Coronary Artery Flow Velocity Is Related To Lumen Area and Regional Left Ventricular Mass

H. Vernon Anderson, MD; Michael J. Stokes, MD; Miltiadis Leon, MD; Subhi A. Abu-Halawa, MD, MPH; Yvonne Stuart, RT; Richard L. Kirkeeide, PhD

Background—Coronary flow velocity varies widely between individuals, even at rest. Because of this variation, indices with less apparent deviation, such as the ratio of hyperemic to resting velocity (coronary flow reserve), have been more commonly studied. We tested the hypothesis that the flow continuity principle could be used to model resting coronary flow, and we examined the resulting velocity relationship.

Methods and Results—We studied coronary velocity in 59 patients using a Doppler wire to measure resting and hyperemic average peak velocities in the left anterior descending artery. Quantitative techniques were used to calculate lumen cross-sectional area and the lengths of all distal coronary branches. Branch lengths were used to estimate regional left ventricular mass. We then calculated the ratio of lumen area to regional mass (A/m). Regional perfusion was estimated from the double product of heart rate and systolic blood pressure. Resting velocity (V) varied inversely with A/m ratio [V = 46.5/(A/m); r = 0.68, P<0.001]. Disease in the left anterior descending artery was categorized as none or luminal irregularities only (n = 22), mild (n = 15), or moderate (n = 22). The A/m ratio declined across these groups (8.7±4.0, 8.5±6.2, and 5.6±3.0 mm²/100 g, respectively; P<0.04), and the resting average peak velocity increased (27±16, 33±11, and 37±20 cm/s, respectively; P=0.06).

Conclusions—Resting coronary artery flow velocity is inversely related to the ratio of lumen area to regional left ventricular mass. Higher resting velocities are found when insufficient lumen size exists for the distal myocardial bed, as occurs with diffuse mild or moderate coronary atherosclerosis. (Circulation. 2000;102:48-54.)

Key Words: blood flow velocity ■ coronary circulation ■ coronary angiography

Coronary artery flow velocity is easily measured with a Doppler guidewire (FloWire).1 Although absolute velocity (in centimeters per second) is measured, this simple number has not been widely used to characterize coronary status. Relative velocity indices are used more frequently; the most common of these indices is the ratio of hyperemic to resting velocity (CFR). This and other relative indices have been used to assess coronary functional status, the hemodynamic significance of stenoses, and the effects of interventions.2,3 One likely reason CFR has been used is the poorly understood variations in velocity between individuals, both during rest and under hyperemic conditions.4,5 In this study, we focused on determinants of resting coronary velocity. We hypothesize from physical principles that resting velocity depends on lumen cross-sectional area, the size of the myocardial bed perfused by the artery (ie, regional left ventricular mass), and resting myocardial perfusion. We thought it likely that atherosclerotic disease that produced coronary lumen encroachment would be reflected in resting velocity.

Methods

Study Population

We studied coronary velocity in 59 patients. These patients were undergoing diagnostic catheterization for the evaluation of chest pain syndromes, congestive heart failure, and known or suspected valvular disease or for preoperative examination before major noncardiac surgery. We excluded patients with remote prior anterior myocardial infarction or any infarction in other areas within the previous 5 days, as well as those found to have any occluded coronary arteries, any visible collateral flow, left main stenosis, critical coronary lesions in the left anterior descending artery (LAD; >90% diameter stenosis by visual estimation), or previous bypass surgery. We deliberately included patients with a range of disease in the LAD, from those with no apparent disease or luminal irregularities only to those with obvious mild (30% to 50%) and moderate (50% to 70%) lesions.

Theoretical Model

We considered the lumen cross-sectional area in the proximal LAD and its regional myocardial perfusion bed as a unit. We modeled it as functioning at resting demand conditions, without ischemia and without collateral supply to or from the bed. Under these conditions, the flow continuity principle states that volumetric flow through the coronary cross-section (Qw) equals the flow required by the meta-
bolic demand of the myocardial bed \( Q_{\text{bed}} \). Recognizing that \( Q_{\text{art}} \) is the product of a spatially averaged resting velocity \( V \) with a cross-sectional area \( A \) at that point \( Q_{\text{art}} = V \times A \) and that \( Q_{\text{bed}} \) is the product of the distal bed’s average perfusion \( q \) measured as milliliters per minute per 100 grams and its mass \( m \), the flow continuity equation can be written as follows.

\[
V \times A = q \times m
\]

This can be rearranged to express the average resting velocity as follows.

\[
V = \frac{q}{A/m}
\]

This second equation states that coronary velocity at rest directly reflects myocardial perfusion \( q \) but is also inversely related to the area-to-mass \( A/m \) ratio. For these studies, resting perfusion \( q \) was estimated by the double-product of heart rate (HR) and systolic blood pressure (SBP) from the following simple but readily available clinical relation.6,7

\[
q = 8 \times [0.7 \times (HR \times SBP) \times 10^{-1}] - 0.4
\]

**Angiographic and Coronary Velocity Measurements**

After diagnostic angiography, a 0.014-inch Doppler guidewire (FloWire) was introduced into the proximal LAD and adjusted to obtain an optimal signal. Position was documented by angiography. Average peak velocity (APV) was recorded. Spatially averaged flow velocity was taken as \( V = \text{APV}/2 \). The hyperemic response to 18 \( \mu \)g of intracoronary adenosine was then recorded, and the ratio of hyperemic to resting velocity was taken as CFR.

Biplane ventriculograms and coronary cinearteriograms were made. Coronary diameter at the site of velocity measurement (5 mm distal to the wire tip and away from any focal narrowing) was determined by quantitative methods (Figure 1).8 Lumen area was calculated from coronary diameter by assuming a circular cross-section. Left ventricular mass \( (M_{LV}) \) was determined by the methods of coronary tree analysis developed and validated by Seiler et al10,11 according to the following formula: \( m = M_{LV} \times L/L_{LV} \), in which \( L \) represents the summed branch lengths of the coronary vessels distal to the wire tip and \( L_{LV} \), the summed branch length of the left coronary artery system. For each patient, the lumen area of the LAD was divided by regional mass to form the \( A/m \) ratio.

**Statistical Analysis**

Continuous variables are reported as mean±1SD. Log-transformation was performed on continuous variables with skewed distributions. Group comparisons were made using ANOVA. Categorical variables were compared using the \( \chi^2 \) or Fisher exact tests. Least squares regression was performed, and product-moment correlation coefficients were calculated. Significance was determined using the \( t \) test. Differences in estimated regression variables were compared using the method of Bland and Altman.12

\[ P \leq 0.05 \text{ was} \]
considered significant, and values between 0.05 and 0.1 indicated a trend.

Results

Patients
Selected characteristics of the 59 study patients are summarized in Table 1.

Angiographic and Hemodynamic Findings
Variables of interest are summarized in Table 2. Men had greater values for left ventricular mass than women (248±687 g; \( P, 0.01 \)), but this correlated with their larger body size (body surface area, 2.02±0.31 versus 1.82±0.22 m²; \( P, 0.01 \)). There were no differences in A/m ratio (6.8±4.6 versus 8.1±4.5 mm²/100 g; \( P=0.29 \)), APV (31±18 versus 32±15 cm/s; \( P=0.82 \)), or CFR (2.3±1.2 versus 2.5±0.8; \( P=0.49 \)) between men and women.

TABLE 1. Clinical Characteristics of 59 Study Patients

<table>
<thead>
<tr>
<th>Feature</th>
<th>n (% )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>27 (46)</td>
</tr>
<tr>
<td>Female</td>
<td>32 (54)</td>
</tr>
<tr>
<td>Age, y, mean±SD</td>
<td>57±13</td>
</tr>
<tr>
<td>Family history of coronary disease</td>
<td>21 (36)</td>
</tr>
<tr>
<td>Elevated cholesterol</td>
<td>24 (41)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>16 (27)</td>
</tr>
<tr>
<td>Smoking</td>
<td>29 (47)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>38 (64)</td>
</tr>
<tr>
<td>Clinical syndrome</td>
<td></td>
</tr>
<tr>
<td>Chest pain</td>
<td>41 (69)</td>
</tr>
<tr>
<td>Post-MI</td>
<td>6 (10)</td>
</tr>
<tr>
<td>CHF</td>
<td>3 (5)</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Valve disease</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>6 (10)</td>
</tr>
</tbody>
</table>

CHF indicates congestive heart failure; MI, myocardial infarction.

TABLE 2. Angiographic and Hemodynamic Data

<table>
<thead>
<tr>
<th>Parameter</th>
<th>n</th>
<th>Range</th>
<th>Average, mean±1SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiographic data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary diameter, mm</td>
<td>59</td>
<td>1.5–4.6</td>
<td>3.0±0.7</td>
</tr>
<tr>
<td>Cross-sectional area, mm²</td>
<td>59</td>
<td>1.8–16.7</td>
<td>7.2±3.5</td>
</tr>
<tr>
<td>Total LV mass, g</td>
<td>59</td>
<td>101–450</td>
<td>216±82</td>
</tr>
<tr>
<td>Regional mass, g</td>
<td>59</td>
<td>29–249</td>
<td>110±47</td>
</tr>
<tr>
<td>A/m ratio, mm²/100 g</td>
<td>59</td>
<td>1.7–20.7</td>
<td>7.5±4.5</td>
</tr>
<tr>
<td>Hemodynamic data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR, bpm</td>
<td>59</td>
<td>48–123</td>
<td>82±15</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>59</td>
<td>90–202</td>
<td>135±27</td>
</tr>
<tr>
<td>HR×SBP, mm Hg/min</td>
<td>59</td>
<td>5432–18 924</td>
<td>10 921±2653</td>
</tr>
<tr>
<td>Myocardial perfusion, q, mL/min per 100 g</td>
<td>59</td>
<td>27–103</td>
<td>58±15</td>
</tr>
<tr>
<td>APV, cm/s</td>
<td>59</td>
<td>10–89</td>
<td>32±17</td>
</tr>
<tr>
<td>CFR</td>
<td>46</td>
<td>1.2–5.9</td>
<td>2.4±1.0</td>
</tr>
</tbody>
</table>

LV indicates left ventricular; HR, heart rate; and SBP, systolic blood pressure.

Figure 2. Relationships between estimates of coronary perfusion. \( Q_{bed} \) estimate is derived from perfusion rate and mass (perfusion×mass), whereas \( Q_{art} \) estimate is derived from velocity and cross-sectional area (velocity×area). A, Significant correlation existed between these values (\( r=0.66, P,<0.001 \)). B, Difference between \( Q_{bed} \) and \( Q_{art} \) and their mean values.

\[ Q_{bed} = 0.96 Q_{art} \]
\[ r = 0.66 \]
\[ p < 0.001 \]

\[ Q_{bed} - Q_{art} \]

\[ 0 \] to \[ 180 \]

\[ 0 \] to \[ 180 \]

\[ 0 \] to \[ 180 \]

\[ 0 \] to \[ 180 \]

Area and Mass
No relationship existed between lumen area and either total or regional left ventricular mass in any of the 59 study patients (\( r=0.11, P=0.39 \) and \( r=0.07, P=0.6, \) respectively). However, in the subgroup with an A/m ratio ≥10 mm²/100 g,
lumen area was strongly related to regional mass \( r = 0.8, P < 0.0001 \); Figure 3). For patients with an A/m ratio \( < 10 \text{ mm}^2/100 \text{ g} \), lumen area was also related to regional mass \( r = 0.34, P = 0.02 \), but it had a different and weaker relationship (slope of regression line) from the group with an A/m ratio \( \geq 10 \text{ mm}^2/100 \text{ g} \).

**Velocity and A/m Ratio**

The relationship between velocity and A/m ratio is shown in Figure 4. An inverse association was found, as predicted by equation 2. When lumen area was large in relation to the mass supplied (larger A/m ratio), resting velocities were correspondingly low. However, when lumen area was small in relation to the mass supplied (smaller A/m ratio), velocities were much higher. For the group with an A/m ratio \( \geq 10 \text{ mm}^2/100 \text{ g} \), average APV was 23±9 cm/s compared with an average APV of 34±18 cm/s in the group with an A/m ratio \( < 10 \text{ mm}^2/100 \text{ g} \) \( P = 0.02 \). Figure 4 also shows the theoretical curves for 2 clinically relevant resting myocardial perfusion rates, 50 and 100 mL/min per 100 g. Our data fall mostly within the area bounded by these 2 perfusion curves. As mentioned above, the overall estimated perfusion rate was 58 mL/min per 100 g.

**Velocity, CFR, and Mass**

No relationship existed between APV and either total or regional mass \( r = 0.25, P = 0.55 \) and \( r = 0.15, P = 0.24 \), respectively. Likewise, no relationship existed between CFR and either total or regional mass \( r = 0.10, P = 0.5 \) and \( r = 0.16, P = 0.29 \), respectively). A weak relationship existed between CFR and A/m ratio \( r = 0.34, P < 0.05 \).

**Coronary Disease Groups**

We grouped patients by LAD disease status as visualized on angiography (Table 3). A total of 22 patients had no evident coronary disease or had minimal luminal irregularities only (\(<30\% \) diameter obstruction at most), whereas 15 patients...
had mild disease (30% to 50%) and 22 patients had moderate disease (50% to 70%). The groups with mild or moderate coronary disease had smaller vessel diameters and lower A/m ratios compared with the group with little or no disease. Trends toward a higher APV and a lower CFR existed in the groups with mild or moderate disease that was assessed this way.

Discussion
The major finding of this study is that resting coronary flow velocity follows a relationship predicted by the flow continuity principle (Figure 4). The relationship was demonstrated for the LAD under resting nonischemic conditions, although it might also apply in other arteries. We studied the LAD because of its ease of instrumentation, ease of visualization on angiograms, and its clinical significance. The results indicate that resting coronary velocity has physical meaning beyond just a measured number. Velocity seems primarily determined by the following 3 parameters: lumen area, bed mass, and regional perfusion. Previously reported variations in resting velocity are likely due to differences in arterial size (including amount of atherosclerosis), regional mass, and oxygen demand.

Myocardial Mass
Coronary size is related to regional myocardial mass. Size increases along with mass in conditions such as hypertension or aortic valve stenosis. Yet compensatory increases in coronary size are usually inadequate to match the increased mass in these conditions, so the A/m ratio declines. For example, in 10 patients with aortic valve stenosis, left ventricular mass increased from 269±60 g at baseline to 339±73 g over a period of 66 months. Although coronary area also increased, the A/m ratio decreased from 10.3±2.3 mm²/100 g at baseline to 8.6±4.0 mm²/100 g at follow-up (P<0.05). With the relief of aortic stenosis by valve replacement, it is possible for both left ventricular hypertrophy and coronary size to resolve toward normal values. The A/m ratio can then return to normal, at least in undiseased arteries. For example, in 15 patients who underwent aortic valve replacement, left ventricular mass decreased from 364±102 g to 250±100 g over a period of 38 months. In consequence, the A/m ratio increased from 7.9±2.1 mm²/100 g before valve surgery to 10.1±4.0 mm²/100 g at follow-up (P<0.05). Therefore, in the absence of atherosclerotic coronary disease, coronary size can increase or decrease to partially compensate for changes in distal bed size. These earlier studies of hypertrophied hearts with no coronary disease suggested a minimum normal A/m ratio of 10 mm²/100 g.

While accepting an A/m ratio ≥10 mm²/100 g as normal (although it was based on a somewhat different clinical scenario of ventricular hypertrophy), we found different relationships between area and mass in patients with a normal A/m ratio (≥10 mm²/100 g) and those with abnormally small ratios (<10 mm²/100 g). Our findings here are consistent with the data of Seiler and colleagues, who discovered different relationships between area and mass for normal coronary arteries and those that were narrowed with atherosclerosis. Both in their data and ours, the slope of the regression line between area and mass for diseased arteries is less steep than the slope for normal arteries. This suggests that coronary disease, not surprisingly, blunts the relationship between artery size and left ventricular mass. Our data are the first to indicate that resting coronary velocity in humans also varies with A/m ratio and that resting velocity differs between normal and diseased arteries.

Lumen Area
As long as resting blood flow is maintained and tissue perfusion is adequate, arterial blood velocity will increase as lumen area diminishes. As mentioned previously, a reduced lumen area for a given amount of myocardium most commonly occurs with atherosclerosis (Figure 5). Although coronary atherosclerosis can produce discrete, focal narrowing, very often it is a diffuse process or there is a combination of focal and diffuse disease. Angiography is limited in detecting diffuse atherosclerosis, as has been repeatedly demonstrated by both postmortem histological sections and in vivo intracoronary ultrasound imaging. Ultrasound has frequently shown that reference segments adjacent to obvious obstructive lesions are not themselves normal, but instead may harbor substantial plaque. In this regard, our data (Table 3) are consistent with those of Leung and colleagues. Using quantitative arteriography, Leung et al. found that the lumen diameters from apparently normal reference segments in coronary arteries with nearby or even distant atherosclerosis were smaller than comparable segments in subjects with entirely normal coronary arteries. Furthermore, they noted a gradient of decreasing reference vessel diameters with proximity of apparent disease to the normal segment, with reference LAD diameters diminishing from 3.55±0.43 mm in normal control subjects to 3.00±0.53 mm in subjects with nearby disease and to 2.54±0.31 mm in subjects with adjacent disease. We did not perform a similar analysis; however, decreased lumen size in reference seg-

<table>
<thead>
<tr>
<th>No Disease or Luminal Irregularities (n=22)</th>
<th>Mild Disease (n=15)</th>
<th>Moderate Disease (n=22)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary diameter, mm</td>
<td>3.2±0.7</td>
<td>3.1±0.7</td>
<td>2.6±0.6</td>
</tr>
<tr>
<td>A/m ratio, mm²/100 g</td>
<td>8.7±4.0</td>
<td>8.5±6.2</td>
<td>5.6±3.0</td>
</tr>
<tr>
<td>APV, cm/s</td>
<td>27±16</td>
<td>33±11</td>
<td>37±20</td>
</tr>
<tr>
<td>CFR</td>
<td>2.8±0.7</td>
<td>2.1±0.5</td>
<td>2.2±1.3</td>
</tr>
</tbody>
</table>
ments can logically result in higher resting velocities in areas that seem to have little or no angiographic evidence of atherosclerosis.

Velocity and CFR
We did not find strong relationships between CFR and either area, mass, or A/m ratio. This may derive from the different measurement conditions for resting flow and CFR, which resulted in distinct and complimentary viewpoints. Resting flow is autoregulated to resting demand. As long as flow is adequate (no ischemia), the presence of disease in other segments of the artery is immaterial. Velocity at any point reflects flow in relation to the local arterial area. However, CFR depends on the stimulation of a hyperemic response, which eliminates autoregulation. Furthermore, hyperemia is related to the number and responsiveness of recruitable arterioles and capillaries, interactions between the endothelium and the smooth muscle cells of the arterial wall, and the presence of microvascular disease or endothelial dysfunction (as occurs in diabetes mellitus or with smoking).20,21 Therefore, CFR is a wider, more integrative measure of the responsiveness of an entire artery-bed system in comparison with the purely local perspective of resting velocity.

Limitations
Our studies were performed in clinically stable patients without evidence of ischemia. We assumed that resting myocardial perfusion was within normal limits. Our simplified estimate of myocardial perfusion, 58±15 mL/min per 100 g, is within the range of resting perfusion values obtained using positron emission tomography with either 15O-labeled water22 or 13N-labeled ammonia.23 Ischemia and certain metabolic abnormalities, such as anemia, thyroid disorders, or myocarditis, could affect our assumptions about perfusion and, therefore, our results might not apply when those conditions exist. Vessels with occluded distal branches or collaterals would not fit the flow continuity assumptions used here. Likewise, the distal myocardium was assumed to be normal; a stunned, hibernating, or infarcted myocardium would also not fit our assumptions.

We deliberately studied patients with a spectrum of coronary disease, ranging from a few luminal irregularities to mild or moderate lesions. We did not study patients with visibly severe lesions in the LAD. Interestingly, by our disease category grouping, even patients with little or no apparent disease angiographically had an average A/m ratio as a group that was less than the previously reported normal value of 10 mm²/100 g. This could imply that some atherosclerotic disease was present in these arteries. Alternatively, the A/m ratio cut point value of 10 mm²/100 g may not be correct. In the future, intracoronary ultrasound imaging to interrogate for plaques not visualized by angiography, combined with simultaneous coronary velocity measurements, might be a more exact way to investigate the possibility of occult atherosclerosis and to establish better estimates of a normal A/m ratio cut point.

Although a good correlation existed between the 2 estimates of flow in the continuity equation (Q_bed and Q_art), substantial scatter also existed. There are ample sources for the scatter we observed in these estimates. For example, the 4-fold variation in calculated regional perfusion seems excessively large (27 to 103 mL/min per 100 g). This may reflect the simplistic method for estimating perfusion using the double-product alone, without attention to sedation state, hypertension, or other contractility measures. The velocity estimate we used (APV/2) assumed a parabolic flow profile in the coronary artery, which may be imprecise. Jenni and colleagues24,25 have described blunted rather than strictly parabolic velocity profiles, which suggests that the spatial average correction coefficient for APV may be greater than the assumed one-half. Nevertheless, many studies have validated APV/2 as a useful approximation of mean velocity.1,26,27 The assumption of circular arterial cross-sectional area may also introduce some scatter. However, many clinical studies have used circular arterial cross-sectional areas calculated from quantitative coronary diameter measurements.28,29 Although intravascular ultrasound imaging might be a more accurate way to quantitate arterial lumen cross-sectional area, studies have shown a good correlation between arterial areas calculated from quantitative arteriograms and

Figure 5. Schematic illustration of increased resting arterial flow velocity (V) due to reduced lumen area (A) caused by atherosclerosis. A, Profile of artery without atherosclerosis. B, Profile of artery with atherosclerosis. Reduction in lumen caliber must be accompanied by increased velocity to provide adequate perfusion and avoid ischemia.
those measured from intravascular ultrasound images in most situations except immediately after angioplasty. Finally, the calculations of total and regional left ventricular mass add additional variability. Despite these technical limitations, the values we obtained are all within the ranges of values previously determined using a variety of methods.

**Clinical Significance of Resting Velocity**

Our results support the concept that the “normal” size for a coronary artery is determined by the size (mass) of the distal myocardial bed it serves. This arterial size may be estimated in 2 ways. It can be assessed most directly by calculating the $A/m$ ratio. This involves measuring cross-sectional area by one of several possible quantitative techniques and estimating bed mass by using either the tree structure analysis (as we did) or another method. Measuring area alone or mass alone is not sufficient; our data and those of others indicate that lumen area and bed mass are closely related in normal arteries but that this relationship is degraded or lost with atherosclerosis. As an alternative to establishing the $A/m$ ratio, vessel size adequacy in general might also be estimated by measuring resting coronary velocities. Higher resting velocity values correlated with lower $A/m$ ratio values, even in segments that, by angiography, did not have apparent atherosclerosis, suggesting lumen encroachment with functionally small size. Although our results support these general principles in a broad sense, their application to individual patients will be meaningful only when the variance we encountered has been reduced.

**Conclusions**

Resting coronary velocity was related to lumen cross-sectional area and regional left ventricular mass. The relationship fit the expectations derived from the flow continuity principle. The clinical usefulness of this knowledge may lie in the eventual ability to assess the presence of diffuse mild or moderate coronary atherosclerosis.

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**References**


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