Quantitative Assessment of Coronary Artery Stenosis by Intravascular Doppler Catheter Technique

Application of the Continuity Equation

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Background. Quantitative assessment of coronary artery stenoses plays a central role in clinical decision making. According to the continuity equation, the ratio of the time–velocity integral of prestenotic to stenotic flow velocities represents the ratio of the cross-sectional area of the stenotic to prestenotic segments. However, no data exist regarding the application of this method to clinical assessment of human coronary artery diseases. Therefore, we attempted to determine the severity of coronary artery stenoses by applying the continuity equation to the coronary circulation.

Methods and Results. Nineteen patients with a stenosis of the proximal left anterior descending coronary artery (LAD) and one patient with a stenosis in an aortocoronary bypass graft to the LAD were studied. Coronary flow velocities at the prestenotic and stenotic segments were measured with an end-mounted Doppler catheter (3F, 20 MHz), and the time–velocity integral ratio was calculated. Percent area stenosis was calculated as \(1 - \text{time–velocity integral ratio} \times 100\). In three patients with severe stenosis (>90% in area stenosis), velocity at the stenosis could not be determined because of aliasing of Doppler signals, and in four, Doppler signals at the stenosis were not measurable because of technical difficulties. The stenotic flow velocity was successfully recorded in 13 patients (65%) with mild to moderate stenosis. The diastolic peak flow velocity at the stenosis was 90±36 cm/sec (mean±SD), and was significantly greater than the velocity at the prestenotic segment, 48±18 cm/sec \((p < 0.01)\). Percent area stenosis determined by Doppler continuity equation correlated closely with that by biplane coronary angiography \((r=0.83, y=0.92x-0.45, p < 0.01)\).

Conclusions. Application of the continuity equation to Doppler catheter measurement of coronary flow velocity can be used to successfully compute the severity of coronary stenoses. This may be a useful alternative method to estimate functional severity of coronary artery disease, although further technical developments will be necessary to improve the sensitivity. (Circulation 1992;85:1786–1791)

Key Words • intravascular ultrasound • coronary stenosis • coronary flow velocity

Quantitative evaluation of coronary stenoses is the fundamental means used to guide therapy of coronary artery disease.\(^1\)\(^-\)\(^2\) Although evaluation of the severity of coronary stenosis is usually performed by coronary angiography, the method has significant limitations. Because angiography provides only a silhouette of the vascular lumen, some studies have documented a poor correlation between percent stenosis and the physiological consequences of coronary obstructions.\(^3\)

Developments of Doppler catheter methods enabled measurement of intracoronary flow velocity in the clinical setting.\(^4\)\(^-\)\(^5\) When combined with a spectrum analysis system, absolute flow velocity can also be determined. This technique may permit assessment of a percent stenosis by application of the continuity equation, which was originally introduced into the measurement of stenotic valve area.\(^6\)\(^-\)\(^7\) Although Johnson et al\(^8\) reported that in a canine model, the cross-sectional area of the coronary stenosis can be calculated by the Doppler catheter method, there have been no studies regarding quantification of coronary stenoses using this method in humans. This may be due to methodological difficulties in measurement of the absolute flow velocity in the human coronary circulation.

Recently, we established the Doppler catheter system, by which absolute velocity of human coronary flow could be measured using fast Fourier transformation (FFT) analysis technique.\(^9\) In the present study, we attempted 1) to measure the velocities in the prestenotic and stenotic segments of the coronary artery using a Doppler catheter, and 2) to determine the functional severity of the stenosis using the continuity equation method.
Methods

Study Patients

We studied 19 patients with coronary artery stenosis at the proximal to midportion of the left anterior descending artery (LAD) and one patient with a stenosis in the saphenous vein bypass graft to the LAD demonstrated by coronary angiography. Because this was a feasibility study, we chose patients with LAD disease because prior experience demonstrated that intracoronary catheter manipulation is easiest in the proximal LAD. This research protocol was directed by the Hospital Medical Ethics Committee of the National Cardiovascular Center. Informed consent for intracoronary Doppler examination was obtained from all patients. Fourteen patients had typical exertional chest pain and six patients had atypical chest pain symptoms. Nine patients had history of previous myocardial infarction. All were men aged 47 to 71 years (mean, 60 years).

Coronary Angiography

Coronary angiography was performed by standard Judkins method using biplane imaging system (System CAS-LA, Toshiba, Tokyo). We used a 7 or 8F guiding catheter (Softip, Schneider) for insertion of a Doppler catheter. After sublingual administration of nitroglycerin (0.3 mg), 6-8 ml of contrast medium (Iopamidol, Schering AG Pharma) was injected into each coronary artery to obtain the angiographic images. Simultaneous biplane orthogonal views in which the stenosis was clearly visualized were selected, and images were recorded on Kodak CSF film at a framing rate of 30 frames per second.

Flow Velocity Measurements

We used a commercially available 3F (1.0-mm) pulsed Doppler catheter with an end-mounted transducer (model DC-201, Millar Inc., Houston Tex.) and a standard signal generator (model MDV-20, Millar Inc.).5 8 The carrier frequency was 20 MHz, and the pulse repetition frequency was 62.5 kHz. The sample volume that was determined by the carrier and pulse repetition frequencies was 0.46 mm in depth and moveable from 1 to 10 mm from the catheter tip. Absolute flow velocity was calculated from Doppler catheter signals using the FFT method previously described.9

Heparin (3,000 units) was administered before diagnostic coronary angiography, and an additional 100 units/kg was given before the Doppler catheter study. The Doppler catheter was preloaded with a 0.014-in., very flexible steerable guide wire (USCI, Galway, Ireland). The guide wire was extended beyond the tip of the Doppler catheter and the entire system passed through the guiding catheter into the native coronary artery or a bypass graft approximately 5 mm proximal to the stenotic segment. After this procedure, the guide wire was withdrawn into the Doppler catheter lumen, which offered improved signal quality. A biplane coronary angiogram was obtained from the identical projections used for diagnosis to confirm the position of the tip of the Doppler catheter. At this time, we used a small amount of contrast medium to prevent driving the Doppler catheter forward.

The Doppler sample volume was set at 3-4 mm beyond the catheter tip, and a phasic tracing of maximal flow velocity proximal to the stenotic segment was obtained by making minor adjustments of the catheter position with the aid of audio signal. Subsequently, the sample volume was advanced 3–5 mm to record the flow velocity at the stenotic segment. The position of the sample volume was adjusted to determine the maximal stenotic flow velocity. Flow velocity pattern was recorded on a strip chart system at a paper speed of 100 mm/sec. The peak flow velocity was measured from the outer border of the spectral display of the recording. Time–velocity integral of flow was also measured by planimetry as the area between the velocity curve and the zero line during one cardiac cycle. In the present study, we calculated the time–velocity integral using spectral peak flow velocity rather than spectral mean flow velocity, because a previous experimental study had indicated the superiority of the use of spectral peak flow velocity in the measurement of cross-sectional area.68 These measurements were performed with an off-line computer system (PC-9801, NEC, Tokyo). All reported measurements represent the average of three to five consecutive beats.

Determination of Percent Area Stenosis

Luminal diameters at the prestenotic and stenotic segments were measured at end diastole from coronary angiograms projected onto a large screen at fivefold magnification with a projector (Tagarno 35CX, Tagarno A.S., Denmark). At this time, a special care was taken to measure the dimension of prestenotic segment at the precise location where the Doppler sample volume was positioned. Cross-sectional area was determined as a product of two orthogonal luminal diameters and \( \pi \times \frac{1}{4} \). Angiographically determined percent area stenosis was calculated as (stenotic cross-sectional area−stenotic cross-sectional area)/stenotic cross-sectional area×100.

The continuity equation method was applied for calculation of Doppler-determined percent area stenosis. According to the continuum equation, coronary flow volume during one cardiac cycle at the prestenotic segment \((Q_1)\) should be equal to that at the stenotic segment \((Q_2)\) if there are no branches between the prestenotic segment and the stenotic segment. Flow volume during one cardiac cycle is determined as a product of cross-sectional area at the point at which velocity is measured and the time–velocity integral.7 8 Then

\[
Q_1 = A_{\text{pre}} \times TVI_{\text{pre}} = A_s \times TVI_s = Q_2
\]

\[
A_s = A_{\text{pre}} \times TVI_{\text{pre}} / TVI_s
\]

where \(A_{\text{pre}}\) is prestenotic cross-sectional area, \(A_s\) is stenotic cross-sectional area, and \(TVI_{\text{pre}}\) and \(TVI_s\) are the time–velocity integrals of the flow over one cardiac cycle at the prestenotic and stenotic segments, respectively. By rearranging the equation, percent area stenosis is determined as

\[
\text{Percent area stenosis} = (A_{\text{pre}} - A_s) / A_{\text{pre}} \times 100 = (1 - TVI_{\text{pre}} / TVI_s) \times 100
\]
Figure 1. Representative angiographic findings and coronary flow velocity patterns. In right anterior oblique view (RAO) (upper left), there was a stenotic lesion of 58% in diameter (arrow). In left anterior oblique view (LAO) (upper right), there were only luminal irregularities (arrow). Typical coronary flow velocity patterns were recorded just proximal to stenosis (lower left). Note that flow pattern represents laminar flow. When a sample volume was set at 8 mm beyond the tip, markedly augmented flow velocity was recorded (lower right). Calculated cross-sectional area stenosis was 60% from angiography and 51% from Doppler continuity equation method.

Statistical Analysis

Data are expressed as mean±SD. The differences between two measures were compared by Student’s t test, and the relation between two parameters was evaluated by a simple regression analysis. We considered results significant when the probability value was less than 0.05.

Results

Coronary Angiography

Two patients had large diagonal branches arising just proximal to the stenotic segment. Therefore, we had to exclude these two patients from the calculation of area stenosis by Doppler technique, because the flow of the branches would disintegrate the assumption of the continuity equation. Calculated percent cross-sectional area stenosis in the remaining 18 patients ranged from 21 to 94% (mean, 63±16%). A representative case with a 60% cross-sectional area stenosis is shown in the upper panels of Figure 1.

Measurement of Premenstotic and Stenotic Flow Velocities

Flow velocity at the prestenotic segment was measured in all patients. The typical flow velocity pattern of the prestenotic segment of the proximal LAD consisted of a large diastolic forward flow preceded by a small systolic forward flow (lower left panel of Figure 1).

Among 20 patients, the flow velocity pattern at the stenotic segments could be recorded in 13 patients (65%) with mild to moderate stenosis. There was also a predominant diastolic forward flow and a relatively small systolic forward flow (lower right panel of Figure 1). In three patients with severe stenosis (>90% in angiographical area stenosis), there were bidirectional flow signals mainly during diastole. These signals could not be analyzed because of aliasing and flow turbulence. In two patients, flow velocity signals from the stenosis could not be recorded possibly because of the inappropriate direction of the Doppler beam. The peak velocity at the stenotic segment of 13 patients was 90±36 cm/sec during diastole and was significantly greater than velocity at the prestenotic segment, 48±18 cm/sec (p<0.01). The time–velocity integral of the flow at the stenotic segment was also significantly greater than at the prestenotic segment (43±18 cm versus 21±6 cm; p<0.01).

Doppler-determined percent area stenosis ranged from 21% to 76% (mean, 48±15%). When these values were compared with stenosis severity by angiography, there was a good correlation (r=0.83, y=0.92x−0.45, n=13, p<0.01; Figure 2).
TABLE 1. Time–Velocity Integrals and Percent Area Stenosis

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>TVI at prestenosis (cm)</th>
<th>TVI at stenosis (cm)</th>
<th>Doppler-derived area stenosis (%)</th>
<th>Angiographic area stenosis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>60</td>
<td>18</td>
<td>36</td>
<td>51</td>
<td>60</td>
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<td>59</td>
<td>26</td>
<td>54</td>
<td>52</td>
<td>60</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>59±7</td>
<td>21±6</td>
<td>43±18</td>
<td>48±15</td>
<td>53±14</td>
</tr>
</tbody>
</table>

All male patients. TVI, time–velocity integral.

There was no complication during catheterization procedures.

Discussion

In the present study, stenotic flow velocity in the human coronary artery was measured with a Doppler catheter system, and the severity of stenosis was quantitatively evaluated by the continuity equation. Although there are several studies in which coronary flow velocity at the site of stenosis was measured in experimental models,8,10 to our knowledge, this is the first report examining the flow velocity of human coronary stenoses.

Flow Velocity at Site of Stenosis

We found that coronary flow velocity at the stenotic segment is markedly increased. It is reasonable to expect that flow velocity becomes progressively higher as the stenosis increases because of a larger pressure gradient across the lesion. The concept has been reported by Gould,10 who proposed that pressure gradients across the stenosis could be determined if stenotic flow velocity could be measured. However, in the human coronary circulation, there are important methodological difficulties in the measurement of the flow velocity at the stenosis.

In the present study, we determined the flow velocity at the stenotic segment by moving the Doppler sample volume (not by moving the catheter). This procedure minimized the effect of the catheter on the measured flow velocity as reported in the experimental study.8 Indeed, the measured flow velocity at the stenosis was similar to those measured by another method,11 suggesting that the present data could be acceptable for the area calculation.

Application of Continuity Equation

The continuity equation is the law of conservation of mass in hydrodynamics and has been applied to measure the aortic and mitral valve areas.6,7 Theoretically, the continuity equation should apply to the mean flow velocity and not the peak flow velocity. Mean and peak velocities will be approximately the same if the flow profile is blunt, a requisite not present in the coronary arteries. However, Johnson et al8 reported that in the canine model, the estimated cross-sectional area of the stenosis using the continuity equation and the spectral mean velocity had a poor correlation with the true cross-sectional area, whereas that using the spectral peak velocity correlated better. There are several reasons for this discrepancy. First, in the measurement of flow velocity at the stenosis, the Doppler sample volume (0.46 mm in depth) may overlap the lower velocities just proximal to the stenosis, thus resulting in calculation of a lower mean velocity at the stenosis. Second, in the measurement of prestenotic flow velocity, the Doppler catheter may be positioned off center, and a relatively high proportion of low-velocity signals near the wall may be included in the calculation of mean velocity. Third, high-pass filters used in the FFT analysis system can reduce low-velocity components as well as artifacts.

![Figure 2. Graph shows relation between percent cross-sectional area stenosis determined by coronary angiogram (CAG) (horizontal axis) and by Doppler continuity equation method (vertical axis).](image-url)
from the vessel wall, resulting in errors in the measurement of true mean velocity. Therefore, practical considerations favor the use of the spectral peak flow velocity in the calculation of the cross-sectional area by the continuity equation. Indeed, we found a good correlation between Doppler-determined percent cross-sectional area stenosis, which was derived from the integral of time and spectral peak velocity, and angiographically determined percent cross-sectional area stenosis.

Other factors that can affect the velocity measurements using a Doppler catheter must also be considered. First, our measurements were performed by placing the sample volume more than 3 mm beyond the catheter tip to avoid flow interference effect, because it has been reported that there would be no effect from the catheter approximately 1 mm beyond the tip. However, in the diseased or curved vessels, flow disturbances at the tip of the catheter may extend beyond 1 mm downstream. This potential problem is mitigated by the use of spectral peak velocity in the calculations; if the true peak velocities are present anywhere in the Doppler beam, the measurement will be accurate. This represents another advantage of the use of the spectral peak velocity for the continuity equation. Second, we measured flow velocity after withdrawing the guide wire into the catheter lumen to avoid any flow interference by the guide wire. This procedure sometimes resulted in difficulty to fix the catheter in the center of the vessel lumen. Further, a free tip of the Doppler catheter might injure the coronary vessel. However, careful and meticulous manipulation of the Doppler catheter while monitoring the flow velocity pattern enabled safe positioning of the catheter near the center of the lumen. Third, the Doppler-derived cross-sectional area at the stenotic segment may be theoretically somewhat smaller than the true cross-sectional area because of the vena contracta effect. Therefore, the stenotic cross-sectional area determined by the continuity equation method represents the effective area rather than the true anatomical area, as suggested in the previous experimental study. This might explain, in part, the smaller cross-sectional area determined by Doppler compared with angiography.

Clinical Implications

Accurate determination of the severity of coronary stenosis is required to evaluate catheter-based interventions. Contrast angiography is not necessarily suitable for the purpose, because recent studies by intravascular ultrasound imaging technique suggested that it is difficult to correctly estimate the stenosis from the angiogram because of the eccentricity of vascular lumen after angioplasty. Regarding intravascular ultrasound imaging technique, the present smallest size of ultrasound catheter is 3.5F and is still too large to be inserted into the tight coronary stenosis. Therefore, measurement of the stenotic cross-sectional area based on the continuity equation method will provide an alternative index of the results of such interventions without inserting the catheter into the stenotic segment. It may also be possible to combine Doppler stenosis sizing with determination of coronary flow reserve. Thus, anatomical and physiological severity of the stenosis could be evaluated with a single Doppler catheter.

Limitations

There remain practical limitations to this new technique. In the present study, only 13 of the 20 patients had acceptable flow recordings at the stenotic segment. This relatively high failure rate (35%) is mainly due to two factors: 1) The measurable flow velocity, which is determined by the carrier and pulse repetition frequencies, is limited to approximately 115 cm/sec, and aliasing occurs when higher coronary flow velocities are encountered. 2) It is impossible to measure the flow velocity at a severe stenosis where coronary blood flow would be markedly augmented. Indeed, in the present study, the velocity signal could not be optimally recorded in three patients with severe stenosis (>90%). However, in these cases with severe stenosis, clinical decisions are not difficult using conventional angiography. Therefore, the present method seems to be useful to evaluate the severity of the clinically important subjects of mild to moderate stenosis. Use of a high-pulse repetition frequency method or continuous-wave Doppler method could overcome this limitation. Our shortcomings include the difficulty in positioning the sample volume in the center of the coronary lumen, especially in the presence of curvature. This technique is also not applicable to long, sequential, or diffuse coronary artery stenoses. The guide wire--type Doppler probe (0.018-in.) may be useful to measure the flow velocity of such stenoses because of its excellent flexibility and small size.

Although we used orthogonal biplane angiograms to minimize errors in the evaluation of stenosis, luminal diameter measured from the angiogram might be misleading in the evaluation of the severity, especially when the lesion is eccentric and/or complex. This may be one of the reasons why there was scatter in the calculated cross-sectional area by the Doppler method. The other reason for this variability may be that angiographic dimensions were determined in diastole, whereas the Doppler indexes were averaged over the cardiac cycle. The distension of the vessel that can occur from presurized injections of contrast may also contribute to the variability. Comparison of the present results with those obtained by another direct method such as intravascular ultrasound imaging will be necessary to confirm the accuracy of Doppler estimation of coronary stenosis.

Because this was a feasibility study to examine the Doppler catheter technique to quantify coronary stenoses, only patients who had a lesion in the LAD or the bypass graft were examined. However, it should be possible to obtain similar results in the left circumflex artery and/or the right coronary artery, although the manipulation of the Doppler catheter may be somewhat more difficult because of the tortuosity of these vessels. Further studies using the improved Doppler catheter may demonstrate the practical usefulness of the present method for the quantitative evaluation of coronary artery stenosis.

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