Magnitude of Dilatation of Large and Small Coronary Arteries by Nitroglycerin

ROBERT L. FELDMAN, M.D., CARL J. PEPINE, M.D., AND C. RICHARD CONTI, M.D.

SUMMARY  Vasodilatory responses of segments of large epicardial left coronary artery (CA), small intramyocardial CAs (0.3–1.0 mm), coronary stenoses and CAs filled by collaterals were determined in 34 patients. Measurements were made before and after nitroglycerin (0.4 mg, sublingual) by means of quantitative magnification coronary angiography using photospot film and a calibrated 6-power viewing device. The left main CA, proximal, middle and distal anterior descending and circumflex segments, and small CAs showed dilatation that varied in magnitude. When magnitude of dilatation was compared with control diameter of the vessel and its location, control diameter proved to be the significant independent variable. CAs with the smallest control diameter showed the greatest magnitude of vasodilatation. CA branches filled by collaterals had vasodilatation similar in magnitude to that of CAs of comparable control diameter. Although coronary stenoses dilated, the magnitude of dilatation was less than that observed in nonstenosed arterial segments of similar control diameter. When areas of stenosis were excluded, however, results were similar regardless of whether the patient had CA disease. These data indicate that a principal determinant of the CA vasodilatory response to nitroglycerin is the size of the artery before nitroglycerin.

DILATATION OF proximal coronary arteries (CAs) is the usual response to nitroglycerin observed during coronary angiography.1-3 However, the response to nitroglycerin of more distal CA segments and smaller intramyocardial CAs has not been quantified in humans. Confusion also exists regarding the response of different-sized CAs to nitroglycerin. In vivo human and animal experiments have both shown that nitroglycerin usually causes dilatation of large epicardial capacitance CAs and constriction of resistance vessels.4-6 Animal experiments using excised large (diameter ~ 2.0 mm) and smaller (diameter ~ 0.5 mm) CAs showed dissimilar dilatation responses to nitrates and adenosine.9 It is not clear whether smaller CAs evaluated in vitro are the same as the resistance vessels of in vivo studies. Studies of the human microcirculation describe arterioles (diameter 0.03–0.1 mm) as having principal control of resistance to flow.10 A review that examined function of small human CAs (diameter 0.1–1.0 mm) did not describe control of resistance as a function of CAs of this diameter.11

The purpose of this study was to quantify left CA dilatation responses to nitroglycerin in patients with and without CA disease (CAD). Special attention was given to the control diameter and location of the CA segment relative to the left coronary ostium. We arbitrarily divided the left CA system into eight large (diameter > 1.0 mm) epicardial CA segments and small (diameter ≤ 1.0 mm) intramural CAs. Vasodilatation responses of these CA segments to nitroglycerin was measured by quantitative angiography.

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Methods

Patient Selection

Thirty-four patients undergoing cardiac catheterization for further evaluation of a chest pain syndrome were studied after giving informed consent. Patients with symptoms or ECG findings suggesting variant angina were excluded. Each patient was taking propranolol (80–480 mg/day) and nitrates for chest pain thought to be caused by transient myocardial ischemia.

Cardiac Catheterization

Propranolol treatment was not interrupted, but nitrates were withheld for at least 6 hours before catheterization. The patients were in a postabsorptive state without premedication when catheterized. A #SF Sones catheter was advanced from the right brachial artery to the left ventricle. Pressures were measured and the catheter was withdrawn to the aortic root. Mean aortic pressure was obtained by electronic filtration.

Coronary Angiographic Technique

Multiple views of the left CA were obtained using conventional 35-mm cine technique. Fluoroscopic images were simultaneously recorded on a video disk recorder (Videomatic disk recorder, General Electric, OM C7560B). These recordings were reviewed and a right anterior oblique projection was chosen to minimize overlapping of proximal left CA branches and maximize visualization of any proximal coronary stenosis. Projections ranged from 10–40° rotation with various degrees of sagittal plane angulation. After ECG and pressure changes related to selective injection of coronary contrast material had reverted (~ 5 minutes), a control 105-mm photospot selective coronary angiogram was filmed using 6 ml of Renografin 76. The filming rate was 4–6 frames/sec, with CA segments of interest positioned in the central portion of the image field. A photospot camera (General Electric), Kodak 2541 film, 11.5-cm or 15-
cm image magnification (General Electric Fluorcon) and a 3-mm focal spot were used with this technique.

After the control angiogram was filmed, the patient was rotated to the horizontal position. When heart rate and aortic pressure were constant (± 5%), they were recorded and the Sones catheter was advanced to the left ventricle to record pressure at low and high gain. A 0.4-mg freshly crushed nitroglycerin tablet (Lilly) was given sublingually. Pressure and ECG were monitored for 5 minutes after the tablet dissolved. Left ventricular pressure recordings were made, and the catheter was withdrawn to the aortic root. An angiogram was filmed after nitroglycerin with the same technique and projection used for the control angiogram.

In three additional patients nitroglycerin was omitted, and 5 minutes after the first control angiogram, a second control angiogram was filmed with the same technique.

Measurements of Coronary Artery Diameter

Our quantitative coronary angiographic technique has been described in detail. Briefly, photospot angiogram frames were viewed on a standard x-ray view box. Frames filmed in end-diastole from both control and nitroglycerin angiograms were selected. A hand-held magnifying comparator (Finescale), fitted with a reticle containing 0.1-mm divisions (No. 122 Finescale), was placed over the opacified artery. Viewed through the eyepiece, the scale and underlying CA segments or catheter were both magnified 6 times. Measurements were made to the nearest 0.1 mm at branch points. All measurements were made near the center of the photographic field, which makes additional correction for pincushion distortion unnecessary.

The Sones catheter was measured at its tip, which was positioned within the left main CA ostium. The epicardial left CA was divided in a manner similar to that proposed by the American Heart Association (fig. 1). The left main CA was measured just before its bifurcation. The anterior descending (AD) CA was measured proximal to the first septal perforating branch (proximal AD), just distal to the second septal perforating branch (middle AD) and at a branch point near the apex (distal AD). The circumflex (Cx) CA was measured proximal to the origin of the obtuse marginal branch (proximal Cx), at the obtuse marginal branch at its origin (middle Cx), as it continued in the atroventricular groove just beyond the origin of the obtuse marginal branch (middle Cx), and at a distal posterior left ventricular branch (distal Cx). To evaluate the response of small CAs in each patient, we also measured three intramyocardial left CA branches, usually septal perforating branches of the AD or branches of the Cx, which when viewed on cine film in two or more views appeared intramyocardial, ranging from 0.3–1.0 mm. Coronary stenoses were measured at their minimal visualized diameter, and the percentage of diameter reduction was calculated by comparing this minimal diameter (one view) to the diameter of the immediate prestenotic segment, which was not apparently involved by atherosclerosis.

Calculations and Statistical Analysis

Actual CA diameters were calculated by reference to the diameter of the Sones catheter tip (1.7 mm). The percentage of dilatation was used to quantify the magnitude of dilatation and was calculated as [(diameter after nitroglycerin − control diameter)/control diameter] × 100%.

The mean and standard deviation were calculated for paired measurements obtained from control and nitroglycerin angiograms and compared using the paired t test. An analysis of variance was used to compare the percentage of change after nitroglycerin for different CA measurements (between proximal AD, middle AD, small CAs, between AD and Cx CAs of similar locations, etc). An analysis of covariance using an F test was used to evaluate the significance of the percentage of dilatation relative to control CA diameter. Thus, if a different percentage of dilatation was observed for different-sized CAs or different locations within the same CA, this statistic tested whether the effect was related to control CA diameter or location. Values from patients with CAD were compared with those in patients without CAD. Coronary artery diameters before and after nitroglycerin for various large CA segments and small CAs were related by simple linear regression analysis and the 95% confidence interval around this regression line was calculated. A p value ≤ 0.05 was considered significant.

Results

Coronary Angiography

Before nitroglycerin, 22 of the 34 patients (average age 53 years, range 35–67 years) had coronary narrowings ≥ 50% diameter reduction involving all three major CA branches. No patients had ≥ 50% diameter narrowing of the left main CA. These 22
patients constituted the CAD group. The group without CAD comprised the 12 other patients (average age 51 years, range 31–64 years) who had coronary angiograms without stenosis.

**Effect of Renografin 76 on Coronary Artery Diameters**

Twenty-seven CA segments from the left main CA through small CAs (range of initial CA diameters 4.2–0.6 mm) were measured from the three sets of paired angiograms done 5 minutes apart without intervention. The diameters were similar (0 ± 2%, p = NS, range –5% to 5%) because only six of the 27 CA segments appeared to change their initial diameter (three increased and three decreased 0.1 mm).

**Hemodynamic and Angiographic Responses to Nitroglycerin**

When patients with and without CAD were compared, hemodynamic and angiographic (excluding coronary stenoses) responses were similar (p ≥ 0.28). Thus, hemodynamic and angiographic values of patients with and without CAD were combined in subsequent analysis of results.

**Effect of Nitroglycerin on Heart Rate and Aortic and Left Ventricular Pressures**

Compared with values obtained after the control angiogram, heart rate increased 5 ± 6 beats/min, mean aortic pressure decreased 10 ± 5 mm Hg and
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The proximal AD segment measured 2.83 ± 0.68 mm before and 3.28 ± 0.66 mm after nitroglycerin (p < 0.01). The proximal Cx segment measured 2.72 ± 0.77 mm before and 3.10 ± 0.72 mm after nitroglycerin (p < 0.01). The average dilatation was 6% (fig. 2A). Diameters of the left main CA after nitroglycerin were related to diameters observed before nitroglycerin by the equation in table 1.

Effect of Nitroglycerin on Diameter of Proximal Anterior Descending and Circumflex Arteries

The equation diameter after nitroglycerin = (slope) [diameter before nitroglycerin] + constant was calculated for each left coronary artery segment.

Figure 2. Coronary artery diameters for each location before (horizontal axis) and after (vertical axis) nitroglycerin (TNG) for all patients with and without coronary artery disease (CAD). (A) left main coronary artery; (B) proximal anterior descending (AD) and circumflex (Cx); (C) middle AD and Cx; (D) distal AD and Cx; (E) small intramyocardial coronary artery; (F) coronary arteries filled by collaterals; (G) coronary narrowings (hatched region represents narrowings ≤ 1.2 mm).

TABLE 1. Summary of the Relationship of Coronary Artery Diameters Before and After Nitroglycerin*

<table>
<thead>
<tr>
<th>Coronary segment</th>
<th>Slope</th>
<th>Constant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left main</td>
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<tr>
<td>Proximal AD</td>
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<td>1.0</td>
</tr>
<tr>
<td>Proximal Cx</td>
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<td>0.9</td>
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<tr>
<td>Middle AD</td>
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<td>0.9</td>
</tr>
<tr>
<td>Middle Cx₁</td>
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<td>0.5</td>
</tr>
<tr>
<td>Middle Cx₂</td>
<td>1.3</td>
<td>0.0</td>
</tr>
<tr>
<td>Distal AD</td>
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<td>0.5</td>
</tr>
<tr>
<td>Distal Cx</td>
<td>1.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Small CA</td>
<td>1.3</td>
<td>0.0</td>
</tr>
</tbody>
</table>

*The equation diameter after nitroglycerin = (slope) [diameter before nitroglycerin] + constant was calculated for each left coronary artery segment.

Abbreviations: AD = anterior descending; Cx = circumflex; CA = coronary artery.
glycerin ($p < 0.01$). Diameters of proximal AD and Cx were similar ($p = \text{NS}$) before and after nitroglycerin. Percentage of dilatation for proximal AD (16%) and Cx (14%) segments were also similar ($p = \text{NS}$). Responses for both proximal AD and Cx segments are shown in figure 2B. Diameters of the two proximal segments after nitroglycerin were related to diameters before nitroglycerin by the equation in table 1.

**Effect of Nitroglycerin on Diameter of Middle Anterior Descending and Circumflex Arteries**

The middle AD segment measured 2.11 ± 0.43 mm before and 2.56 ± 0.48 mm after nitroglycerin ($p < 0.01$). The middle Cx1 segment measured 1.98 ± 0.58 mm and 2.37 ± 0.60 mm ($p < 0.01$), and the middle Cx2 segment measured 1.79 ± 0.47 mm and 2.18 ± 0.60 mm before and after nitroglycerin, respectively (both $p < 0.01$). Diameters of middle Cx1 and Cx2 were similar ($p = \text{NS}$). Percentages of dilatation for middle AD (21%), middle Cx1 (20%) and Cx2 (22%) were similar ($p = \text{NS}$). Responses for the three middle segments are shown in figure 2C. Diameters of middle AD, Cx1 and Cx2 after nitroglycerin were related to diameters before nitroglycerin by the equation in table 1.

**Effect of Nitroglycerin on Diameter of Distal Anterior Descending and Circumflex Arteries**

The distal AD segment measured 1.51 ± 0.34 mm before and 1.90 ± 0.37 mm after nitroglycerin ($p < 0.01$). The distal Cx segment measured 1.34 ± 0.31 mm before and 1.67 ± 0.36 mm after nitroglycerin ($p < 0.01$). The diameters of the distal AD and Cx were similar ($p = \text{NS}$) before and after nitroglycerin. Percentages of dilatation of distal AD (26%) and Cs (25%) were similar ($p = \text{NS}$). Responses for distal AD and Cx are shown in figure 2D. Diameters of distal AD and Cx after nitroglycerin were related to diameters before nitroglycerin by the equations in table 1.

**Effect of Nitroglycerin on Diameter of Small Coronary Arteries**

The diameter of small intramyocardial CAs measured 0.64 ± 0.19 mm before and 0.79 ± 0.22 mm after nitroglycerin ($p < 0.01$) (fig. 2E). The average percentage of dilatation was 23%. Diameters of small CAs after nitroglycerin were related to diameters before nitroglycerin by the equation in table 1.

**Effect of Nitroglycerin on Arteries Filled by Collaterals**

The diameter of CAs filled by collaterals was 0.99 ± 0.52 mm before and 1.27 ± 0.60 mm after nitroglycerin (fig. 2F). The average dilatation was 0.28 mm (28%, $p < 0.01$).

**Differential Effect of Nitroglycerin on Proximal, Middle and Distal Anterior Descending and Circumflex CA Segments**

The percentage of dilatation of proximal, middle and distal segments and of small CAs, comparing AD with Cx, showed that segments of similar location dilated similarly ($p \leq 0.40$). Therefore, in analysis of possible differential responsiveness, similar locations of AD and Cx CAs were combined. Responses of coronary narrowings were not included in the following analysis.

The percentage of dilatation of the left main CA was less than that of proximal, middle, and distal AD and Cx CAs, small CAs and CAs filled by collaterals ($p < 0.05$). The percentage of dilatation of proximal CAs was less than that of middle and distal AD and Cx CAs, small CAs and CAs filled by collaterals ($p < 0.05$). The percentage of dilatation of middle and distal AD and Cx CAs, small CAs and CAs filled by collaterals was similar ($p = \text{NS}$).

These percentages of dilatation were related to control CA diameter ($p < 0.01$) but not to location (left main, proximal, middle and distal CAs, small CAs, and CAs filled by collaterals) ($p = \text{NS}$) (fig. 3). For example, the percentage of dilatation of a 2-mm CA was usually greater than dilatation observed in a 3-mm CA, regardless of location.

**Effect of Nitroglycerin on Coronary Stenoses**

The minimal diameter of each of 41 coronary stenoses ranged from 0.5-2.5 mm. The average diameter before nitroglycerin was 1.42 ± 0.40 mm and after nitroglycerin was 1.51 ± 0.46 mm ($p < 0.05$) (fig. 3).
Dilatation averaged 6%, but varied; 18 of 41 dilated at least 0.1 mm. The diameter of a stenosed CA before nitroglycerin had a bearing on whether or not it dilated. Only two of 14 narrowed segments with a diameter ≤ 1.2 mm dilated at least 0.1 mm (average 2%, p = NS), whereas 16 of 27 narrowed segments ≥ 1.3 mm in diameter dilated at least 0.1 mm (average 11%, p < 0.01).

The average percentage of coronary diameter reduction was 46 ± 15% before nitroglycerin and 50 ± 14% after nitroglycerin (p < 0.01). The range of change was −9% to 18%. Of the 41 narrowed segments the percentage of narrowing increased in 29, decreased in seven and was unchanged in five (fig. 4). This tendency to an increase in percentage of narrowing after nitroglycerin was usually the result of greater dilatation in the prestenotic segment (0.38 ± 0.23 mm) than in the narrowed segment (0.10 ± 0.13 mm, p < 0.01). In patients with CAD, the changes in proximal and middle AD and Cx segments immediately proximal to a narrowing (16 ± 11%) were not significantly different (p = NS) from changes in CA segments of similar location (22 ± 14%) that were not adjacent to a narrowing. Additionally, these changes were similar (p = NS) to changes in CA segments of similar location (21 ± 15%) from patients with normal angiograms.

Discussion

The purpose of this study was to quantify the dilatative effects of nitroglycerin on the left CA. Dilatation was observed in all regions of the left CA visualized with coronary angiography (figs. 5 and 6). The percentage of dilatation of individual epicardial and small
intramyocardial CAs varied, but some group responses differed. Differences in response to nitroglycerin were inversely related to the size of the CA before nitroglycerin. Contrary to concepts derived from pathologic studies, suggesting that coronary stenoses are "fixed," many stenoses dilated after nitroglycerin. This finding was similar to our previous findings using a different quantitative technique, in which approximately one-fourth of right and left CA stenoses dilated after nitroglycerin. However, stenoses likely to limit coronary blood flow usually did not dilate. However, slight changes in stenosis diameter (< 0.1 mm) may not have been detected by the technique used. Other investigators have shown that some coronary stenoses dilated after nitroglycerin. Magnitude of dilatation of CAs visualized by collateral filling was similar to that of CAs of comparable location or size. Whether dilatation after nitroglycerin was related to alterations in regional flow, collateral perfusion pressure, left ventricular wall stress and preload, or whether it was solely a direct action of nitroglycerin, could not be determined.

Our quantitative coronary angiographic technique using 105-mm photospot films and 6× magnification has been described in detail. We find an acceptable intraobserver and interobserver reproducibility when measuring the same angiogram. Although we have not detected coronary artery dilatation related to contrast medium from pairs of angiograms obtained 5 minutes apart, angiogram pairs might show differences if they were obtained temporally closer together, before multiple coronary injections, or with larger amounts of contrast medium. The limiting factor with this technique is CA edge definition, which is particularly apparent in some small CAs ≤ 0.5 mm diameter.

Before nitroglycerin, diameters of the left main and proximal epicardial CA were slightly less than those reported by MacAlpin et al. and Vieweg et al. This discrepancy was probably related to the specific site measured. MacAlpin et al. made proximal AD and Cx measurements closer to the left main CA bifurcation. Vieweg et al. did not specify where measurements were made. In both studies, nitrates may sometimes have been administered before angiography, and some patients were probably receiving propranolol, whereas others were not. All of our patients were receiving propranolol, which may have affected our results. Beta blockade could cause a decrease in CA diameter and alter the dilatation response to nitroglycerin. Because CAs taper as the distance from the ostium increases and the percentage of dilatation depends on CA size, it was also important to define the exact site measured.

Before nitroglycerin the diameter of all left CA segments and the percentage of dilatation were similar in patients with and without CAD. In contrast, Vieweg et al. reported that the CA lumen was slightly smaller in patients with CAD than in those with normal angiograms. Gensini et al. observed less CA dilatation in patients with CAD who received 5 mg of isosorbide dinitrate compared with patients with normal arteriograms. After 10 mg of isosorbide dinitrate, dilatation was similar in patients with CAD and in those with normal CAs. Our data did not show significant differences between patients with CAD and
those with normal CAs when obviously narrowed segments were excluded. A trend that was not significant suggested that certain CA segments immediately adjacent to a stenosis dilated less than others farther from stenoses. It was possible that these CA segments were less affected by the atherosclerotic process, e.g., less than stenoses but more than CA segments farther from stenoses. This lack of difference compared with findings of Gensini et al. could relate to the dose of nitroglycerin used by us or to different techniques. Perhaps measurements made at obviously diseased locations will show a decreased responsiveness, whereas more dilatation will occur in other CA segments from patients with CAD. Similar hemodynamic effects of nitroglycerin occurred in patients with and without CAD in this study and in our previous reports.

Small AD and Cx intramyocardial CA branches (0.3–1.0 mm) dilated after nitroglycerin. Winbury and co-workers found that nitroglycerin decreased pressure gradients across epicardial CAs for long periods of time, although total resistance transiently decreased and then increased. From these observations, they postulated that nitroglycerin preferentially dilated large CAs compared with small resistance vessels. In experiments using animal models with a ligated CA, nitroglycerin usually improved perfusion and function of regions supplied by the ligated CA. To explain the potential for improved perfusion of the ischemic region after nitroglycerin, Winbury et al. proposed that intramyocardial tributary CAs connecting epicardium with endocardium dilate after nitroglycerin; therefore, flow to collaterally perfused vessels increases. These tributary CAs were thought to respond to nitroglycerin in a manner similar to that of large epicardial CAs, but no direct measurements within intramyocardial CAs were made. Dilatation of small intramyocardial CAs observed in this study supports the theory of Winbury and colleagues that nitroglycerin can dilate some intramyocardial CAs. This effect would potentially increase flow to regions dependent on collateral flow. In addition to dilatation of tributary arteries, the physiologic effect of nitroglycerin will depend on nitroglycerin-induced changes in heart rate, coronary perfusion pressure and left ventricular filling pressure. Recent animal experiments by several groups also show that vasoactive drugs may change distal coronary pressure and alter coronary hemodynamics separate from changes in aortic pressure. It is not known whether these changes occur in patients with coronary stenoses, but that possibility should be considered when speculating on the action of nitroglycerin in patients with CAD. Additionally, although hemodynamic and angiographic values for patients with and without CAD were combined in the analysis, reduced perfusion pressure may have different effects in patients with and in those without CAD with respect to the diameter of coronary vessels distal to a stenosis.

In contrast to the supportive observations of Winbury and co-workers, findings of in vitro studies by other investigators differed from ours in that large and small CAs responded differently to nitroglycerin. Schnaar and Sparks compared the effects of nitroglycerin on isolated large (diameter ~ 2.0 mm) and small (diameter ~ 0.5 mm) CAs in dogs and found quantitatively different degrees of relaxation. Harder et al. using a similar preparation, observed quantitatively different effects of nitroglycerin on the action potential of large (diameter > 1.0 mm) and small (diameter < 0.5 mm) CAs. Both groups reported that nitroglycerin had a greater effect on large CAs. In both studies, adenosine, believed to predominantly affect resistance vessels, had an action opposite to that of nitroglycerin on these responses. These findings suggested that CAs 0.3–0.5 mm in diameter have a major effect on coronary resistance.

Observations of investigators comparing responses of different-sized CAs may be important because similar responses were observed comparing small CAs and large CAs. Krishnamurty et al. using intact perfused CAs, found that mannitol dilated medium (diameter 0.5–1.0 mm) and small CAs (diameter < 0.5 mm) similarly. Borda et al. studied intact perfused epicardial arteries, helical strips and arterial rings from large (diameter 0.8–1.2 mm) and small (diameter 0.4–0.7 mm) CAs and found that the three preparations had quantitatively similar responses to catecholamine stimulation. Why different responses of small and large CAs have been observed by different investigators is not clear. Important methodologic differences are not apparent in the various reports.

In a review of small arteries of the heart, James defined small CAs as being 0.1–1.0 mm in diameter and did not discuss control of coronary resistance as one of their functions. Sherf et al. described coronary arterioles as having a diameter of 0.03–0.1 mm. These authors described constriction, relaxation and distribution of flow as the function of arterioles. Schaper and Schaper stated that resistance vessels range in size from small arteries to precapillary arterioles but did not estimate their size. In preliminary studies, Tillmanns et al. using a calibrated microscope in vivo, directly measured CA diameters on the surface of beating intact cat and rat hearts. They observed that larger arterioles (average diameter 0.127 mm) were more responsive to nitroglycerin than to dipyridamole. In contrast, small arterioles (average diameter 0.02 mm) did not dilate after nitroglycerin but dilated after dipyridamole. These studies suggest that small CAs as defined by James and as viewed by coronary angiography are different from vessels usually considered as part of the microcirculation.

What causes the apparent nitroglycerin-induced differential vasodilatory responses of CAs of different initial diameters is unclear. Actual magnitude of dilatation (diameter aster nitroglycerin minus control diameter) is greater for larger CAs. When the actual magnitude of dilatation is normalized for control diameter, the resulting value (termed relative dilatation) is greater for smaller CAs. An increase in capacitance of the entire CA bed after nitroglycerin may contribute to the physiologic action of nitroglycerin.
Decreased extravascular compression related to decreased left ventricular pressure and volume may also be important. Increased capacitance could result in increased volume of blood stored in epicardial CAs during systole. This blood would be delivered through epicardial and intramyocardial tributaries to the microcirculation, not visualized by angiography, during diastole. The actual volume of blood flow delivered is regulated by the microcirculation, particularly coronary arterioles, again not seen by angiography. In left ventricular regions supplied by normal CAs, there may be no need for an increase in perfusion, and coronary autoregulation would limit flow. In contrast, in regions with diseased CAs, resistance vessels may always be nearly maximally dilated, and nitroglycerin-induced CA dilatation could allow more perfusion during diastole. Thus, a decrease in extravascular compression could also enhance flow through intramyocardial collaterals. This hypothesis is supported by observations of coronary flow in selected patients with and without CAD.7,8

In conclusion, the magnitude of CA dilatation after nitroglycerin differed in segments of the left CA and small CAs. The smaller the CA diameter before nitroglycerin, the greater the relative dilatation after nitroglycerin. Coronary stenoses often dilated, but the more narrowed stenoses were less likely to dilate. These data may also help assess dilative responses of other patient groups. Our preliminary observations suggest that dilatation by certain CA segments of patients with variant angina is greater after nitroglycerin than the dilatation observed here in patients without variant angina.9

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Acute Effect of Intravenous Dipyridamole on Regional Coronary Hemodynamics and Metabolism

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SUMMARY The acute coronary hemodynamic and metabolic effects of intravenous dipyridamole were studied in 13 patients. Total left ventricular (LV), anterior (supplied by the left anterior descending coronary artery) and inferior (supplied by circumflex and right coronary arteries) regional flows and metabolic responses were assessed from the coronary sinus and great cardiac vein. Perfusion to LV regions was classified as potentially "normal" or "abnormal," based on coronary angiographic findings.

Before dipyridamole, LV oxygen delivery and lactate extraction in both the normal and abnormal regions were similar. Within 1 minute after injection of 20 mg of dipyridamole by i.v. bolus, total coronary flow increased 51% (p < 0.05). Fifteen minutes after injection the flow increase persisted. Flow decreased to approximately control level by 20 minutes. The major component of this increased total coronary flow resulted from increased flow in normal regions (75% at 1 minute, p < 0.05). Mean regional LV oxygen delivery and lactate extraction were not changed significantly in either normal or abnormal regions. However, lactate production occurred more often after dipyridamole in abnormal regions.

These results suggest that during dipyridamole-induced hyperemia, regional coronary flow and metabolic responses depend upon the status of the arteries supplying the LV region. Regional differences in flow and metabolism occur independent of major changes in heart rate and aortic and LV pressures.

EXPERIMENTS in anesthetized dogs with a normal coronary circulation showed that i.v. dipyridamole has a more pronounced action on the coronary circulation than on the circulation of other organs.1, 2 Both coronary blood flow and coronary venous oxygen were increased, but whether the increase in coronary blood flow is potentially useful has not been clearly defined.

Results from studies of canine models of acute and chronic ischemic heart disease have conflicting concerning effects of dipyridamole on regional left ventricular (LV) blood flow. When one left coronary branch was acutely occluded or narrowed, flow supplied by the normal coronary branch uniformly increased.3, 7 However, flow and oxygen delivery responses varied in regions supplied by a narrowed branch. Becker observed that dipyridamole increased flow to the region perfused by an occluded branch when other branches were normal,5 but decreased flow if other branches were narrowed.6 Several investigators found that when one branch was occluded, dipyridamole decreased the predicted size of myocardial infarction associated with increased ischemic region flow.6, 9 In contrast, Marshall and Parratt7 used an acute model similar to Becker’s,9 with one totally occluded branch and the others normal, and observed that dipyridamole decreased flow to the region perfused by the occluded branch. Nakamura et al.4 and Flameng et al.8 used a different model, which had decreased flow to the inferior region, and found that dipyridamole caused nonhomogeneous transmural flow distribution and, in some experiments, redistributed flow away from the inferior region. Further, in models of chronic coronary occlusion, dipyridamole alone or dipyridamole plus rapid pacing caused nonhomogeneous flow distribution and in some experiments decreased flow in the region supplied by collaterals.8, 11 This reported variability of dipyridamole’s effect on ischemic myocardium did not relate to drug-induced changes in heart rate, coronary perfusion pressure or LV filling pressure.

Results of clinical trials using either oral or i.v.
Magnitude of dilatation of large and small coronary arteries of nitroglycerin.
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