] The intracoronary Doppler catheters, however, cannot be used in very severe coronary stenoses because their relatively large diameter (1 mm) induces an almost complete obstruction to flow when the catheter is

From The Cardiac Catheterization Laboratory, Division of Cardiology, Thoraxcenter, Erasmus University, Rotterdam, The Netherlands.

Address for reprints: Patrick Serruys, MD, PhD, Cardiac Catheterization Laboratory, Division of Cardiology, Thoraxcenter, Ee 2332, Erasmus University, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands.

advanced into the stenosis. Adjustment of the distance of the Doppler sample volume from the catheter tip has been used to investigate the stenotic jet without crossing the stenosis. This technique, however, is applicable only for short stenoses and induces an inaccurate estimation of the velocity ratio if the change of position of the Doppler sample volume is performed within the area of flow distortion distal to the catheter tip (10 times the catheter diameter).[6] Further, frequency aliasing precludes the recording of velocities higher than 110 cm/sec because of the high frequency and relatively low repetition rate of these systems. The ultraminiaturized Doppler probes mounted at the tip of a steerable angioplasty guidewire (0.018 inch) can be introduced through moderate stenoses without generally inducing a significant obstruction to flow. Further, the use of spectral analysis and the lower frequency and higher repetition rate of the Doppler guidewire system allow the recording of velocities as high as 6 m/sec without frequency aliasing.[7]

To assess the feasibility of the measurement of maximal velocity in the stenosis with a Doppler guidewire, velocity data were obtained in 52 consecutive patients during coronary angioplasty. The accuracy of the relative measurements of cross-sectional area reduction based on the ratio of the velocity measurement in a normal arterial segment and in the stenosis was also compared with the corresponding quantitative angiographic measurements.

METHODS

Study patients: The study group consisted of 52 consecutive patients (mean age 57 ± 10 years, 43 men and 9 women) undergoing coronary balloon angioplasty or other nonsurgical revascularization procedures with the use of the Doppler guidewire for the angioplasty. Arteries with complete or functional occlusion (Thrombolysis in Myocardial Infarction [TIMI] flow class 0–1) or arteries with extreme tortuosity were excluded from this study. In 9 patients the Doppler guidewire was used in 2 arteries before dilation, so that a total of 61 arteries were studied. The Doppler guidewire was successfully used to cross the coronary stenosis in 58 arteries (95%). The study angioplasty artery was the left anterior descending coronary artery in 36 cases (59%), the left circumflex in 7 (12%), the right coronary artery in 13 (21%), and a saphenous vein bypass graft in 5 (8%).

Catheterization procedure: After intravenous administration of 10,000 IU of heparin and 250 mg of acetylsalicylic acid, an 8 F guiding catheter was advanced up to the coronary ostium. After isosorbide dinitrate (2–3 mg intracoronary), cineangiograms suitable for quantitative assessment were obtained in 1–3 angiographic views.

The Doppler guidewire was advanced into the artery to be dilated and a baseline flow velocity recording was obtained in a straight angiographically normal or minimally diseased segment of the artery proximal or distal to the lesion. Care was taken to avoid the presence of major side branches between the site of the flow velocity measurement and the stenosis. When prestenotic acceleration and poststenotic deceleration of flow were identified, the guidewire position was readjusted. A new angiogram was obtained with the Doppler guidewire in place in order to locate the position of the Doppler sample volume and measure the corresponding cross-sectional area. When the guidewire approached the stenosis, the probe was slowly advanced and, if a high velocity signal was observed, carefully rotated and/or moved in order to optimize the Doppler recording. The duration of these attempts before crossing the lesion ranged between 50 and 560 sec (mean 140 sec).

Doppler guidewire and flow velocity measurements: The Doppler angioplasty guidewire is a 0.018-in (diameter 0.46 mm), 175-cm long, flexible and steerable guidewire with a floppy distal end mounting a 12 MHz piezoelectric transducer at the tip[7] (Cardiometrics, Mountain View, CA). The sample volume is positioned at a distance of 5.2 mm from the transducer. At this distance, the sample volume has a width of approximately 2 mm due to the divergent ultrasound beam so that a large part of the flow velocity profile is included in the sample volume also in case of eccentric positions of the Doppler guidewire. The pulse repetition frequency (17–96 kHz) varies with the velocity range selected (50–600 cm/sec full scale) so that flow velocities up to 6 m/sec can be recorded without frequency aliasing (Figure 1). In order to increase the reliability of the measurements, a real-time fast Fourier transform algorithm is used for the analysis of the Doppler signal.[8] The flow velocity measurements obtained with this system have been validated in vitro and in an animal model using simultaneous electromagnetic flow measurements for comparison.[7] The Doppler system calculates and displays on-line several spectral variables, including the instantaneous peak velocity and the time-averaged (mean of 2 beats) peak velocity (APV). Mean blood flow velocity was estimated 50% of the time-averaged peak velocity

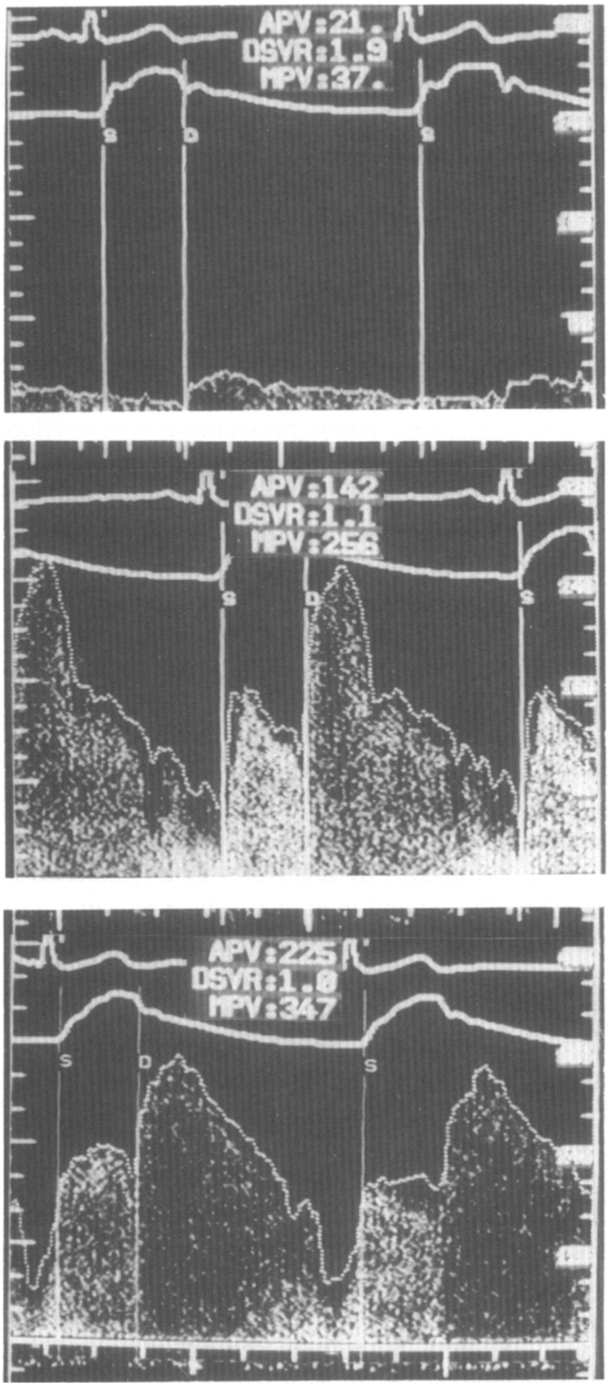

FIGURE 1. ***Upper panel:*** **Doppler flow velocity tracing proximal to a 70% cross-sectional area stenosis of the left anterior descending coronary artery (scale, 0–400 cm/sec).** ***Middle panel:*** **when the Doppler probe is advanced into the stenosis, the flow velocity shows a large increase of the average peak velocity and especially of the systolic flow velocity component (decrease of the diastolic/systolic velocity ratio from 1.9 to 1.1; scale, 0–400 cm/sec).** ***Lower panel:*** **a further increase is observed after contrast-induced hyperemia. Note the perfectly defined Doppler envelope despite the presence of flow velocities of 3.5 m/sec (scale, 0–480 cm/sec). APV = time-averaged peak flow velocity (cm/sec); DSVR = ratio of the time-averaged diastolic and systolic flow velocity components; MPV: maximal peak velocity (cm/sec). All these measurements were automatically performed after spectral analysis of the Doppler signal (FloMap, Cardiometrics).**

(APV), assuming a fully developed velocity profile.[9,10] Coronary flow (CoBF) was calculated from the corresponding mean blood flow velocity and cross-sectional area (CSA) as:

$$\text{CoBF (mL/min)} = 0.6 \times \text{CSA (mm}^2) \times \frac{\text{APV}}{2} \text{(cm/sec)}$$

where 0.6 is the conversion factor for mm^2/cm^2 and min/sec (Figures 2 and 3). The Doppler-derived percent cross-sectional area stenosis (CSA_{St}) is calculated from the following:

$$\%CSA_{St} = (1 - APV_{Ref}/APV_{St}) \times 100$$

where APV_{Ref} is the reference APV and APV_{St} is the stenosis APV. Absolute minimal cross-sectional area (MlCSA) of the stenosis was calculated as:

$$\text{Doppler MlCSA} = CSA_{Ref} \times APV_{Ref}/APV_{St}$$

with the reference cross-sectional area (CSA_{Ref}) measured with quantitative angiography from the corresponding diameter at the site of the Doppler sample volume assuming a circular cross-section.[11]

Quantitative angiographic measurements: The guiding catheter, filmed without contrast medium, was used as a scaling device.[12] A previously validated on-line analysis system operating on digital images[13] (ACA-DCI; Philips, Eindhoven, The Netherlands) and a cine-film based off-line system[14] (CAAS System; Pie Medical Data, Maastricht, The Netherlands) were used. After automatic detection of the vessel centerline, a weighted first and second derivative function with predetermined continuity constraints was applied to the brightness profile on each scan line perpendicular to the vessel centerline to determine the contours of the lumen.[11] From the measured minimal luminal diameter (MLD), the minimal luminal cross-sectional area was calculated assuming a circular cross-section (average of the measurements in the 8 patients in whom multiple views were acquired). Percent cross-sectional area stenosis was calculated using the cross-sectional area at the site of the Doppler measurement as reference using the following formula:

$$\%CSA_{St} = (1 - CSA_{St}/CSA_{Ref}) \times 100$$

Statistical analysis: A two-tailed paired Student's *t* test was used to compare the difference between the coronary flow calculated in the stenosis and in the reference segment and between the Doppler-derived and the angiographic percent

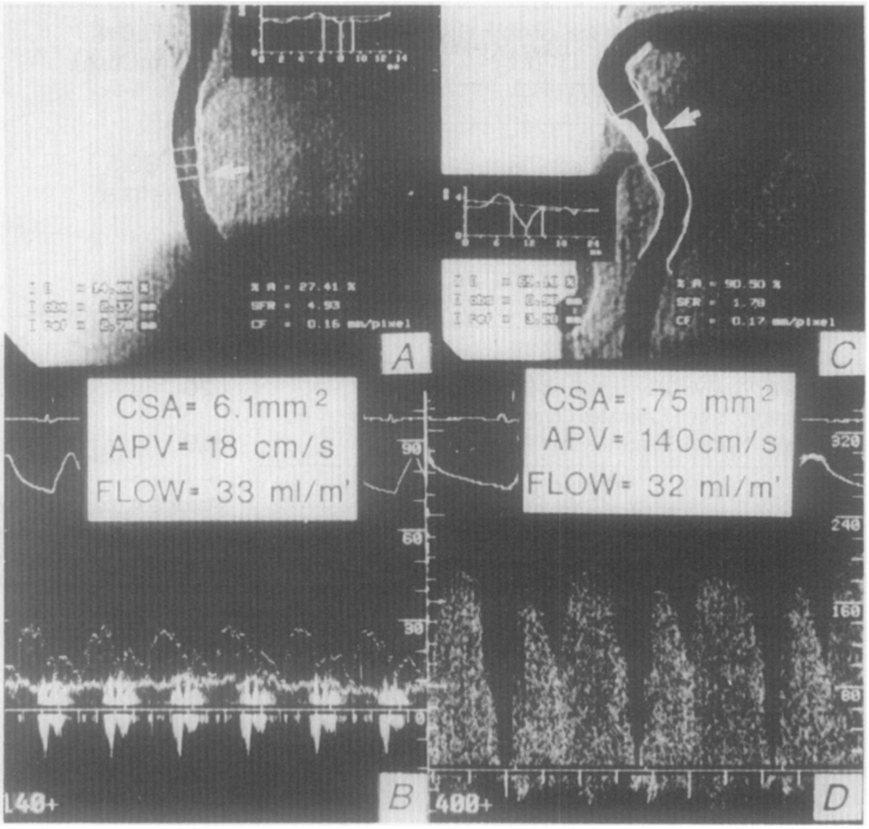

FIGURE 2. ***Upper panels:*** **magnified digital angiogram of the middle segment of a right coronary artery with a severe coronary stenosis.** ***A*, measurement at the site of the Doppler sample volume, distal to the stenosis;** ***C*, minimal luminal diameter (Philips DCI-ACA analysis package).** ***Lower panels:*** **flow velocity recordings distal to the stenosis (*B*) and in the stenosis (*D*). Note the large velocity increase (maximal velocity of 210 cm/sec). APV = average peak velocity; CSA = cross-sectional area (mm²). Note that the scale is changed from 0–90 cm/sec in *B* to 0–320 cm/sec in *D* for jet analysis.**

cross-sectional area stenosis and minimal luminal cross-sectional area stenosis. Linear regression analysis was used to compare percent cross-sectional area stenosis and minimal luminal cross-sectional area measured with quantitative angiography with the corresponding values derived from the Doppler flow velocity measurements. The difference between Doppler-derived and measured stenosis minimal luminal cross-sectional area was plotted versus the stenosis minimal luminal cross-

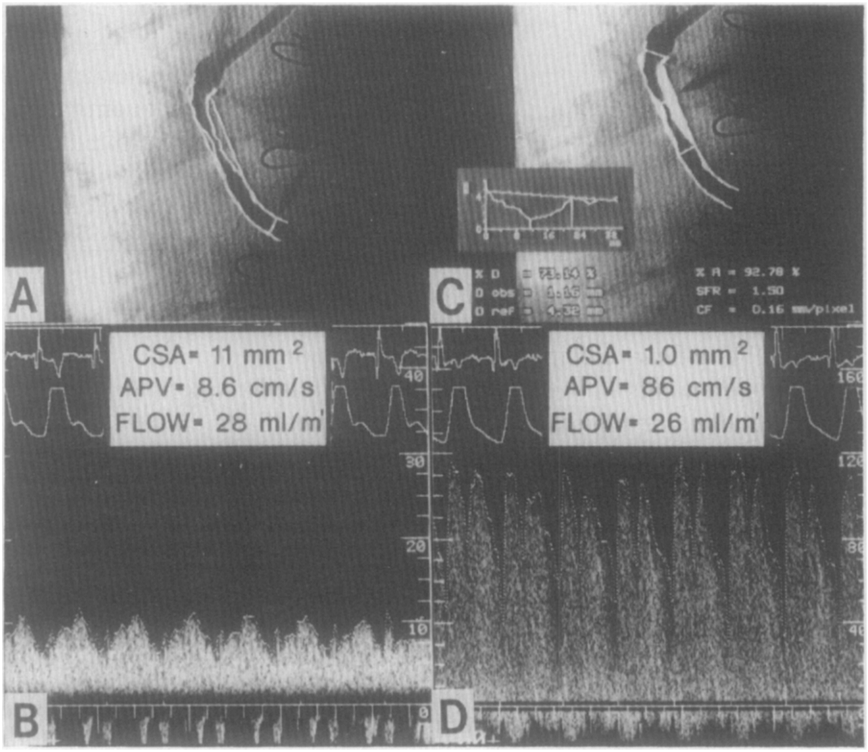

FIGURE 3. ***A*, *C*, magnified digital angiogram of a saphenous vein bypass graft with a severe proximal stenosis (92% area stenosis).** ***B*, *D*, corresponding Doppler flow velocity tracings and automatic measurements of a severe proximal stenosis and of the site of the flow velocity measurement in the reference segment (in this particular example, necessarily distal to the very proximal stenosis). Note that the scale is changed from 0–40 to 0–320 cm/sec for jet analysis.**

TABLE I Detection of High Transstenotic Flow Velocities in the Study Population

Examined Vessel	LAD	LCX	RCA	SVBG	Total
Vessels examined (n)	36	7	13	5	61
Detection of velocity increase in the stenosis	8 (22%)	2 (29%)	4 (31%)	3 (60%)	17 (28%)
Doppler recordings suitable for quantization	4 (11%)	1 (14%)	3 (23%)	2 (40%)	10 (16%)

LAD = left anterior descending; LCX = left circumflex; RCA = right coronary artery; SVBG = saphenous vein bypass graft.

TABLE II Flow Velocity and Cross-Sectional Area Measurements and Estimated Coronary Blood Flow in a Reference Normal Segment and in the Stenosis

	Reference			Stenosis		
Patients	CSA mm^2	BFV cm/sec	Flow mL/min	CSA mm^2	BFV cm/sec	Flow mL/min
CE (92/275)	12.10	21	76	0.97	138	40
KD (92/239)	9.10	9	25	0.75	90	20
ME (92/339)	6.30	18	34	1.27	77	29
HR (91/1,838)	10.90	9	28	1.00	86	26
WD (92/1,132)	6.29	11	21	0.66	118	24
MV (92/1,065)	7.06	11	23	0.59	137	24
SM (92/822)	5.06	12	18	0.50	130	19
GF (91/1,860)	6.10	18	33	0.75	140	32
RA (92/1,792)	8.75	18	47	2.06	90	56
GF (92/1,504)	4.77	21	30	1.46	142	62
Mean	7.64	15	33.5	1.00	115	33.2
± SD	2.47	5	17.0	0.48	26	14.9

BFV = blood flow velocity; CSA = cross-sectional area.

sectional area according to the method proposed by Bland and Altman.[15] Statistical significance was defined as $p < 0.05$. All data were expressed as mean ± SD.

RESULTS

The minimal luminal diameter of the 61 studied arteries was 1.07 ± 0.32 mm (percent diameter stenosis 62 ± 6.8%). A Doppler signal could be obtained in the stenosis in 17 arteries (28%). In only 10 cases (16%), however, was the quality of the Doppler recording satisfactory to allow the measurement of the time-averaged peak velocity (Table I). The flow velocity and the cross-sectional area measurements in the reference segment and in the stenosis are reported in Table II for the 10 arteries in which recordings suitable for quantitative analysis were obtained. The time-averaged peak velocity increased from 15 ± 5 to 115 ± 26 cm/sec from the reference normal segment to the stenosis. An inverse change was observed in the corresponding angiographically measured cross-sectional areas (7.75 ± 2.55 vs 1.05 ± 0.61 mm^2 for the reference and stenosis areas, respectively). Consequently, the coronary flow in the stenosis and in the reference segment showed no significant

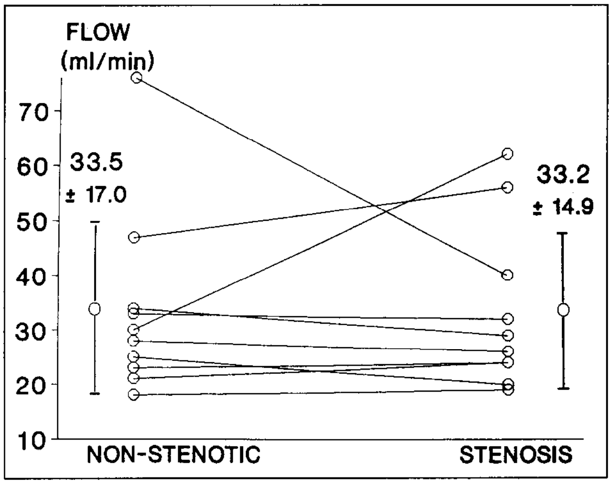

FIGURE 4. Diagram illustrating the individual measurements of coronary flow from the Doppler flow velocity and angiographic cross-sectional area measurements in a nonstenotic reference segment and in the stenosis.

difference (33.2 ± 14.9 vs 33.5 ± 17.0 mL/min, respectively, Table II). Figure 4 illustrates the individual differences between coronary flow calculated from Doppler velocity and cross-sectional area measurements in the stenosis and in the reference segment.

The percent reduction of cross-sectional area calculated from the quantitative angiographic measurements and from the Doppler flow velocity measurements is plotted in Figure 5. The Doppler-derived percent cross-sectional area stenosis showed a significant correlation with the angiographic percent cross-sectional area stenosis (86.7 ± 5.1 vs 85.9 ± 7.9%; $r = 0.64$, $p < 0.05$). Similar minimal luminal cross-sectional areas were calculated from the stenotic velocity ratio and from quantitative angiography (mean difference, 0.0–0.005 ± 0.37 mm^2, difference not significant; Figure 6).

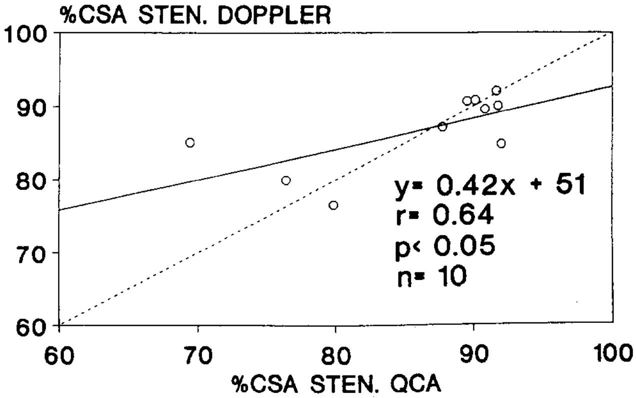

FIGURE 5. Linear regression analysis of the percent cross-sectional area stenosis measurements obtained from quantitative angiography and derived from the Doppler stenotic velocity ratio. CSA = cross-sectional area (mm^2); QCA = quantitative coronary angiography; STEN. = stenosis.

DISCUSSION

Application of the continuity equation in the assessment of stenosis severity: These results demonstrate the ability of intracoronary Doppler to obtain accurate flow velocity data in the normal segment of the artery and, in conjunction, to measure higher jet velocity within a severe stenosis. In the first study consistently applying the principle of the continuity of flow in the human coronary circulation, Nakatami et al[5] used 20 MHz Doppler catheters with a pulse repetition frequency of 62.5 kHz. With this system, unfortunately, flow velocities >115 cm/sec were not recorded because of the development of frequency aliasing. As a result of this technical limitation, all the flow velocity measurements were obtained only in mild-to-moderate coronary stenosis, with a percent cross-sectional area reduction <75% (diameter stenosis <50%).

In the current study, patients with significant coronary stenoses undergoing coronary balloon angioplasty were studied. The use of steerable Doppler guidewires with smaller diameter and cross-sectional area (0.17 mm^2), larger sample volume, lower carrier frequency (12 MHz), and higher pulse repetition rate (up to 96 kHz) allowed the recording of higher jet velocities within severe coronary stenoses. With these Doppler probes the continuity equation can be applied also in severely stenotic coronary arteries, providing a measurement of percent cross-sectional area reduction independent of angiography.

This approach, however, has practical and theoretical limitations. The first problem is the choice of the reference "normal" segment. Epicardial and intravascular ultrasound has confirmed pathologic findings showing that diffuse or focal intimal thickening is present in angiographically normal arterial segments.[16,17] An abnormally high flow velocity measurement is obtained in a segment already narrowed by atherosclerotic wall encroachment. In this case, the percent cross-sectional area stenosis calculated from the velocity measurements will underestimate the true hemodynamic severity of the stenosis. The hemodynamic significance of a coronary stenosis is influenced by all the elements defining lesion geometry, including length of the narrowed segment and inflow–outflow angles. The stenotic velocity ratio, however, can calculate only the percent reduction in cross-sectional area.

An additional problem with the use of the continuity equation is the interposition of major side branches between the site of the measurement and the stenosis. In particular, experience obtained

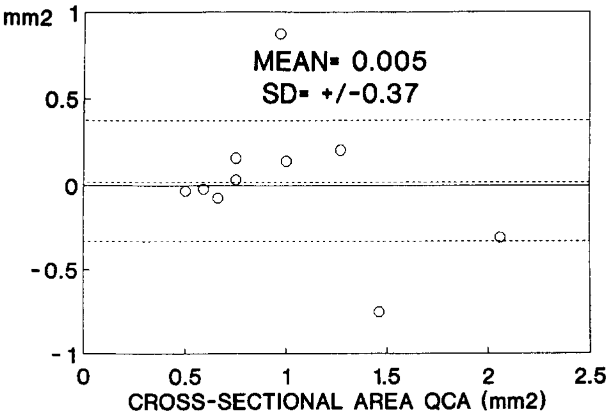

FIGURE 6. The difference between minimal luminal cross-sectional area calculated from the Doppler measurements and from quantitative angiography is plotted against the angiographic minimal luminal cross-sectional area. CSA = minimal luminal cross-sectional area (mm^2); QCA = quantitative coronary angiography.

with the Doppler guidewire in intermediate stenoses has shown that in branching arteries the ratio between the flow velocity recorded proximal and distal to a stenosis can be used as an indirect index of stenosis severity.[18] In the presence of severe stenoses, the flow will be preferentially directed to the prestenotic branches so that high proximal-to-distal flow velocity ratios will be obtained. Proximal flow velocity was used when possible, assuming minimal redistribution by intervening branches and avoiding the segment of proximal lesion acceleration in the zone of convergence. In practice, however, we were forced to record the reference flow velocity in a segment distal to the stenosis in 7 of our 10 cases, possibly inducing a further obstruction to flow due to the guidewire.[19]

A more important limitation is related to the measurement of the flow velocity in the stenosis. The comparison of the time-averaged peak flow velocities in the stenosis and in the reference segment is based on the assumption that maximal and mean velocities are linked by a fixed ratio in the presence of a fully developed parabolic flow velocity profile (2:1 for a perfect Newtonian fluid). In the presence of abrupt changes of vascular diameter, however, a vascular segment several times longer than the vascular diameter is required to obtain a fully developed parabolic profile, as predicted from classic models and confirmed experimentally.[10] It is obvious, therefore, that for a short stenosis the use of the maximal velocity will lead to a predictable underestimation of the percent cross-sectional area stenosis. A possible alternative is the direct measurement of the mean flow velocity from the Doppler spectrum. This measurement, however, is unreliable because of the unavoidable presence of nonflow-related signals (wall thumps, artifacts), the inability to include the entire velocity profile of the artery in the sample volume, and the different signal intensity induced by the higher density of scatterers in the central flow lamina.[20,21]

Despite all these theoretical limitations, in our experience the percent cross-sectional area stenosis measured with quantitative angiography and estimated from the ratio of stenosis/reference velocity showed a significant correlation, with closer values being obtained in the most severe coronary stenoses. The accuracy of the Doppler-derived measurements in these cases cannot obscure the fact that Doppler recordings suitable for quantization were obtained within the stenosis only in a minority of the study population. The inability to record the flow velocity in severe stenoses is the most important practical limitation to the applicability of the continuity equation from Doppler measurements obtained with guidewire-type intracoronary probes. The failure to record the intrastenotic velocities is in contrast with the high acquisition rate of adequate Doppler signals in normal or near-normal arterial segments, proximal or distal to the lesion.

Yuan and Shung[22] have shown that the ultrasonic backscatter from flowing whole blood is dependent on the shear rate. The ultrasonic backscatter of porcine whole blood measured at a shear rate of 22 sec^{-1} was 15 dB lower than the ultrasonic backscatter measured at a shear rate of 2 sec^{-1}, probably as a consequence of a reduced rouleaux formation. In the stenoses evaluated in this study a much higher shear rate can be expected: a shear rate of 2,600 sec^{-1} can be estimated in the presence of a peak velocity of 100 cm/sec in a lumen of 1 mm. Consequently, the amount of intact rouleax in the stenosis can be minimal and explain the reduced echointensity of the stenotic jet. An alternative possible explanation of this difference is the greater difficulty in orientating the Doppler sample volume in the narrowed tapering segment immediately proximal to the lesion and the very small dimension of the stenotic jet in comparison to the Doppler sample volume, leading to an unfavorable signal-to-noise ratio. A more extensive manipulation of the Doppler guidewire in front of the stenotic lesion, reshaping the distal end of the guidewire if necessary, might have resulted in a higher success rate in the acquisition of high-velocity signals in the stenosis. The potential risk to induce flow-limiting intimal lesions while the access to the distal vessel has not been secured makes this approach hazardous and of limited clinical applicability. The low success rate obtained in the assessment of flow velocity within the stenosis in patients undergoing coronary angioplasty cannot be extrapolated to the assessment of less severe stenoses. The clinical applicability of the use of flow velocity measurements obtained with a Doppler guidewire in moderate or intermediate coronary stenoses as well as after coronary interventions remains to be tested.

Additional application of intracoronary Doppler flow velocity for the assessment of stenosis severity: Other indices than the coronary flow reserve and the intrastenotic/normal segment velocity ratio can be obtained from the measurements of flow velocity distal to the stenosis. An abnormal phasic flow velocity pattern recorded during individual cardiac cycles and, in particular, a low diastolic-to-systolic velocity ratio has been proposed as an index of stenosis severity that can be easily obtained in almost all the cases using the Doppler guidewire.[18,23,24] In addition, in severely stenotic arteries the velocity in the proximal segment is much higher than the distal velocity, because of preferential flow toward the prestenotic branches of lower resistance. The presence of a high proximal-to-distal velocity ratio appears to differentiate arteries with flow-limiting stenoses from normal arteries.[24] More sophisticated indices, based on the instantaneous hyperemic diastolic pressure–flow velocity relation and implemented in animal experimental laboratories[25,26] can be applied in the catheterization laboratory with this intracoronary Doppler guidewire technology.[27] Further, the combined simultaneous assessment of the transstenotic pressure gradient and flow velocity using Doppler and pressure microsensors with guidewire technology provides all the elements required for a complete hemodynamic characterization of the stenosis severity.

CONCLUSION

The measurement of blood flow velocity in the stenotic jet in patients with severe coronary stenoses is possible with ultraminiaturized Doppler probes tip-mounted on angioplasty guidewires. High-quality Doppler recordings, suitable for quantization, can be obtained only in a small subset of the studied vessels. When measurable, however, the percent cross-sectional area stenosis derived from the stenosis velocity shows a significant correlation with the angiographic percent cross-sectional area stenosis. In summary, although accurate for quantification of lesion significance, use of the continuity equation employing intrastenotic jet velocity recordings is difficult and impractical for clinical application even when using flow velocity spectra obtained with a Doppler guidewire.

Acknowledgment: The contribution to the acquisition of the data of the medical, technical, and nursing staff of the Catheterization Laboratory, Thoraxcenter, Dijkzigt University Hospital, is gratefully acknowledged.

REFERENCES

1. Hatle L, Angelsen B. Pulsed and continuous wave Doppler in diagnosis and assessment of various heart lesions. In: Hatle L, Angelsen B, eds. Doppler ultrasound in cardiology. Philadelphia: Lea & Febiger, 1985;97–282.
2. Sibley DH, Millar HD, Hartley CJ, Whitlow PL. Subselective measurement of coronary blood flow velocity using a steerable Doppler catheter. *J Am Coll Cardiol* 1986;8:1332–1340.
3. Blasini R, Schad H, Huttl S, Mendler N, Blomer H. Intracoronary Doppler catheter: determination of the cross-sectional area of coronary artery stenoses by improved frequency analysis. (Abstr.) *Eur Heart J* 1992;13:362.
4. Johnson EL, Yock PG, Hargrave VK, Manubens SM, Seitz W, Ports TA. Assessment of severity of coronary stenoses using a Doppler catheter. Validation of a method based on the continuity equation. *Circulation* 1989;80:625–635.
5. Nakatami S, Yamagishi M, Tamai J, Takaki H, Haze K, Miyatake K. Quantitative assessment of coronary artery stenosis by intravascular Doppler catheter technique. *Circulation* 1992;85:1786–1791.
6. Tadaoka S, Kagiyama M, Hiramatsu O. Accuracy of 20 MHz Doppler catheter coronary artery velocimetry for measurement of coronary blood flow velocity. *Cathet Cardiovasc Diagn* 1990;19:205–213.
7. Doucette JW, Corl PD, Payne HM, Flynn AE, Goto M, Nassi M, Segal J. Validation of a Doppler guidewire for intravascular measurement of coronary artery flow velocity. *Circulation* 1992;85:1899–1911.
8. Di Mario C, Roelandt JRTC, de Jaegere P, Linker DT, Oomen J, Serruys PW. Limitations of the zero-crossing detector in the analysis of intracoronary Doppler. A comparison with fast Fourier analysis of basal, hyperemic and transstenotic blood flow velocity measurements in patients with coronary artery disease. *Cathet Cardiovasc Diagn* 1992;27:28:56–64.
9. Di Mario C, de Feyter PJ, Slager CJ, de Jaegere P, Roelandt JRTC, Serruys PW. Intracoronary blood flow velocity and transstenotic pressure gradient using sensor-tip pressure and Doppler guidewires. *Cathet Cardiovasc Diagn* 1993;28: (in press).
10. Caro CG, Pedley TJ, Schroter RC, Seed WA. The mechanics of the circulation. Oxford: Oxford University Press, 1978;53.
11. Reiber JHC, Serruys PW, Koojman CJ, Wijns W, Slager CJ, Gerbrands JJ, Schumblers JCH, den Boer A, Hugenholtz PG. Assessment of short-, medium-, and long-term variations in arterial dimensions from computer-assisted quantization of coronary cineangiograms. *Circulation* 1985;71:280–288.
12. Di Mario C, Hermans WRM, Rensing BJ, Serruys PW. Calibration using angiographic catheters as scaling devices. Importance of filming the catheters not filled with contrast medium. *Am J Cardiol* 1992;69:1377–1378.
13. Haase J, Di Mario C, Slager CJ, van der Giessen WJ, den Boer A, de Feyter PJ, Reiber JHC, Verdouw PD, Serruys PW. In-vivo validation of on-line and off-line geometric coronary measurements using insertion of stenosis phantoms in porcine coronary arteries. *Cathet Cardiovasc Diagn* 1992;27:16–27.
14. Di Mario C, Haase J, den Boer A, Reiber JHC, Serruys PW. Videodensitometry versus edge detection for the assessment of in vivo intracoronary phantoms. *Am Heart J* 1992;124:1181–1189.
15. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986;ii:307–310.
16. Nissen SE, Gurley JC, Grines CL, Booth DC, McClure R, Berk M, Fisher C, DeMaria AN. Intravascular ultrasound assessment of lumen size and wall morphology in normal subjects and patients with coronary artery disease. *Circulation* 1991;84:1087–1099.
17. StGoar FG, Pinto FJ, Alderman EL, Fitzgerald PJ, Stadius ML, Popp RL. Intravascular ultrasound of angiographically normal coronary arteries: an in-vivo comparison with quantitative angiography. *J Am Coll Cardiol* 1991;18:952–958.
18. Donohue TJ, Kern MJ, Bach RG, Aguirre F, Bell C, Wolford T, Penick D. Transstenotic pressure-gradient-flow velocity relationships in patients with coronary artery disease. *Circulation* 1992;86:I-855.
19. De Bruyne B, Vantrimpont P, Stockbroekx J, Demoor D, Heyndrickx GR. Influence of a PTCA wire on stenosis dynamics. *Circulation* 1992;86:I-322.
20. Evans DH, Schlindwein FS, Levene MI. The relationship between time averaged intensity weighted mean velocity and time averaged maximum velocity in neonatal cerebral arteries. *Ultrasound Med Biol* 1989;15:429–435.
21. De Kroon MGM, Slager CJ, Gussenhoven WJ, Serruys PW, Roelandt JRTC, Bom N. Cyclic changes of blood echogenicity in high-frequency ultrasound. *Ultrasound Med Biol* 1991;17:723–728.
22. Yuan YW, Shung KK. Ultrasonic backscatter from flowing whole blood. I: Dependence on shear rate and hematocrit. *J Acoust Soc Am* 1988;84:52–58.
23. Ofili E, Kern MJ, Tatineni S, Deligonul U, Aguirre F, Serota H, Labovitz AJ. Detection of coronary collateral flow by a Doppler-tipped guide wire during coronary angioplasty. *Am Heart J* 1991;222:221–225.
24. Segal J, Kern MJ, Scott NA, King SB, Doucette JW, Heuser RR, Ofili E, Siegel R. Alterations of phasic coronary artery flow velocity in humans during percutaneous coronary angioplasty. *J Am Coll Cardiol* 1992;20:276–286.
25. Mancini GBJ, Cleary RM, DeBoe SF, Moore NB, Gallagher KP. Instantaneous hyperemic flow-versus-pressure slope index: microsphere validation of an alternative to measures of coronary reserve. *Circulation* 1991;84:862–870.
26. Mancini GBJ, McGillem MJ, DeBoe SF, Gallagher KP. The diastolic hyperemic flow versus pressure relation: a new index of coronary stenosis severity and flow reserve. *Circulation* 1989;80:941–950.
27. Serruys PW, Di Mario C, Meneveau N, de Jaegere P, Strikwerda S, de Feyter PJ, Emanuelsson H. Intracoronary pressure and flow velocity from sensor-tip guidewires. A new methodological comprehensive approach for the assessment of coronary hemodynamics before and after coronary interventions. *Am J Cardiol* 1993;71:41–53.