Impaired Left Ventricular Filling Dynamics During Percutaneous Transluminal Angioplasty for Coronary Artery Disease

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The effects of brief periods of major coronary artery occlusion on global and regional peak left ventricular (LV) filling rates were studied during angioplasty in 10 patients. No patient had had a previous myocardial infarction. High-fidelity LV pressure and volume were determined by angiography before and 20 and 50 seconds after the onset of transluminal coronary occlusion and soon after the last balloon inflation. Segmental wall motion was analyzed frame by frame along 20 hemiaxes. Global peak filling rate decreased significantly both after 20 (29%, $p < 0.05$) and 50 seconds (27%, $p < 0.05$) from the onset of the occlusion. The term $\Sigma\Delta t_1$ was defined as the sum of the absolute values of the time differences from the occurrence of global peak filling rate and the segmental peak filling rate in 20 segments. This variable increased significantly during both periods of transluminal occlusion (by 73% and by 72% [both $p < 0.005$], respectively), indicating asynchrony in the occurrence of regional peak filling rate. Simultaneously, the sum of intervals between aortic valve closure (end systole) and occurrence of peak segmental shortening, $\Sigma\Delta t_2$, measured in the 20 segments, increased by 63% after 20 seconds and by 87% after 50 seconds (both $p < 0.005$), showing major asynchrony in segmental contraction. A significant negative correlation was found between global peak filling rate and both $\Sigma\Delta t_1$ and $\Sigma\Delta t_2$ ($r = 0.64$, $p < 0.001$ and $r = 0.70$, $p < 0.0001$, respectively). Our findings suggest that during coronary transluminal occlusion, early asynchrony in regional peak filling rate occurs that appears to be related to delayed and asynchronous peak segmental shortening.

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In patients with coronary artery disease (CAD), abnormalities may occur in left ventricular (LV) filling dynamics, even in the presence of normal systolic function.[1–4] The relation between the regional and global LV filling has been investigated in patients with 1-vessel CAD, using radionuclide angiography, and asynchrony in diastolic filling of the ischemic regions in the absence of regional systolic dyshomogeneity has been reported.[5,6] We previously observed that in humans, a transient ischemia induced by luminal occlusion of a major coronary artery during percutaneous transluminal angioplasty (PTCA) caused a shift in timing of the peak inward wall displacement of the ischemic segments, from end systole to early diastole.[7] To investigate the relation between such temporal nonuniformity of contraction and abnormalities in LV filling dynamics during ischemia, we studied regional wall displacement in systole and diastole during transient ischemia induced by balloon inflation at PTCA.

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Methods

Study population: After a preliminary study to confirm the absence of effects of nonionic contrast media (metrizamide [Amipaque®]) on LV function, permission was obtained from the Thoraxcenter Ethics Committee to perform LV angiography during balloon inflation at PTCA. All patients involved in the study gave

informed consent and no complications related to the research procedure occurred. Ten patients with CAD undergoing PTCA were studied. All met the selection criteria: (1) isolated, obstructive lesion of left anterior descending coronary artery without angiographically demonstrable collateral circulation; (2) normal global and regional LV wall motion at rest, as determined at prior diagnostic catheterization with an automated analysis system (described herein); and (3) no intraventricular conduction abnormalities on the rest electrocardiogram.

Standard antianginal therapy was allowed until the day of the study, but no particular medication was administered to the patients before or during the procedure. The medications consisted of a combination of a calcium antagonist, a β-blocking agent and long-acting nitrates (except for 4 patients who had only the 2 former types of drugs).

Study protocol: LV pressure was recorded during ventriculography (30° right anterior oblique view at 50 frames/s) carried out before balloon dilatation, at a mean occlusion time of 20 seconds during the second dilatation, at a mean occlusion time of 48 seconds during the fourth dilatation and at a mean of 12 minutes after the last dilatation. According to the recommendation of the ethics committee, no investigational occlusions were carried out after completion of a technically successful dilatation. In 4 patients, this result was achieved after 3 dilatations so that angiographic data after the fourth occlusion are only available in 6 of 10 patients. Three to 10 occlusions were performed and the duration of balloon inflation ranged from 15 to 75 seconds. Each consecutive balloon inflation was made only when end-diastolic pressure and LV pressure-derived isovolumic measures of contractility and relaxation, which were available on line during the procedure,[8,9] had returned to basal values. Care was taken to maintain uniform patient position relative to x-ray equipment during sequential angiograms, which were performed with the breath held in shallow inspiration.

Analysis of pressure and pressure-derived indexes: LV pressure was measured with a tipmanometer on a No. 8Fr pigtail catheter and digitized at 250 samples/s, allowing a beat-to-beat analysis. End-diastolic pressure was defined as the point on the pressure trace at which the derivative of the pressure first exceeded 200 mm Hg/s; end-systole or aortic valve closure was assumed to occur simultaneously with the dicrotic notch on the central aortic pressure.

For off-line analysis of pressure relaxation the following definitions were used: (1) pressure at the beginning of isovolumetric relaxation (P_b) is the pressure at the point at which dP/dt is minimal (maximal negative dP/dt) and (2) pressure at end of isovolumetric relaxation (P_c) is the pressure less than or equal to the previous end-diastolic pressure but not less than 1 mm Hg. The semilogarithmic model used was: $P(t) = P_o e^{-t/T}$, where P = pressure, t = time, and $P_o = P_b$ when a true exponential decay is present starting from the time of peak negative dP/dt. A biexponential fit for isovolumic relaxation was determined that was characterized by the 2 exponential time constants; the fit for the first 40 ms, τ_1 and the fit after the first 40 ms, τ_2.[7,9] Isovolumic relaxation period was defined as the interval between aortic valve closure and mitral valve opening. This latter was defined during left ventriculography as occurring in the last frame preceding the entry of non-opacified blood into the left ventricle from the left atrium. The LV pressure corresponding to this frame was considered to reflect left atrial pressure.[10]

Analysis of global left ventricular function: A complete cardiac cycle was analyzed frame by frame from each cineangiogram; care was taken to exclude from analysis postextrasystolic beats that could have affected LV function during ischemia. Ventricular contours were automatically detected by an analysis system[11] and instantaneous volume was calculated according to Simpson's rule. End-diastolic and end-systolic volumes, cardiac index, stroke index and ejection fraction were derived. LV volume data were smoothed by determining for each data point the least-square-error fit of a straight line through that point and the 2 neighboring volume values. The slope of this last regression line represents the derivative of volume relative to time (dV/dt). Peak ejection rate was taken as the peak negative dV/dt after end diastole, peak global filling rate as the peak positive dV/dt after mitral valve opening, and time to peak filling rate as the interval between aortic valve closure and peak dV/dt.

A computer-generated a system of coordinates along which segmental LV wall motion was determined. The wall motion analysis system we used is based on the motion pattern of small irregularities appearing at the LV endocardial border (endocardial landmarks), which can be detected in the contrast cineangiogram with the above-mentioned automated endocardial outlining system.[11,12] Such an endocardial landmark pathway, previously tested in 23 normal human left ventricles and validated in pigs with metal endocardial markers inserted through a percutaneous, retrograde, transvascular approach,[12] appears to reflect the motion pattern of actual anatomic structures. Over a full cardiac cycle, beginning with end diastole, segmental wall displacement was determined in 20 segments, 10 in the anterior and 10 in the inferoposterior wall. The peak segmental inward and outward velocity was calculated as the first derivative relative to time of the segmental wall displacement after a 3-point smoothing function had been applied to the data (Fig. 1).

Analysis of regional left ventricular function: We applied to the cineangiographic data the method proposed by Yamagishi et al[5] to quantitate LV regional asynchrony in filling. We measured in each segment the interval between occurrence of the global peak filling rate and that of peak velocity of segmental outward displacement (Fig. 2), which corresponds in time to the segmental peak filling rate. Accordingly, we defined $\Sigma\Delta t_1$ as the sum of the absolute values of the time differences between global peak filling rate and peak velocity of outward displacement for each of the 20 wall segments. We defined $\Sigma\Delta t_2$ as the sum of the

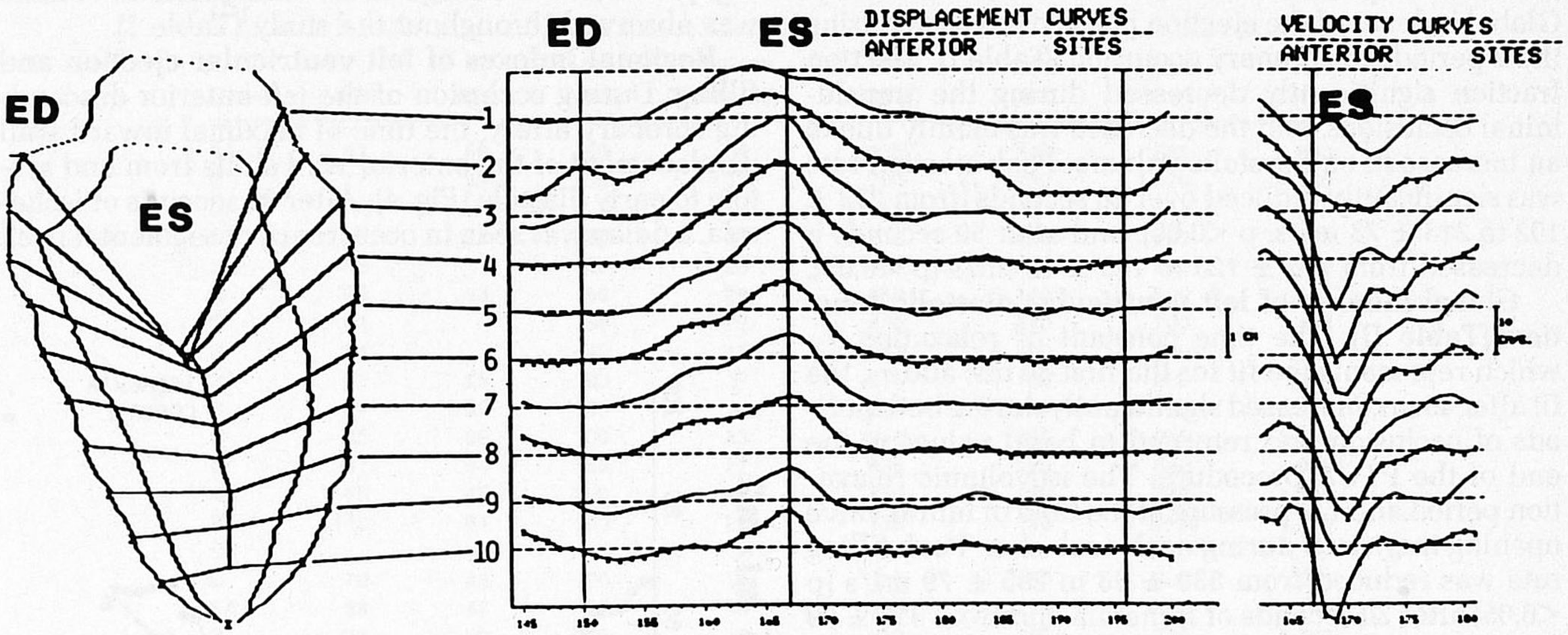

FIGURE 1. Computer output showing the end-diastolic (ED) and end-systolic (ES) contours of the 30° right anterior oblique left ventriculogram. Left ventricular segmental wall displacement is determined along a system of coordinates derived from endocardial landmark trajectories in normal persons and is studied in 20 separate segments, 10 in the anterior and 10 in the inferoposterior wall. Left ventricular wall velocity, the first derivative of wall displacement, is derived from these data.

absolute values of the time differences between occurrence of aortic valve closure and peak segmental inward displacement (Fig. 2). The terms $\Sigma\Delta t_1$, $\Sigma\Delta t_2$ are thus indexes reflecting variations in the synchrony of ventricular filling and contraction, respectively, their increase corresponding to a greater asynchrony.

Statistical analysis: Values are mean ± standard deviation; statistical analysis was performed using the *t* test for paired data. The relations between peak filling rate and the regional indexes reflecting asynchrony of contraction and filling were analyzed by regression analysis.

Results

Global indexes of left ventricular systolic function (Table I): An example of frame-to-frame analysis of LV volume before and during ischemia induced by balloon inflation is shown in Figure 3 with its derivative (dV/dt). Heart rate, pressures and volumes measured before, during and after transluminal occlusion

TABLE I Global Systolic and Diastolic Function Before Angioplasty, 20 and 50 Seconds After the Onset of Occlusion and After Angioplasty

	Before PTCA				After PTCA	
Variables	Total Group (n = 10)	Subgroup (n = 6)	20-Second Occlusion (n = 10)	50-Second Occlusion (n = 6)	Subgroup (n = 6)	Total Group (n = 10)
HR (beats/min)	62 ± 17	61 ± 22	60 ± 12	66 ± 15	62 ± 13	62 ± 10
MAP (mm Hg)	97 ± 15	92 ± 16	95 ± 9	91 ± 15	93 ± 10	97 ± 10
EF (%)	60 ± 6	60 ± 6	51 ± 8†	43 ± 12†	66 ± 7	64 ± 7
SV (ml/m²)	48 ± 10	50 ± 12	42 ± 12*	35 ± 14†	52 ± 10	50 ± 9
PER (ml/s)	253 ± 102	277 ± 123	213 ± 73*	183 ± 65*	264 ± 72	240 ± 67
TPER (ms)	174 ± 51	183 ± 61	180 ± 63	173 ± 50	186 ± 96	164 ± 81
ESP (mm Hg)	96 ± 13	92 ± 15	94 ± 9	91 ± 23	93 ± 13	92 ± 13
ESV (ml/m²)	31 ± 9	29 ± 7	38 ± 8†	44 ± 4†	26 ± 5	28 ± 7
Pmin (mm Hg)	10 ± 6	7 ± 3	10 ± 4	15 ± 5†	7 ± 4	8 ± 3
LVEDP (mm Hg)	22 ± 9	18 ± 7	23 ± 8	29 ± 4*	20 ± 4	20 ± 6
EDV (ml/m²)	81 ± 15	80 ± 12	80 ± 14	80 ± 12	81 ± 7	78 ± 10

*$p < 0.05$; †$p < 0.005$ (compared with before PTCA, paired Student *t* test).

EDV = end-diastolic volume; EF = ejection fraction; ESP = end-systolic pressure; ESV = end-systolic volume; HR = heart rate; LVEDP = left ventricular end-diastolic pressure; MAP = mean aortic pressure; PER = peak ejection rate; Pmin = minimal left ventricular diastolic pressure; SV = stroke volume; TPER = time to peak ejection rate.

are listed in Table I. No changes in heart rate and mean aortic pressure were observed over the study. Global indexes of the ejection phase decreased during the 2 periods of coronary occlusion (Table I). Ejection fraction significantly decreased during the transluminal occlusions, and the decrease was mainly due to an increase in end-systolic volume. Peak ejection rate was significantly reduced over 20 seconds (from 253 ± 102 to 213 ± 73 ml/s, $p < 0.05$), and after 50 seconds it decreased from 277 ± 123 to 183 ± 63 ml/s ($p < 0.05$).

Global indexes of left ventricular diastolic function (Table II): The time constant of relaxation τ_1, which represents the fit for the first 40 ms, and τ_2, the fit after 40 ms, increased significantly during both periods of occlusion and returned to basal values at the end of the PTCA procedure. The isovolumic relaxation period and LV pressure at the time of mitral valve opening increased during each occlusion. Peak filling rate was reduced from 330 ± 86 to 235 ± 79 ml/s ($p < 0.05$) after 20 seconds of ischemia and from 313 ± 89 to 227 ± 115 ml/s ($p < 0.05$) after 50 seconds. The mean rate of volume inflow, measured during the early filling period between mitral valve opening and minimal diastolic pressure, declined significantly both at 20 seconds (from 181 ± 90 to 99 ± 84 ml/s, $p < 0.005$) and 50 seconds (from 218 ± 101 to 136 ± 88 ml/s, $p < 0.005$) from the onset of occlusion. LV end-diastolic pressure did not change after 20 seconds of ischemia, increasing significantly after 50 seconds (from 22 ± 9 to 29 ± 4 mm Hg, $p < 0.05$). No change in LV end-diastolic volume was observed throughout the study (Table I).

Regional indexes of left ventricular ejection and filling: During occlusion of the left anterior descending coronary artery, the time of maximal inward wall displacement of the anterior wall shifts from end systole to early diastole (Fig. 4). After 20 seconds of ischemia, a delay was seen in occurrence of segmental peak

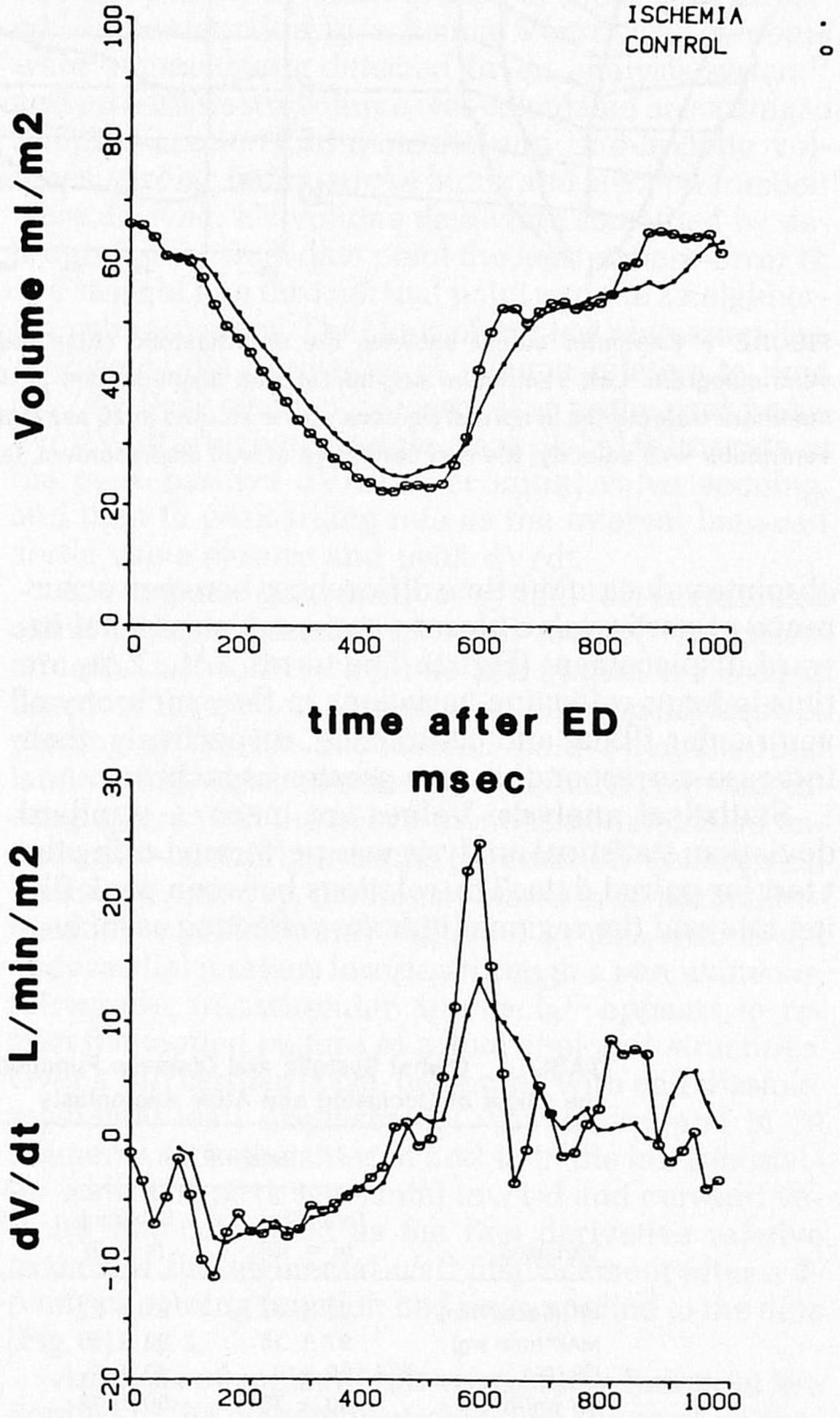

FIGURE 3. *Top*, left ventricular volume curves for the same patient, derived from angiographic volumes every 20 ms throughout a complete cardiac cycle, before and during transluminal occlusion. *Bottom*, instantaneous left ventricular volume derivative (dV/dt) curves for the same patient, measured every 20 ms throughout a complete cardiac cycle, before and during transluminal occlusion. During ischemia a decrease in peak dV/dt was observed. ED = end-diastole.

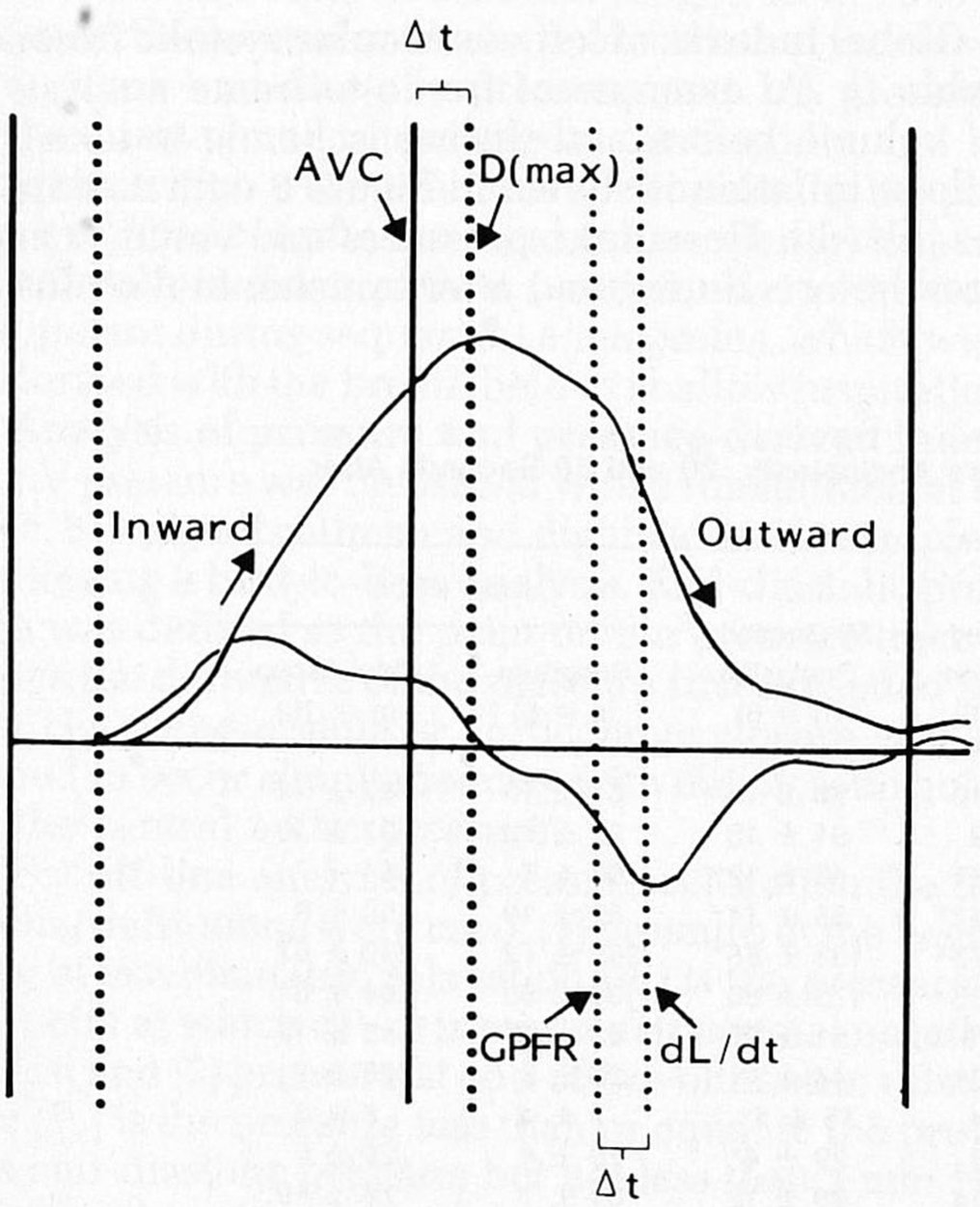

FIGURE 2. Segmental wall displacement and its first derivative, superimposed to show the temporal relation between inward and outward phases with aortic valve closure (AVC). The intervals (Δt) between AVC and maximal inward wall displacement (Dmax) and between global peak filling rate (GPFR) and peak velocity of outward displacement (dL/dt) were measured in every segment.

TABLE II Early Diastolic Function and Regional Asynchrony in Contraction and Filling Before Angioplasty (A), 20 (B) and 50 (C) Seconds After the Onset of Occlusion and After Angioplasty (D)

Case	τ_1 (ms)	τ_2 (ms)	IRP (ms)	MVOP (mm/Hg)	PFR (ml/s)	TPFR (ms)	$\Sigma\Delta t_1$ (ms)	$\Sigma\Delta t_2$ (ms)
1A	51	50	60	32	233	140	580	800
B	77	33	80	13	283	180	1,320	1,540
C	. . .	. . .	. . .	. . .	. . .	. . .	. . .	. . .
D	40	32	60	31	216	120	860	460
2A	56	. . .	60	20	483	140	460	760
B	88	63	80	29	450	140	600	1,100
C	64	. . .	60	22	416	140	700	1,480
D	54	. . .	40	16	533	100	580	660
3A	61	55	80	17	316	180	560	940
B	57	52	120	18	283	160	1,100	1,360
C	85	69	100	33	200	180	1,040	1,360
D	61	54	80	27	333	120	640	980
4A	65	45	100	12	350	120	740	1,100
B	113	61	100	27	133	120	1,520	1,440
C	. . .	. . .	. . .	. . .	. . .	. . .	. . .	. . .
D	70	45	100	16	150	160	1,600	1,581
5A	59	47	80	18	300	120	400	740
B	86	52	120	15	233	140	720	1,280
C	75	59	60	31	283	120	560	1,360
D	59	50	80	16	316	160	380	1,140
6A	48	36	40	. . .	283	140	600	680
B	56	46	80	14	133	220	1,020	1,580
C	57	49	80	27	83	200	1,080	1,240
D	45	40	80	17	166	140	720	1,060
7A	50	35	80	13	283	140	360	1,160
B	76	52	80	25	200	160	880	1,460
C	68	60	80	25	150	140	640	1,380
D	57	37	100	12	316	140	200	960
8A	58	59	40	25	416	100	540	960
B	87	61	80	33	133	140	800	1,900
C	. . .	. . .	. . .	. . .	. . .	. . .	. . .	. . .
D	56	45	60	33	216	120	540	1,020
9A	47	39	80	17	216	100	640	500
B	70	47	100	19	216	120	980	1,720
C	74	65	100	20	233	140	1,180	1,980
D	50	44	80	19	266	120	340	820
10A	58	48	60	25	416	120	880	1,320
B	69	42	80	27	283	100	1,040	1,240
C	. . .	. . .	. . .	. . .	. . .	. . .	. . .	. . .
D	50	. . .	60	23	366	80	780	800
Mean all patients								
A	53	41	68	18	330	130	576	896
B	78†	51†	82†	22†	235†	148	998†	1,462†
D	54	35	74	19	288	126	664	948
Subgroup 6 patients								
A	54	35	70	17	314	136	503	796
C	70†	50†	80	26*	227*	153	866†	1,488*
D	54	37	74	19	322	130	476	936

*$p < 0.05$ †$p < 0.005$ compared with before PTCA.

IRP = isovolumic relaxation period; MVOP = LV pressure at mitral valve opening PFR = peak filling rate; $\Sigma\Delta t_1$ = sum of the time intervals between the occurrence of global PFR and peak velocity of segmental outward displacement (dL/dt); $\Sigma\Delta t_2$ = sum of the time intervals between the occurrence of the aortic valve closure and segmental peak filling inward displacement; τ_1 and τ_2 = time constants of isovolumic relaxation; TPFR = time to PFR.

velocity of outward displacement (dL/dt) with respect to aortic valve closure, particularly in the apical region (segments 10 and 20 in Fig. 4) and the absolute value of the dL/dt was clearly reduced in the ischemic segments (Fig. 5). In the nonischemic segments showed a compensatory increase in dL/dt as well as in maximal outward displacement (Fig. 5). A relation between the asynchrony of segmental dL/dt and the reduction of global peak filling rate was sought by measuring the sum of the absolute values of the time differences from global peak filling rate to the occurrence of regional peak filling rate (peak dL/dt) in each of the 20 segments ($\Sigma\Delta t_1$). This sum increased significantly during both the first and second occlusions, indicating asynchrony in filling (Table II).

To determine if the decrease in global peak filling rate was related to asynchrony in regional peak filling rate rather than to other causes, we correlated global

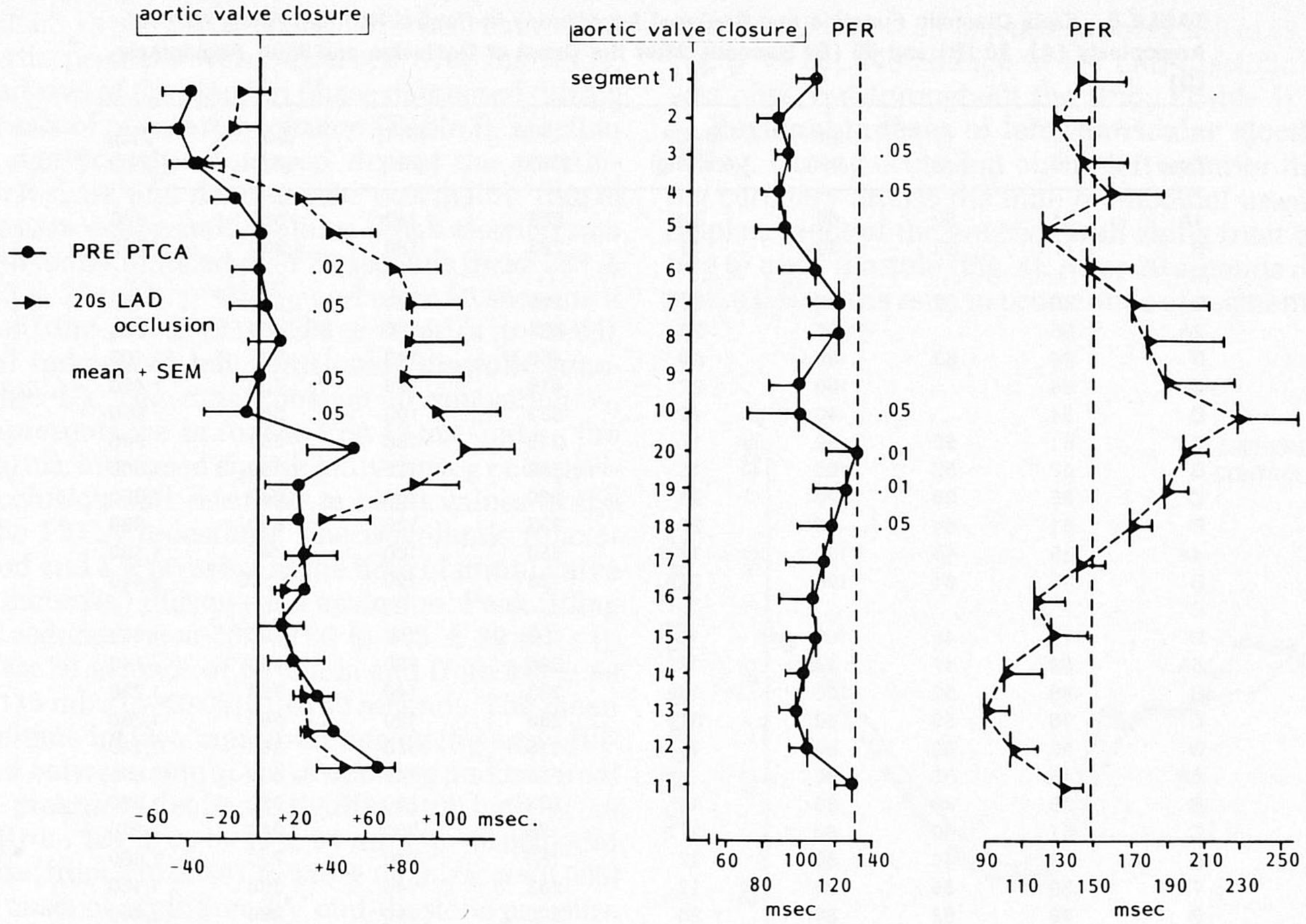

FIGURE 4. ***Left*****, time relation between aortic valve closure and maximal inward wall displacement before and after 20 ms of occlusion of the left anterior descending coronary artery (LAD).** ***Right*****, time relation between aortic valve closure and occurrence of peak velocity of segmental outward displacement before and after 20 seconds of occlusion of the LAD. PFR = global peak filling rate; PTCA = percutaneous transluminal coronary angioplasty; SEM = standard error of the mean.**

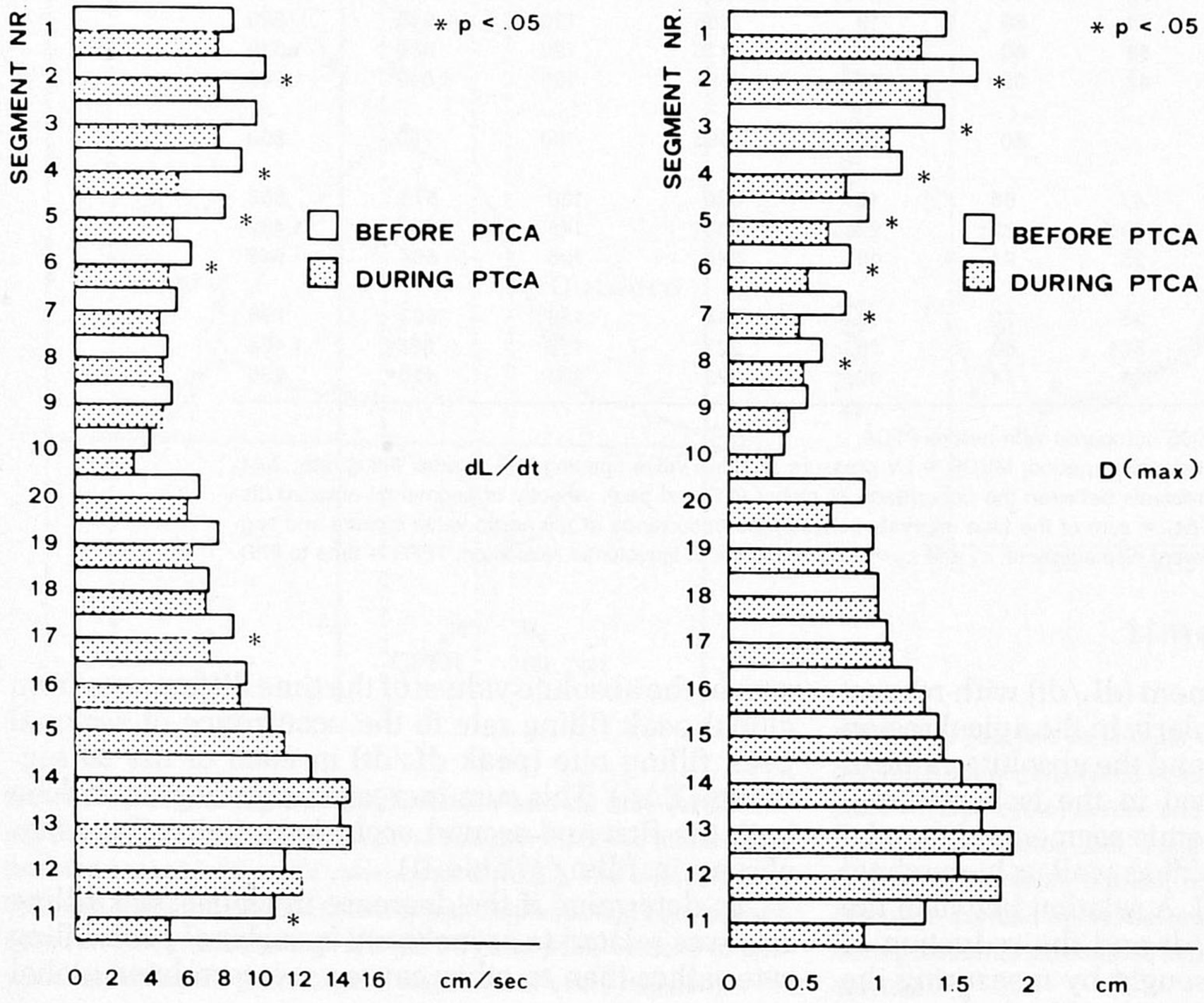

FIGURE 5. ***Left*****, mean changes in peak velocity of segmental outward displacement (dL/dt) in 10 anterior and 10 posterior segments before and during occlusion of the left anterior descending coronary artery.** ***Right*****, mean changes in maximal outward displacement (Dmax) in 10 anterior and 10 posterior segments before and during occlusion of the left anterior descending coronary artery. While the ischemic segments show a decreased outward displacement, in the nonischemic segments a greater outward displacement was observed, suggesting a compensatory increase in filling to allow augmentation of stroke volume by the Starling effect.[24] PTCA = percutaneous transluminal coronary angioplasty.**

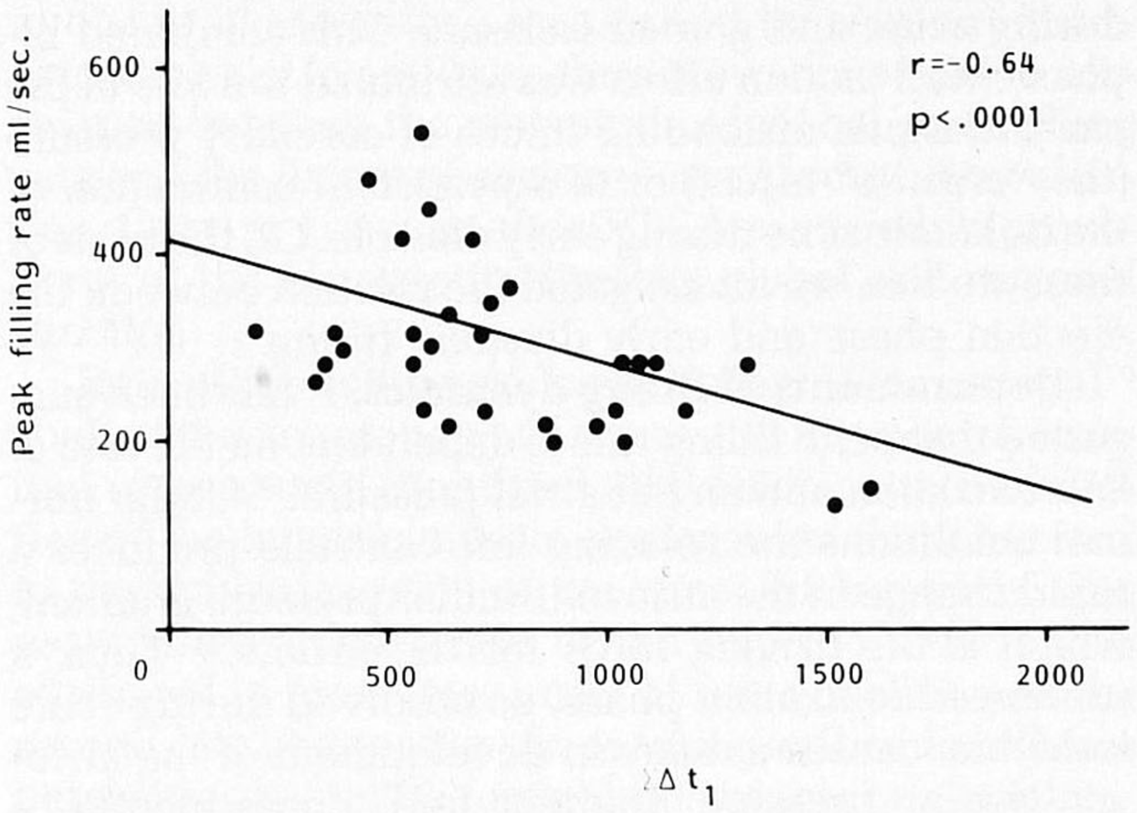

FIGURE 6. Negative correlation between the global peak filling rate and the $\Sigma\Delta t_1$ as an index of segmental asynchrony in filling in patients with left anterior descending artery disease.

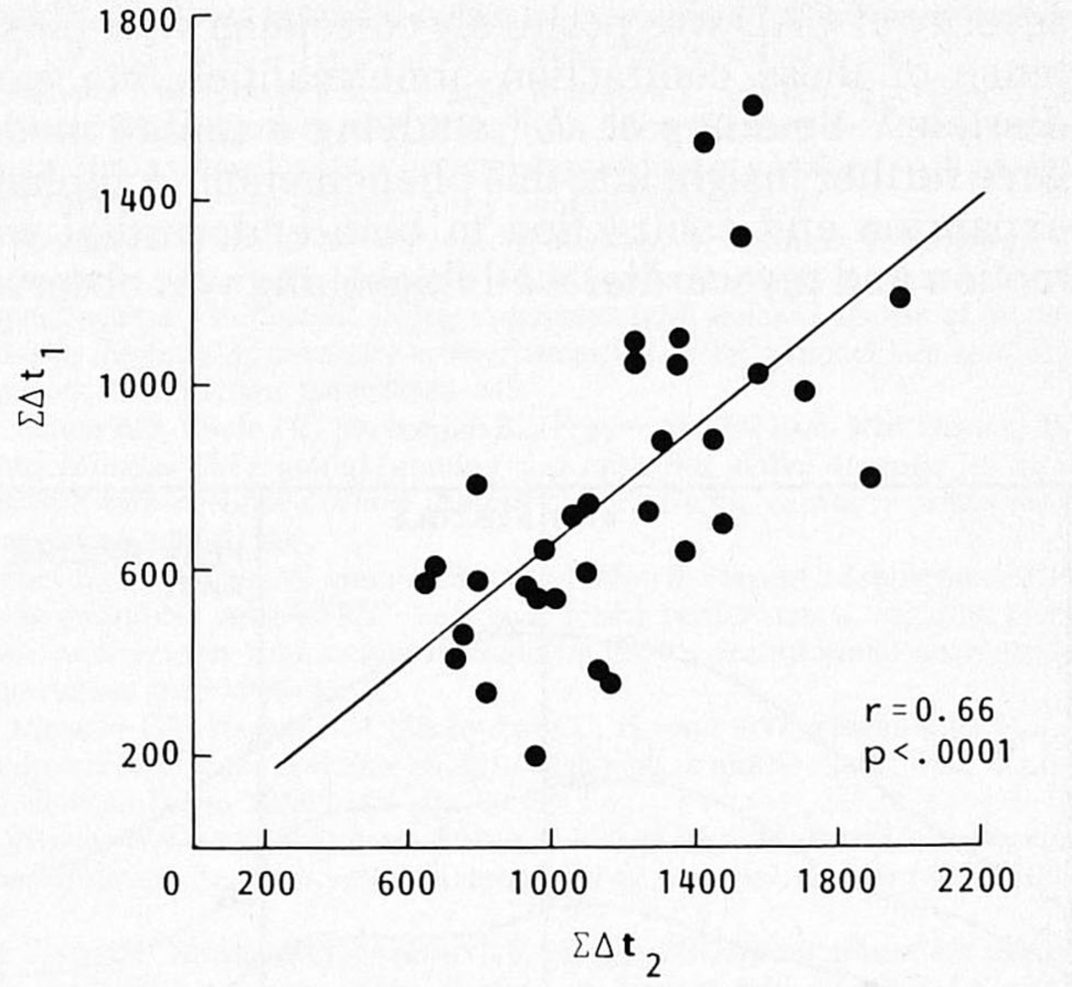

FIGURE 7. Correlation between $\Sigma\Delta t_1$ as an index of segmental asynchrony in filling and $\Sigma\Delta t_2$ as an index of segmental asynchrony in contraction.

peak filling rate with $\Sigma\Delta t_1$ and found a significant negative correlation ($r = 0.64$, $p < 0.0001$), showing that a greater degree of asynchrony was associated with a reduction in peak filling rate (Fig. 6).

To determine whether asynchrony in regional filling was an isolated phenomenon or an effect of a temporal nonuniformity in inward wall displacement, we quantified this systolic nonuniformity by measuring the time relation between aortic valve closure (end systole) and segmental peak inward displacement. The sum of the absolute time differences between aortic valve closure and the peak regional inward wall displacement ($\Sigma\Delta t_2$) was used as an index of systolic asynchrony, and during coronary occlusion $\Sigma\Delta t_2$ increased in the same fashion as $\Sigma\Delta t_1$ (Table II). We also found a significant correlation ($r = 0.66$, $p < 0.0001$) between $\Sigma\Delta t_2$ and $\Sigma\Delta t_1$ (Fig. 7), suggesting that a greater asynchrony of contraction was associated with impaired filling dynamics. This temporal interdependence between inward and outward wall displacement is illustrated in Figure 4. Further evidence for an interrelation between contraction and filling was given by the significant negative correlation between the global peak filling rate and $\Sigma\Delta t_2$ ($r = -0.70$, $p < 0.0001$) (Fig. 8).

Thus, the greater the asynchrony in the pattern of contraction the greater the decrease in peak filling rate. All these data indicate that nonuniformity of LV contraction contributes to the early asynchrony in the occurrence of the regional filling with subsequent decreases in peak filling rate. To clarify the dynamic interplay between asynchrony in contraction and abnormalities in early diastolic phase, we correlated $\Sigma\Delta t_2$ with parameters of the relaxation phase, such as time constants of relaxation (τ_1 and τ_2), isovolumic relaxation period and mitral valve opening pressure, and these latter variables with the peak filling rate. A significant correlation was observed between $\Sigma\Delta t_2$ and τ_1 ($r = 0.75$, $p < 0.0001$) and between τ_1 and the duration of isovolumic relaxation period ($r = 0.58$, $p < 0.001$). A weak negative correlation was found between the global peak filling rate and the isovolumic relaxation period ($r = -0.53$, $p < 0.01$), whereas no correlations were observed between time constants of relaxation and global peak filling rate. Thus, severity of impairment of global filling dynamics during the early phase of acute ischemia is related to magnitude of segmental LV systolic and diastolic asynchrony.

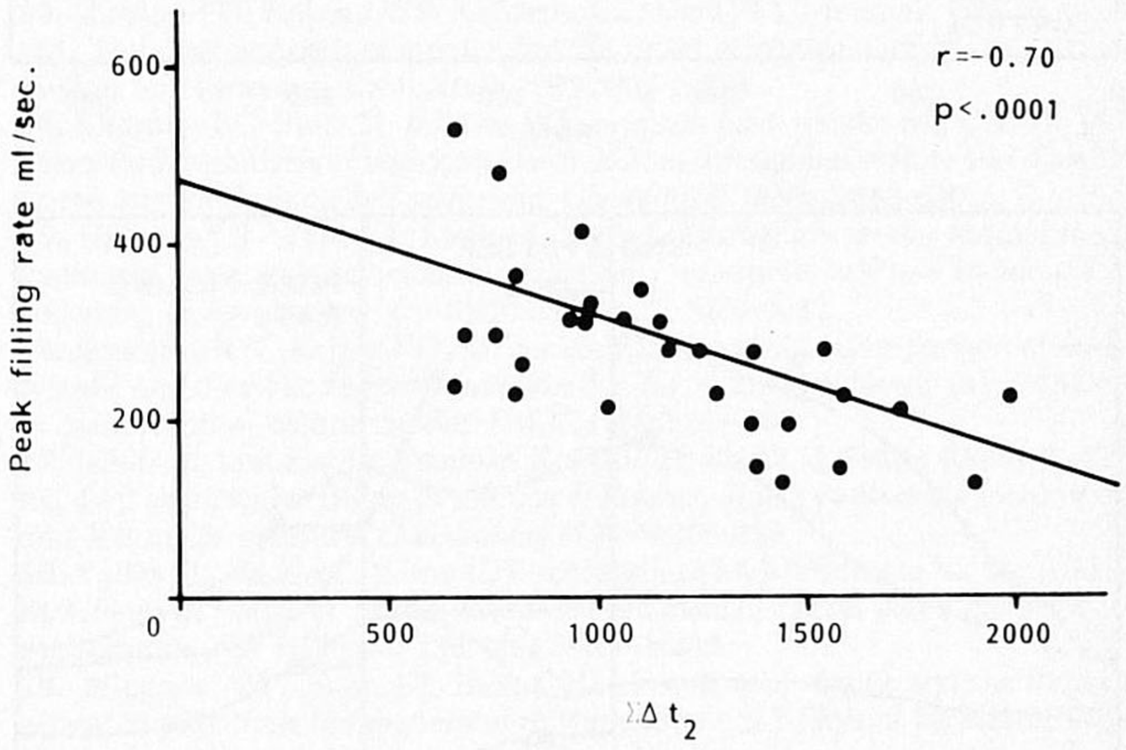

FIGURE 8. Negative correlation between global peak filling rate and $\Sigma\Delta t_2$ as an index of segmental asynchrony in contraction in patients with left anterior descending coronary artery disease.

Discussion

Variability in the temporal sequence of regional LV contraction in normal subjects has been previously observed and attributed to variations in the sequence of electrical activation or to other factors playing an important role in determining ventricular geometry such as ventricular volume and fiber orientation.[13,14] In patients with CAD, the completion of ejection was delayed, whereas the onset of ejection was not and the

severity of CAD was positively correlated with persistence of these contraction abnormalities into early diastole.[15] Smalling et al,[16] studying a canine model, gave further insight into this phenomenon. A biphasic expansion and contraction in both endocardial wall motion and myocardial wall thickening was observed during acute and graded ischemia This combined biphasic wall motion effect was attributed to a loss of the early diastolic distending forces of coronary pressure (the "erectile" effect) or to a persistent contraction of the ischemic zone during early diastole. On the basis of these studies, we investigated the relation between the ejection phase and early diastolic filling.

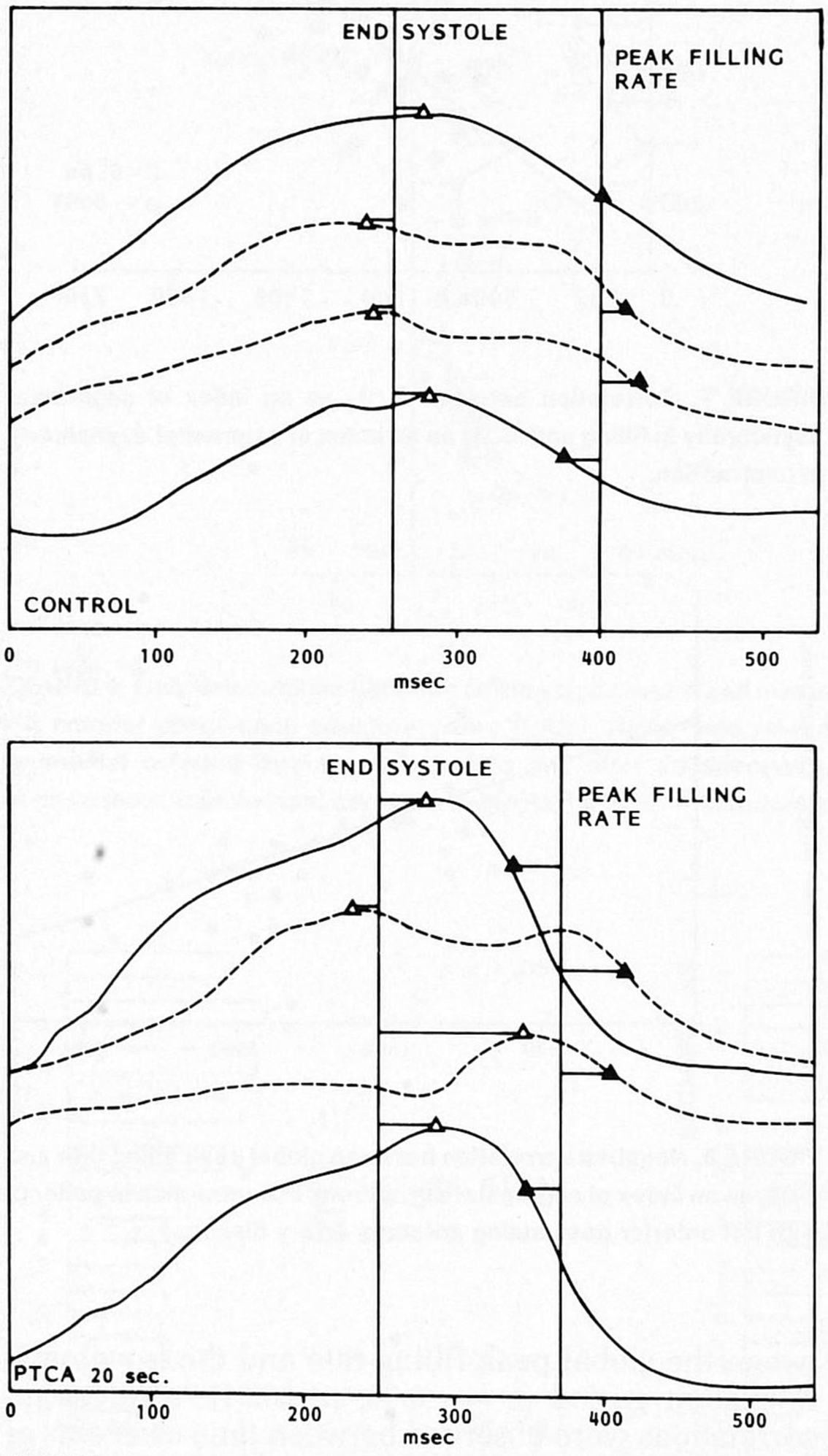

FIGURE 9. Variation in patterns of segmental displacement in the same patient before and after 20 minutes of left anterior descending coronary artery occlusion. *Solid line* indicates nonischemic segments and *dashed line* ischemic segments. *Open* and *black triangles* indicate segmental peak shortening and peak filling rate, respectively. End systole refers to the occurrence of the aortic valve closure. During occlusion a major asynchrony both in contraction and filling is observed; particularly, the upper ischemic segment (located in the peripheral ischemic area) shows biphasic motion and the lower ischemic segment (located in the core of the ischemic area) shows late peak shortening during early diastole. The occurrence of segmental peak filling rate is consequently delayed. The nonischemic segments show an accelerated outward displacement with early occurrence of segmental peak filling rate.

Determinants of filling dynamics: It has been suggested that peak filling rate is dependent on the rate of LV relaxation and on left atrial pressure.[17] Under normal conditions the relaxing left ventricle produces a rapid change in the atrioventricular pressure gradient, which is the driving force for the inflow.[18] Thus, a prolonged relaxation phase, as observed during acute ischemia, causes a delay in development of the atrioventricular pressure gradient and, consequently, a greater left atrial pressure is required to open the mitral valve. In fact, we observed a consistent delay in the relaxation rate occurring 20 seconds after the onset of ischemia and, concomitantly, both the isovolumic relaxation period and the left atrial pressure required for mitral valve opening increased. The significant relation between $\Sigma\Delta t_2$ and τ_1 and between this latter variable and duration of the isovolumic relaxation period suggests that during acute ischemia, the atrioventricular dynamic interplay occurring during early diastole is affected by the asynchronous LV contraction. Ishida et al[17] showed in the dog that under conditions of similar left atrial pressure at mitral valve opening, prolongation of the time constant of relaxation decreases the rate and amplitude of filling, whereas under conditions of similar LV pressure during relaxation, an increase of left atrial pressure increases the amplitude of early filling. Thus, the lack of correlation between the peak filling rate and single variables of the relaxation phase was expected because these latter, during acute ischemia, are changing in opposite directions.

A decrease in peak filling rate has been extensively reported in patients with CAD with or without previous myocardial infarction. Until recently no data were available in the literature regarding the relation between global and regional LV filling. Yamagishi et al[5] investigated this relation using radionuclide angiography in normal persons and in patients with left anterior descending CAD without previous myocardial infarction and found differences in peak filling rate that differentiated normal persons from those with CAD. To explain this difference they analyzed regional filling dynamics and identified that asynchrony in regional filling was a major determinant of decrease in peak filling rate. The sum of the absolute time differences between the global and regional peak filling rate was inversely correlated to the global peak filling rate and proposed as an index of asynchrony in diastolic filling. More recently, Bonow et al[6] studied with radionuclide angiography the relation between regional LV diastolic asynchrony and global diastolic filling, before and after PTCA in patients with 1-vessel CAD. Before PTCA impaired global diastolic filling was found and was related to regional variations in the timing of LV relaxation and filling determined by vari-

ations in phase among sectors and by regional quadrant analysis. In addition, they showed a negative correlation between the magnitude of global peak filling rate and the extent of regional asynchrony. Reevaluation 1 day to 1 month after PTCA revealed improvement of the changes in diastolic global and regional function.

Role of asynchronous contraction: Wiegner et al[19] studied the interaction of normal and hypoxic myocardial muscles and identified a biphasic pattern of motion of the hypoxic muscle analogous to that observed in the ischemic region of the intact left ventricle. The early lengthening phase of the hypoxic muscle was attributed to premature onset of force decline and the second late shortening phase was ascribed to either a persisting contractile force of the muscle or a manifestation of stored force from elastic recoil of previously stretched passive muscle elements. Furthermore, they indicated the negative role of late shortening on filling dynamics. Similar types of wall motion abnormalities have been described in animals,[20-23] during chronic CAD in humans[24,25] and, more recently, during transluminal coronary occlusion.[26] In our angiographic study, frame-by-frame analysis of anterior wall displacement during brief occlusion of the left anterior descending coronary artery showed a variety of biphasic wall motion patterns. After 20 seconds of occlusion, the segment adjacent to the ischemic area exhibited late inward wall displacement in early diastole (Fig. 9). This phenomenon was mirrored by an accelerated outward displacement of the normal segment. The interaction between ischemic and nonischemic segments resulted in segmental asynchrony in occurrence of peak velocity of outward displacement. Since this measurement reflects the segmental peak filling rate, asynchrony in segmental outward displacement corresponds to asynchrony in the filling phase, with a decrease in the global peak filling rate. The crucial question is whether diastolic asynchrony was a direct, intrinsic manifestation of altered relaxation properties of the myocardium (inactivation) or a consequence of dysfunction of the contractile properties of the myocardium (activation).[27,28]

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