

Effects of acute coronary occlusion and previous ischaemic injury on left ventricular wall motion in humans

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Abstract

Objective—To assess the acute effects of single and repeated coronary artery occlusions, during percutaneous transluminal coronary angioplasty (PTCA), on left ventricular long axis function in patients with stable and unstable angina.

Design—Prospective examination of ventricular systolic and diastolic long axis function using M mode echocardiography and transmitral Doppler in patients with significant coronary artery stenosis and either stable or unstable angina, during routine PTCA.

Setting—A tertiary referral centre for heart disease with cardiac catheterisation and echocardiographic facilities.

Subjects—36 patients, age (SD) 60 (8) years, with significant coronary artery disease undergoing PTCA (mean duration 100–130 seconds) to the left anterior descending coronary artery (LAD) in 18 patients, native LAD or its vein graft in eight, and right coronary artery in 10. Controls were 21 normal subjects, age 58 (11) years.

Results—*At baseline:* in systole, total long axis excursion was reduced at septal, posterior, and right sites in patients with LAD disease, at right site in those with vein grafts, and at septal and right sites in patients with right coronary artery disease. Peak shortening rate was often reduced in all patients and onset of shortening delayed with respect to the Q wave in patients with LAD disease. In diastole, onset of lengthening was always delayed, peak lengthening rate reduced, and relative A wave amplitude increased in all patients. There was a consistent abnormal shortening of the long axis during the isovolumic relaxation period in the 14 patients with unstable angina, not seen in the others. Transmitral A wave velocity was also increased and the onset of E wave delayed with respect to A2. *At first balloon inflation:* the extent of pre-existing systolic and particularly diastolic abnormalities consistently increased in patients with LAD or right coronary artery occlusion. This was associated with further delay in the onset of the transmitral Doppler E wave as its peak velocity fell and E/A ratio increased. In unstable angina, balloon inflation caused minor changes only in systolic function and no change in diastolic function. *At second balloon inflation:* systolic changes were

the same as with the first inflation, while diastolic changes were attenuated by 10–15%.

Conclusions—In stable angina intracoronary balloon inflation aggravated pre-existing systolic and diastolic abnormalities in the territory of the occluded vessel, indicating the dependence of both on coronary flow. In unstable angina balloon inflation caused only minor deterioration in systolic function, and diastolic changes—including the characteristic abnormal shortening during isovolumic relaxation—were unaffected. Thus resting abnormalities of left ventricular function in unstable angina are effectively dissociated from acute changes in coronary flow. Overall, the severity of systolic disturbances was unaltered by a second balloon inflation, but diastolic disturbances were attenuated by 10–15%, compatible with ischaemic preconditioning or recruitment of collaterals.

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Keywords: balloon inflation; long axis function; preconditioning; myocardial injury

The function of the left ventricle depends on the coordinate action of circumferentially and longitudinally oriented myocardial fibres. The latter, which can readily be studied by echocardiography, are very sensitive to the presence of coronary artery stenoses. In patients with stable angina, ventricular long axis disturbances are present in the absence of symptoms,¹ and tend to normalise after successful coronary angioplasty.² In unstable angina, these long axis disturbances are more severe and more generalised, and their severity is related to that of the symptoms rather than that of the coronary artery disease itself.³ Against this background, we designed the present study to observe the acute effects of an occlusion of a single coronary artery on left ventricular long axis function, by balloon inflation, during routine coronary angioplasty. We aimed to observe how acute occlusion of the subtending coronary artery would interact with the pre-existing long axis disturbances and to define differences in response between patients with stable and unstable angina. Finally, we wanted to compare any differences in the wall motion response between first and second coronary balloon inflation in these patients which might be attributed to ischaemic preconditioning.

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Table 1 Angiographic results. Values are means (SD)

Variables	LAD (n = 18)	CABG (n = 8)	RCA (n = 10)
Age (years)	60 (11)	62 (8)	56 (11)
History of myocardial infarction	7	4	5
Site of target lesion:			
Proximal	9	5	4
Mid-vessel	9	3	6
Baseline vessel stenosis (%)	80 (8)	90 (5)*	93 (8)*
Residual vessel stenosis (%)	15 (7)	11 (6)	13 (10)
1st balloon inflation:			
Pressure (atm)	7.2 (3.6)	8.4 (6.0)	7.0 (3.5)
Duration (s)	100 (35)	110 (55)	130 (80)
2nd balloon inflation:			
Pressure (atm)	7.8 (1.6)	9.6 (4.5)	9.0 (1.5)
Duration (s)	115 (40)	120 (55)	60 (5)
Duration between 1st and 2nd inflations (min)	12 (1.5)	11 (1.4)	10 (1.5)

*P < 0.005 v LAD (unpaired t test).

Methods

PATIENTS

We studied 36 patients with significant coronary artery disease (> 70% stenosis) in whom percutaneous transluminal coronary angioplasty (PTCA) was being performed, mean (SD) age 60 (8) years, four females, 32 males. The site of the angioplasty and the number of inflations, along with their pressure and duration, were determined on standard clinical indications. Eighteen patients underwent left anterior descending angioplasty, 10 of whom had isolated left anterior descending coronary artery (LAD) disease; additional right coronary artery disease was present in five, and circumflex artery disease in three. Eight patients, who had had previous coronary artery grafting, required coronary angioplasty either to the native left anterior descending or to the vein graft. Ten patients underwent right coronary artery angioplasty, five of whom had isolated right coronary disease, three had additional left anterior descending disease, and two also had circumflex disease.

Twenty two of the patients had a clinical diagnosis of chronic stable effort induced

angina. The remaining 14 patients, who had experienced rest pain within the previous week, were diagnosed as having unstable angina: six with left anterior descending artery disease, four with previous coronary grafts, and four with right coronary artery disease. All these 14 latter patients had been stabilised on antianginal treatment with intravenous heparin and nitrate infusion before the angioplasty, and treatment was continued throughout the procedure. In all, the most recent attack had been within the preceding 48 hours but none experienced pain at the time of the procedure. Sixteen patients had a documented history of previous myocardial infarction. No patient had had a myocardial enzyme rise or electrocardiographic signs of acute myocardial infarction in the six months before PTCA and none had decompensated heart failure or significant chest disease. Clinical and angiographic details are summarised in table 1.

Twenty one normal subjects, mean age 58 (11) years, 10 females, 11 males, served as controls; none had a history of coronary artery disease, hypertension, or diabetes. Patients and controls were all studied echocardiographically by the same investigator.

METHODS

Patients were studied in the catheterisation laboratory during routine coronary angioplasty. We used a Hewlett-Packard 500 Sonos echocardiograph with a 2.5 phased array transducer interfaced to it with electrocardiograph and phonocardiograph. The echocardiograph was placed to the right side of the patient, on the left of the interventionist, at the head of the catheterisation table. A baseline echocardiographic examination was performed immediately before the start of the procedure and repeated during the last 30 seconds of the first minute of the first and second balloon inflations. The exact time interval between the two inflations varied for technical reasons connected with the conduction of the procedure. We obtained cross sectional guided M mode scans of left and right ventricular long axes, represented by the longitudinal mitral and tricuspid valve ring motion. The M mode cursor was positioned across the left and septal angles of the mitral ring and across the lateral angle of the tricuspid ring from the apical four chamber view, then across the posterior angle of the mitral ring from the apical two chamber view.¹ We also obtained a recording of transmitral pulsed Doppler flow velocities with the sample volume at the tips of the mitral valve leaflets from the apical four chamber view. All records were made with the patient in quiet expiration. An electrocardiogram and phonocardiogram were superimposed on each M mode and transmitral Doppler trace. All were made at a paper speed of 100 mm/s, using a photographic recorder. M mode echocardiograms were later digitised off line.⁴

From each long axis trace (fig 1) we measured the total long axis excursion as the extent of motion between the innermost point (towards the ventricular cavity), around the second heart sound, and the outermost point

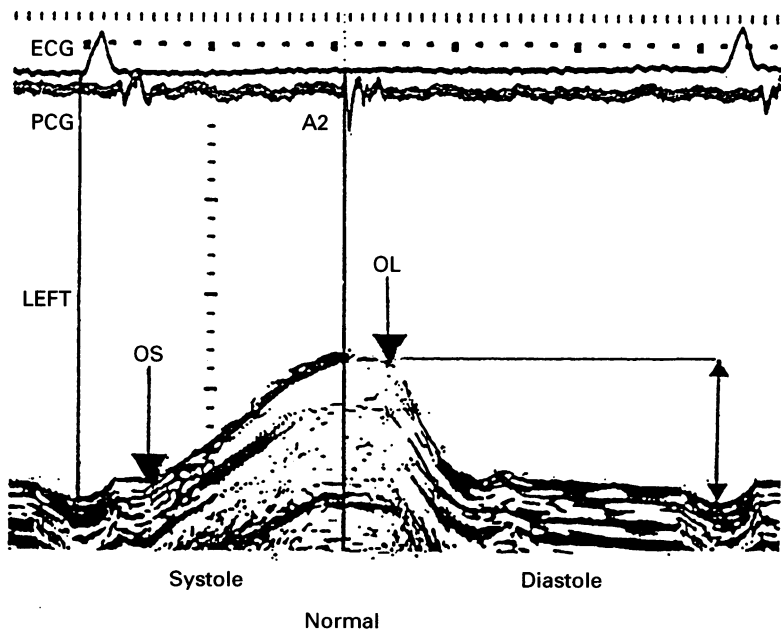


Figure 1 An example of M mode recording of the left sided long axis along with an electrocardiogram and phonocardiogram. First vertical line represents the onset of the Q wave and the second represents the first high frequency component of the aortic component of the second heart sound. OS, onset of shortening; OL, onset of lengthening; A2, aortic component of the second heart sound; ECG, electrocardiogram; PCG, phonocardiogram.

Table 2 Reproducibility of long axis variables

Variables	Intraobserver CV (%)	Interobserver CV (%)
Total excursion	3.2	4.0
Shortening during isovolumic relaxation	11.5	15
Peak shortening rate	4.2	5.4
Peak lengthening rate	5.0	6.0
q-onset of shortening	6.5	7.0
A2-onset of lengthening	5.5	6.0

(towards the atrium) at the nadir of the A wave, in late diastole. The A wave itself was taken as the backward displacement of the mitral and tricuspid rings (towards the atrium) after the P wave of the electrocardiogram, and the relative contribution of the atrial component to the total excursion was calculated. We measured two time intervals: from the Q wave of the electrocardiogram to the onset of long axis shortening, and from A2, first high frequency component of the aortic component of the second heart sound on the phonocardiogram, to the onset of long axis lengthening. From the digitised traces we measured peak rate of ventricular shortening (in systole) and peak rate of lengthening (in early diastole), as well as peak rate of shortening during atrial systole. We also measured the time intervals from the same traces: from Q wave of the electrocardiogram to the peak shortening rate time, and from A2 to the peak lengthening rate time. Finally, the extent of any abnormal shortening after A2, during the isovolumic relaxation time, was also measured as the amplitude between the long axis at A2 and the innermost excursion point. From the transmitral pulsed Doppler trace we measured peak early and late velocities of left ventricular filling and hence calculated the E/A ratio. The time interval between A2 on the phonocardiogram and the onset of transmitral early diastolic flow "E wave" was measured and referred to as the Doppler isovolumic relaxation time. Patients and controls were all studied by the same investigator.

REPRODUCIBILITY

The reproducibility of long axis measurements was assessed in a sample of 20 patients from duplicate determination of long axis total excursion, peak shortening and lengthening velocities, and timing with respect to Q wave and the second heart sound. Within observer

and between observer values were determined independently. Reproducibility was assessed as root mean square (RMS) difference between duplicate measurements, and the corresponding value of coefficient of variation as the ratio RMS difference/absolute value (table 2).

STATISTICAL ANALYSIS

Baseline results, presented as mean (SD), were compared with normal values using the Student *t* test. Baseline, first, and second balloon inflation values were investigated using a one way analysis of variance test (ANOVA); when this was significant individual values were compared using a paired *t* test.

Results

The results of diagnostic coronary angiography, along with the site and effect of balloon angioplasty on the stenoses, are summarised in table 1. Baseline long axis results and the effects of the first balloon inflation are compared in tables 3-6.

BASELINE RESULTS

Systolic and diastolic long axis function was frequently abnormal (fig 2).

In systole (table 3)—Total long axis excursion was consistently reduced at the septal, posterior, and right sites in patients with LAD disease, the right site only was involved in patients with vein grafts, and the septal and the right sites in patients with right coronary artery disease. Peak shortening rate was frequently reduced in at least three of the four sites in each group. The onset of long axis shortening (table 3) was delayed with respect to the Q wave at the three left ventricular sites in patients with LAD disease and only at the septal site in the other two groups.

In diastole (tables 4 and 5)—the time interval between A2 and the onset of long axis lengthening was nearly always prolonged. Peak lengthening rate was frequently reduced but there was no consistent shortening during isovolumic relaxation in any of the three groups of patients with stable angina. A relative increase in A wave excursion was commonly present in late diastole. Thus localisation of the abnormalities in the resting state was clearly related to the vessel to be

Table 3 Systolic long axis function. Values are means (SD)

Variables	Normal (n = 21)	LAD (n = 18)		CABG (n = 8)		RCA (n = 10)	
		Pre	Inflation	Pre	Inflation	Pre	Inflation
Total excursion (cm):							
Left	1.5 (0.25)	1.38 (0.3)	1.15 (0.2)§‡	1.4 (0.3)	1.25 (0.4)	1.4 (0.4)	1.4 (0.3)
Septal	1.5 (0.3)	1.33 (0.2)*	0.98 (0.2)§‡	1.2 (0.5)	1.0 (0.5)§†	1.25 (0.3)*	1.26 (0.3)
Posterior	1.6 (0.2)	1.3 (0.3)†	1.3 (0.2)	1.4 (0.3)	1.1 (0.6)	1.4 (0.4)	1.2 (0.6)
Right	2.6 (0.3)	2.35 (0.4)*	1.9 (0.35)	1.7 (0.4)‡	1.4 (0.1)	2.3 (0.2)¶	2.0 (0.4)§*
Peak shortening rate (cm/s):							
Left	8 (1.5)	6.3 (2.2)†	5.2 (1.4)	6.3 (1.7)*	5.8 (1.7)	5.3 (1.6)‡	5.5 (1.4)
Septal	7.5 (1.2)	5.6 (1.6)‡	4.1 (0.97)§†	5.0 (1.7)†	4.0 (1.7)	5.1 (1.1)‡	4.4 (1.3)
Posterior	8 (1.5)	5.8 (1.1)‡	5.9 (0.9)	6.2 (3)*	5.7 (2.3)	6.2 (1.3)‡	5.4 (2.0)
Right	10 (2.0)	10 (3.0)	9.0 (4.0)	9.0 (3.0)	7.0 (1.4)	8.0 (1.6)†	7.4 (2.4)
q-onset of shortening (ms):							
Left	90 (20)	105 (15)*	120 (40)	105 (20)	100 (20)	105 (20)	105 (15)
Septal	80 (10)	92 (20)*	115 (15)§‡	96 (30)*	105 (35)	105 (15)‡	110 (10)
Posterior	100 (15)	115 (25)*	130 (12)	115 (40)	125 (30)	105 (15)	135 (35)§*
Right	85 (20)	80 (25)	87 (20)*	85 (25)	70 (30)	85 (15)	105 (10)

LAD, left anterior descending coronary artery; CABG, coronary artery bypass graft; RCA, right coronary artery.

*P < 0.05, †P < 0.01, ¶P < 0.005, ‡P < 0.001 v normal (unpaired *t* test), § v pre inflation (paired *t* test).

Table 4 Isovolumic relaxation time (IVRT) and dimension change. Values are means (SD)

Variables	Normal (n = 21)	LAD (n = 18)		CABG (n = 8)		RCA (n = 10)	
		Pre	Inflation	Pre	Inflation	Pre	Inflation
Abnormal shortening during IVRT (mm):							
Left	-1.0 (0.7)	-0.2 (1.7)	0.2 (1.6)	-0.7 (2.0)	-0.6 (1.0)	-0.5 (1.6)	-0.55 (1.6)
Septal	-1.0 (0.6)	-0.2 (1.6)	0.4 (1.3)	0.04 (1.03)	-0.3 (1.4)	-0.6 (1.1)	0.2 (1.8)
Posterior	-1.0 (0.7)	-0.7 (1.1)	-0.3 (1.3)	-0.1 (2.0)	0.7 (1.8)	-1.4 (1.2)	-0.8 (1.0)
Right	-2.0 (1.5)	-3.1 (2.0)	-2.0 (0.7)	-2.7 (2.3)	-3.3 (4.6)	-3.3 (3.0)	-2.0 (1.7)
A2 to onset of lengthening (ms):							
Left	58 (11)	92 (28)‡	100 (10)	78 (25)¶	85 (10)	80 (10)‡	95 (15)
Septal	60 (9)	86 (12)‡	105 (10)‡	80 (18)‡	90 (20)	92 (10)‡	105 (20)‡*
Posterior	65 (10)	90 (16)‡	100 (12)	80 (25)*	95 (20)	90 (13)‡	105 (12)‡*
Right	11 (20)	40 (35)†	50 (45)‡¶	20 (40)	40 (55)	50 (35)‡	75 (25)‡*

LAD, left anterior descending coronary artery; CABG, coronary artery bypass graft; RCA, right coronary artery.
*P < 0.05, †P < 0.01, ¶P < 0.005, ‡P < 0.001 v normal (unpaired t test), § v pre inflation (paired t test).

Table 5 Early and late diastolic long axis function. Values are means (SD)

Variables	Normal (n = 21)	LAD (n = 18)		CABG (n = 8)		RCA (n = 10)	
		Pre	Inflation	Pre	Inflation	Pre	Inflation
Peak lengthening rate (cm/s):							
Left	10 (2.5)	6.9 (2.0)‡	4.7 (1.6)‡§	6.0 (2.9)‡	5.5 (2.0)	5.5 (2.2)‡	5.6 (2.4)
Septal	6.5 (1.0)	5.9 (1.4)	3.0 (1.8)‡§	4.7 (2.2)¶	3.6 (1.5)	5.2 (1.5)¶	4.3 (1.6)
Posterior	9 (1.5)	5.5 (1.9)‡	5.0 (1.9)	5.9 (3.2)¶	2.7 (5.0)	6.4 (3.0)‡	5.5 (3.7)‡*
Right	10 (2.5)	9.8 (2.6)	7.0 (2.8)	6.5 (1.7)‡	8.3 (1.1)	8.4 (0.9)	5.8 (3.1)‡*
Relative A wave (%):							
Left	29 (6)	40 (9)‡	51 (11)‡¶	41 (11)‡	51 (11)‡§	38 (10)¶	41 (12)
Septal	33 (8)	43 (8)‡	57 (15)‡§	46 (8)‡	53 (10)	45 (12)‡	45 (15)
Posterior	30 (5)	43 (14)‡	38 (9)	42 (13)‡	52 (16)	37 (9)†	31 (13)‡*
Right	33 (5)	42 (18)*	35 (6)	42 (13)*	41 (2)	39 (15)	47 (10)

LAD, left anterior descending coronary artery; CABG, coronary artery bypass graft; RCA, right coronary artery.
*P < 0.05, †P < 0.01, ¶P < 0.005, ‡P < 0.001 v normal (unpaired t test), § v pre inflation (paired t test).

Table 6 Transmitral Doppler. Values are means (SD)

Variables	Normal (n = 21)	LAD (n = 18)		CABG (n = 8)		RCA (n = 10)	
		Pre	Inflation	Pre	Inflation	Pre	Inflation
E wave velocity (cm/s)	0.7 (0.1)	0.7 (0.15)	0.4 (0.2)‡	0.8 (0.2)	0.6 (0.4)‡*	0.6 (0.2)	0.45 (0.25)‡¶
A wave velocity (cm/s)	0.5 (0.1)	0.6 (0.12)†	0.6 (0.2)	0.6 (0.3)	0.7 (0.3)	0.65 (0.2)†	0.65 (0.25)
E/A ratio	1.4 (0.4)	1.2 (0.45)	0.8 (0.5)‡†	1.6 (0.8)	1.15 (1.0)	1.1 (0.6)	0.7 (0.3)
A2-onset of E wave (ms)	80 (10)	90 (6)‡	105 (15)‡‡	85 (25)	90 (25)	100 (10)‡	120 (45)

LAD, left anterior descending coronary artery; CABG, coronary artery bypass graft; RCA, right coronary artery; E, early diastolic velocity; A, late diastolic velocity; A2, aortic component of the second heart sound.
*P < 0.05, †P < 0.005, ‡P < 0.01, ‡‡P < 0.001 (unpaired t test), § v pre inflation (paired t test).

dilated, which was the site of the most severe stenosis.

Transmitral Doppler (table 6) showed an increase in the A wave velocity and delayed onset of the E wave in patients with LAD disease and in those with right coronary artery disease, but both variables were normal in the patients with vein grafts.

When the patients with unstable angina (table 7) were considered in isolation, the pattern of abnormalities was similar to that in patients with stable angina, except that abnormal shortening during isovolumic relaxation was consistently present at left and posterior sites. This was not seen in patients with stable angina, the difference between the two groups being highly significant (P < 0.01).

When patients with isolated LAD or right coronary artery disease were separated from the others with mixed coronary disease and compared with the normal controls, they again showed the same nature of abnormalities except that the total excursion was reduced only in patients with isolated LAD disease. No specific pattern of localisation could be identified among the other measurements.

DURING FIRST BALLOON INFLATION

The extent of pre-existing long axis systolic and diastolic abnormalities increased (fig 2).

In systole (table 3)—Total long axis excursion was frequently affected, falling at the septal and left sites in patients with LAD disease, at the septal site in patients with vein grafts, and at the right site in patients undergoing right coronary angioplasty. The onset of shortening was less consistently affected, but the time interval from the Q wave to the onset of shortening increased at the septal site in patients with LAD disease and at the posterior site in patients with right coronary artery disease. By contrast, peak rate of shortening fell only at the septal site in patients with LAD disease. The time interval between Q wave and peak shortening did not change in any patient group. Systolic changes were minor in patients with unstable angina and localised to the septal site (table 7).

In diastole (tables 4 and 5)—The effects of balloon inflation were more pronounced than during systole. The onset of lengthening was further delayed with respect to the second heart sound, and peak lengthening rate fell in at least two sites in the patients in whom native arteries were occluded, though not in those with vein grafts. The relative A wave excursion increased at two sites in patients undergoing LAD occlusion but only at one site in the remainder. Abnormal shortening during isovolumic relaxation never appeared

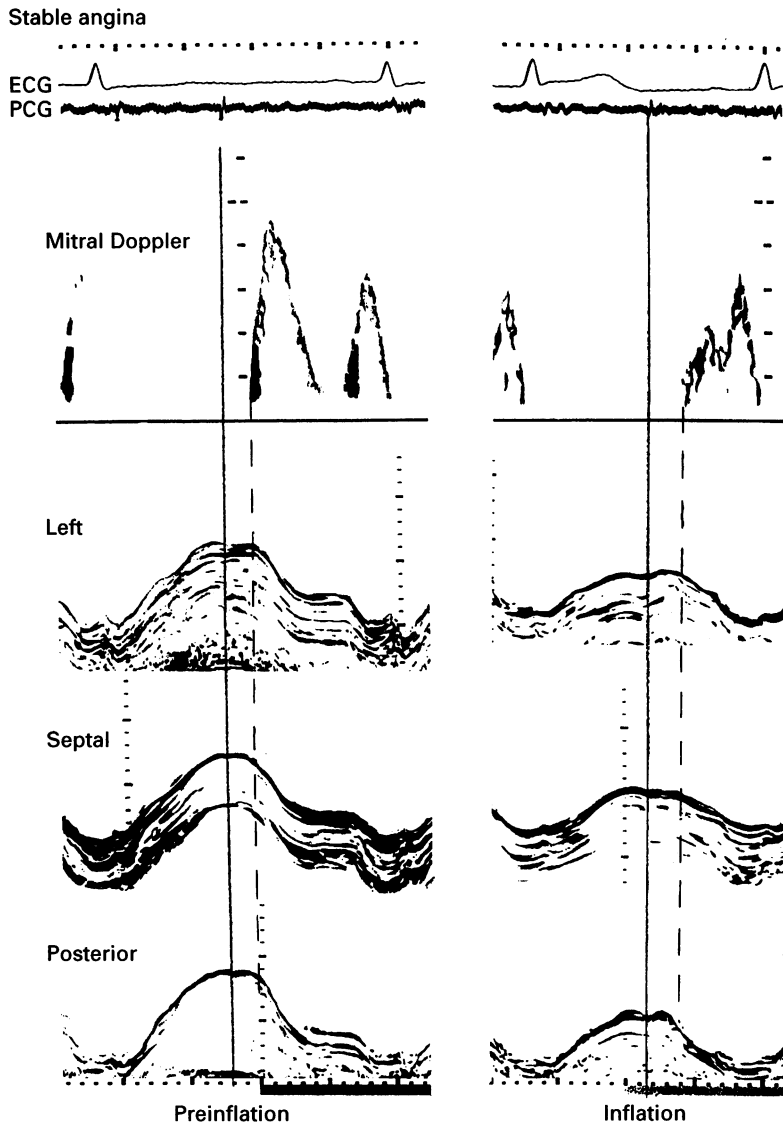


Figure 2 An M mode example of the left ventricular three long axes; left, septal, and posterior taken from a patient with left anterior descending coronary artery stenosis. Baseline recording on the left and during balloon inflation on the right, along with transmitral Doppler flow velocities at the top. Note the significant reduction in the total long axis amplitude of motion, shortening and lengthening velocities, the delay in the onset of lengthening (dotted line) with respect to A2, and the increase in A wave excursion. There is also a corresponding increase in the transmitral A wave velocity. A2, aortic component of the second heart sound; ECG, electrocardiogram; PCG, phonocardiogram.

with balloon inflation in patients with stable angina. These diastolic disturbances were associated with changes in transmitral Doppler (table 6); E wave velocity fell in all three groups. With LAD occlusion the E/A ratio also fell and the onset of the E wave with respect to A2 was delayed. In unstable angina (table 7, fig 3), balloon inflation was without any consistent effect on any of the 16 variables studied reflecting long axis behaviour or transmitral velocities.

In patients with multivessel disease and LAD angioplasty the effect of balloon inflation selectively affected the septum both in systole and diastole. However, in patients with isolated LAD disease, only the systolic abnormalities were exaggerated at the septum, while the diastolic abnormalities deteriorated consistently at the septum and the free wall. Only the latter condition was associated with a reduction in transmitral E wave velocity and E/A ratio and with delayed onset of the E wave

from A2. In patients with right coronary disease, there was no significant difference in the response to balloon inflation between patients with single and multivessel disease.

COMPARISON BETWEEN FIRST AND SECOND BALLOON INFLATIONS

In 22 patients (table 8), five with unstable angina, we were able to obtain long axis recordings during the first and second balloon inflations of the procedure. The extent of alteration in systolic function was effectively the same with first and second inflations. However, in diastole, apart from the abnormal shortening during isovolumic relaxation which did not change, the effect of the second inflation on the remaining variables was consistently less than the first at the left site. Here, the onset of lengthening was less delayed, lengthening velocity greater, the extent of A wave excursion reduced, and the peak rate of atrial shortening increased. In the remaining patients studied it was not technically possible to obtain long axis recordings during the second inflation.

Discussion

It has been appreciated since the time of William Harvey that normal left ventricular contraction involves the coordinated action of circumferentially and longitudinally directed fibres.⁵ Shortening and lengthening patterns of the longitudinally directed fibres are frequently abnormal in coronary artery disease,¹ and indeed a series of disturbances was present in our patients under baseline conditions similar to those we have described previously in stable² and unstable angina.³ These disturbances were both systolic and diastolic in timing. In systole, there was a reduction in total long axis excursion, delayed onset of shortening with respect to the Q wave of the ECG, and reduced shortening velocity. In diastole, the onset of lengthening with respect to the second heart sound was delayed, early diastolic lengthening velocity was reduced, and relative A wave excursion was increased. The subgroup of patients with unstable angina also showed a marked abnormal shortening during isovolumic relaxation.³

The results of this study show that coronary occlusion by a balloon inflation of mean duration 100–130 seconds had clear effects in patients with chronic stable angina. In systole there was a further reduction of total excursion, delay in the onset of shortening, and reduction in shortening velocity. In diastole the onset of long axis lengthening was further delayed with respect to the second heart sound, lengthening velocity was reduced, and A wave excursion increased. These disturbances nearly always occurred in previously abnormal segments. They were very similar in their nature to those occurring under resting conditions, although their extent was greater. However, they were more clearly localised to the septal site in patients with two vessel coronary artery disease and LAD occlusion, to the septal and left sided long axes with isolated left

Table 7 Stable v unstable angina (LAD). Values are means (SD)

Variables	Stable angina (n = 12)		Unstable angina (n = 6)	
	Baseline	Inflation	Baseline	Inflation
<i>Systolic function</i>				
Total excursion (cm):				
Left	1.43 (0.3)	1.17 (0.2)	1.3 (0.4)	1.15 (0.3)
Septal	1.35 (0.3)	1.0 (0.2)¶	1.3 (0.2)	1.0 (0.3)*
Posterior	1.5 (0.2)	1.3 (0.15)	1.1 (0.25)‡	1.3 (0.3)
Peak shortening rate (cm/s):				
Left	7.1 (3.0)	5.1 (1.1)	5.2 (1.5)	5.3 (1.9)
Septal	5.6 (1.4)	4.1 (1.0)¶	5.7 (2.0)	4.2 (1.0)
Posterior	6.1 (1.5)	5.7 (0.3)	5.5 (0.6)	6.2 (1.3)
q-onset of shortening (ms):				
Left	102 (13)	116 (40)	112 (20)	130 (30)
Septal	93 (24)	116 (20)†	90 (15)	110 (10)†
Posterior	102 (24)	130 (10)	130 (25)§*	133 (15)
<i>Diastolic function</i>				
Abnormal shortening during IVRT (mm):				
Left	-1.05 (1.6)	-0.4 (1.6)	0.7 (1.5)§*	1.2 (1.0)
Septal	-0.5 (1.8)	0.7 (1.3)	0.3 (0.9)	-0.3 (1.0)
Posterior	-1.3 (0.7)	-0.5 (1.3)	0.2 (1.0)§‡	0.25 (1.8)
A2 to onset of lengthening (ms):				
Left	85 (9)	102 (11)¶	103 (45)	100 (10)
Septal	87 (9)	105 (10)‡	85 (20)	100 (10)
Posterior	82 (5)	103 (15)	100 (20)§†	100 (10)
Peak lengthening rate (cm/s):				
Left	7.2 (1.8)	4.4 (1.5)‡	6.6 (2.4)	5.3 (1.7)
Septal	6.2 (1.2)	2.8 (2.0)‡	5.4 (1.8)	3.4 (1.6)
Posterior	6.2 (1.6)	4.5 (1.3)	4.8 (2.1)§*	5.5 (2.6)
A wave amplitude (cm):				
Left	0.58 (0.1)	0.6 (0.15)	0.5 (0.15)	0.58 (0.18)
Septal	0.55 (0.1)	0.6 (0.15)	0.58 (0.14)	0.46 (0.1)
Posterior	0.6 (0.1)	0.6 (0.1)	0.46 (0.13)	0.65 (0.1)
Transmitral Doppler:				
E wave velocity (m/s)	0.68 (0.15)	0.4 (0.17)‡	0.7 (0.16)	0.47 (0.23)
A wave velocity (m/s)	0.6 (0.12)	0.64 (0.2)	0.6 (0.1)	0.58 (0.2)
E/A ratio	1.2 (0.5)	0.74 (0.4)*	1.2 (0.4)	1.0 (0.7)
A2-onset of E wave (ms)	91 (5)	105 (17)¶	88 (8)	100 (5)

*P < 0.05, ¶P < 0.005, †P < 0.01, ‡P 0.001 (paired t test), § v baseline stable angina.

LAD, left anterior descending coronary artery; A2, second heart sound; E, early diastolic left ventricular filling; A, late diastolic left ventricular filling.

anterior descending artery occlusion, and to the right and posterior long axes with right coronary artery angioplasty. They were much less obvious when the left anterior descending artery and a vein graft were in parallel. In contrast to patients with stable angina, balloon inflation was almost without effect in those with unstable angina, even though the degree of coronary artery stenosis was similar and the extent of resting abnormalities greater. In no case of stable or unstable angina did coronary balloon inflation aggravate the extent of abnormal shortening during isovolumic relaxation commonly seen under control conditions, particularly in the latter patients. We conclude, therefore, that in patients with stable angina intracoronary balloon inflation usually aggravates systolic and diastolic abnormalities that are already present under

control conditions. It does not produce any new long axis disturbance. On a segmental level, the effects of balloon inflation are reasonably well localised bearing in mind the differences in the severity of stenoses between patients, the adequacy of collateral circulation, and the normal variability of coronary artery anatomy. Finally, balloon inflation has only minor systolic effects and does not significantly alter diastolic long axis behaviour at all in unstable angina even though the resting abnormalities are greater than those in stable angina and the degree of stenosis and the characteristics of inflation no different.

These results are compatible with previous invasive studies on the effect of balloon angioplasty on left ventricular function in patients with coronary artery disease and stable angina.⁶⁻¹¹ These have shown a prompt reduc-

Figure 3 A patient with unstable angina with inward wall motion during isovolumic relaxation (arrow) which is unaffected by balloon inflation. A2, aortic component of the second heart sound; ECG, electrocardiogram; PCG, phonocardiogram.

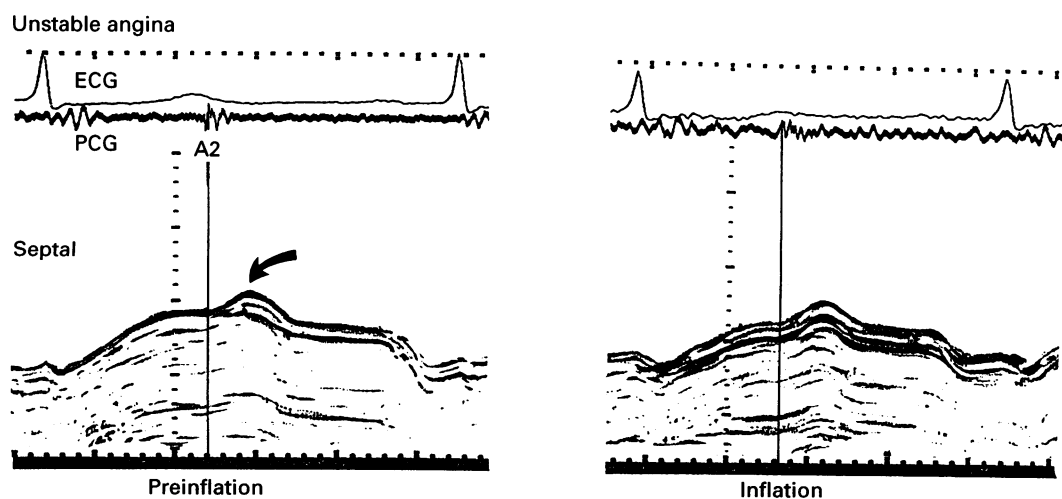


Table 8 Comparison between first and second inflations. Values are means (SD)

Variables	1st Inflation	2nd Inflation	P value
<i>Systolic function</i>			
Total excursion (cm):			
Left	1.2 (0.3)	1.24 (0.37)	NS
Septal	1.0 (0.25)	1.1 (0.4)	NS
Posterior	1.2 (0.3)	1.2 (0.4)	NS
q-onset of shortening (ms):			
Left	125 (30)	120 (30)	NS
Septal	115 (25)	110 (30)	NS
Posterior	125 (30)	120 (35)	NS
Peak shortening velocity (cm/s):			
Left	5.3 (1.6)	5.6 (1.7)	NS
Septal	4.0 (1.1)	4.0 (1.0)	NS
Posterior	6.3 (1.4)	6.8 (1.9)	NS
<i>Diastolic function</i>			
Abnormal shortening during			
IVRT (mm):			
Left	-0.2 (1.6)	-0.5 (2.0)	NS
Septal	0.1 (1.7)	-0.03 (1.5)	NS
Posterior	2.5 (0.5)	1.5 (1)	NS
A2-onset of lengthening (ms):			
Left	96 (14)	90 (12)	< 0.03
Septal	100 (12)	98 (10)	NS
Posterior	110 (10)	90 (14)	NS
Peak lengthening rate (cm/s):			
Left	4.5 (1.5)	5.2 (1.4)	< 0.05
Septal	3.2 (1.4)	3.3 (1.6)	NS
Posterior	3.3 (1.0)	4.6 (0.6)	NS
A wave amplitude (mm):			
Left	0.65 (0.2)	0.45 (0.15)	< 0.05
Septal	0.68 (0.18)	0.57 (0.2)	< 0.005
Posterior	0.35 (0.3)	0.5 (0.3)	NS
Peak atrial shortening rate (cm/s):			
Left	6.4 (2.0)	7.1 (1.7)	< 0.05
Septal	5.7 (2.2)	6.0 (2.0)	NS
Posterior	9 (2)	9.5 (3)	NS

-, Outward movement during isovolumic relaxation; A2, second heart sound; IVRT, isovolumic relaxation time.

tion in the peak rate and time constant of left ventricular pressure fall, followed by an increase in left ventricular end diastolic pressure. Though we did not measure pressure directly, prolongation of pressure fall in early diastole would be anticipated from our finding of delayed onset and reduced rate of long axis lengthening, and indeed in one study delay in the onset of outward wall motion in the affected area was apparent angiographically.⁸ Changes in isovolumic relaxation time reflect the competing effects of an increase in end diastolic pressure, which could tend to shorten it,¹² and a reduction in relaxation rate, as occurred with left anterior descending artery inflation. Doppler indices of diastolic function would be affected in the same way by these two competing effects, a raised end diastolic pressure increasing and slow ventricular relaxation reducing the height of the E wave, with exactly opposite effects on E wave deceleration time and A wave amplitude. These interactions may well explain the relative insensitivity of Doppler measurements in our own as well as previous studies.^{13,14} Variable depression in the overall and regional systolic amplitude of wall motion has also been demonstrated angiographically,^{10,11} corresponding with our observations on the rate and extent of long axis shortening.

Changes in wall motion were not identical during the second balloon inflation compared to the first, even though it lasted longer and a higher inflation pressure was used. The extent of diastolic changes during the second inflation was consistently less, though those in systole were apparently unaltered. The reduction in severity of long axis disturbances with second balloon inflation amounted to 10–15% of that occurring with the first and appeared

most consistently in the left long axis, representing the left ventricular free wall.

These results shed light on the pathophysiology of the disturbances of long axis motion seen in coronary artery disease. In chronic stable angina, acute coronary occlusion consistently aggravates long axis abnormalities which already exist before balloon inflation, in the territory of the affected artery. This is compatible with the idea that under resting conditions disturbances in long axis function directly reflect the severity of the stenosis in the subtending coronary artery. On the other hand, in unstable angina balloon occlusion had only minor effects on pre-existing systolic long axis abnormalities and none at all on those in diastole. In particular, in no case did coronary occlusion induce or aggravate abnormal shortening during isovolumic relaxation, the characteristic abnormality in unstable angina.³ This dissociation between balloon inflation and functional change suggests that in unstable angina the disturbance to long axis function no longer reflects the severity of coronary stenosis, and therefore that another mechanism must be involved. This additional factor is likely to be some form of reversible myocardial injury, no longer directly dependent on coronary blood flow, though caused by previous ischaemia. A reduction in the severity of the manifestations of myocardial ischaemia with a second balloon inflation has been interpreted in previous studies as being a model of ischaemic preconditioning of the myocardium.¹⁵ If this is indeed the case and if these ideas can be extrapolated to the long axis, then in the human heart ischaemic preconditioning appears to have a greater influence on diastolic than on systolic myocardial function, as shown by its effect in patients with isolated left anterior descending coronary artery disease. There is, in fact, little published information about the nature of the improvement in diastolic left ventricular function caused by ischaemic preconditioning in the clinical setting,^{15–17} though mean pulmonary artery pressure and left ventricular end diastolic pressure are lower with the second inflation.

This study had technical limitations. The degree of coronary artery stenosis was estimated visually, in line with current clinical practice. Obviously, there were no normal controls for coronary angioplasty, so that changes in long axis behaviour with balloon inflation had to be interpreted in the light of the pre-existing changes. We did not formally quantify the extent of collaterals, and so are unable to assess any role they may have had in modifying the results, particularly in explaining differences between the effects of first and second balloon inflations.¹⁸ The duration of balloon inflation was determined purely on clinical criteria, so that in a minority values were below 90 seconds, which has been suggested as a threshold in man.^{19,20} It is also possible that the development of pain in the 48–72 hours before the procedure might have itself led to preconditioning by the "second window" effect. Although the long axis motion

can readily be recorded and measured from the apical four chamber view, the operator's access to the patient's chest was limited during an invasive procedure, as was the time allowed for recording, so it did not prove feasible to obtain a series of long axis recordings throughout the procedure and the recovery period or between balloon inflations. More females were involved in the control group, but in previous studies we have shown that gender has no effect on long axis function.²¹

Our results provide further evidence underlining the validity of left ventricular long axis measurements as a useful non-invasive method of investigation for coronary artery disease in clinical practice. They are sensitive to acute as well as chronic ischaemia, suggesting that the abnormalities present at rest and in the absence of symptoms in patients with stable angina directly reflect the presence of coronary stenosis. Inward motion during isovolumic relaxation, as occurs in unstable angina, appears qualitatively different and seems to represent a form of ischaemic myocardial injury not directly dependent on coronary blood flow. Nevertheless, all these segments showed active shortening during systole, and thus performed external work to the circulation, so that myocardial infarction could be excluded. The dissociation of abnormal myocardial function from acute alterations in coronary flow therefore corresponds closely with myocardial stunning as occurs in animal models,²² and indeed might form a functional definition of it in man. Finally, the difference between the effects of the first and second balloon inflations has been attributed to the effects of ischaemic preconditioning. If this is the case, then these appear to be more obvious in diastole than in systole in humans. Further studies might be useful in confirming the effects of coronary angioplasty on diastolic function as a practical model for defining the effect to which myocardial injury depends directly on coronary flow and for investigating possible effects of ischaemic preconditioning on ventricular function in man. Both would have obvious theoretical and clinical consequences.

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