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CLINICAL STUDIES

Effect of Coronary Occlusion During Percutaneous Transluminal Angioplasty in Humans on Left Ventricular Chamber Stiffness and Regional Diastolic Pressure-Radius Relations

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The effect of repeated (3 to 10 second) and transient (15 to 75 second) abrupt coronary occlusion on the global and regional chamber stiffness was studied in nine patients undergoing angioplasty of a single proximal left anterior descending coronary artery stenosis. The left ventricular high fidelity pressure and volume relation was obtained before and after the procedure as well as during coronary occlusion, after 20 seconds (n = 9) and after 50 seconds (n = 5). During ischemia, there was an upward shift of the pressure-volume relation. The nonlinear simple elastic constant of chamber stiffness increased from 0.0273 ± 0.017 before angioplasty (mean ± SD) to 0.0621 ± 0.026 after 20 seconds of occlusion ($p < 0.05$) and 0.0605 ± 0.015 after 50 seconds of occlusion ($p < 0.01$). In five patients, the postangioplasty value remained higher than the control value, but at the group level the mean value (0.0529 ± 0.037) was not statistically different.

The regional stiffness was determined from the changes in the length of six segmental radii during diastole, from the lowest diastolic to the end-diastolic pressure. The regional constant of elastic stiffness was unaffected in the nonischemic zone. In the adjacent and ischemic zones, the regional stiffness was increased during occlusion ($p < 0.05$). These regional abnormalities in diastolic function persisted at the time of postangioplasty measurements, 12 minutes after the end of the procedure. This suggests that recovery of normal diastolic function after repeated ischemic injuries is delayed after restoration of normal blood flow and systolic function.

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An increase in left ventricular diastolic pressure relative to volume has been described in patients during cardiac pacing and exercise-induced ischemia (1,2) as well as during spontaneous angina at rest (3). The observed upward shift of the entire pressure-volume curve reflects an increased chamber stiffness. From these data, it cannot be inferred that the intrinsic diastolic properties of the myocardium were altered because many other factors, such as delayed and incomplete left ventricular relaxation or extrinsic compression by the right ventricle and the pericardium, may be involved (4,5). More recent studies (6,7), however, were able to relate the shift in the left ventricular pressure-volume relation observed after pacing-induced ischemia to a regional increase in myocardial stiffness of the ischemic zone.

When low flow (as opposed to high demand) ischemia was induced by acute coronary occlusion in the experimental laboratory (8,9), an increase in myocardial stiffness with or without upward shift of the diastolic pressure-volume curve was described. A recent study in conscious dogs (10) showed that the upward shift was prevented by inferior vena cava occlusion evidencing the modulating role of right ventricular loading conditions.

In patients with coronary artery disease, interruption of blood flow induced by transient balloon inflation during percutaneous transluminal coronary angioplasty is a situation that mimics the experimental abrupt coronary occlusion in the animal laboratory. This provides a unique opportunity to study the mechanical and metabolic effects of low flow ischemia in humans. Earlier, we reported the dynamic changes in the left ventricular hemodynamics and geometry during

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coronary angioplasty (11) and demonstrated the perfect reversibility after the procedure of the abnormalities in global and regional systolic function induced by repeated transluminal occlusion.

The aim of the present study was to further characterize the changes in diastolic function induced by coronary occlusion in conscious humans. We determined whether an upward shift in the diastolic pressure-volume relation was actually observed and whether this increase in chamber stiffness, if any, was reversible and could be ascribed to an increased regional stiffness of the ischemic zone.

Methods

Patients. The present study includes nine patients (one woman and eight men) with normal left ventricular function and wall motion at rest who underwent percutaneous transluminal coronary angioplasty of a proximal and isolated left anterior descending coronary artery stenosis. No patient had had a previous infarction. The distal vessel was not filled by collateral circulation, as shown by diagnostic angiography. One of the 10 previously reported (11) patients was excluded because the small number of available data points due to a higher heart rate precluded analysis of the diastolic function. All patients gave their informed consent and there were no complications related to the research procedure. The patient's medications were not discontinued on the day of the procedure, but no particular medication was administered to the patient before dilation. The medications consisted of a combination of a calcium channel blocker, a beta-adrenergic blocking agent and a long-acting nitrate (except for Patients 2, 7, 8 and 9 who had only the first two drugs). Before approval of the protocol by the Thoraxcenter ethics committee, a feasibility study was performed including an analysis of the effect of various nonionic contrast media on left ventricular function. Other details regarding the angioplasty procedure used in our laboratory have been published previously (12).

Study protocol. Simultaneous left ventricular pressure and volume were obtained by contrast ventriculography before the angioplasty procedure was started (n = 9), after a median occlusion of 20 seconds (range 15 to 27) during the second dilation (n = 9), after a median occlusion of 48 seconds (range 46 to 59) during the fourth dilation (n = 5) and after a median time of 12 minutes after the end of the angioplasty procedure (n = 9). A total of 3 to 10 occlusions were performed; the duration of each balloon inflation ranged from 15 to 75 seconds. According to the recommendation of the ethics committee, no investigational occlusions were carried out after completion of a technically successful dilation. In four patients, this result was achieved after three dilations so that angiographic data after 48 seconds (fourth occlusion) are available only in five of nine patients.

These sequential angiograms were made only after the return to baseline of the end-diastolic pressure and of the left ventricular pressure-derived isovolumic variables of contractility and relaxation, which were available on line during the procedure. The interval between two angiograms was at least 10 minutes. Care was taken to maintain the patient's position unchanged and to decrease diaphragm movement by encouraging shallow inspiration.

The left ventricular pressure was measured with a Millar micromanometer on an 8F pigtail catheter. The contrast ventriculograms (30° right anterior oblique at 50 frames/s) were obtained by injection of 0.75 ml/kg of a nonionic contrast medium (metrizamide, Amipaque). As noted by others (13), we found that this contrast agent has virtually no persistent effects on left ventricular hemodynamics.

Data analysis. Frame by frame left ventricular volumes and the corresponding pressures were simultaneously obtained from a complete cardiac cycle as previously described (14). The ventricular contours were automatically detected with the Contouromat (15) and the volumes calculated according to Simpson's rule. The end-diastolic pressure was defined as that point on the pressure trace at which the derivative of the pressure is first greater than 200 mm Hg/s (14), and in all cases this coincided with the largest left ventricular volume. End-systole was defined with reference to the pressure tracing, at the occurrence of the dicrotic notch of the central aortic pressure. The left ventricular pressure decay during the isovolumic relaxation was quantified as previously described (11) using a biexponential model, where Tau_1 represents the time constant of early relaxation (during the first 40 ms after the peak negative first derivative of pressure [dP/dt]). To detect the ventricular contours and analyze the segmental wall motion, the previously described "endocardial landmark model" (15,16) was used. As shown in pigs with endocardially implanted metal markers, the automated detection throughout the cardiac cycle by a computerized high resolution outlining system of specific sites of the endocardium accurately reflects the motion pattern of the actual anatomic structures.

From the mean trajectories of these endocardial landmarks in 23 subjects without hemodynamic, coronary or angiographic abnormalities, a system of 20 segmental radii was defined and generalized as a mathematic expression amenable to automatic data processsing. The range of normal values was defined from these data. In the present study, the length of the 20 segmental radii defined by the model was measured frame by frame and among them, we selected for analysis 6 radii located in the core of the ischemic segment (anterior, anterolateral and apical radii) or in the nonischemic segment (anterobasal and posterobasal radii), as well as the inferior radius immediately adjacent to the ischemic segment (Fig. 1). The linear correlation coefficients between repeated measurements of radius length in 20 patients ranged from 0.96 to 0.99 (SEE = 0.4 to 1.4%) for

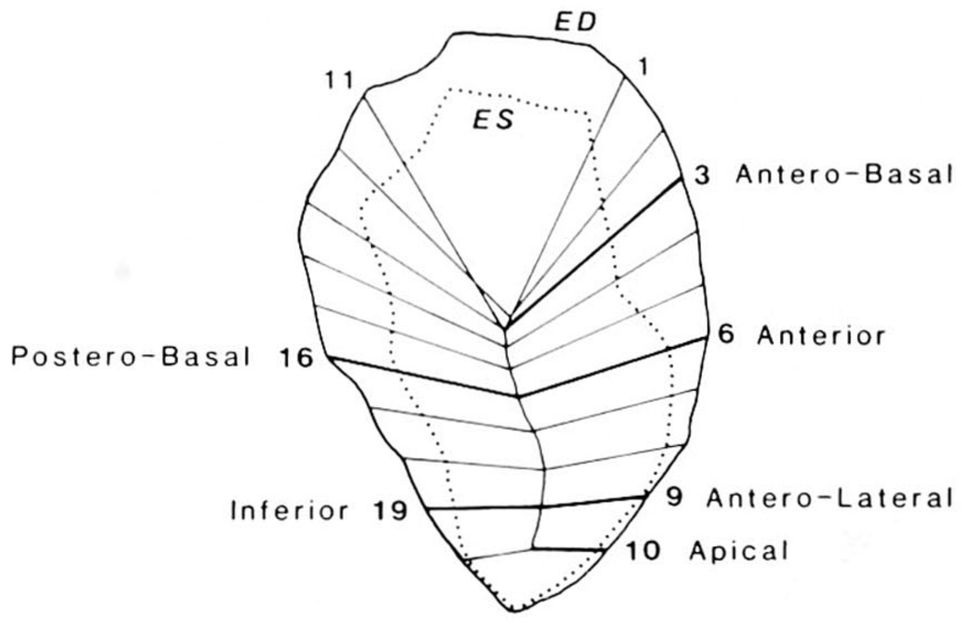

Figure 1. The end-diastolic (ED) and end-systolic (ES) contours of a left ventriculogram during transluminal occlusion are displayed with the system of 20 radii along which regional wall displacement was determined. For the analysis of regional diastolic function, we selected radii 6, 9 and 10 within the ischemic zone, radii 3 and 16 within the nonishchemic zone as well as radius 19 in the adjacent inferior zone.

the same operator and from 0.91 to 0.99 (SEE = 0.4 to 2.3%) for two different operators.

Calculations. *For the evaluation of global chamber stiffness*, the left ventricular pressure (P) and volume (V) data obtained every 20 ms starting at the lowest diastolic pressure and ending at the end-diastolic pressure were fitted by a simple elastic model: $P = \alpha e^{\beta V} + C$, where α = intercept (mm Hg), β = constant of elastic chamber stiffness, C = baseline pressure (mm Hg) and e is the base of the natural logarithm. The three constants of this equation (α, β and C) were determined using an iteration procedure until the best nonlinear curve fit was obtained (17).

For the evaluation of regional chamber stiffness, the left ventricular pressure and the segment radius length (L) data were fitted in a similar way for each of the six (1,2, . . . n) analyzed segmental radii: $P = \alpha_n e^{\beta_n L} + C_n$, where β_n represents the regional elastic stiffness constant for a given radius. The same approach was applied previously by others to pressure-length relations obtained either by ultrasonic subendocardial crystals (18) or by contrast ventriculography (7,8).

Statistical analysis. Results are given for all patients (n = 9) and the subgroup is analyzed after 50 seconds of occlusion (n = 5) either as mean ± SD or as median values using analysis of variance for repeated measurements. Comparisons among preangioplasty, postangioplasty and 20 seconds of occlusion conditions were performed in nine patients. The data obtained before angioplasty, after 50 seconds of occlusion and after angioplasty were compared in the appropriate subgroup of five patients. In both cases, when overall significance was found, multiple comparisons were used to delineate which paired comparisons were significantly different at the 0.05 level.

Results

Global pressure-volume relations. The left ventricular volume at the lowest diastolic pressure as well as at end-diastole did not change significantly during and after angioplasty, whereas the end-systolic volume and Tau_1, the time constant of early relaxation, had increased markedly ($p < 0.01$) after 20 seconds of occlusion (Table 1).

The lowest diastolic ($p < 0.05$) and the end-diastolic ($p < 0.01$) pressures were increased in the subgroup of patients studied after 50 seconds of anterior descending coronary artery occlusion. After completion of the procedure, all the hemodynamic variables returned toward control values.

The increase in pressure relative to volume during transluminal occlusion resulted in an upward shift of the entire pressure-volume relation, as shown for two representative patients (Cases 2 and 7) (Fig. 2). In only two instances (Cases 6 and 9) we observed a shift downward and to the right of the pressure-volume relation.

The calculated variables of global chamber stiffness showed a similarly increased constant of elastic stiffness (β) after 20 seconds as well as after 50 seconds of occlusion. The baseline pressure (C) increased significantly ($p < 0.01$) only after 50 seconds of coronary occlusion. No change in the intercept (α) was observed (Table 2). All patients except one (Case 8) showed an increase in chamber stiffness during coronary occlusion which, after the procedure, returned to values not significantly different from the preangioplasty value. However, the postangioplasty elastic constant remained higher than the control value in five instances (Cases 4, 5, 6, 7 and 9). This is further illustrated in Figure 2 where the pressure-volume relation obtained after the procedure is nearly superimposed on the control curve in Patient 2 (Fig. 2A) whereas the postangioplasty curve remains shifted upward in Patient 7 (Fig. 2B).

Regional pressure-radius length relations. There was no significant difference during the procedure in the length at end-diastole of the various segmental radii (Table 1). Plots of the left ventricular pressure against a representative radius within the ischemic segment (radius 6, 9 or 10) are shown in Figure 3. During occlusion, the slope of the pressure-radius length relation increased; this was often accompanied by an upward shift. The postangioplasty curves either showed a return toward the control relation or remained parallel to the curves during occlusion. The latter instance was mainly observed in Patients 4, 6, 7 and 9, all of whom had persistent global increased chamber stiffness after the procedure, as mentioned earlier.

These relations were fitted with the same elastic model used for calculation of the global chamber stiffness. The changes in the constant of regional chamber stiffness (β_n) showed a marked and persistent increased stiffness in the ischemic segment as well as in the adjacent inferior segment (radius 19). The regional stiffness in the nonischemic seg-

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Table 1. Hemodynamic Variables Before Angioplasty (Pre), During Coronary Occlusion (20 and 50 seconds) and After the Dilation Procedure (Post) in Nine Patients

Case	LVP_{min} (mm Hg)	LVV at P_{min} (ml/m^2)	LVEDP (mm Hg)	LVEDV (ml/m^2)	LVESV (ml/m^2)	Tau_1 (ms)	Radius Length at End-Diastole (mm)					
							Radius 3	Radius 6	Radius 9	Radius 10	Radius 16	Radius 19
1												
Pre	8	49	13	78	28	61	44	32	19	14	28	17
20 seconds	12	72	19	88	33	57	43	33	23	15	33	23
50 seconds	20	56	31	88	39	85	42	32	22	13	34	24
Post	13	53	26	91	28	61	45	34	23	17	33	21
2												
Pre	2	47	10	78	32	50	38	26	15	11	35	21
20 seconds	11	50	21	82	39	76	42	30	16	11	29	16
50 seconds	15	62	24	76	49	68	40	30	16	10	29	16
Post	4	45	16	85	32	57	42	31	17	12	30	16
3												
Pre	5	52	16	82	28	47	49	32	20	13	29	16
20 seconds	11	55	23	88	44	70	39	30	19	11	34	21
50 seconds	12	59	24	87	44	74	41	31	22	14	32	19
Post	6	53	18	86	28	50	42	32	21	14	30	18
4												
Pre	8	63	16	92	29	56	45	31	19	11	32	30
20 seconds	13	60	23	110	36	88	48	34	23	15	32	25
50 seconds	8	59	24	105	38	64	45	32	20	14	35	32
Post	3	53	18	96	23	54	47	32	19	14	32	27
5												
Pre	12	49	20	72	28	59	41	33	17	13	30	18
20 seconds	8	54	22	73	36	86	41	32	20	12	31	20
50 seconds	22	70	36	81	51	75	43	36	22	14	31	21
Post	10	40	18	73	27	59	43	35	19	13	29	19
6												
Pre	20	48	35	65	22	58	38	29	22	14	26	15
20 seconds	13	38	25	59	28	87	33	26	16	11	28	19
Post	9	39	19	64	24	56	37	27	18	11	26	18
7												
Pre	6	82	16	113	52	65	52	36	22	17	32	19
20 seconds	13	64	21	96	57	113	48	33	19	15	32	19
Post	8	57	17	94	47	70	48	31	18	12	32	20
8												
Pre	15	64	35	96	43	68	42	33	20	12	33	22
20 seconds	14	58	31	82	39	69	41	30	18	12	32	20
Post	13	47	31	82	27	50	44	28	19	13	32	19
9												
Pre	19	39	30	68	26	51	38	28	18	13	29	17
20 seconds	0	43	14	72	35	77	38	29	19	14	28	19
Post	6	35	19	67	21	40	40	27	18	13	28	18
Median values												
All patients (n = 9)												
Pre	8	50	20	78	28	58	42	31	19	13	30	18
20 seconds	12	55	22	82	36†	77‡	42	30	19	12	32	20
Post	8	53	18	84	27	56	43	31	19	13	30	18
Subgroup (n = 5)												
Pre	8	50	16	78	28	56	43	32	18	12	30	18
50 seconds	15*	59	30†	87	44‡	74*	42	32	21	14	32	19
Post	6	53	18	86	28	57	43	32	19	14	30	18

*$p < 0.05$; †$p < 0.01$; ‡$p < 0.001$. LVEDP = left ventricular end-diastolic pressure; LVEDV = left ventricular end-diastolic volume; LVESV = left ventricular end-systolic volume; LVP_{min} = left ventricular minimal diastolic pressure; LVV = left ventricular volume; P_{min} = minimal diastolic pressure; Tau_1 = time constant of early relaxation; each radius (3 through 19) refers to the radii selected for analysis as defined in Figure 1; probability values versus pre- and postangioplasty.

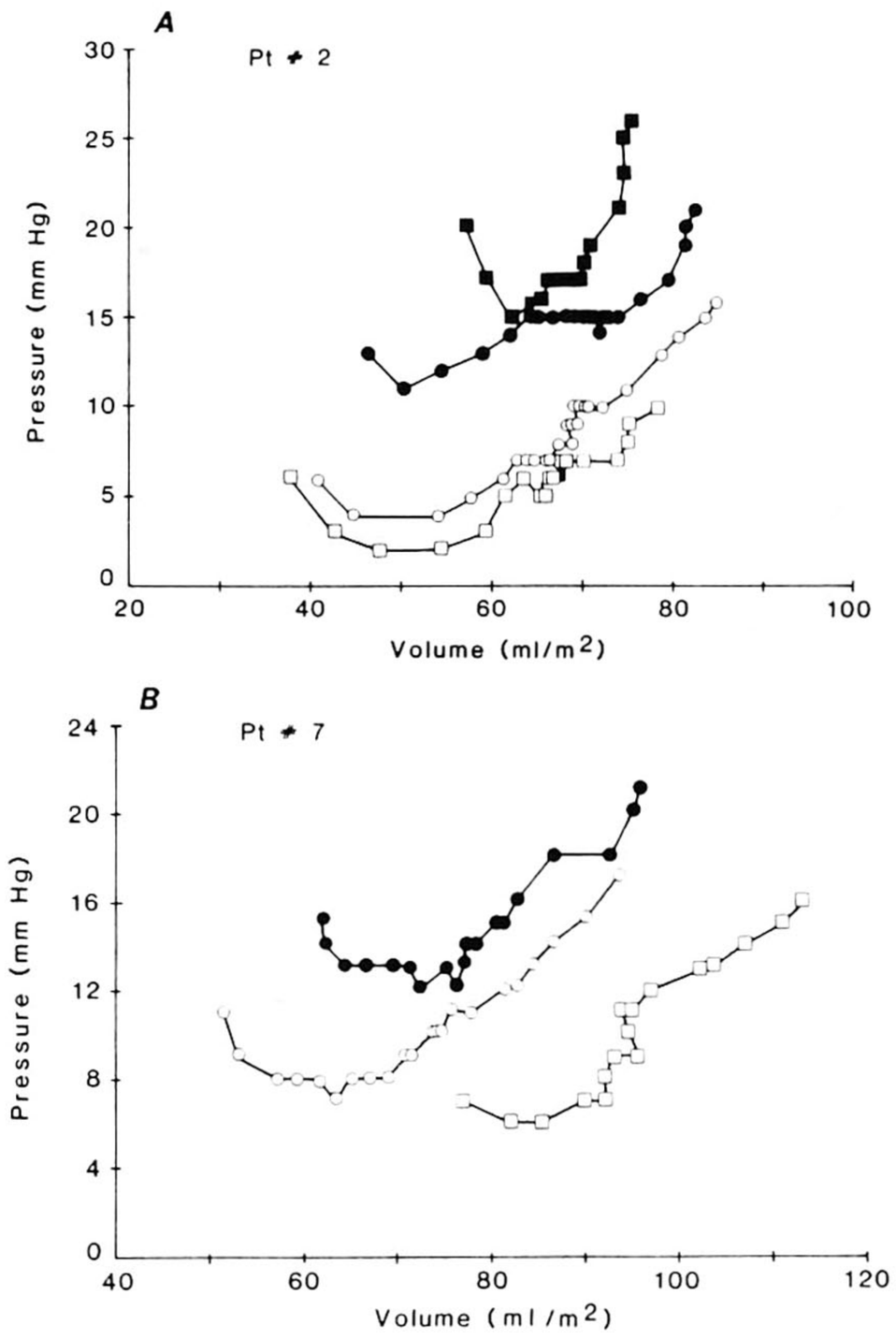

Figure 2. Diastolic pressure-volume relation in two representative patients. Note the upward shift of the relation during coronary occlusion. In Patient 2 (**A**), the postangioplasty relation returned toward control whereas it remained shifted upward in Patient 7 (**B**). **Open squares** = preangioplasty; **closed circles** = 20 seconds of occlusion; **closed squares** = 50 seconds of occlusion; **open circles** = postangioplasty.

ments was not significantly affected by the coronary occlusions (Table 3). There were also no significant changes in the nonlinear elastic constant (α_n). Similar shifts in the baseline pressure (C) and global diastolic function were observed because the same left ventricular pressure data were used for calculations of both global and regional chamber stiffness.

Discussion

Postischemic diastolic abnormalities. Our major finding was that ischemia induced by complete occlusion of the left anterior descending coronary artery increased the regional chamber stiffness of the ischemic anterior wall, even during an occlusion as short as 20 seconds. Parallel to this increase in regional stiffness, the global stiffness of the left ventricle increased significantly. In experimental studies (8–10), an increase in global chamber stiffness was seen only when the area rendered ischemic was large, such as during acute occlusion of the left anterior descending coronary artery.

The baseline pressure (constant C) increased slightly from −1.4 to 5.2 mm Hg at 20 seconds and from −5.8 to 9.4 mm Hg at 50 seconds after acute coronary occlusion (Table 2). This increase in baseline pressure reflects the upward shift of the diastolic pressure-volume relation during coronary occlusion, which was 6.6 mm Hg after 20 seconds and 15.2 mm Hg after 50 seconds.

Twelve minutes after the end of the procedure, including repeated (3 to 10 second) and brief (15 to 75 second) occlusions, angiocardiography was repeated. The variables of global and regional systolic function were back to normal, as shown by the indexes of isovolumic contraction, relaxation and segmental wall motion (11). In contrast, the variables of regional diastolic function were still abnormal (Table 3), whereas the constant of global chamber stiffness and the baseline pressure remained slightly elevated. This suggests the persistence of postischemic diastolic abnormalities while complete recovery of systolic function and relaxation has already occurred.

Significance of the upward shift in pressure-volume and pressure-radius relations. The significance of the upward shift in the pressure-volume or pressure-radius length relation, or both, is still the subject of controversy. In previous studies (5–10,19,20), this shift was attributed to any or a combination of the following factors: changes in intrinsic diastolic myocardial stiffness, delayed left ventricular relaxation, loss of elastic recoil due to ventricular asynergy,

Table 2. Global Left Ventricular Chamber Stiffness (simple elastic model)

	α Intercept (mm Hg)	β Constant of Elastic Stiffness	C Baseline Pressure (mm Hg)
All patients (n = 9)	NS	*	NS
Preangioplasty	4.6 ± 4.9	0.0273 ± 0.017	−1.4 ± 9.5
20 seconds of occlusion	1.2 ± 3.3	0.0621 ± 0.026*	5.2 ± 8.3
Postangioplasty	1.2 ± 1.5	0.0529 ± 0.037	2.8 ± 4.7
Subgroup (n = 5)	NS	†	†
Preangioplasty	5.3 ± 5.9	0.0214 ± 0.007	−5.8 ± 7.4
50 seconds of occlusion	0.2 ± 0.3	0.0605 ± 0.015*	9.4 ± 2.7†
Postangioplasty	1.9 ± 1.8	0.0396 ± 0.027	0.8 ± 5.6

*$p < 0.05$; †$p < 0.01$. Values are mean ± 1 SD; overall and paired (versus preangioplasty) significance values are given.

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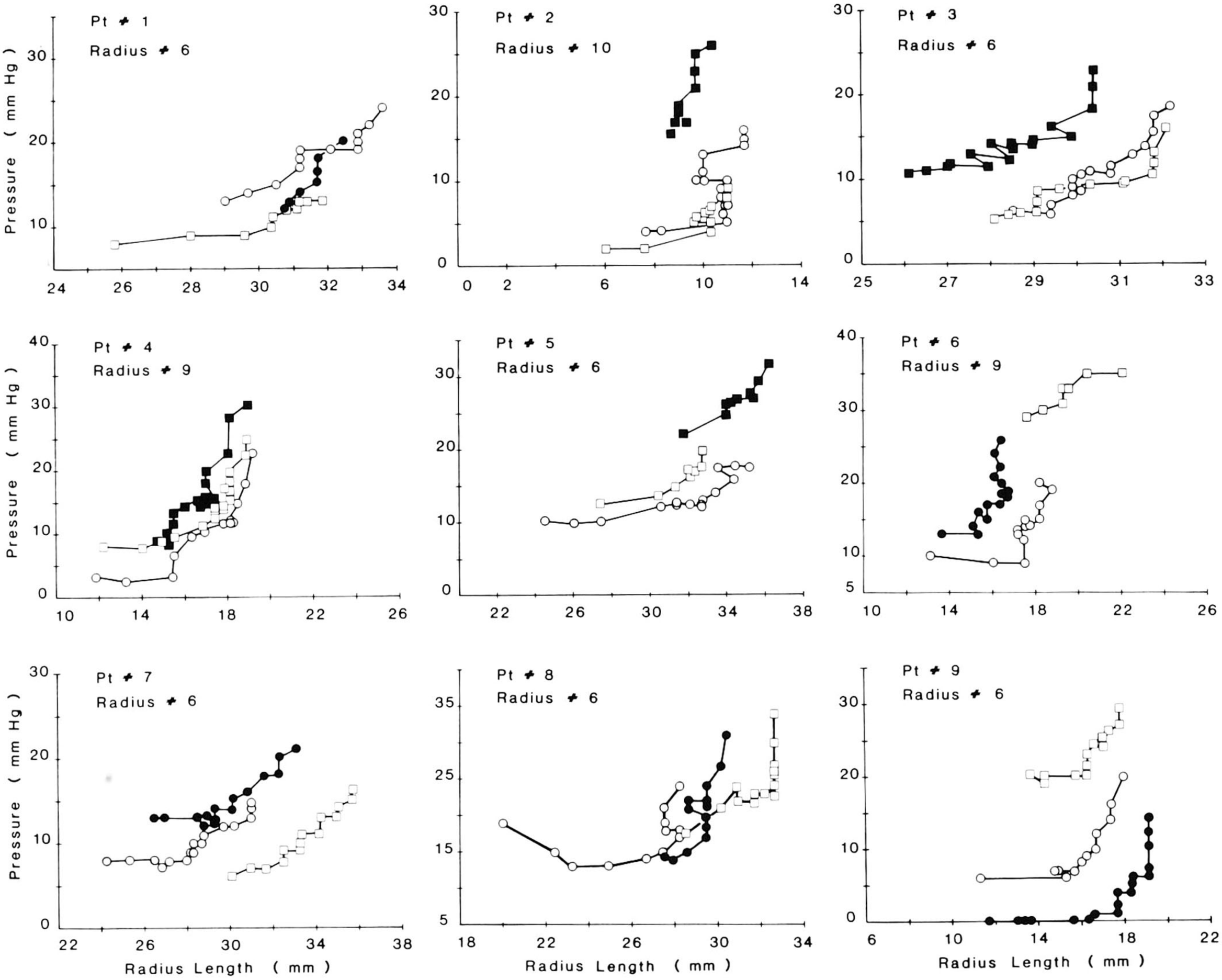

Figure 3. Plots of left ventricular pressure versus radius length in the ischemic zone in the nine patients. During occlusion the slope of this relation increased as compared with the slope before angioplasty. The increased slope was mostly accompanied by an upward shift. The postangioplasty curves either showed a return toward the control relation or remained parallel to the curves observed during occlusion (Cases 4, 6, 7 and 9). Symbols as in Figure 2. Radius number refers to specific radius in Figure 1.

changes in right ventricular loading conditions, effects of the pericardium and coronary perfusion. A limitation of the present study is that we cannot directly address these specific issues. For instance, fitting of the pressure-volume relation by a simple elastic model, as we did, does not allow one to infer that the intrinsic diastolic properties of the myocardium were affected by acute coronary occlusion because this would require analysis of left ventricular stress and strain (4). For this purpose, regional wall thickness measurements are needed which cannot be obtained accurately at 20 ms intervals from the left ventricular angiocardiograms. Also, the strain data should be normalized for a reference unloaded muscle length, that is, at a transmural pressure of 0 mm Hg, which cannot be obtained easily during cardiac catheterization in humans. As far as extrinsic factors are concerned, we believe that the coronary perfusion, or the so-called erectile effect, is not likely to account for the increased stiffness in the core of the ischemic segment.

During occlusion of the left anterior descending coronary artery, inflation of the dilation balloon results, on average, in a 44% decrease in regional blood flow (21), thereby decreasing the myocardial wall blood volume. Similarly, the postangioplasty measurements were obtained at a time when any increased myocardial turgor due to reactive hyperemia had worn off (21). Interestingly, the increase in regional stiffness observed in the adjacent inferior segment could be related to an increased turgor as the collateral flow to that area might increase during left anterior descending artery occlusion (22).

Table 3. Regional Left Ventricular Chamber Stiffness (β_n)

	Zone					
	Nonischemic Anterobasal	Ischemic			Adjacent Inferior	Nonischemic Posterobasal
		Anterior	Anterolateral	Apical		
Radius	3	6	9	10	19	16
All patients (n = 9)	NS	NS	*	NS	NS	NS
Preangioplasty	1.59	3.92	3.11	2.93	2.76	4.03
20 seconds of occlusion	3.03	4.03	5.63	4.97	6.59	5.01
Postangioplasty	2.73	2.59	6.45*	7.16	5.98	3.64
Subgroup (n = 5)	NS	NS	‡	‡	†	NS
Preangioplasty	1.59	3.45	2.81	1.09	1.52	2.59
50 seconds of occlusion	4.13	4.81	5.39	6.16	7.56*	5.54
Postangioplasty	1.98	3.71	5.59	7.16	6.93	4.35

*$p < 0.05$, †$p < 0.01$, ‡the statistical significance was borderline at the 0.05 level. β_n = constant of regional elastic stiffness; median values and overall and paired (versus preangioplasty) probability values are given.

Comparison with animal models of acute low flow ischemia. Coronary angioplasty mimics experimental coronary occlusion in the animal laboratory and induces transient acute low flow ischemia. In their animal model, Hess et al. (10) showed that "myocardial wall stiffness is increased during complete coronary occlusion when there is systolic thinning of the ischemic wall." In their conscious chronically instrumented dogs, the ischemic alteration in the intrinsic diastolic properties of the muscle resulted in an upward shift of the pressure-volume control curve. The authors observed an average 27% increase in diastolic wall stiffness, which compares well with the 35% increase in global chamber stiffness after 50 seconds of left anterior descending coronary artery occlusion in our data. It is worth mentioning that in the animal study, the upward shift of the pressure-volume curve was prevented by inferior vena cava obstruction. This emphasizes the modulating role of right ventricular loading conditions and the ventricular interaction, which can offset the increase in pressure. Thus, the observed changes in global and regional diastolic chamber stiffness are in accordance with previous experimental studies (8,10,18) demonstrating an increase in myocardial stiffness during coronary occlusion.

Mechanism of increased myocardial stiffness. The mechanism by which ischemia increases myocardial stiffness remains speculative and may depend on the pathophysiology (9) and the duration (23) of a given ischemic condition. In the acute coronary occlusion model (8,10), systolic overstretch of the akinetic muscle fibers by adjacent nonischemic myocardium was thought to be responsible for the diastolic thinning of the ischemic wall and the increase in muscle length at rest. This "creep" effect causes the ischemic myocardium to operate at a higher point on the pressure-sarcomere length relation and therefore at an increased stiffness level. Although we observed no significant changes in end-diastolic volume throughout the procedure, it cannot be excluded that creep actually occurred. Echocardiographic evidence of wall thinning during angioplasty and during attacks of variant angina supports this hypothesis (24,25).

The other major mechanism refers to the concept of residual diastolic actin-myosin interaction (26). An increase in cytosolic ionic calcium and a decrease in adenosine triphosphate available for cross bridge dissociation could result in the presence of an abnormal myocardial "tone." This mechanism is unlikely after prolonged occlusion because the ischemic segment becomes akinetic or dyskinetic and systolic cross bridge formation is probably minimal or absent. However, after 20 seconds of occlusion, we observed asynchrony and late shortening of the ischemic wall (11,23), which were shown to affect the stiffness of rat heart trabeculae (27). Also, the persistent abnormalities in diastolic function observed after the procedure could be related to an abnormal myocardial tone despite normalization of the rate of relaxation. As was recently reported (7,9), such failure of complete myofilament inactivation implies a decreased extent of relaxation that is not necessarily synonymous with a decreased rate of relaxation, as measured from the time constant of isovolumic left ventricular pressure decay.

Finally, it should be realized that the increase in calculated stiffness constant could also be related to an increased resistance to early filling. It was shown recently in humans (28) that early diastolic filling can be kept normal during ischemia despite delayed relaxation and loss of elastic recoil (increase in end-systolic volume) by increasing the left atrial driving pressure. Under these conditions, the diastolic properties of the myocardium would be better characterized by a viscoelastic model rather than by a simple elastic stress-strain relation (29,30). We used a simple elastic model because the present angiocardiographic data did not allow proper quantitation of the strain rates, which are essential for determining diastolic viscous effects. Therefore, our calculated stiffness constant includes both elastic and viscous forces.

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Conclusion and clinical implications. Repeated complete coronary occlusions of the left anterior descending coronary artery in conscious humans are associated with profound alterations in diastolic chamber stiffness that persist well after restoration of myocardial blood flow and normal systolic function. Further study is needed to document the time course of the recovery to a normal regional diastolic function and to address the responsible derangement of subcellular metabolism because the mechanisms of the observed abnormalities are not yet fully understood.

From the clinical point of view, many factors have contributed to increase the extent and severity of iatrogenic ischemia during angioplasty: longer balloon inflation time, dilation of multiple lesions during a single setting and inclusion of patients with unstable angina or impaired left ventricular function. This has prompted studies attempting to modify ischemic changes induced by balloon inflation by various means of intervention (21,31,32).

Together with our previous studies (11,23), the present data suggest that the analysis of diastolic function may prove to be a sensitive tool in assessing the possibly deleterious effects of repeated coronary occlusion during angioplasty and could be a useful end point in evaluating the efficacy of cardioprotective interventions.

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