

Use of the Continuity Equation for Transesophageal Doppler Assessment of Severity of Proximal Left Coronary Artery Stenosis: A Quantitative Coronary Angiography Validation Study

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Objectives. We tested the value of transesophageal Doppler echocardiography (TEDE) for quantitating proximal left coronary artery (LCA) stenosis by using the continuity equation.

Background. The continuity equation applied to a stenosis states that the ratio of the time-velocity integral (TVI) of prestenotic to stenotic flow velocities is equal to the ratio of stenotic to prestenotic cross-sectional areas. TEDE allows the measurement of coronary blood flow velocities within the proximal part of the LCA.

Methods. Forty-one patients with a stenosis of the proximal or mid left anterior descending coronary artery or with a nonostial stenosis of the left main coronary artery were studied. Coronary flow velocities were recorded by TEDE guided by color flow imaging. Prestenotic velocities were recorded by pulsed Doppler echocardiography and transstenotic velocities were recorded by pulsed or high pulse repetition frequency or continuous wave Doppler echocardiography. The prestenotic and transstenotic diastolic TVIs were calculated and the TEDE-derived percent area

stenosis was calculated as $(1 - \text{TVI ratio}) \times 100$. Quantitative angiography lesion analysis was performed using a computer-assisted automated edge-detection system.

Results. TEDE recordings were successful in 35 of the 41 patients. A good linear correlation was found between TEDE and quantitative angiographically derived percent area stenosis ($r = 0.89$, $p = 0.0001$, SEE 5.7). However, TEDE measurements underestimated the actual percent area stenosis (slope of regression 0.54). A better agreement (slope 1.08) was obtained after dividing prestenotic velocity by 2 in the continuity equation, based on the assumption of a parabolic cross-sectional velocity profile in the prestenotic segment.

Conclusions. TEDE may be used for quantitating stenosis of the proximal part of the LCA with the use of a modified continuity equation that takes into account the parabolic velocity profile in the normal prestenotic segment.

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Quantitative evaluation of coronary stenosis is clinically important. Quantitative coronary angiography is usually performed for estimating the severity of coronary stenosis. Intracoronary blood flow velocity measurements using Doppler catheters or Doppler ultrasound guide systems have also been proposed as an alternative method for evaluating the functional severity of coronary stenosis at baseline as well as for assessing the results of interventional procedures (1-5). Johnson et al. (1) demonstrated, in a canine model, that the cross-sectional area (CSA) of the coronary stenosis can be calculated with a Doppler catheter using the continuity equation, which was originally introduced for measuring stenotic valve area (6,7). More recently, Nakatani et al. (2) showed, in 13 patients with mild to moderate stenosis, that application of the continuity equation to Doppler catheter measurement of

coronary flow velocity can be used to successfully compute the severity of coronary stenosis. These methods, however, remain invasive, requiring cardiac catheterization, and cannot be repeated without risk during serial follow-up studies. Furthermore, in a consecutive series of 52 patients undergoing percutaneous transluminal coronary angioplasty, Di Mario et al. (8) found that, although the percent CSA stenosis derived from the intracoronary guide wire Doppler measurements based on the continuity equation were significantly correlated with the corresponding quantitative angiographic measurements, this determination could be achieved in only 16% of cases. Recently, it has been demonstrated that coronary blood flow velocity can be recorded in the proximal part of the left coronary artery (LCA) with the use of transesophageal Doppler echocardiography (TEDE) (9-15). In the present study, we tested whether the percent reduction of CSA of the stenosis can be quantitated by TEDE using the continuity equation.

Methods

Study group. Forty-one patients with a left main coronary artery (LMCA) distal stenosis or a stenosis at the proximal or

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Abbreviations and Acronyms

CSA	=	cross-sectional area
DS	=	diameter stenosis
LAD	=	left anterior descending coronary artery
LCA	=	left coronary artery
LMCA	=	left main coronary artery
MLD	=	minimal lumen diameter
TEDE	=	transesophageal Doppler echocardiography
TVI	=	time-velocity integral

mid segment of the left anterior descending coronary artery (LAD), with no side branch involved in the lesion, were prospectively studied from January to September 1995. We chose patients with LMCA or proximal or mid LAD disease because, in our experience, TEDE recordings are easier to obtain in these portions of the LCA. A high quality TEDE signal was obtained in 35 patients (25 men and 10 women, mean age 63 years [range 38 to 77]). Among these 35 patients studied, 11 had an LMCA distal stenosis, 19 had a stenosis at the proximal segment of the LAD and 5 had a stenosis of the mid segment of the LAD. Written informed consent for TEDE examination was obtained in all patients.

Coronary angiography and quantitative coronary angiography. Coronary angiography was performed using the standard Judkins method with the femoral approach. Coronary injections were performed using multiple views, and images were recorded on Kodak CFE 746 film at a framing rate of 25 frames/s. Film images were converted into digital format using a video camera and a video-digital converter interfaced with a computer-assisted automated edge-detection system (ARTREK, ImageComm, Quinton Systems). This quantitative coronary angiographic system has been validated previously (16). Quantitative analysis of stenosis was performed using the average of results obtained from two orthogonal projections, when available, or the most severe narrowing of several nonorthogonal angiographic projections. Three recognized quantitative variables of stenosis severity (17,18) were automatically computed by the ARTREK analysis software: percent diameter stenosis (DS), minimal lumen diameter (MLD) and percent CSA stenosis.

Transesophageal Doppler echocardiographic measurements. Transesophageal echocardiography was performed with a 5-MHz probe connected to a Hewlett-Packard Sonos 1000 or Vingmed CFM 800 echocardiographic system within 24 h of the angiographic study. A multiplane probe was used in 25 patients and a single-plane probe was used in the remaining 10 patients. Transesophageal examination was performed in each patient after sedation with sublingual midazolam hydrochloride and oropharyngeal anesthesia by lidocaine. The LMCA was visualized by placing the transducer just above the aortic leaflets. Small adjustments in transducer orientation were necessary to visualize the bifurcation of the vessel into the LAD and circumflex artery. Prestenotic and transstenotic coronary flow velocities were then measured as follows: coro-

nary blood flow was first visualized by color flow imaging and a localized color aliasing phenomenon corresponding to a local flow acceleration was searched; pulsed wave Doppler echocardiography was then sampled in the site immediately upstream from the area of color aliasing; second, the sample volume was moved slightly downward in the area of color aliasing. High pulse repetition frequency or continuous wave Doppler echocardiography was used to quantitate the magnitude of transstenotic velocities if these velocities were too high to be measured by pulsed Doppler echocardiography without aliasing, the choice between the two techniques being left to the discretion of the operator based on the best quality signal. Small adjustments in the transducer orientation allowed alignment of the ultrasound beam with the long axis of the interrogated proximal portion of the LCA. The peak flow-velocity curve was traced from the outer border of the Doppler spectral signal, and the time-velocity integral (TVI) was obtained by planimetry as the area under this peak flow-velocity curve during diastole. We and other investigators have previously reported good interobserver and intraobserver reproducibility of coronary flow transesophageal Doppler velocity recording in the proximal part of the LCA (9-15). Two examples of typical phasic coronary flow-velocity signals recorded by TEDE in the prestenotic and transstenotic regions are illustrated in Fig. 1.

Transesophageal Doppler echocardiographic determination of percent area stenosis. According to the continuity equation, coronary flow volume at the prestenotic segment is equal to that at the stenotic segment in the absence of branches between the two segments. As flow volume is derived from the product of CSA with the TVI, thus,

$$\text{Prestenotic CSA} \times \text{Prestenotic TVI} = \text{Stenotic CSA} \times \text{Stenotic TVI}. \quad [1]$$

The percent area stenosis (%CSA) is written as

$$\% \text{CSA} = 100 (1 - \text{Stenotic CSA} / \text{Prestenotic CSA}). \quad [2]$$

Rearranging Equations 1 and 2 leads to

$$\% \text{CSA} = 100 (1 - \text{Prestenotic TVI} / \text{Stenotic TVI}). \quad [3]$$

Transesophageal measurements and calculations were performed with the observer having no knowledge of the quantitative coronary angiographic data.

Statistical analysis. All data are expressed as the mean value \pm SD. Prestenotic and stenotic velocities were compared using a two-tailed paired *t* test. A *p* value <0.05 was considered significant. The correlations between angiographic percent CSA stenosis and TEDE coronary flow-velocity derived indexes were obtained using linear regression analysis, and the agreement between both measurements was evaluated using the method of Bland and Altman (19).

Results

Coronary angiographic data. No patient had a large diagonal or septal branch arising immediately proximal to the

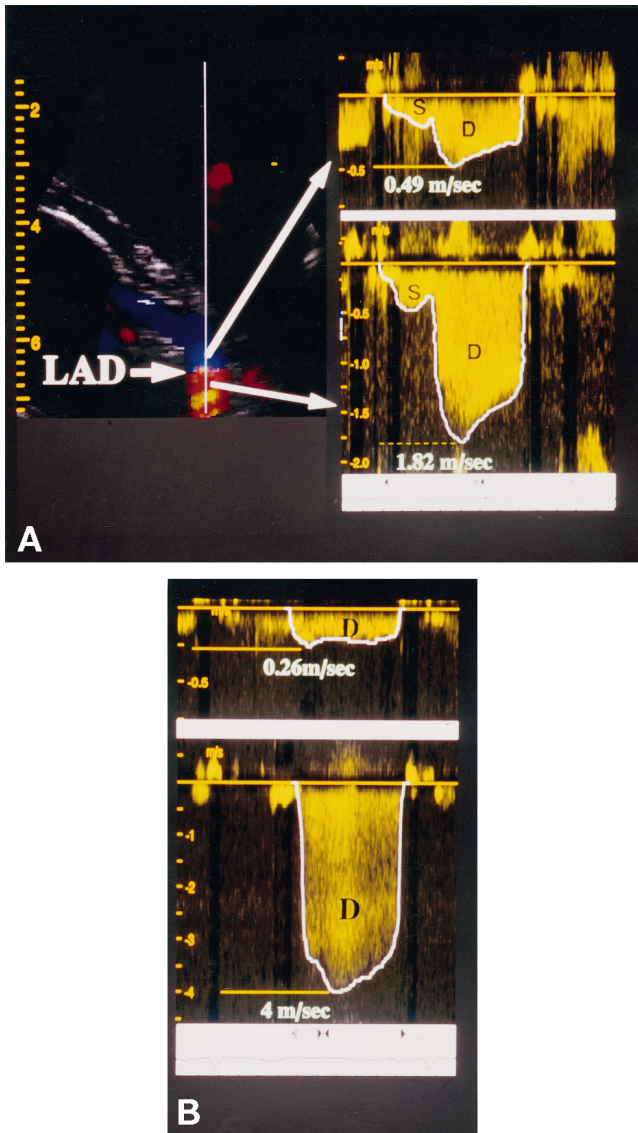


Figure 1. Examples of transesophageal Doppler coronary flow recording in two different patients with stenosis of the proximal part of the LAD. **A**, Example of a patient with a moderate stenosis of the proximal part of the LAD. **Left panel**, Color Doppler flow mapping; note the changes in the color flow map, with blue indicating low velocities in front of the stenosis and a typical localized color aliasing at the site of the stenosis. **Right upper panel**, Pulsed Doppler recording upstream from the zone of color aliasing (prestenotic area); the peak diastolic velocity is 49 cm/s and the diastolic TVI is 25 cm. **Right lower panel**, High pulse repetition frequency Doppler recording of velocities at the site of color aliasing (stenotic area); velocities are significantly increased, with a peak diastolic velocity of 182 cm/s and a TVI of 64 cm. **B**, Example of a patient with a critical stenosis of the proximal part of the LAD. In this patient, only the diastolic velocity wave tracing can be well delineated. **Upper panel**, Pulsed Doppler recording in the prestenotic area; the peak diastolic velocity is 26 cm/s and the diastolic TVI is 12 cm. **Lower panel**, High pulse repetition frequency Doppler echocardiography allows the recording of velocities at the site of the stenotic area as high as 4 m/s, with a TVI of 198 cm. S = systolic wave; D = diastolic wave.

stenosis, so the assumption of the continuity of flow could be applied. The calculated percent DS ranged from 27% to 82% (mean $50 \pm 12\%$); MLD ranged from 0.45 to 3.04 mm (mean

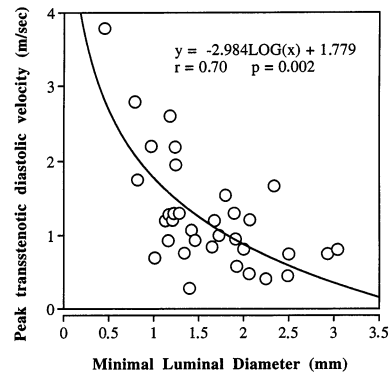


Figure 2. Relation between the catheterization-derived MLD and the TEDE-derived peak diastolic velocity across the stenosis.

1.6 ± 0.6); and percent CSA stenosis ranged from 47% to 97% (mean $73 \pm 12\%$).

Transesophageal Doppler echocardiographic data. A localized increase in velocity appeared on Doppler color flow mapping as a localized area of aliased and disturbed signal in all 35 patients studied. In all patients, peak diastolic velocity and diastolic TVI at the prestenotic site were obtained by pulsed Doppler echocardiography; transstenotic diastolic peak velocity and TVI were obtained in all patients with the use of either pulsed Doppler echocardiography or high pulse repetition frequency Doppler or continuous wave Doppler echocardiography. The peak diastolic velocity at the stenotic region was 126 ± 74 cm/s and was significantly higher than that measured at the prestenotic segment (51 ± 19 cm/s, $p = 0.0001$). The diastolic TVI was also higher at the stenotic segment (39 ± 24 cm) than at the prestenotic region (15 ± 6 cm, $p = 0.0001$). A significant inverse curvilinear relation was found between the catheterization-derived MLD and the peak transstenotic diastolic velocity derived from TEDE ($r = -0.70$, $p = 0.002$) (Fig. 2). A good linear correlation was found between the catheterization-derived and TEDE-derived percent CSA stenosis ($r = 0.89$, $p = 0.0001$) (Fig. 3). Despite this good linear relation, analysis of the linear regression showed that TEDE measurements significantly underestimated the actual percent CSA stenosis. As an example, Figure 3 shows that a 70% CSA reduction calculated by catheterization corresponded to only a 47% TEDE-derived CSA reduction. After dividing by 2 the values of prestenotic Doppler TVIs, the accuracy of TEDE for predicting the catheterization-derived percent CSA reduction was improved, as shown in Figure 4. As shown in Figure 5, a good linear relation was also found between the catheterization-derived percent DS and the simple prestenotic to stenotic TVI ratio, which was a good discriminator for distinguishing patients with $\geq 50\%$ diameter reduction from those with $< 50\%$ diameter reduction. All patients with $\geq 50\%$ diameter reduction stenosis at catheterization had a TVI ratio ≤ 0.5 and only two of the 21 patients with $< 50\%$ diameter reduction had a TVI ratio ≤ 0.5 . Thus, a TVI ratio ≤ 0.5 predicted $\geq 50\%$ diameter reduction with 100% sensitivity and 90% specificity.

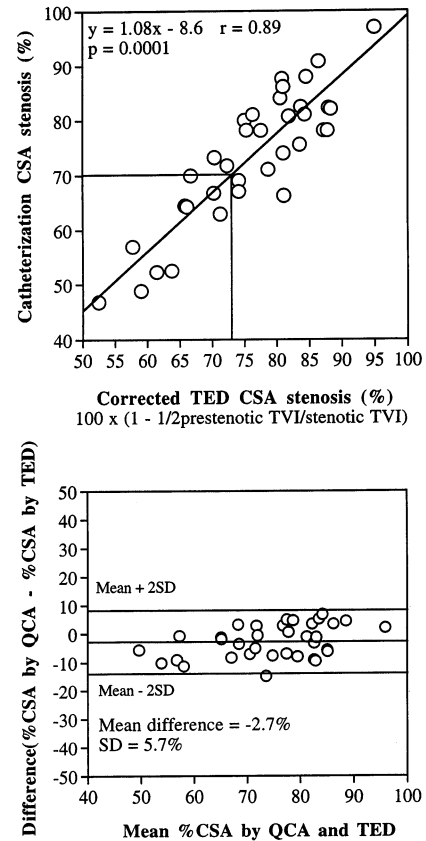
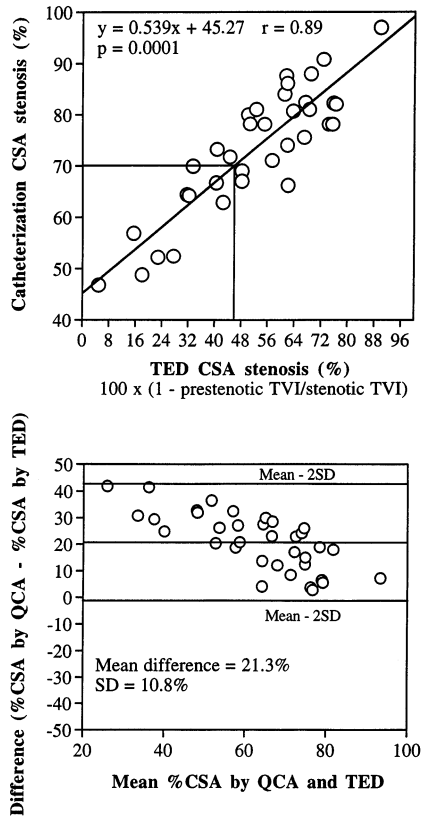


Figure 3. Upper panel, Relation between catheterization-derived percent CSA stenosis and TED-derived percent CSA stenosis, using the continuity equation. Lower panel, Plot of the difference of the values obtained by the two methods versus the mean of the values. QCA = quantitative coronary angiography. TED = transesophageal Doppler echocardiography.

Figure 4. Upper panel, Relation between catheterization-derived percent CSA stenosis and TED-derived percent CSA stenosis, using the corrected continuity equation (i.e., by dividing the prestenotic TVI by 2). Lower panel, Plot of the difference of the values obtained by the two methods versus the mean of the values. QCA = quantitative coronary angiography; TED = transesophageal Doppler echocardiography.

Discussion

The present study demonstrates that velocity measurements derived from TEDE can be used for quantitating stenosis of the LMCA and proximal LAD. To our knowledge, this is the first report to validate, by comparison with digital quantitative angiographic data, the use of TEDE for quantitating coronary artery stenosis based on the application of the continuity equation.

Transstenotic velocity measurements. Our study shows that coronary flow velocity measured by TEDE at the site of the stenosis is significantly increased compared with that recorded in the normal prestenotic segment. Previous published clinical and animal studies (1,2) based on Doppler catheter measurements have shown that coronary flow velocity increases at the site of a stenosis. Yamagishi et al. (11), using TEDE, showed that flow velocity recorded by pulsed Doppler echocardiography at the site of the LMCA stenosis in 10 patients was significantly higher than that recorded in the LMCA of 21 patients without coronary stenosis. More recently, Caiati et al. (15) showed in 16 patients that a percent increase in TEDE-derived peak diastolic velocity of at least 50% at the site of color aliasing detected a significant proximal

stenosis of the LAD, with a sensitivity of 93% and a specificity of 100%. However, in their study, Caiati et al. (15) did not perform quantitative coronary angiography, and these investigators defined significant stenosis as $\geq 50\%$ diameter reduction assessed visually. Beside its limitations for estimating the severity of coronary stenosis, visual assessment does not allow accurate and systematic comparison between angiographic and TEDE data.

In our study, we found only a fair, although significant, inverse relation between the catheterization-derived MLD and the TEDE-derived peak transstenotic diastolic velocity (Fig. 2). Indeed, for a given MLD, the transstenotic velocity varies with coronary flow rate, which in turn is dependent on many physiologic variables like aortic pressure, heart rate, myocardial contractility and intramyocardial coronary vascular tone. Thus, different hemodynamic conditions may modify transstenotic velocities independently of the MLD.

Use of the continuity equation. Three previously published reports (1,2,8) based on invasive Doppler measurements have proposed the application of the continuity equation to estimate the severity of coronary stenosis. However, the methods used

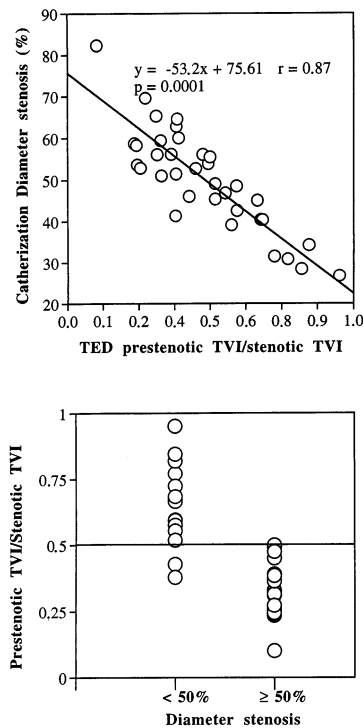


Figure 5. Upper panel, Relation between catheterization-derived percent DS and the TED-derived ratio of prestenotic to stenotic VTIs. Lower panel, Individual data for the ratios of prestenotic to stenotic VTIs in patients subclassified according to the catheterization-derived percent DS (<50% or ≥50%). TED = transesophageal Doppler echocardiography.

in these previously published studies (1,2,8) remain invasive, requiring cardiac catheterization, and cannot be repeated without risk during serial follow-up studies. Furthermore, in their consecutive series of 52 patients undergoing percutaneous transluminal coronary angioplasty, Di Mario et al. (8) found that, although accurate for quantitation of lesion significance, use of the continuity equation employing intracoronary guide wire Doppler measurements is difficult and impractical for clinical application because high quality intrastenotic Doppler signals are obtained in only a minority of cases.

In our study, we used a noninvasive approach—TEDE—which can be used more easily in a clinical setting. We found a good linear relation ($r = 0.89$) between catheterization-derived and TEDE-derived percent CSA stenosis using the continuity equation. Despite this good linear relation, TEDE measurements significantly underestimated the actual percent CSA stenosis. This discrepancy between transesophageal Doppler measurements and the actual percent CSA may be explained by differences in the cross-sectional velocity profile that may occur between the prestenotic and stenotic segment sites. Fluid mechanics theory and previous published experimental studies suggest that cross-sectional velocity profile in a small conduit, like coronary arteries, is parabolic at a low Reynolds number, but flattens when velocities increase, like in a stenosis where flow becomes turbulent (20–24). We have recently confirmed in a clinical study, based on computer analysis of digitally

transferred transesophageal color coronary flow maps, that the cross-sectional velocity profile is parabolic in the normal proximal LAD, whereas it becomes flatter when velocities increase, like at the site of stenosis or after intravenous injection of dipyridamole (25). Accordingly, one should divide by 2 the velocities in the normal prestenotic segment when applying the continuity equation (see Appendix). This theoretic hypothesis is supported by our data. Figure 3 shows that a 50% CSA reduction predicted by TEDE using the simple TVI ratio in the continuity equation corresponds to an actual 72% CSA reduction calculated by catheterization. After dividing by 2 the values of prestenotic Doppler TVIs, the accuracy of TEDE for predicting the catheterization-derived percent CSA reduction was improved, as shown in Figure 4. For clinical purposes, however, as shown in Figure 5, the simple TVI ratio may be used for predicting with good accuracy the percent DS, which is also a well recognized variable of stenosis severity.

Clinical implications. Our data suggest that TEDE allows quantitation of stenosis of the LMCA and proximal LAD. This method offers the advantage of a noninvasive technique, which can be applied in many echocardiographic laboratories.

Our TEDE method might also represent an adjunct to coronary angiography to evaluate mild to moderate stenosis. Conventional angiography with visual interpretation, as currently used in many catheterization laboratories, has significant limitations in the assessment of coronary stenosis (26). In patients with severe coronary diameter reduction on the angiogram, there is usually no difficulty in ascertaining the functional severity of the lesion and in making clinical decisions. In contrast, in some patients with angiographically documented mild to moderate stenosis, it is sometimes difficult to evaluate the actual physiologic consequences of the obstruction. Also, contrast angiography, even when using quantitative angiography, is not necessarily suitable for evaluating the results of catheter-based interventions owing to the eccentricity of the vascular lumen after angioplasty (27). As TEDE measurements using the continuity equation do not rely on any geometric assumption, it might help to confirm the functional severity of stenosis visualized by angiography, especially in cases of mild to moderate lesions and after catheter-based interventions.

TEDE also provides a method for quantitating the severity of the stenosis without inserting any catheter or guide wire into the stenotic segment. In contrast, Doppler catheters or guide wires reduce the actual CSA of the stenosis and may disturb flow field, thus leading to some errors in measurements.

Study limitations. Some limitations of this new technique must be addressed. In our study, we were able to obtain interpretable TEDE flow recordings at the site of both prestenotic and stenotic regions in only 35 of 41 patients, which represents a success rate of 85%.

The present study was designed to test the ability of TEDE, in comparison with digital quantitative angiographic data, for quantitating proximal LCA stenosis based on the continuity equation. However, the accuracy of this method in detecting

the absence or presence of a significant stenosis in the proximal LCA in patients with various heart diseases on a large screening basis remains to be determined.

Only patients with stenosis of the LMCA or LAD were studied, and no attempt was made to explore circumflex and right coronary arteries. Owing to more severe angulation and tortuosity of these vessels, adequate Doppler signals, as well as a good alignment between the ultrasound beam and the axial flow direction, appear to be more difficult to obtain in the right coronary artery and the circumflex artery. However, computation of severity of stenosis of the LMCA and proximal LAD provides clinically important information, because a major amount of myocardium is perfused by these vessels.

The absolute value of MLD could be theoretically computed using the continuity equation if the diameter of the prestenotic segment were known. In the present study, we did not attempt to calculate this variable because we believe that the lateral resolution of the two-dimensional sector scan is too low to allow reliable measurements of dimensions of coronary arteries.

Theoretically, the continuity equation applies to flow velocity measurements in a nonbranching system. In our study, no patient had a large diagonal or septal branch arising immediately proximal to or within the stenosis. This method might have limitations for quantitating the severity of bifurcation stenosis involving both the parent vessel and the ostium of a side branch.

Appendix

Continuity Equation in Coronary Artery Stenosis

At any instant and at any site, the coronary flow rate (CFR) is equal to the product of spatial average velocity with the CSA:

$$\text{CFR} = \text{Spatial average velocity} \times \text{CSA.} \quad [1]$$

In the prestenotic segment, assuming a parabolic velocity profile—that is, spatial average velocity is equal to half the peak axial velocity—CFR is written as

$$\text{CFR} = \text{Spatial average prestenotic velocity} \times \text{Prestenotic CSA} \quad [2]$$

$$\approx \frac{1}{2} \text{Peak axial prestenotic velocity} \times \text{Prestenotic CSA.} \quad [3]$$

In the stenotic segment, assuming a flat velocity profile—that is, spatial average velocity is equal to peak axial velocity—CFR is written as

$$\text{CFR} = \text{Spatial average stenotic velocity} \times \text{Stenotic CSA} \quad [4]$$

$$\approx \text{Peak axial stenotic velocity} \times \text{Stenotic CSA.} \quad [5]$$

Rearranging Equations 3 and 5 demonstrates that the percent CSA reduction may be written as

$$\begin{aligned} \% \text{CSA} &= 100(1 - \text{Stenotic CSA/Prestenotic CSA}) \\ &= 100 \left(1 - \left[\frac{1}{2} \text{Peak axial prestenotic velocity} \right] / \text{Stenotic peak axial velocity} \right). \end{aligned} \quad [6]$$

Owing to the width of the pulsed Doppler sample volume and of the continuous wave Doppler beam compared with the small diameter

of the coronary vessel, one can assume that peak velocity measurements derived from TEDE correspond to the actual peak axial velocity within the vessel at any instant. In our study, TVIs were measured by planimetry of the peak velocity curve obtained by tracing the outer border of the Doppler spectral display on the recording, so that Equation 6 can be rewritten by substituting peak velocity by TVI:

$$\% \text{CSA} = 100 \left(1 - \left[\frac{1}{2} \text{Prestenotic TVI} \right] / \text{Stenotic TVI} \right). \quad [7]$$

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