Zeitschrift für
Kardiologie

Z. Kardiol. 72, Suppl. 3, 116–123 (1983)

Contribution of Dynamic Vascular Wall Thickening to Luminal Narrowing During Coronary Arterial Vasomotion

P. W. Serruys, J. M. Lablanche*, J. H. C. Reiber, M. E. Bertrand*, and P. G. Hugenholtz

Thoraxcenter, Erasmus University and University Hospital "Dijkzigt", Rotterdam, The Netherlands
* Hôpital Cardiologique, Lille, France

Summary: The hypothesis has been developed that increased coronary artery vasomotor tone superimposed on a preexisting obstruction is a possible mechanism responsible for resting and exertional angina. In 18 patients (22 stenotic lesions), the maximal changes in coronary artery diameter (mm) induced by an ergometrine test followed by an injection of isosorbide dinitrate were assessed by a quantitative computer-based angiographic system. If we assume that there is no change in the length of the artery as the result of changes in its diameter, then at any point of the artery the area of the arterial wall on a transverse cross section of the vessel will be constant regardless of its state of its contraction or dilatation. As vasoconstriction occurs, the luminal diameter decreases proportionally more than the outer diameter of the vessel and the wall thickness increases. Using elementary geometric principles, we calculated and reconstructed the changes that might occur at the stenotic sites as the result of vasomotion acting on the entire coronary segment. From the reference diameter in the control state (*Ri:* 3.7 ± 1.1 mm) and after vasoconstriction (*Ric:* 3.3 ± 1.0 mm) and the obstruction diameter in the control state (*ri:* 2.2 ± 0.9 mm), the minimal obstruction diameter after vasoconstriction (*ric:* 1.0 ± 0.8 mm) was derived using the following equation: $ric^2 = ri^2 - Ri^2 + Ric^2$. In four of 22 lesions, the decrease in diameter of the lumen of the normal vessel was fully translated to the stenotic point and the decrease in diameter at the stenosis was correctly predicted. In six lesions the vessel wall constricted less at the site of the lesion than predicted. Finally, 12 lesions exhibited clear arterial hypercontractility at the site of the stenosis (true spasm). These results demonstrate how unpredictable the effects of changes in vasomotor tone can be on large coronary arteries in individual patients. Understanding of these changes is essential before a rational definition of a critical stenosis can be made.

Zusammenfassung: Es wurde die Hypothese aufgestellt, daß ein erhöhter vasomotorischer Tonus der Koronararterie auf eine bereits vorhandene Obstruktion ein möglicher Mechanismus ist, der mitverantwortlich für Angina im Ruhezustand und bei Belastung ist. Bei 18 Patienten (22 stenotische Läsionen) wurden die maximalen Veränderungen des Durchmessers der Koronararterie (mm), die mittels eines Ergometrintests nach einer intrakoronaren ISDN-Injektion ausgelöst wurden, mit einem quantitativen, auf Computer basierenden, angiographischen System ausgewertet. Wenn man davon ausgeht, daß sich die Arterienlänge nicht als Folge der Veränderungen ihres Durchmessers ändert, dann ist die Fläche des Querschnitts der Arterienwand an jedem Punkt der Arterie ungeachtet ihres Kontraktions- oder Dilatationszustandes konstant. Mit auftretender Vasokonstriktion verringert sich der luminale Durchmesser verhältnismäßig mehr als der äußere Durchmesser des Gefäßes, und die Wanddicke nimmt zu. Unter Anwendung von elementaren geometrischen Prinzipien haben wir die Veränderungen, die an den stenotischen Läsionen aufgrund vaskulärer Veränderungen an dem ganzen koronaren Segment auftreten könnten, berechnet und rekonstruiert. Von dem Referenzdurchmesser im Kontrollzustand (*Ri:* 3,7 ± 1,1 mm) und nach Vasokonstriktion (*Ric:* 3,3 ± 1,0 mm) und dem Obstruktionsdurchmesser im Kontrollzustand (*ri:* 2,2 ± 0,9 mm) wurde der minimale Obstruktionsdurchmesser nach Vasokonstriktion (*ric:* 1,0 ± 0,8 mm) mittels der folgenden Gleichung abgeleitet: $ric^2 = ri^2 - Ri^2 + Ric^2$. Bei 4 von 22 stenotischen Läsionen wurde die Verringerung des Durchmessers des normalen Gefäßlumens ganz auf die stenotische Lokalisation übertragen, und die Verringerung des Durchmessers an der Stenose wurde errechnet. Bei 6 Läsionen war die Konstriktion der Gefäßwand an den Stenoselokalisationen geringer als erwartet. Schließlich wurde bei 12 Läsionen eine deutliche arterielle Hyperkontraktilität an den Stenoselokalisationen gezeigt (Spasmus). Diese Ergebnisse zeigen, wie unberechenbar Veränderungen des vasomotorischen Tonus auf große Koronararterien bei einzelnen Patienten sein können. Das Verstehen dieser Veränderungen ist von wesentlicher Bedeutung für eine rationale Definition einer kritischen Stenose.

Key words: vasomotion, quantitative coronary angiography

Introduction

When trying to establish what constitutes a physiologically significant obstruction to blood flow in the

the coronary system of patients with exertional angina, we implicitly assume that the pathogenesis of exertional angina pectoris is based primarily on the concept of a "fixed" stenosis that causes angina when flow requirements of the myocardium exceed the flow capacity of the diseased vessel.

Recently, the hypothesis has been developed that increased coronary arterial vasomotor tone superimposed on a preexisting obstruction in a coronary artery is an important pathophysiologic mechanism responsible for causing angina pectoris not only at rest, but also during exercise (1, 2). On the other hand, it has been clearly established that the arteries of patients with spontaneous spasm or inappropriate vasomotor tone are hypersensitive to ergonovine at the sites of atherosclerotic lesions (3–10).

MacAlpin (11) recently proposed that this hypersensitivity is due in fact to the amplification of normal vasoconstriction at sites of atheromatous luminal encroachments, the degree of vasoconstriction being related to the severity of encroachment (geometric theory).

We undertook the present study to determine whether this geometric theory could explain the hypersensitivity of arteries in patients with vasospastic angina. We tried to assess the amount of coronary tone present in 18 patients to have exertional and resting angina by measuring the maximal changes in coronary arterial diameter induced by a provocative test (methylergobasine; Methergin) followed by an intracoronary (i.c.) injection of isosorbide dinitrate (Risordan).

Using elementary geometric principles, we calculated and reconstructed the changes that might occur at the stenotic sites as the result of "normal" vasomotion of the nonstenotic segment adjacent to the obstructive lesion.

Methods

Patient Selection and Vasomotor Tone Testing

In a highly selected group of 18 patients known to have exertional and resting angina, we tried to explore the entire spectrum of coronary vasomotor tone by measuring the maximal changes in coronary arterial diameter, induced by a provocative test (i.v. bolus of 0.4 mg Methergin) followed by an intracoronary (i.c.) injection of 3 mg isosorbide dinitrate. A total of 20 stenotic coronary segments were selected for quantitative angiographic analysis. Before the pharmacologic intervention, a baseline coronary angiogram (control) was performed. Five minutes later, 0.4 mg Methergin was injected intravenously.

A second arteriogram was obtained 5 min after the injection of Methergin or as soon as the patient developed chest pain and/or ST-T changes on the electrocardiogram. The third coronary angiogram was recorded 2 min after an i.c. injection of 3 mg isosorbide dinitrate.

The X-ray system was maintained in exactly the same position during the sequential angiographic studies in a particular patient, i.e., no differences in projection occurred.

Quantitative Angiographic Analysis System

In the present study, for each individual patient arterial dimensions were measured at specific distances from identifiable branch points in end-diastolic frames before and after Methergin and isosorbide dinitrate administration.

The quantitative analysis of selected coronary segments was carried out with the help of a computer-based coronary angiography analysis system (CAAS) which has been described extensively elsewhere (12–14).

To analyze a selected 35-mm cineframe, the film is placed on a specially constructed cine-video converter consisting of a standard 35-mm Vanguard cinefilm transport mechanism, a drum with six different lens systems allowing the selection of the desired optical magnification, and a high-resolution video camera mounted on a motor-driven x-y stage (12). By means of this converter, any portion of the 35-mm cineframe can be selected with the appropriate magnification factor. The cinefilm transport, the selection of the optical magnification, and the x-y positioning of the video camera are all operated through a PDP 11/44 host computer. The magnified portion of the cineframe is displayed on a video monitor; in practice, an optical magnification factor of 2 is used for the coronary segments. Regions of interest in the image can be digitized and stored in computer memory for subsequent processing. Graphics and the computer-detected contours of a coronary arterial segment can be superimposed in the video image displayed on the monitor. Operator interaction is possible with a writing table.

The computer analysis of a selected coronary segment requires the manual definition of a number of center positions within the segment by means of the writing table. A smooth continuous curve, the centerline, is subsequently generated through these center positions. This centerline determines the regions of interest 96×96 pixels in size, encompassing the arterial segments to be digitized. Contour positions are detected along scanlines perpendicular to the local centerline directions on the basis of a minimum-cost contour-detection algorithm (14). The cost of a pixel is defined as the inverse of the weighted sum of the first and second derivative values of the brightness information. If the user does not agree with part of the detected contours, these positions may be corrected interactively. On the basis of the detected contour positions, a new centerline is computed and the contour detection procedure is repeated. This interactive approach has been implemented to minimize the influence of the user definition of the center points on the detected contours. Finally, a smoothing procedure is applied to each of the contours. As a next step, all the

contour positions are corrected for pincushion distortion introduced by the image intensifier. A correction vector for each pixel in the image is assessed at an earlier stage from a digitized image of a centimeter grid and stored in memory.

Calibration of the diameter data is achieved by using the intracardiac catheter as a scaling device. To this end, the contours of part of the projected catheter are detected automatically in a way similar to that described above for the arterial segment; in addition, a priori information is included in the iterative edge-detection procedure, based on the fact that the selected part of the catheter is the projection of a cylindrical structure. The optical magnification factor for the catheter is usually chosen as $2\sqrt{2}$. A mean diameter value is determined in pixels, so that the calibration factor can be computed from the known size of the catheter.

From the final contours, the diameter function (D-function) is determined by computing the shortest distances between the left and right contour positions (curves in Figures 1a-c). As a next step the computer algorithm determines the position of the obstruction by searching for the minimal diameter value in the D-function. This position can be changed interactively by the user if more than one focal obstruction is to be processed within the analyzed arterial segment. The extent of the selected obstruction is determined from the D-function on the basis of curvature analysis and expressed in millimeters. The detected boundaries of the obstruction are indicated in the D-function with two dotted lines. For the purpose of determining the percentage diameter reduction of an obstruction, the reference diameter is computed as the average of 11 diameter values in a symmetric region with center at a user-defined reference position.

For parts of the analyzed segments proximal and/or distal to the obstructions which show no abnormalities in size, mean proximal and/or distal diameters can be calculated respectively. The user indicates the two boundary positions of such part with the writing tablet, and the mean diameter value is computed.

The accuracy of the quantification method has been validated with perspex models of coronary arteries with circular cross sections. The diameter reduction percentages and the absolute obstruction dimensions of the models were measured with the described procedure at various settings of the X-ray system and with different concentrations of the contrast agent. The average deviation from the true values for the percentage diameter stenosis was 2.00 % ± 2.32 % (mean ± SD) and for the absolute minimal obstruction diameter −0.03 ± 0.10 mm (14).

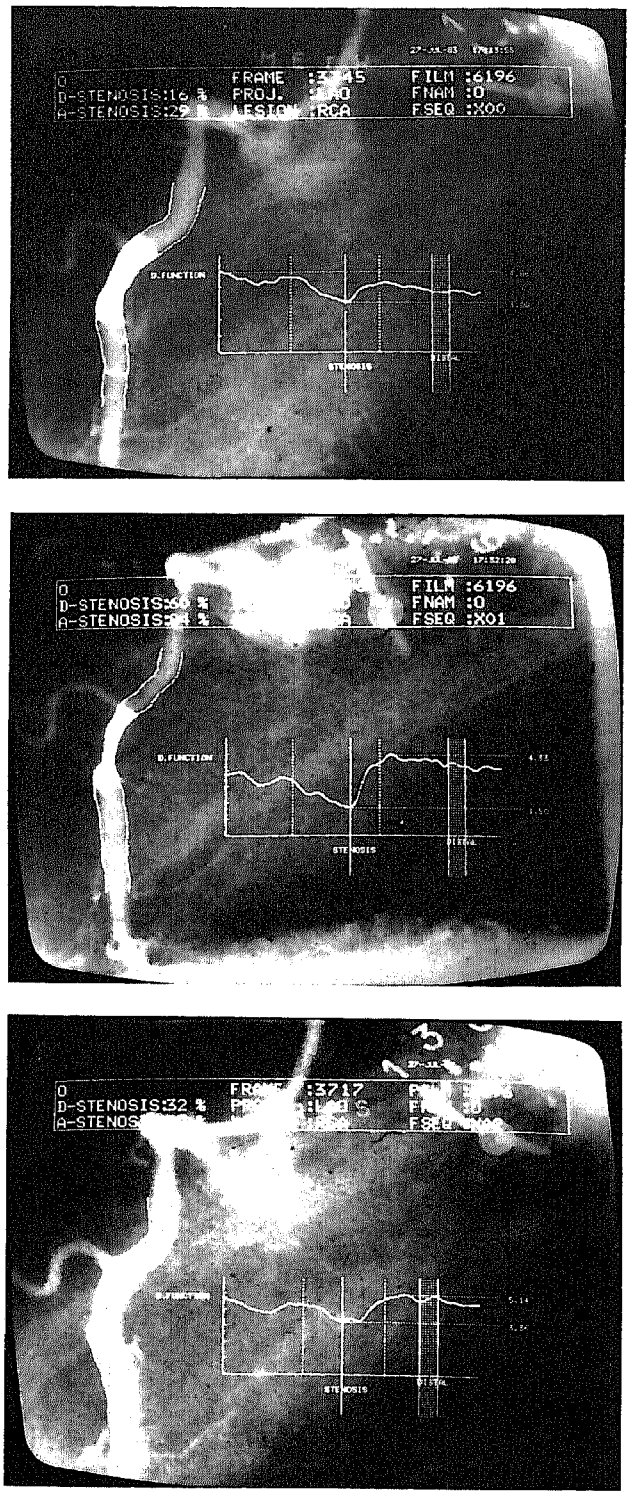

Fig. 1 a–c. Computer output of an analyzed lesion in right coronary artery at different states of vasomotion. a Control state; b after i.v. Methergin; c after i.c. isosorbide dinitrate.

Geometric Considerations: Dynamic Vascular Wall Thickening

Quantitation of vasomotion observed by angiography is limited to comparing the luminal diameter in two ore more states of vasomotion. Because we cannot see the arterial wall itself, we do not always appreciate the changes occurring in it that produce the variations in luminal dimensions which we call "vasomotion" (11, 15, 16).

The elementary geometric principle used to predict the narrowing expected at a lesion site, given the severity of the lesion and the degree of vasoconstriction of the adjacent normal segment, is shown in Figures 2–4.

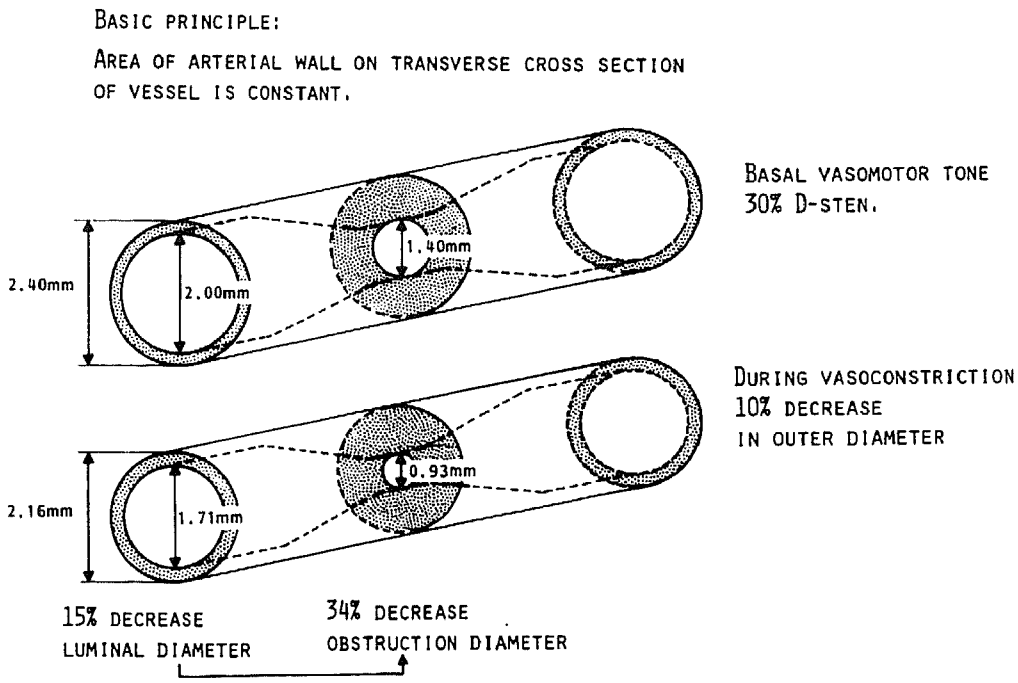

Fig. 2. Contribution of dynamic vascular wall thickening to luminal narrowing during coronary arterial constriction.

Let us assume a coronary artery that is circular in cross section when distended by a normal blood pressure and has an outer diameter $2Ro$ (e.g., 2.4 mm) including the media but excluding the adventitia (Figure 2). Furthermore, there is a coronary obstruction in the segment under consideration with a minimal (luminal) obstruction diameter $2ri$ (e.g. 1.4 mm); the luminal reference diameter in the normal prestenotic segment equals $2Ri$ (e.g., 2.0 mm).

Figure 3 shows the cross sections at the reference position and at the site of the obstruction with the definitions of the different radii. The area A_R of the arterial wall at the reference cross section equals $A_R = \pi (Ro^2 - Ri^2)$ and the area A_s at the obstruction $A_s = \pi (Ro^2 - ri^2)$. These diameter and area values define the control situation.

A new situation is created as vasoconstriction occurs (Figures 2 and 4). For practical purposes, the material of the arterial wall is plastic but not incompressible. If we assume that there is no change in the length of the artery as the result of changes in its diameter, and no extrusion of tissue from the constricted area into nonconstricted, adjacent parts of the artery, then at any point of the artery the area of the arterial wall on a transverse cross section of the vessel will be constant regardless of the state of its contraction or dilation. If we denote the new outer diameter Roc, the luminal obstruction diameter ric, and the reference diameter Ric in the state of vasoconstriction, then the following equations hold:

(1) $A_R = \pi (Roc^2 - Ric^2) = \pi (Ro^2 - Ri^2)$

(2) or $Ro^2 - Roc^2 = Ri^2 - Ric^2$

(3) and $A_s = \pi (Roc^2 - ric^2) = \pi (Ro^2 - ri^2)$

(4) or $Ro^2 - Roc^2 = ri^2 - ric^2$

Then Equations (2) and (4) yield:

(5) $ric^2 = ri^2 - Ri^2 + Ric^2$

Thus if we know the reference diameter in the control state (Ri) and after vasoconstriction (Ric) and the obstruction diameter ri in the control state, then we can predict the minimal obstruction diameter ric after vasoconstriction from Equation (5).

It should be clear that the equations (1) to (5) are equally valid for vasoconstriction and vasodilation situations.

At the top of Figure 2 we see a coronary stenotic lesion with a 30% diameter stenosis in the basal condition. Now let us assume that a 10% decrease in the outer diameter occurs as a result of vasoconstriction, i.e., the outer diameter becomes 2.16 mm (bot-

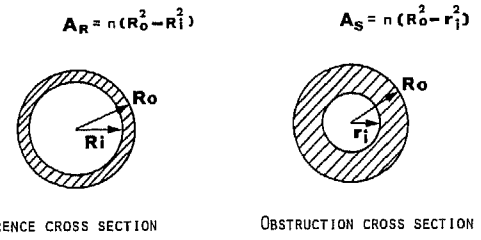

Fig. 3. A hypothetical coronary artery with circular cross sections (A_R and A_s) at a prestenotic reference position and at the site of a coronary obstruction respectively.

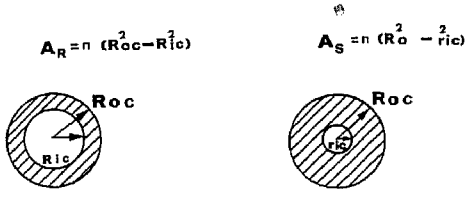

Fig. 4. Cross sections of Figure 3 after vasoconstriction.

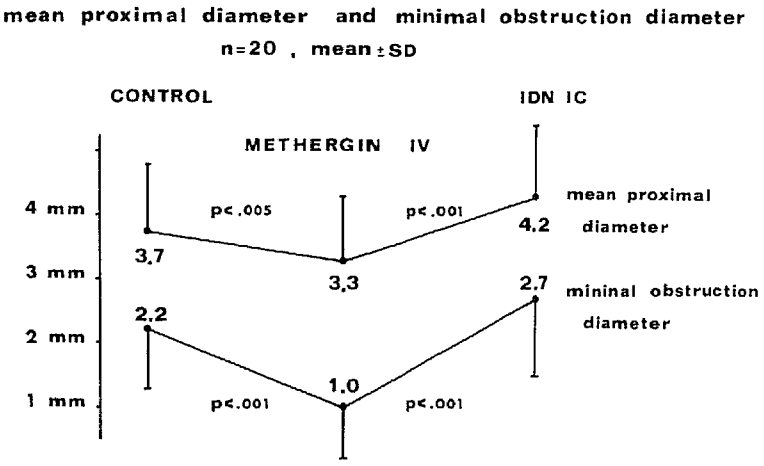

Fig. 5. Effects of i.v. Methergin and of i.c. isosorbide dinitrate (IDN) on mean proximal diameter and minimal obstruction diameter.

tom drawing of Figure 2). Under the assumption of a constant transverse cross section, it can be derived from the simple geometric principles given above that a 15 % decrease occurs in the luminal diameter of the prestenotic segment.

At the stenotic site, because of the modest mural thickening due to disease, the luminal diameter decreases in greater proportion; in the present case a 34 % decrease in obstruction diameter can be predicted from Equation (5).

Results

The effects of i.v. Methergin and i.c. isosorbide dinitrate on the mean proximal diameter and on the minimal obstruction diameter are shown in Figure 5.

Table 1. Results from quantitative analysis of coronary arteries in different states of vasomotion

Patient	Artery	Reference diameter (mm)	Obstruction diameter (mm)	Percentage diameter stenosis (user defined)	Mean proximal diameter (mm)	Mean distal diameter (mm)
1 Va	1 RCA	4.93	4.20	14.9	4.89	4.75
	2 RCA	5.39	2.79	28.3	5.24	4.33
	3 RCA	6.03	4.88	19.0	5.76	5.19
2 Gh	1 LAD	2.80	0.90	68.0	2.70	3.70
	2 LAD	totally occluded			2.10	
	3 LAD	3.01	1.76	41.4	2.99	3.48
3 Ol	1 RCA	4.48	3.34	25.4	4.1	3.8
	2 RCA	3.22	1.68	47.8	3.14	4.21
	3 RCA	4.15	3.57	14.0	4.36	4.99
Ol	1 RCA	4.04	3.34	17.3	4.1	3.8
	2 RCA	4.14	1.68	59.4	3.14	4.21
	3 RCA	5.02	3.57	28.8	4.36	4.99
4 Be	1 RCA	5.96	2.79	53.2	5.82	4.46
	2 RCA	totally occluded			4.98	
	3 RCA	6.36	2.88	54.7	6.52	5.97
5 Cr	1 RCA	5.34	3.16	40.9	5.21	
	2 RCA	5.11	1.37	73.1	4.85	
	3 RCA	5.29	3.90	26.3	5.26	
6 Flc	1 RCA	3.73	1.63	56.3	3.72	
	2 RCA	3.63	0.94	74.1	3.55	
	3 RCA	4.01	1.88	53.1	4.09	
Flc	1 RCA	3.73	2.09	43.8	3.72	
	2 RCA	3.52	1.42	59.6	3.55	
	3 RCA	3.98	2.44	38.6	4.09	
7 Duf	1 RCA	3.21	2.62	18.6	3.65	3.15
	2 RCA	2.21	1.56	29.5	3.24	2.22
	3 RCA	3.00	2.77	7.7	3.83	2.97
8 Flm	1 RCA	4.75	2.48	47.7	4.80	4.25
	2 RCA	4.02	1.36	66.2	4.00	2.54
	3 RCA	5.30	4.59	13.3	5.29	4.21

Table 1 (continued)

Patient	Artery	Reference diameter (mm)	Obstruction diameter (mm)	Percentage diameter stenosis (user defined)	Mean proximal diameter (mm)	Mean distal diameter (mm)
9 Dup	1 LCX	5.88	2.65	54.9	6.11	3.69
	2 LCX	4.94	2.14	56.7	4.73	3.62
	3 LCX	7.01	4.59	34.6	7.02	5.11
10 Ti	1 LAD	2.38	1.22	48.7	2.36	2.62
	2 LAD	totally occluded			2.16	
	3 LAD	3.39	1.44	57.6	3.18	2.69
11 No	1 RCA	3.16	1.83	42.0		3.16
	2 RCA	2.89	0.38	86.7		2.76
	3 RCA	3.31	1.79	45.9		3.16
12 De	1 RCA	3.11	1.49	52.0	3.04	3.54
	2 RCA	totally occluded			2.38	
	3 RCA	3.94	0.99	74.9	3.88	3.77
13 Dum	1 LAD	3.23	1.29	60.1	3.08	
	2 LAD	2.67	1.14	57.3	2.70	
	3 LAD	3.97	2.03	49.0	3.96	
14 Paz	1 LAD	2.43	1.27	47.6		2.41
	2 LAD	totally occluded			2.64	
	3 LAD	3.58	2.32	35.4	2.60	3.22
15 Pat	1 LAD	2.85	2.09	26.8		2.70
	2 LAD	2.31	1.23	46.6		2.05
	3 LAD	2.82	2.19	22.2		2.71
16 Me	1 RCA	3.75	2.96	21.0	2.83	
	2 RCA	4.24	1.50	64.6	3.94	2.70
	3 RCA	3.60	3.44	4.5	3.55	3.69
17 Gr	1 LAD	3.24	1.65	49.0	3.06	3.36
	2 LAD	totally occluded			2.70	
	3 LAD	3.38	1.33	60.8	3.50	3.0
18 Jo	1 RCA	2.94	1.41	51.9		2.98
	2 RCA	1.98	1.37	30.7		1.94
	3 RCA	2.90	1.56	46.3	2.88	3.39

1, control; 2, Methergin; 3, isosorbide dinitrate
Abbreviations: RCA, right coronary artery; LAD, left anterior descending artery; LCX, left circumflex artery

The differences in value between the reference diameter and mean proximal diameter (Table 1) stem from the fact that the reference diameter is computed over only 11 pixel positions, which corresponds to a width of approximately 1 mm, whereas the mean proximal diameter is usually computed over a much larger width, e.g., 100–200 pixel positions or approximately 10–20 mm.

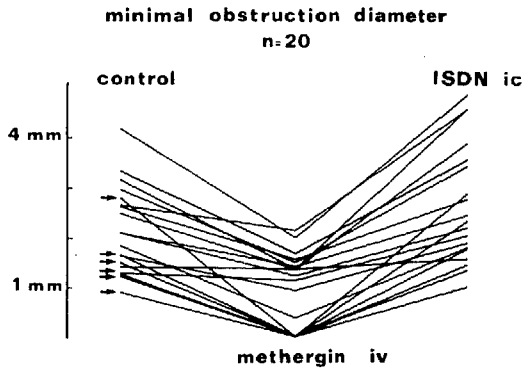

Fig. 6. Individual changes in minimal obstruction diameter after i.v. Methergin and i.c. isosorbide dinitrate (ISDN). Six of the 20 analyzed stenotic lesions (marked with *arrows*) are transiently occluded during the provocative test.

During the provocative test the mean proximal diameter decreases significantly ($p < 0.005$) by 11% with respect to the basal condition, from 3.7 to 3.3 mm, whereas the minimal obstruction diameter is reduced by more than 50% from 2.2 to 1.0 mm ($p < 10^{-7}$). The i.c. injection of isosorbide dinitrate provokes a very significant vasodilation of the obstructive lesion from 1.0 mm to 2.7 mm, $p < 10^{-8}$), as well as a significant increase in mean proximal diameter from 3.3 mm to 4.2 mm ($p < 10^{-6}$).

The individual changes in minimal obstruction diameter are given in Figure 6. After Methergin six of the 20 analyzed stenotic lesions (marked with arrows in Figure 6) became transiently occluded, whereas i.c. isosorbide dinitrate increased the luminal diameters of all the obstructive lesions which were vasoconstricted during the provocative test. In terms of percentage diameter stenosis, the severity of the obstructive lesions increased on the average from 41% to 70% ($p < .0001$) during the provocative test and returned

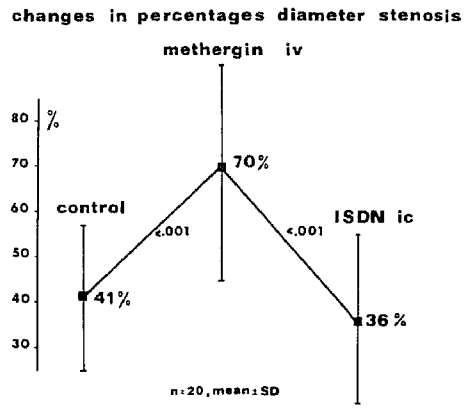

Fig. 7. Changes in percentage diameter stenosis during the provocative test and after the i.c. injection of isosorbide dinitrate.

to an average value of 36 % after i.c. isosorbide dinitrate (Figure 7).

Using the elementary geometric principles described above in Methods, we calculated and reconstructed the changes that might occur at the stenotic sites as the results of vasomotion acting on the entire coronary segment. In Figure 8, the decrease of luminal diameter of a normal prestenotic segment is plotted against the expected decrease in luminal diameter of the stenotic segment for a stenosis with a 20 % diameter reduction. In this example, a 20 % decrease in luminal diameter of the normal segment causes a 33 % decrease in diameter of the stenotic segment.

When applying this theoretical relationship to the different strates of vasomotion measured in our group of 18 patients, we found that the behavior of the stenotic lesions during vasoconstriction deviated considerably from this theoretical relationship, some stenotic lesions being hypercontractile, some others being hypocontractile (Figure 9).

As a matter of fact, during vasoconstriction only four stenotic lesions did react as predicted by the theory, and we can conclude that their decrease in

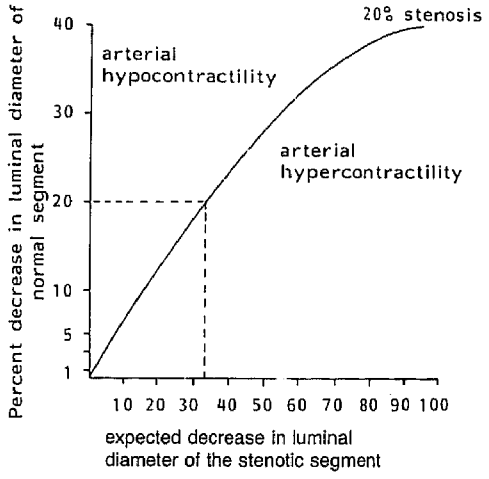

Fig. 8. The percentage decrease in luminal diameter of a normal prestenotic segment plotted against the expected decrease in luminal diameter of the stenotic segment for a stenosis with a 20 % diameter reduction.

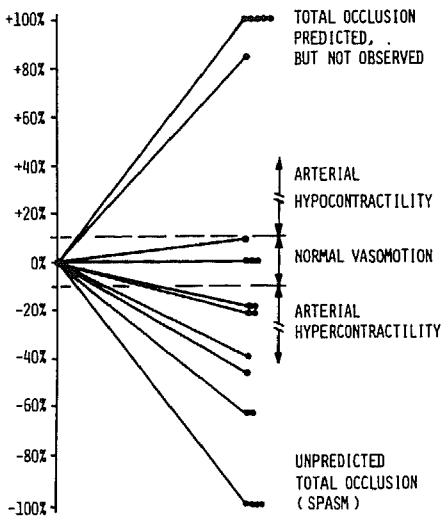

Fig. 9. Percentage deviation of the obstruction diameters from predicted values after Methergin.

luminal diameter at the stenotic sites was simply the result of an increase in vasomotor tone superimposed on an organically narrowed vessel.

Six stenotic lesions were hypocontractile, and the vessel wall at the site of the lesion actually constricted less than suggested by the theoretical model. In five cases we even predicted a total occlusion which was not observed.

As for the 12 remaining lesions, they all showed arterial hypercontractility, and four of them unexpectedly became totally occluded during vasoconstriction.

Concluding Remarks

MacAlpin (11) proposed that the increased sensitivity of arteries at the sites of lesions is a direct consequence of the luminal encroachments by atheroma and the resulting increase in wall thickness at that point. Our results do not support this theory and demonstrate once more how unpredictable the effects of changes in vasomotor tone can be on the large coronary artery.

The present study, like other previous work, supports the hypothesis that coronary artery spasm results from increased sensitivity of coronary arteries to vasoconstrictors, localized at the sites of atheromatous lesions. Although it is not known why a mild atheromatous lesion causes arterial hypersensitivity to ergonovine, recent work by Henry and Yokoyama (17) suggests that this hypersensitivity is mediated by a serotonergic mechanism which they postulated was due to accumulation of cholesterol in the vessel wall.

References

1. Serruys PW, Steward R, Booman F, Michels R, Reiber JHC, Hugenholtz PG (1980) Can unstable angina pectoris be due to increased coronary vasomotor tone? Eur Heart J 1 (suppl B): 71
2. Epstein SE, Talbot TL (1981) Dynamic coronary tone in precipitation, exacerbation and relief of angina pectoris. Am J Cardiol 48: 797

3. Maseri A, Serveri S, DeNes M, L'Abbate A, Chierchia S, Marzilli M, Ballestra AM, Parodi O, Biagine A, Distante A (1978) "Variant" angina: one aspect of a continuous spectrum of vasospastic myocardial ischaemia. Am J Cardiol 42: 1019
4. MacAlpin RN (1980) Relation of coronary arterial spasm to sites of organic stenosis. Am J Cardiol 46: 143
5. Heupler FA, Proudfit WL, Razavi M, Shirey EK, Greenstreet R, Sheldon WC (1978) Ergonovine maleate provocative test for coronary arterial spasm. Am J Cardiol 41: 631
6. Schroeder JS, Bolen JL, Quint RA, Clark DA, Hayden WG, Higgins CB, Wexler L (1977) Provocation of coronary spasm with ergonovine maleate. Am J Cardiol 40: 487
7. Waters DD, Theroux P, Szlachcic J, Dauwe F, Crittin J, Bonan R, Mizgala HF (1980) Ergonovine testing in a coronary care unit. Am J Cardiol 46: 922
8. Curry RC, Pepine CJ, Sabom MB, Feldman RL, Christie LG, Conti CR (1977) Effects of ergonovine in patients with and without coronary artery disease. Circulation 56: 803
9. Freedman SB, Dunn RF, Bernstein L, Richmond DR, O'Neill G, Kelly DT (1980) Coronary artery spasm: use of ergonovine in diagnosis. Aust NZ J Med 10: 6
10. Freedman B, Richmond DR, Kelly DT (1982) Pathophysiology of coronary artery spasm. Circulation 66: 705
11. MacAlpin RN (1980) Contribution of dynamic vascular wall thickening to luminal narrowing during coronary arterial constriction. Circulation 61: 296
12. Reiber JHC, Gerbrands JJ, Kooijman CJ, et al. (1983) Quantitative coronary angiography with automated contour detection and densitometry; technical aspects. In: Just H, Heintzen PH (eds) Angiocardiography: current status and future developments. Springer. Berlin Heidelberg New York Tokyo (in press)
13. Reiber JHC, Gerbrands JJ, Booman F, et al. (1982) Objective characterization of coronary obstructions from monoplane cineangiograms and three-dimensional reconstruction of an arterial segment from orthogonal views. In: Schwartz MD (ed) Application of computers in medicine. IEEE Cat No Th 0095–0: 93–100
14. Kooijman CJ, Reiber JHC, Gerbrands JJ, et al. (1982) Computer-aided quantitation of the severity of coronary obstructions from single view cineangiograms. International symposium on medical imaging and image interpretation. IEEE Cat No 82CH1804–4: 59–64
15. Folkow B, Grimby G, Thulesius O (1958) Adaptive structural changes of the vascular walls in hypertension and their relation to the control of the peripheral resistance. Acta Physiol Scand 44: 255
16. Conway J (1958) Vascular reactivity in experimental hypertension measured after hexamethonium. Circulation 17: 807
17. Henry PD, Yokoyama M (1980) Supersensitivity of atherosclerotic rabbit aorta to ergonovine: mediation by a serotonergic mechanism. J Clin Invest 66: 306

Authors' address:

P. W. Serruys, Catheterization Laboratory, Thoraxcenter, Erasmus University, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands