LEFT VENTRICULAR PERFORMANCE DURING CORONARY ANGIOPLASTY

M.D. THESIS

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ABSTRACT

Left ventricular (LV) performance during elective single vessel coronary angioplasty (PTCA) was assessed in 67 patients with intravenous digital subtraction ventriculography. Left ventriculography, following right atrial contrast injection, was well tolerated and produced images suitable for analysis in all cases.

During balloon inflation, marked contractile abnormalities developed rapidly in ventricular segments subtended by the treated artery. The degree of contractile dysfunction was lessened in the presence of collateral vessels and was independent of short (20 secs) or long (60 secs) balloon inflation, and the presence or absence of additional coronary disease.

During PTCA LV end-diastolic volume remained unchanged and LV end-systolic volume increased. However, ECG R wave amplitude decreased, supporting the view that during ischaemia LV volumes are independent of R wave amplitude.

"Reciprocal" ECG changes were examined in patients with single vessel disease undergoing left anterior descending PTCA. Despite the development of inferior ST segment depression, inferior LV segmental contraction remained unaltered while inferobasal contraction was augmented. This confirms that these remote ECG changes did not indicate additional ischaemia but represented only an electrical phenomenon.

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In patients undergoing PTCA after successful thrombolysis for acute myocardial infarction, balloon occlusion was used to "reproduce" thrombotic coronary occlusion. A deterioration was apparent in global and regional LV performance during balloon inflation which may represent the extent of myocardium salvaged by thrombolytic therapy.

In the 37 patients studied after PTCA, segmental contraction had returned to baseline values confirming that multiple balloon coronary occlusions of up to 60 seconds do not produce sustained abnormalities of LV contraction detectable by this method.

PTCA allows a unique opportunity to examine the immediate effects of controlled coronary occlusion on LV performance. Intravenous digital subtraction ventriculography provides a valuable method with which to study these changes.

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CHAPTER ONE

INTRODUCTION

Since Andreas Gruentzig reported the first coronary balloon
angioplasty in 1977 (1), this technique has become an
established therapy for the treatment of obstructive coronary
artery disease. In 1985 it was estimated that more than
100,000 patients worldwide had undergone the procedure (2) and
by the end of 1988 approximately a quarter of a million
patients had been treated (3).

The initial results with percutaneous transluminal coronary
angioplasty (PTCA) have markedly improved over the last
decade. Increasing operator experience and expertise,
together with improved guidewire, catheter and balloon
design, have resulted in primary success rates of
approximately 90% in most centres (4) compared with 60% to 70%
10 years ago (5). Similarly, the incidence of acute
complications during the procedure has fallen such that one
may anticipate myocardial infarction in 3%, the need for
urgent coronary artery surgery in 2% and death in less than
1% of cases (4).

In addition to improved results, advances in technology have
also widened the application of the technique. Initially,
PTCA was considered only in patients with single vessel
disease and a concentric, non-calcific stenosis situated
proximally in a major coronary vessel (6). Currently,
patients suitable for PTCA may have multivessel disease and

undergo balloon dilatation at multiple sites. Distal or eccentric stenoses may also be dilated as may acute coronary thromboses and chronic total occlusions (7).

Although the immediate outcome of the PTCA procedure is favourable in the majority of patients, long term results are less so. Restenosis at the site of initially successful dilatation occurs in up to 30% of patients within 6 months of the procedure (8), and may then be responsible for recurrent symptoms. Repeat PTCA is feasible in most cases but restenosis nevertheless represents a major drawback of the technique.

Various therapeutic regimens have been applied in an attempt to improve the long term result of PTCA but none has significantly modified the incidence of restenosis (9,10).For this reason attention has been focussed on factors related to the dilatation procedure itself. Kaltenbach (11) has suggested that prolonged balloon inflation may result in a more favourable longterm outcome and a number of studies are currently testing this hypthesis.

If the duration of balloon inflation is an important determinant of the longterm outcome of PTCA, it is pertinent to consider initially the effect of balloon coronary occlusion on left ventricular performance and those factors that may modify this effect.

PTCA requires the temporary and near-complete obstruction of a coronary artery and thus the technique provides a unique model of controlled, reversible myocardial ischaemia in the human subject. Since the pioneering work of Tennant and Wiggers (12) it has been appreciated that coronary occlusion results in the rapid development of regional myocardial dysfunction. The use of PTCA as a tool with which to examine this process has been the subject of previous study (13). In particular, the effect of balloon coronary occlusion on left ventricular contraction has been assessed using either echocardiography (14-20), or direct left ventricular cineangiography (21-23).

Echocardiographic Studies

In 1983, Das reported findings using continuous M-Mode echocardiography in a patient with single vessel coronary disease undergoing left anterior descending (LAD) PTCA (14). The duration of balloon inflations ranged from 30 to 65 seconds with inflation pressures of 3 to 5 atmospheres. Echocardiography, at the chordal level, initially demonstrated an increase in both end-systolic and end-diastolic dimensions, apparent after the 7th cardiac cycle following the onset of balloon inflation (approximately 5 seconds). Septal systolic motion became absent at the 28th cycle (22 seconds after balloon occlusion). ST segment changes on the accompanying ECG did not occur until after 13 seconds. Echocardiographic abnormalities returned to baseline 28 seconds after balloon deflation although ST changes had

resolved previously. Thus, from this early study it was apparent that changes in LV performance occur soon after balloon coronary occlusion and precede ECG changes.

Hauser (15) used 2-Dimensional echocardiography in 18 patients during a total of 52 episodes of balloon occlusion. It is noteworthy that 24 patients were studied before PTCA but in 5 endocardial visualisation was considered suboptimal and these were therefore excluded from the study. ECG was monitored using 6 limb leads together with lead V5 in those patients undergoing LAD PTCA. During balloon inflation abnormal LV wall motion developed in 16 of 18 previously normal LV segments. Further deterioration in wall motion in previously abnormal segments was seen in 2 patients. No new abnormality was observed in 3 patients: one patient had a preexisting extensive area of anteroapical asynergy while another was undergoing circumflex artery dilatation and in this instance abnormal posterolateral wall motion may not have been appreciated. In the remaining patient the arterial segment distal to an LAD stenosis was filled distally by collateral vessels and as will be discussed in Chapter 4 these may have modified the ischaemic response to balloon occlusion. Abnormal wall motion was observed 19 seconds after the onset of the initial balloon inflation, similar changes being observed after the onset of the final inflation (20 seconds). Abnormal wall motion began to improve 20 seconds after balloon deflation and in all cases wall motion was qualitatively unchanged after the procedure compared with

that before PTCA. ST segment change developed in only 8 patients (elevation in 4 and depression in 4), and this was seen 30 seconds after the onset of balloon inflation.

This study underlined the sequence of ischaemic events consequent on balloon coronary occlusion. Thus, the initial development is one of abnormal LV mechanics. This may be followed by ST segment alteration while the last, and by no means universal manifestation of myocardial ischaemia, may be chest pain.

Alam (16) similarly used 2-Dimensional Echocardiography in 12 patients of whom 10 developed reduced septal systolic excursion during LAD PTCA and reduced posterior wall contraction in the remaining 2 patients during right coronary angioplasty. Interestingly, he was not able to demonstrate augmented contraction of the septum during right coronary PTCA, or of the posterior wall during LAD PTCA. Both LV end-systolic and end-diastolic dimensions increased. The changes he observed occurred 15 to 20 seconds after balloon occlusion and had resolved 20 seconds after deflation. He did not document a rebound increase in contraction after the procedure in those segments rendered ischaemic during PTCA. In this study, ECG changes occurred in all the 10 patients who developed echocardiographic evidence of ischaemia. The 2 patients without either echocardiographic or ECG abnormalities both had extensive collateral supply to the treated artery.

Wohlgelernter (17) studied 14 patients with 2-D echo during LAD PTCA, none of whom had angiographically demonstrable

collateral vessels. 12 lead ECG monitoring was incorporated and in this study, as in that of Hauser's, 3 patients had to be excluded because of suboptimal echocardiographic visualisation. The onset of regional LV dysfunction during balloon inflation occurred after 12 seconds, profound dysfunction being observed in all patients. Recovery in wall motion was apparent 15 seconds after balloon deflation and was complete in all patients by 70 seconds (mean 43 seconds). Another group of 6 patients were studied during the first and last of multiple inflations. There was no difference in the time to the onset of regional dysfunction between the first and the last study (19 vs 17 seconds). Similarly there was no difference in the time to the onset of resolution (13 vs 15 seconds) or to the completion of recovery (37 vs 36 seconds). In 3 of the 14 patients he was able to demonstrate overshoot of regional LV function above baseline levels after the procedure. Predictably, changes on ECG monitoring lagged behind those detected by 2-D echocardiography. After 20 seconds of balloon inflation only 9 of the 14 patients had developed ST alteration. Two patients had no ECG change despite echocardiographic evidence of marked ischaemic LV dysfunction. It was apparent in this study that 12 lead ECG monitoring detected ischaemia in more patients than did a 3 lead system comprising leads I, aVL and V5.

Visser studied 15 patients with 2-D echocardiography (18). He observed the development of segmental asynergy in all 15 patients 8 seconds after balloon inflation which resolved 19

seconds after deflation. As in Wohlgelernter's study, overshoot of regional function was manifest as hyperkinesis in 12 patients 25 seconds after deflation. Four of Visser's patients developed ST change in limbleads and 5 patients complained of chestpain during balloon inflation. The typical timecourse in the 3 patients who developed all 3 ischaemic manifestations was initially LV asynergy 11 seconds after inflation. ST change occurred after 21 seconds and chestpain after 27 seconds. With balloon deflation, recovery progressed in the reverse order. Thus, chestpain resolved after 13 seconds and ST change after 16 seconds. LV segmental asynergy was the last ischaemic manifestation to return to baseline 22 seconds after balloon deflation.

Faletra (19) also used 2-D echocardiography in 9 patients undergoing a total of 33 episodes of LAD balloon occlusion. Asynergy was seen in 8 patients after 13 seconds while ECG changes were observed in only 2 after 36 seconds. Only 1 patient developed angina and this occurred after 36 seconds of coronary occlusion.

Khaja (20) has evaluated LV performance during PTCA using continuous wave Doppler. Peak velocity of blood in the ascending aorta - an index of global LV function - was measured in 26 patients during balloon inflation. 15 of these patients developed both angina and ECG changes of ischaemia and in this group peak aortic velocity fell from 17 to 11 m sec-2. None of the vessels in this group was collateralised. In contrast, of the 11 patients who developed neither chestpain nor ECG abnormality there was no change in aortic

blood velocity. 10 of these patients had collateral vessels supplying the treated artery.

Cineangiographic Studies

Serruys (21) reported an evaluation of LV performance during PTCA using direct left ventricular cineangiography. 14 patients were studied before and after PTCA, and after 20 and 50 seconds of balloon coronary occlusion. There was a minimum of 10 minutes between ventriculograms and in all cases haemodynamics had returned to baseline values prior to each study. 20 seconds of balloon inflation resulted in an increase in LV end-systolic volume (ESV;31 to 38 ml m-2) while LV end-diastolic volume (EDV) remained unchanged at 81 ml m-2. After 50 seconds of coronary occlusion LV ejection fraction (EF) had fallen from 62% to 48%. Concurrent monitoring of LV pressure enabled an end-diastolic pressure/volume relationship to be derived. During PTCA there was a shift of this relationship upwards and to the right suggesting a decrease in LV compliance. A profound effect on anterolateral and apical regional LV wall motion was documented after 20 seconds of occlusion. The changes in volume, pressure derived indices and regional wall motion were shown to be perfectly reversible, returning to baseline values after the PTCA procedure.

Doorey (22) used direct cine left ventriculography to investigate the effect of intravenous nitroglycerin on myocardial ischaemia during balloon inflation. 10 patients

undergoing LAD PTCA were studied, the extent of their coronary disease not being stated. They were studied before PTCA and after 30 seconds of balloon inflation. A third study was performed after 30 seconds of a separate inflation which followed the administration of nitroglycerin. During the initial balloon inflation LVEF fell from 66% to 44%. LV end-diastolic and end-systolic volumes both increased from 87 to 93 and 30 to 52 ml m-2 respectively. LV contraction, assessed for 9 regions, decreased markedly in the anterior, anteroapical, apical and inferoapical regions. Anterobasal and inferobasal contraction did not change. Eight of the 10 patients developed angina after 29 seconds of inflation while 7 developed ST change greater than 1 mm after 30 seconds, detected on ECG monitoring of leads 1, 2 and 3. Following nitroglycerin, these manifestations of LV ischaemia were either reduced or delayed. Interestingly, although anteroapical contraction was no different to that pre-nitroglycerin, inferoapical contraction did improve.

Bertrand (23) has also used direct cine ventriculography during PTCA. He studied 8 patients after 30 seconds and another 6 patients after 50 seconds of balloon LAD occlusion. All had single vessel disease and no collateral vessels. After 30 seconds LV end-diastolic volume increased from 98 to 102 ml m-2 as did end-systolic volume from 25 to 54 ml m-2. The resulting fall in stroke volume was manifest as a fall in LVEF from 73% to 46%. There was a marked decrease in anterior and anteroapical LV segmental shortening with systolic outward displacement suggesting true dyskinesia in some

cases. Augmentation of inferior contraction was not documented. After 50 seconds there was only a slight further deterioration in these measurements. All the changes observed by Bertrand were transient and totally reversible.

Previous studies have therefore demonstrated that changes in LV performance are a sensitive and early indicator of myocardial ischaemia during PTCA. Thus, the assessment of global and regional LV contraction in this setting can provide a valuable insight into various aspects of transient, but controlled, coronary occlusion.

During PTCA however both the techniques described above have limitations. Direct cine left ventriculography requires the insertion of a second arterial catheter thus making the procedure more invasive. Furthermore a direct intraventricular injection of contrast medium frequently provokes ventricular ectopic activity and this may produce difficulty when selecting cine frames for volume and wall motion analysis (24,25).

Echocardiography, although ideal for repeated or continuous studies, is dependent on patient suitability and operator expertise. The positioning of the patient supine on a catheter laboratory table is not ideal for producing acceptable echocardiograms and studies satisfactory for detailed analysis may not be available in all cases. In 2 of the studies described above, some patients were excluded because of suboptimal echocardiographic visualisation (15,17).

I therefore chose to examine left ventricular performance during PTCA using intravenous digital subtraction left ventriculography. This method has been shown to produce diagnostic left ventriculograms from central venous contrast injection. Recent studies demonstrate a good correlation with direct cine ventriculograms in terms of LV volumes and regional wall motion (24-27). Additional central venous cannulation does not significantly increase the invasive nature of PTCA and has the advantage that contrast injection is less likely to provoke ectopic beats. Global and regional LV peformance during PTCA were therefore assessed to determine factors that may modify the consequences of balloon coronary occlusion.

CHAPTER TWO

METHODS

Digital Subtraction Ventriculography (DSA)

This is a radiographic technique, similar to conventional angiography, that requires the introduction of contrast medium and subsequent computer processing of information in order to construct images of vascular structures. The computer manipulation of data allows lower concentrations of contrast to be detected (28).

Commercial DSA systems became avilable in 1980 and comprise a number of components. An X-ray source directs the X-ray beam towards a region of interest. An X-ray detector and image intensifier increases the brightness of the radiographic image which is then converted into a video signal by a video camera. The analogue video signal is translated into digital information with an analogue-to-digital converter (ADC) and this data is then stored onto computer.

The ADC samples the analogue video signal at regular time intervals expressing its amplitude at each sampling point in digital form. The rate at which the ADC samples the video image is usually equal to the number of lines scanned by the video camera. Thus, if the camera scans 256 lines the ADC will sample 256 times for each line on the video image. This process, repeated for all 256 lines, results in an image which will be represented as a matrix of 256 x 256 points. Each of these points is called a picture element or pixel. The greater the number of pixels used to represent an

image, the smaller is the area covered by each individual pixel. The spatial resolution of a DSA system is dependent on pixel size being high if the pixels are small and low if they are large. High ADC sampling rates which may produce a 1024 x 1024 pixel matrix however, may impose too great an amount of data for computer manipulation.

Each pixel, representing the amplitude at one point of the video signal, is given a value expressed in binary form. This is usually an eight digit binary number or bit, which can have any value from 0 to 255. Thus any point on the video signal can be represented on the computer as up to 256 levels of grey. The accuracy of the digital representation may be further enhanced if each pixel has a greater number of possible values e.g. 0 to 1023 but this also increases the amount of data that has to be stored on computer and subsequently manipulated.

The basic principle of digital subtraction is to produce a series of images that represent attenuation of the X-ray beam only by the contrast containing structure. This is achieved by taking 2 images of the study region. The first is taken before the introduction of contrast and termed the mask. The second is acquired after contrast injection and referred to as the live image. Both images are stored in digital form and the data from the mask image is then subtracted from that in the live image on a pixel-by-pixel basis. The resultant image displays only the contrast containing structure with the surrounding soft tissues and bone etc., subtracted. This

process allows lower concentrations of contrast to be used. Importantly it also means that arterial structures can be demonstrated with intravenous contrast administration.

In order that subtraction of the mask image is accurate it is important that both the mask and the live image are well registered i.e. that they are in the same position. If movement occurs between the acquiring of the two images misregistration will occur and degradation of the subtracted image will result. Misregistration can be reduced by the patient holding his breath and minimising any movement.

When imaging moving vascular structures such as the heart movement artefact is reduced by ECG gating. The R wave of the ECG is used as a trigger to initiate a set sequence of acquisitions. Subsequent image subtraction can then be undertaken with frames at similar points in the cardiac cycle. Images may be further enhanced by manipulating the mask and producing a composite mask derived from a number of frames. Image quality can also be increased by remasking which allows subtraction of a mask derived at varying intervals prior to the live image. One drawback of this technique is that if the mask is selected late and already contains some contrast, the amount of contrast in the final subtracted image will be reduced.

Digital subtraction angiography has been used increasingly for the assessment of global and regional LV function. Previous studies have used either direct intraventricular injections of reduced volumes of contrast media (29,30) or more recently, intravenous contrast injection (24-27). Some of these

studies have examined the optimum dose and contrast medium together with the site and rate of injection in order to acheive optimum imaging. Others have established the validity of the technique in comparison with cine left ventriculography in the determination of ventricular volumes, ejection fraction and segmental wall motion.

Injection Site

The haemodynamic effects of contrast injection cannot be ignored. Although changes in pulmonary artery pressure, pulmonary artery wedge pressure and right atrial pressure are similar with both intravenous and intraventricular injection these changes are minimal (31). Similarly, alteration in cardiac output, heart rate, blood pressure and LV end-diastolic pressure are small with both techniques, although changes following intravenous delivery are slightly less marked.

Contrast Medium

Non-ionic contrast has been shown to produce less marked alteration of LV haemodynamics (32,33) and is associated with decreased toxicity. This is related to their reduction in osmolality and negligible sodium content. In addition to the minimal effect on haemodynamics, non-ionic contrast has a negligible effect on the ECG. Thus, Mancini has shown no effect on the QT interval with Iohexol in comparison with Renograffin (34,35). DSA following intraventricular injection

requires a lower contrast dose with volumes of 7 ml being employed. Intravenous studies require a greater volume of contrast injection in order to achieve sufficient opacification of the LV after transit of the contrast bolus through the pulmonary circulation. The total dose injected may be reduced by diluting the contrast with dextrose. Contrast doses have ranged from 30 to 50 ml in previous studies. The rate of contrast injection has varied in previous studies, from 10 to 30 ml per sec. The majority of workers have used injection rates of 20 ml sec-1.

A pilot study initially investigated varying both the contrast volume and delivery rate required for optimum image acquisition. A dose of 40 ml injected at 17 ml sec-1 was selected which is in accordance with others' experience.

Analysis of Global LV Function

Previous studies using intravenous DSA have established the validity of the technique when compared with direct cine left ventriculography. Norris (25) found a correlation between the two techniques, deriving LV volumes using a standard area length formula (LVEDV, r = 0.88; LVESV, r = 0.89 respectively). DSA derived LVEF was thus found to correlate closely with that from cine studies (r = 0.81). This particular study noted the superiority of DSA over cine in terms of the decreased incidence of ectopic activity.

Tobis (24) found a similar degree of correlation between the two techniques (EDV r=0.82, ESV r=0.93, LVEF r=0.96). He also

noted a high incidence (10 of 33 patients) of ventricular ectopic activity during direct cine left ventriculography which resulted in 6 patients being withdrawn from this comparative study.

Goldberg (26) found an even closer correlation (EDV r=0.96, ESV r=0.97, LVEF r=0.98) while Greenbaum (36) also noted a satisfactory correlation (LVEF r=0.90). Importantly, studies have shown that this acceptable degree of correlation remains valid even for patients with impaired LV function.

Felix (37) and Nissen (38) have shown satisfactory correlation between DSA and cine studies in patients with impaired LV function, previous infarction and LVEF less than 50%. This is particularly relevant in patients undergoing PTCA in whom LVEF may fall profoundly during balloon inflation. A correlation in patients with reduced LV function has not been found in all workers, although in these patients more rapid contrast injection may compensate for such impaired LV performance.

Analysis of Regional LV Function

Studies comparing DSA and cine left ventriculograms have also produced acceptable concordance in terms of regional LV performance. In Greenbaum's (36) study subjective analysis was used to assess overall LV function in 25 patients investigated with intravenous DSA and results agreed with those of cine angiography in all cases. In a comparative study by Tobis (24), 5 of 6 patients with abnormal LV wall motion, were detected qualitatively by both techniques. The

remaining patient had an apical LV aneurysm which was visualised with intravenous DSA but not with direct cine angiography because of inadequate mixing of the contrast with the intracavity blood pool.

Semiquantitative methods have also been employed and correlate well with cine studies. In Golberg's comparative study of 155 LV segments (26), there was absolute concordance in 123 (79%). In 29 of the remaining 32 segments over which there was disagreement, discordance involved only the degree of abnormality rather than its presence or absence. Similarly Kronenberg (27) showed correspondence in 45 of 54 segments (83%). Nichols (29) compared DSA ventriculograms following both intravenous and intraventricular contrast injection and found a satisfactory overall correlation in terms of abnormal LV segments (r=0.81). Correlations for each of the 5 LV segments examined were anterobasal r=0.72, anterolateral r=0.77, apical r=0.86, diaphragmatic r=0.76 and posterobasal r=0.64.

In addition to validating the technique other studies have capitalised on the relatively non-invasive nature of intravenous DSA. Thus, it has been employed with atrial pacing (39) and exercise (40,41) in patients with coronary disease, or as an outpatient assessment of LV function (36).

STUDY PROTOCOL

PTCA

Patients were studied during elective single vessel angioplasty. 2 hours before the procedure they received oral premedication comprising a long acting nitrate, calcium antagonist and either lorazepam or intramuscular papaveretum. Angioplasty was performed via the femoral approach. An intravenous bolus of heparin (100 i.u./kg) was given at the start of the procedure together with atropine (up to 1.2 mg) if the heart rate fell below 50 per minute. All dye injections incorporated non-ionic contrast. Steerable guide wires and balloon catheters with diameters varying from 2.5 to 3.5 mm were used. The number of balloon inflations ranged from 2 to 12 (mean 5). Inflation pressures used ranged from 5 atm for initial inflations, up to 12 atm (mean 8 atm). Inflation duration ranged from 15 to 95 seconds (mean 57 secs), and the mean total inflation duration was 162 secs.

ECG Monitoring

Standardised 12 lead ECG was monitored throughout the PTCA procedure using a Seimens Elema Mingograf 804 and Mingograf 62 with a frequency response of 0.05 to 100 Hz. In order that the chest electrodes did not interfere with fluoroscopy during the PTCA procedure, Medicotest (A-50-VS, Cambmac) electrodes were used. The ECG was recorded at 25 mm sec-1 immediately prior to and throughout each balloon inflation.

Balloon inflation and deflation was marked on the ECG which was recorded at the same paper speed until any changes had resolved.

Ventriculography

A 5 Fr Pigtail catheter (Superflow, Cordis) was inserted via the femoral vein and the tip positioned in the right atrium. For each ventriculogram, 40 ml of non-ionic contrast (Omnipaque, Nycomed) was injected at 17 ml sec-1. A delay of 7 seconds was allowed for transit of the contrast bolus through the pulmonary circulation and its subsequent arrival in the left ventricle. A digital ventriculogram was then acquired, in held inspiration, in a 30 degree RAO projection. ECG gated images were acquired at 12.5 frames sec-1 onto a 256 x 256 pixel matrix using a Siemens Digitron connected online to a Siemens Elema Angioskop D imaging system. Acquisition times ranged from 5 to 10 seconds. The digital information was then transferred onto hard computer disc and then to magnetic tape for subsequent recall and analysis.

ANALYSIS

Electrocardiography

ST segment alteration was measured 80 msec after the J point, a change of at least 1mm being regarded as significant. During balloon inflation, the 10 consecutive complexes prior to left ventriculography were analysed to avoid the possibility of contrast injection producing spurious ECG changes.

ECG R wave amplitude was determined from leads V4, V5 and V6. The R wave was measured from the PQ segment to the peak of the R wave using a hand held digitiser capable of measuring to 0.1 mm. For each of the three leads analysed, the mean of 10 consecutive complexes was calculated in order to allow for respiratory variation, and the mean R wave amplitude for the all three leads calculated.

Left Ventriculography

Each digital acquisition was recalled onto hard disc and reviewed in order to identify end-diastolic and end-systolic frames suitable for analysis. Ectopic cycles were excluded. End-diastolic frames were identified using an R wave marker. The subsequent end-systolic frame was identified visually as that frame with minimum LV dimensions. Remasking, using a 16 frame composite mask, was employed in order to produce optimal images prior to outlining. Allowance for X-ray

magnification was made using calibration markers. LV volume was determined using an area-length method and ejection fraction derived (42).

In a pilot study the reproducability of this method was assessed. End-diastolic and end-systolic images from a patient with normal LV contraction were repeatedly outlined in order to obtain multiple values for LV ejection fraction. The mean LVEF from 33 determinations was 81% (SD = 1.4%, SEM = 0.2%) with a range of 79% to 85%.

LV Wall Motion

For LV wall motion analysis a previously described method (43) was employed which does not make assumptions concerning LV geometry. It avoids the necessity of identifying the apex of the ventricle such as would be required using a centre-line method. In this study, this was particularly relevant as location of the LV apex is unreliable in patients with coronary disease, and this task becomes even more uncertain during PTCA.

Once end-diastolic and end-systolic frames were identified they were manually outlined. Care was taken to ensure that the end-systolic outline incorporated the papillary muscles. A computer programme translated the two outlines in order to superimpose the centres of each aortic valve plane. A series of radii were then constructed every 8 degrees, from the anterior margin of the aortic valve plane of the end-

diastolic frame, in a clockwise sweep, to the opposite aortic valve margin. These radii had their centre at the geometric centre of gravity of the end-systolic frame (Fig. 1). The percentage shortening of each radius, from the end-diastolic to the end-systolic outline, was calculated. This was represented as a point on a wall motion plot, showing percentage shortening for each radius in turn, in a clockwise sequence beginning at the anterior margin of the aortic valve plane (Fig.2).

The LV perimeter was divided into 5 equal radial segments to represent anterobasal, anterior, apical, inferior and inferobasal LV regions. The percentage shortening of the radii in each of these 5 segments was averaged in order to quantify regional contraction (Fig. 3).
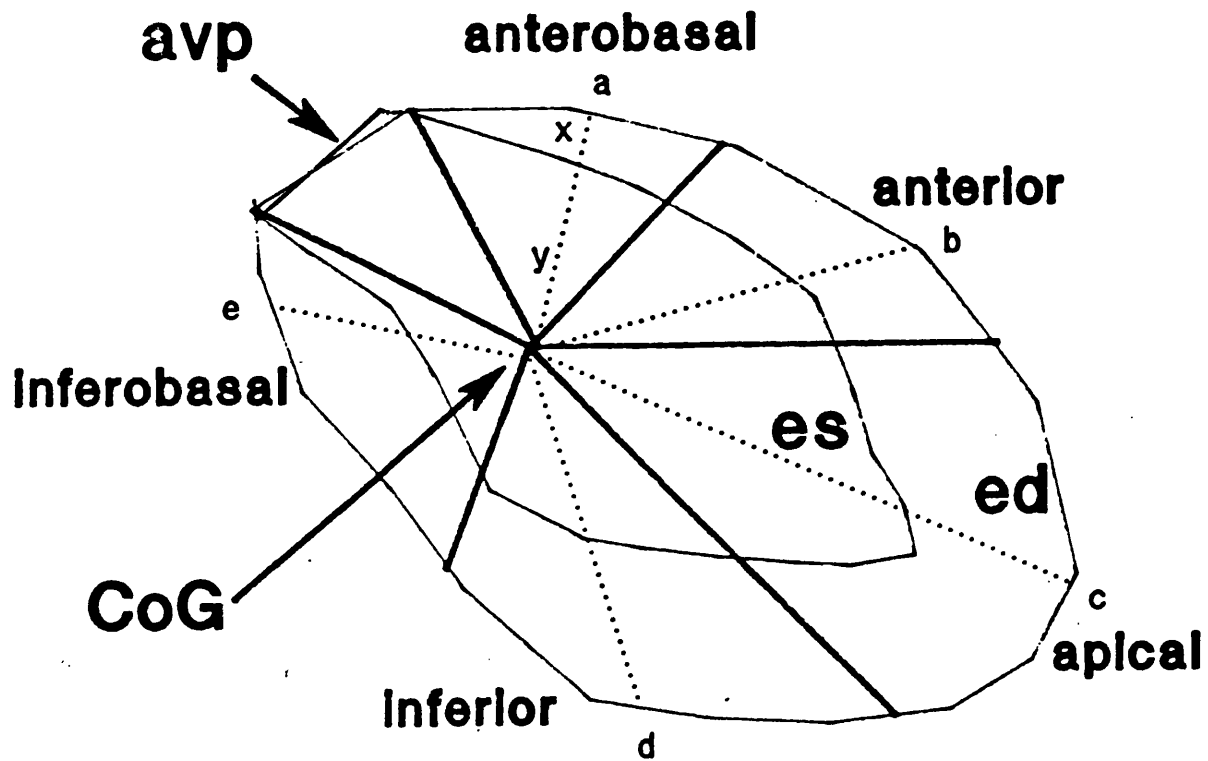
Fig. 1.

Schematic representation of wall motion analysis. End-systolic (es) and end-diastolic (ed) outlines are transposed to superimpose the centres of aortic valve planes (avp). Sample radii (a-e) are shown in each LV segment. Percentage shortening (e.g. radius a) = x/x+y x 100. CoG = end-systolic centre of gravity.
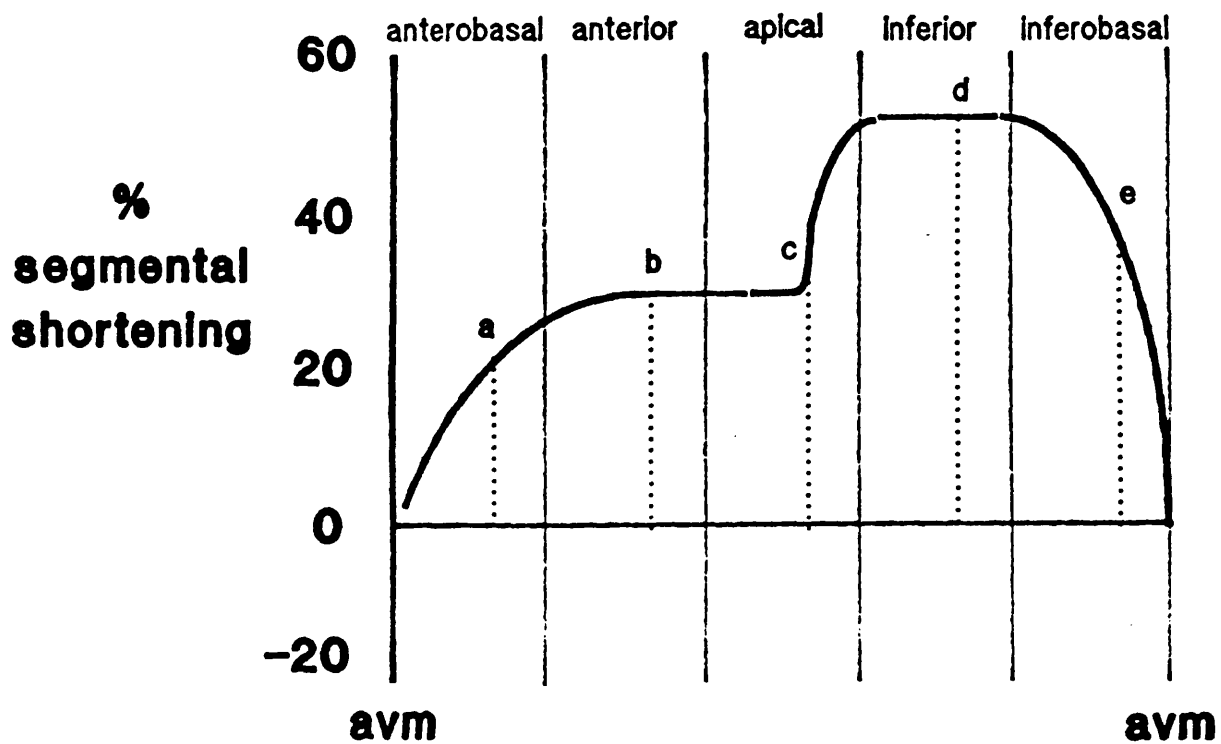
Fig. 2.

Percentage systolic shortening of each radius (e.g. a-e) is
represented on a wall motion plot in a clockwise sequence
beginning at the anterior aortic valve margin (avm).
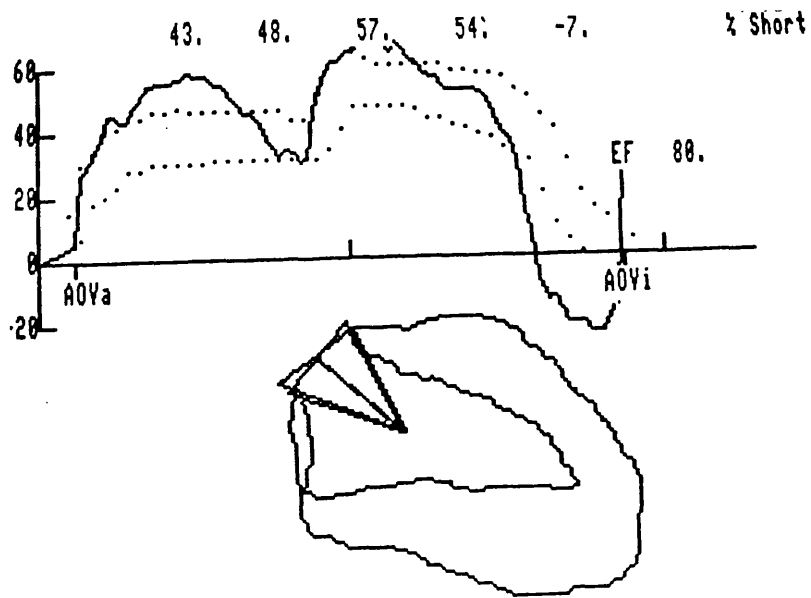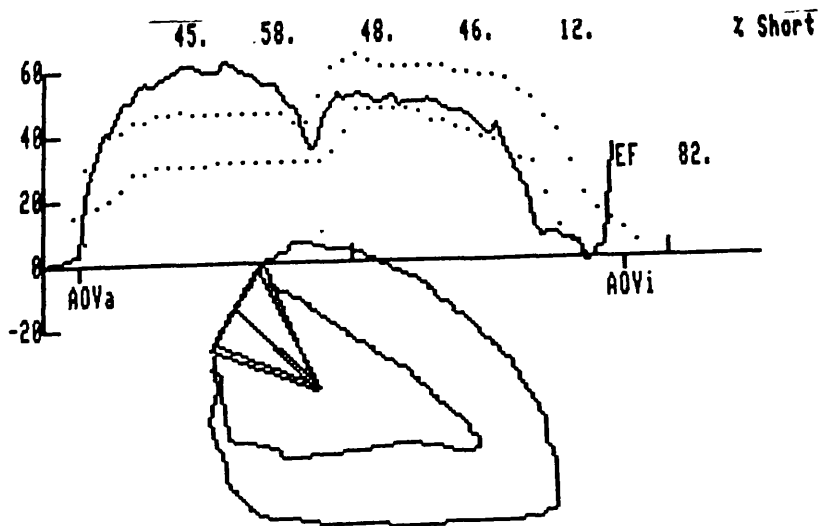
Fig. 3.

Examples of wall motion analysis in 2 patients with normal LV
contraction before PTCA. EF = ejection fraction (%).
Percentage systolic shortening (% short) is shown for each of
5 LV segments. Dotted lines = normal range.

Individual patient data was put onto the London Chest Hospital computer (PRIME) using a word processing package (TEXT, Appendix 1.). This was then converted into a file which would allow statistical analysis using an appropriate software package (STATS).

The changes in LV ejection fraction and regional wall motion within patient subgroups were examined using Student's paired t tests. A number of patient subgroups were identified: those undergoing LAD, RCA or LCX dilatation (Chapter 3.); those with and without collateral supply (Chapter 4.); those with single and multivessel disease (Chapter 5.); those studied after 20 and 60 second ballon inflations (Chapter 6.); those with and without remote ST segment depression (Chapter 8.). These groups were compared by examining the change from baseline in regional wall motion during PTCA, in absolute percentage points, and comparing this change between subgroups using unpaired t tests. Simple correlation and regression analysis was used to examine the relationship between R wave amplitude and LV volumes (Chapter 7.), and LV ejection fraction and ST segment alteration (Chapter 3.). In order to relate ST alteration and ejection fraction to the degree of collateral supply (Chapter 4.), Spearman's rank correlation was used.

Ethical Considerations

The study was approved by the ethical committee of the
National Heart and Chest Hospitals and all patients gave
written, informed consent.
Some aspects require specific comment:

1. Radiation exposure

The acquisition parameters that were used in these studies
were chosen specifically to allow optimum images with minimum
radiation exposure. The frame rate (12.5 sec -1) and duration
(maximum 10 seconds) of image acqisition was calculated as
exposing the patient to approximately the same dose of
radiation as with conventional cine left ventriculography.
Prior to elective PTCA it was thought not unreasonable to
justify the intial digital ventriculogram on the grounds that
LV function could have altered since diagnostic angiography had
been performed. Digital ventriculography during balloon
inflation was an essential part of the study and as such was
considered ethically acceptable. 37 patients underwent a
third digital ventriculographic study on completion of the
PTCA procedure. It should be emphasised that this study was
witheld if the PTCA had been particularly protracted or had
already incorporated excessive amounts of radiation because
of procedural difficulties and the need for frequent
flouroscopy and arteriography. Otherwise it was considered an
acceptable aspect of the study in order to document that LV
function had returned to baseline.

2. Contrast Dose

A non-ionic medium (Omnipaque) was used for both selective arteriography and digital ventriculography in all cases. The use of this contrast medium allowed the acquistion of 3 ventriculograms in some patients. This would not have been possible with standard contrast which would have imposed a significant ionic load. As above, it should be noted that a third ventriclogram was witheld if PTCA had been protracted or had already required large volumes of contrast.

3. Additional Vascular Access

The use of digital subtraction allowed satisfactory left ventriculography following a central venous contrast injection. This obviated the need for additional arterial cannulation which would have been required if direct cineventriculography had been undertaken during PTCA. It is common practice to insert a venous sheath into a femoral vein prior to PTCA in order to gain reliable venous access for drugs and a temporary pacing catheter if required. The utilisation of this access in these studies did not therefore increase the invasive nature of the PTCA procedure.

Each digital acquisition required only a maximum of 20 seconds. Thus, even in those patients undergoing 3 studies, the total duration of the PTCA procedure was not significantly prolonged.

CHAPTER THREE

LEFT VENTRICULAR PERFORMANCE DURING PTCA

Introduction

PTCA has provided an attractive setting in which to study the left ventricle during short, controlled and reversible episodes of myocardial ischaemia (13). As discussed earlier, previous studies have used either echocardiography (14-20) or cine left ventriculography (21-23) but during PTCA both these methods may have limitations. Intravenous digital subtraction left ventriculography has advantages over other methods. It does not rely on patient characteristics that may limit echocardiography and is less invasive than cine ventriculography also being unlikely to provoke ventricular ectopic activity. The use of this method during PTCA in order to evaluate left ventricular performance has not been described by others previously.

Patient Population

52 patients were studied. Their characteristics are summarised on Table 1. They comprised 45 males and 7 females with a mean age of 53 years (range 39 - 73 years). All patients had stable, but limiting, angina despite medical therapy. Their regular medication which included nitrates, calcium antagonists and, in 47 patients, a beta adrenergic blocking agent, was continued. No patient was taking digoxin and none had evidence of valvular disease.

A resting ECG demonstrated sinus rhythm in all cases and no

patient had evidence of bundle branch block. An ECG recorded during either spontaneous chest pain or a symptom limited treadmill exercise test, had revealed objective evidence of myocardial ischaemia in all patients manifest as at least 1 mm of ST segment alteration.

Coronary Anatomy

Previous diagnostic coronary arteriography had demonstrated single vessel disease, defined as at least an estimated 70% reduction in luminal diameter, in 37 patients. Of the remaining 15 patients 12 had 2 vessel and 3 had three vessel disease. In all but one patient the right coronary artery (RCA) was a dominant vessel, giving rise to the posterior descending artery.

Lesions Attempted

PTCA was undertaken to the LAD in 35 patients, the RCA in 7 and the circumflex artery (LCX) in 8 patients (including one patient with a dominant LCX system). The remaining 2 patients underwent PTCA to lesions in the first diagonal branch of the LAD. There were no occluded vessels and in all cases the target stenoses allowed anterograde flow of contrast. The lesions ranged in severity of luminal narrowing from 60% to 99% (mean 92%).

Digital Ventriculography

Ventriculograms were performed prior to the PTCA procedure and after either 20 seconds (28 patients) or 60 seconds (24 patients) of balloon inflation. 36 patients were studied during the third balloon inflation. Of the remainder 1 was studied during the second inflation, 8 during the fourth, 3 during each of the fifth and sixth and 1 during the eighth balloon inflation.

TABLE 1.

CHARACTERISTICS OF STUDY PATIENTS

No.	Sex	Age	PTCA Vessel	Coll. Grade	Add. Disease	PRE-PTCA LVEF (%)	WALL MOTION (%)				
							AB	A	AP	I	IB
1	M	56	LAD	0		78	30	35	55	65	11
2	M	47	RCA	0		58	30	38	42	48	0
3	M	52	LAD	0		76	37	50	51	44	0
4	M	60	LAD	0	LCX	71	33	35	41	55	15
5	M	52	LAD	1		77	50	45	55	52	0
6	M	50	LCX	0		55	15	5	0	60	50
7	M	39	LAD	1		78	35	40	48	59	38
8	M	47	RCA	0	LAD	55	35	21	11	40	30
9	M	63	LCX	3		63	41	26	39	40	8
10	F	43	LAD	0		73	37	40	46	52	38
11	M	54	LCX	0	RCA	66	15	29	30	39	8
12	M	56	LAD	3		82	20	43	63	69	0
13	F	54	LAD	0	RCA	51	11	21	40	45	0
14	M	53	RCA	0		79	12	35	58	60	10
15	M	59	LCX	0	LAD RCA	71	12	21	35	58	4
16	M	51	DIAG	0	RCA LCX	69	15	26	29	50	7
17	M	50	LAD	1		78	27	29	60	46	0
18	M	58	LAD	2		74	47	45	68	36	-10
19	M	60	LAD	1	RCA LCX	61	40	17	0	42	25
20	F	61	LAD	1	LCX	70	45	27	26	36	20
21	M	45	RCA	0	LAD	83	42	41	68	61	0
22	M	50	LAD	2		62	52	17	25	45	22
23	M	51	RCA	0	LCX	61	17	28	48	40	5
24	M	58	LAD	0	RCA	69	28	30	61	43	9
25	M	55	LAD	0		80	52	49	63	57	4

<u>STUDY</u> <u>PATIENT</u> <u>CHARACTERISTICS</u> <u>(cont.)</u>

No.	Sex	Age	PTCA Vessel	Coll. Grade	Add. Disease	LVEF (%)	P R E - P T C A WALL MOTION (%)				
							AB	A	AP	I	IB
26	M	56	LAD	0		58	30	38	40	11	0
27	F	44	LAD	0		68	43	37	39	52	10
28	M	51	LAD	0		75	20	14	65	57	0
29	M	45	LCX	0	LAD	58	25	11	21	58	10
30	M	64	LCX	0		77	40	47	53	57	-10
31	F	41	LAD	0		70	50	32	58	42	5
32	M	60	LAD	0		78	30	25	59	65	10
33	F	57	LAD	1		85	37	41	67	60	0
34	M	71	LAD	1		81	21	38	62	21	0
35	M	47	LCX	0		81	15	6	59	66	19
36	M	69	LAD	0	LCX	82	45	58	48	46	12
37	M	54	RCA	0		70	50	37	27	12	0
38	M	50	LCX	0		83	51	55	59	38	-7
39	M	56	LAD	1		79	51	56	48	34	-11
40	M	57	LAD	3		73	46	57	40	37	0
41	M	60	DIAG	0		75	45	50	45	33	2
42	F	48	LAD	0		81	44	42	59	55	-5
43	M	45	LAD	0		75	33	39	46	55	0
44	M	51	LAD	0		72	47	40	42	34	9
45	M	52	LAD	0		71	37	43	45	43	1
46	M	42	RCA	1		86	46	66	55	37	5
47	M	57	LAD	0	LCX	81	41	47	61	54	-11
48	M	66	LAD	3	LCX	73	43	40	35	54	32
49	M	49	LAD	2		78	33	48	55	53	0
50	M	55	LAD	0		71	36	38	44	43	14
51	M	63	LAD	3		90	39	56	68	70	20
52	M	51	LAD	0		79	31	43	49	48	23

RESULTS

Practical Considerations

Ventriculograms suitable for analysis were obtained in all 52 patients. Although patients were required to maintain held inspiration for up to 10 seconds in order to allow data acquisition during balloon inflation, this did not prove to be problematical.

The interval allowed for pulmonary transit of the contrast bolus was variable. In some patients, an interval of 7 seconds after right atrial contrast injection was too short to coincide with the arrival of contrast in the LV, resulting in the first 30 to 50 frames of the ventriculogram being contrast free. In others, even after only a 5 second delay, contrast was already clearing from the LV as acquisition was started. The duration of pulmonary transit did not seem to relate to either the heart rate or the degree of any preexisting ventricular dysfunction.

Complications

Despite right atrial contrast injection, ectopic activity was observed during ventriculography. This was seen in 3 patients in the study undertaken before PTCA (supraventricular in 2, ventricular in 1) and in 6 others during balloon inflation (supraventricular in 3, ventricular in 3). In all these cases the ectopics were single and therefore did not interfere with data analysis.

Intravenous digital subtraction left ventriculography was tolerated by the majority of patients. Transient atrial fibrillation occurred in 1 patient immediately after contrast injection for the pre-PTCA ventriculogram. This was asymptomatic and did not recur during subsequent ventriculograms. As this arrythmia was also shortlived, it did not affect ventriculographic analysis.

LV Performance Before PTCA (52 Patients)

The mean LV ejection fraction of all 52 patients was 73% (SD = 9%, range 51%-90%). Regional wall motion for each of the 5 LV segments assessed in individual patients is shown in Table 1. with mean values shown in Table 2. The normal range of regional shortening derived from 10 patients with normal coronary arteries and normal LV contraction is also indicated.

Table 2.

Segmental LV contraction before PTCA in 52 patients

Values = mean % shortening (SD)

LV Segment	Regional Shortening	Normal Range
Anterobasal	35 (12)	28-40
Anterior	36 (13)	30-45
Apical	46 (16)	42-62
Inferior	47 (13)	40-58
Inferobasal	8 (13)	0-20

1. LV Ejection Fraction (LVEF, 52 Patients)

Individual results for LV ejection fraction, regional wall motion and ST segment change are detailed in Appendix 1.During balloon inflation ejection fraction decreased in all but one patient. The mean fall in ejection fraction was from 73% to 57% (p<0.001). This decrease in LVEF was no different in the 36 patients studied during the third balloon inflation (74% to 57%) than in the 8 studied during the fourth inflation (70% to 59%) and the 7 patients studied during subsequent inflations (72% to 56%).

The effect on LVEF of LAD, RCA and LCX dilatation is summarised in Table 3. There was no difference in control LVEF between groups. In the 35 patients undergoing LAD PTCA, LVEF fell from 74% to 55%, (p < 0.001). In the 7 undergoing RCA inflation, LVEF fell from 70% to 60%, (p< 0.01) while in the 8 undergoing LCX PTCA, LVEF fell from 69% to 61%, (p< 0.01). The magnitude of the fall in LVEF during LAD inflation (19%) was greater than that during both RCA, (10%, p < 0.05) and LCX balloon occlusion (8%, p< 0.01).

2. Regional LV Wall Motion (52 Patients)

To assess the effect of balloon occlusion on segmental LV performance, patients were separated into groups according to the vessel in which the treated stenosis was located. The results for patients undergoing LAD, RCA and LCX inflations are summarised on Table 4. and the changes in regional wall

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motion within groups compared between groups in Table 5.

LAD Dilatation (35 patients, Fig 4.)

During balloon inflation regional shortening in the anterobasal, anterior and apical LV segments decreased from 37% to 28%, (p < 0.002), 39% to 13%, (p< 0.001) and 50% to 14%, (p< 0.001) respectively. There was no change in inferior segmental contraction (48% to 46%, NS) but inferobasal contraction increased from 8% to 25%, (p< 0.001; Fig. 5).

RCA Dilatation (7 patients, Fig. 6)

Balloon occlusion resulted in a fall in both inferior and apical contraction from 43% to 24%, (p< 0.01) and 44% to 38%, (p< 0.02) respectively. There was no significant change in inferobasal (7% to 0%, NS) anterior (38% to 34%, NS) or anterobasal contraction (33% to 30%, NS; Fig. 7).

LCX Dilatation (8 patients)

Balloon inflation did not produce significant changes in any LV segment examined. The largest falls were in apical and inferior contraction, of 10% and 11% respectively, but these were not significant (Fig. 8).

Diagonal Dilatation (2 patients)

In these 2 patients balloon inflation produced a fall in LVEF from 73% to 59%. The LV segments rendered dysfunctional were the anterior and apical regions in which contraction was reduced from 35% and 40% to 14% and 5% respectively. Inferior contraction did not change appreciably but inferobasal contraction increased from 3% to 25%. None of these changes in regional contraction proved to be statistically significant.

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Table 3.

LVEF in Patients Undergoing LAD, RCA and LCX PTCA

Values = % (SD)

Vessel Dilated (pts)	Pre- PTCA	During PTCA	p
LAD (35)	74(8)	55(13)	<0.001
RCA (7)	70(14)	60(14)	<0.01
LCX (8)	69(10)	61(12)	<0.01

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Table 4.

Shortening of 5 LV segments before and during PTCA

in patients undergoing LAD, RCA and LCX dilatation.

Mean % (SD). AB = Anterobasal, A = Anterior, AP = Apical,

I = Inferior, IB = Inferobasal.

	LAD (35 patients)			RCA (7 patients)			LCX (8 patients)		
LV Segment	Pre- PTCA	During PTCA	p	Pre- PTCA	During PTCA	p	Pre- PTCA	During PTCA	p
AB	37(10)	28(15)	<.002	33(14)	30(12)	NS	27(15)	22(14)	NS
A	39(11)	13(18)	<.001	38(14)	34(12)	NS	25(18)	19(25)	NS
AP	50(14)	14(19)	<.001	44(19)	38(20)	<.02	37(20)	27(26)	NS
I	48(13)	46(14)	NS	43(17)	24(18)	<.01	52(11)	41(14)	NS
IB	8(13)	25(17)	<.001	7(11)	0(14)	NS	10(18)	18(20)	NS

Table 5.

Comparison of Change in Regional Wall Motion
Between Patients undergoing LAD, RCA or LCX PTCA

Values = mean reduction in shortening (%), (SD)
Negative values indicate increased shortening

LV Segment	LAD PTCA (n=35)	RCA PTCA (n=7)	p
Anterobasal	9(14)	3(4)	NS
Anterior	25(15)	4(8)	<0.002
Apical	35(19)	6(5)	<0.001
Inferior	1(15)	19(11)	<0.01
Inferobasal	-16(19)	7(13)	<0.01

LV Segment	LAD PTCA (n=35)	LCX PTCA (n=8)	p
Anterobasal	9(14)	4(13)	NS
Anterior	25(15)	5(18)	<0.01
Apical	35(19)	10(12)	<0.002
Inferior	1(15)	10(16)	NS
Inferobasal	-16(19)	-7(18)	NS

LV Segment	RCA PTCA (n=7)	LCX PTCA (n=8)	p
Anterobasal	3(4)	4(13)	NS
Anterior	4(8)	5(18)	NS
Apical	6(5)	10(12)	NS
Inferior	19(11)	10(16)	NS
Inferobasal	7(13)	-7(18)	NS
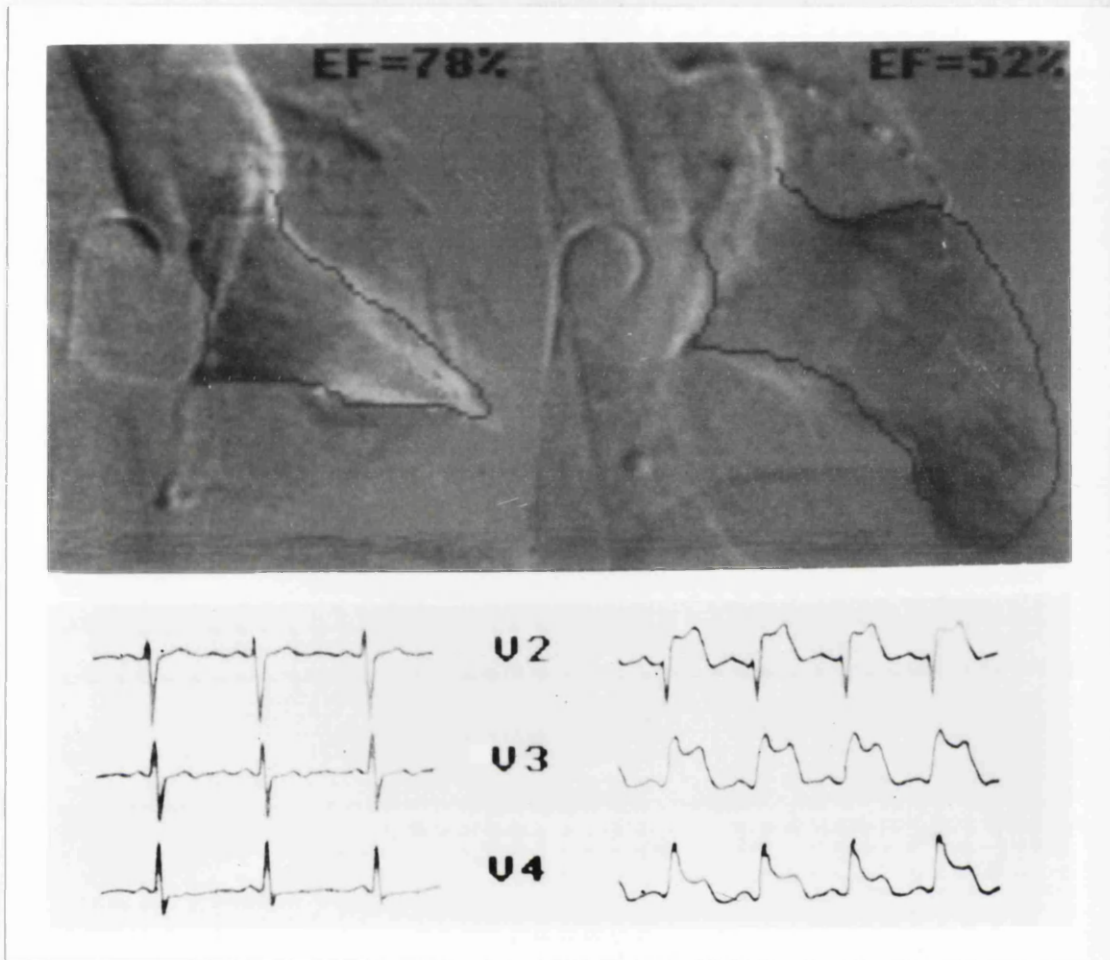
Fig. 4.

Outlined end-systolic images and ECG before (left) and during (right) LAD balloon inflation (30 degree RAO projection). The pigtail catheter in the right atrium and the balloon catheter markers (right) can also be seen. Pronounced anteroapical akinesis is apparent associated with anterior ST segment elevation. Ejection fraction (EF) falls from 78% to 52%
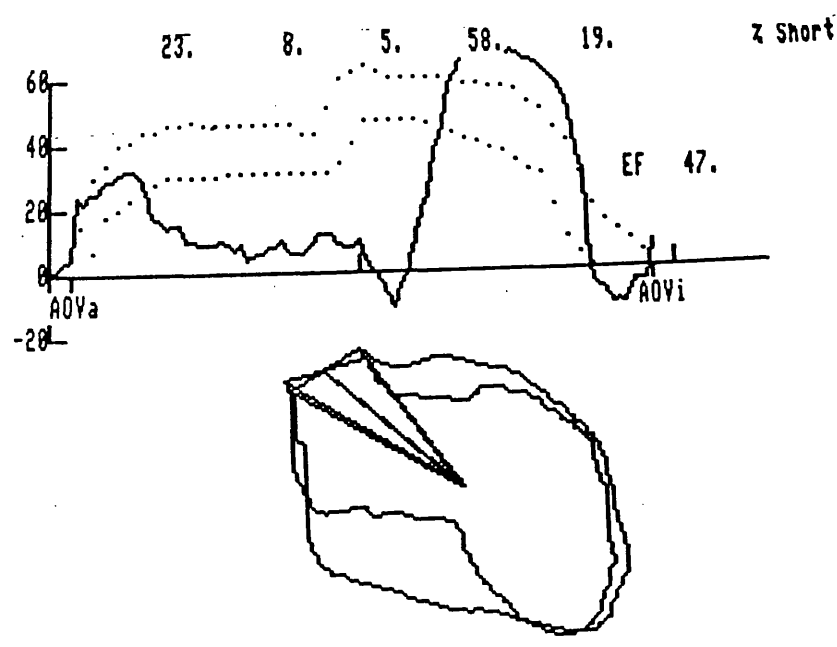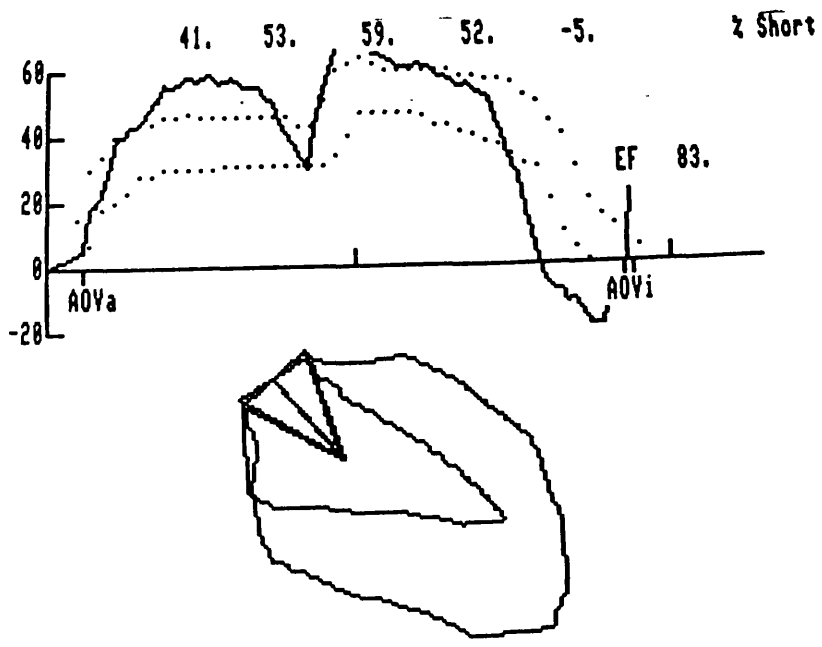
Fig. 5.

Example of LV wall motion before (top) and during (bottom)
LAD PTCA. Shortening of anterobasal, anterior and apical
segments is reduced during balloon inflation associated
with enhanced inferobasal contraction. Ejection fraction (EF)
has fallen from 83% to 47%.

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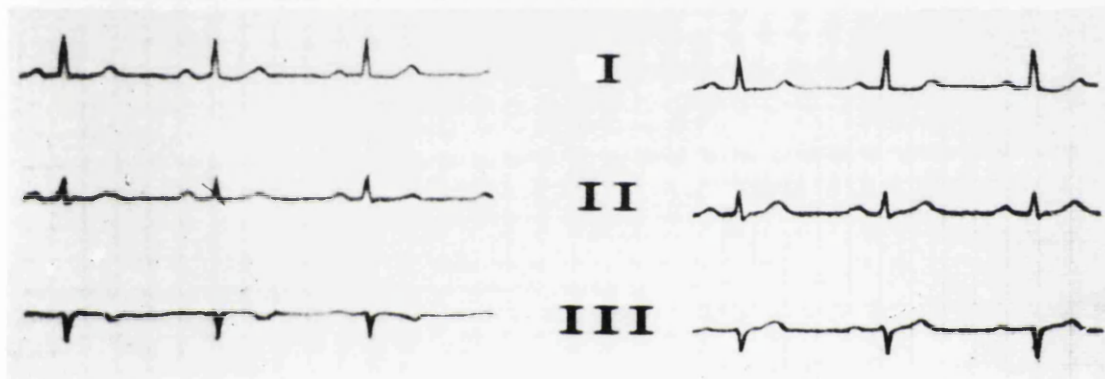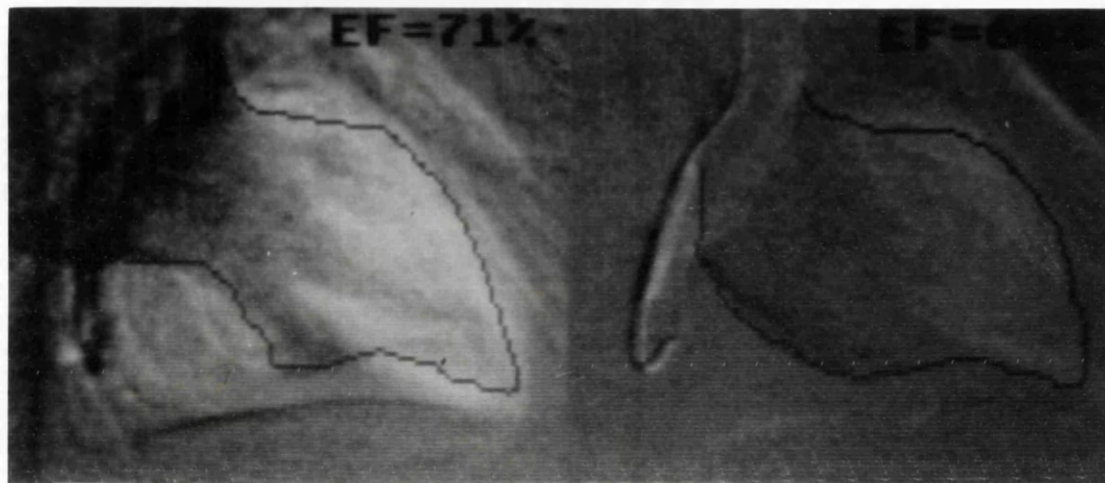
Fig. 6.

Outlined end-systolic images and ECG before (left) and during (right) right coronary PTCA. Inferobasal akinesis is apparent associated with normalisation of a previously inverted T wave in lead III. Ejection fraction (EF) has fallen from 71% to 60%
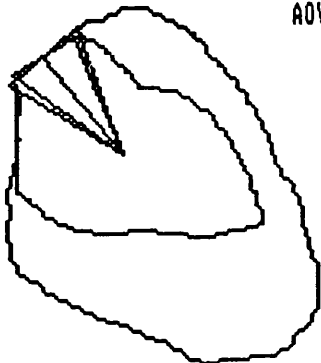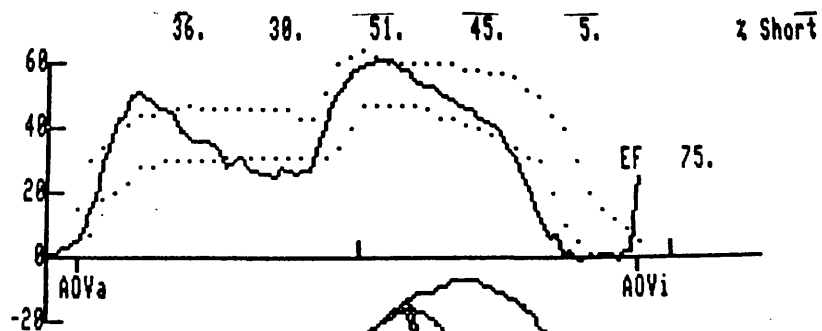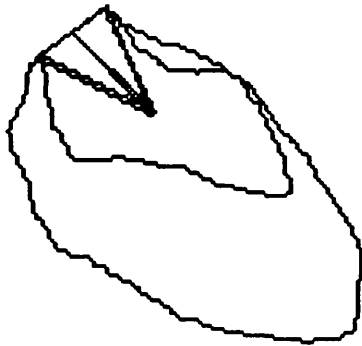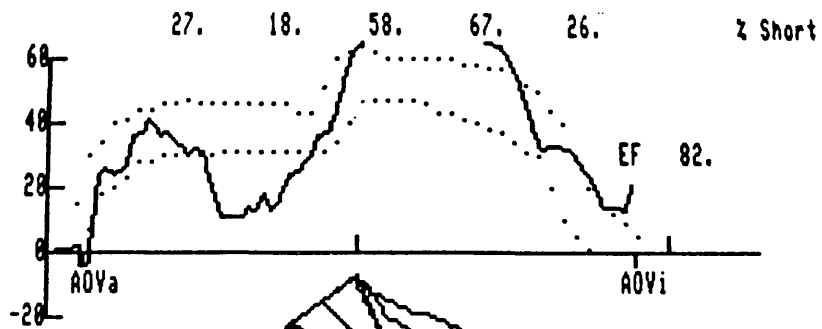
Fig. 7.

Example of LV wall motion before (top) and during (bottom)
right coronary PTCA. Inferior and inferobasal shortening is
reduced and ejection fraction (EF) has fallen from 82 to 75%
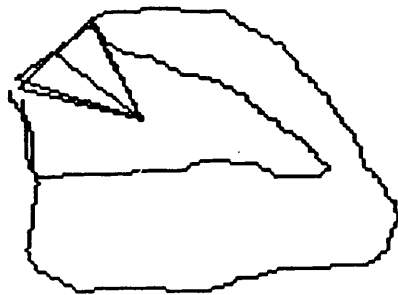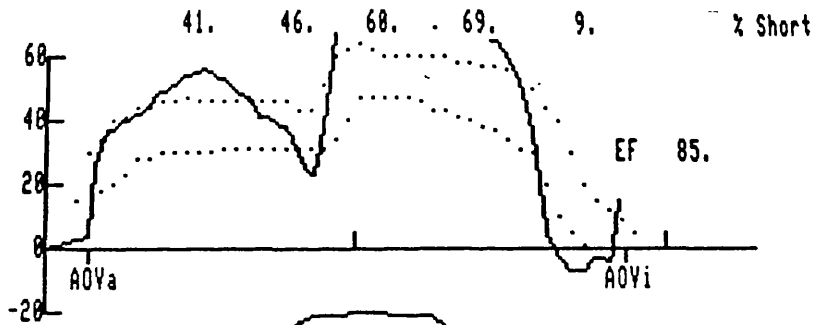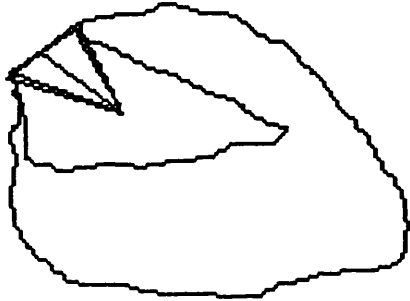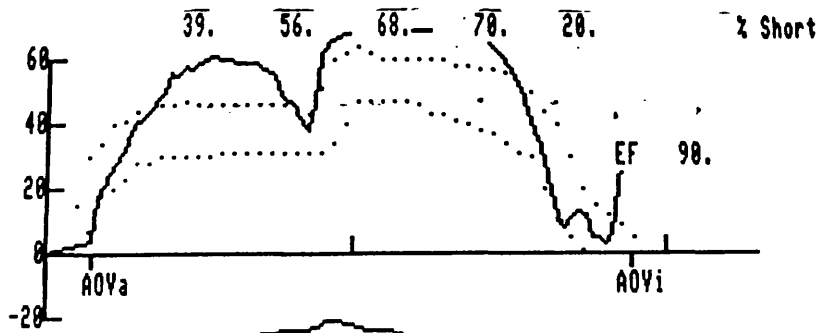
Fig. 8.

Example of LV wall motion before (top) and during (bottom)
circumflex PTCA. No discrete reuction in segmental shortening
occurs and ejection fraction falls only from 90% to 85%.

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3. ECG Changes (52 Patients)

Although LVEF fell during balloon inflation in 51 of the 52 patients, ST segment alteration developed in only 33. 32 patients developed ST elevation (mean 3.9 mm, range 1 - 9 mm). In all cases this occurred in leads overlying the myocardial territory supplied by the occluded artery. 25 patients developed ST depression (mean 1.9 mm, range 1 - 3 mm) while in 24 patients both ST elevation and depression were seen.

Before PTCA LVEF was similar in patients who subsequently developed ST elevation during balloon inflation (74%) compared with those who did not (72%, NS). However, during balloon inflation the fall in LVEF was more marked in those patients with ST elevation (21%) than in those without (9%, $p < 0.001$). Furthermore, there was a positive correlation between the magnitude of ST elevation during balloon inflation and the reduction in LVEF ($r = 0.637$, $p < 0.001$, Fig. 9.).

Similarly, there was a less strong though positive correlation between the degree of ST segment depression and the fall in LVEF, ($r = 0.396$, $p < 0.01$).
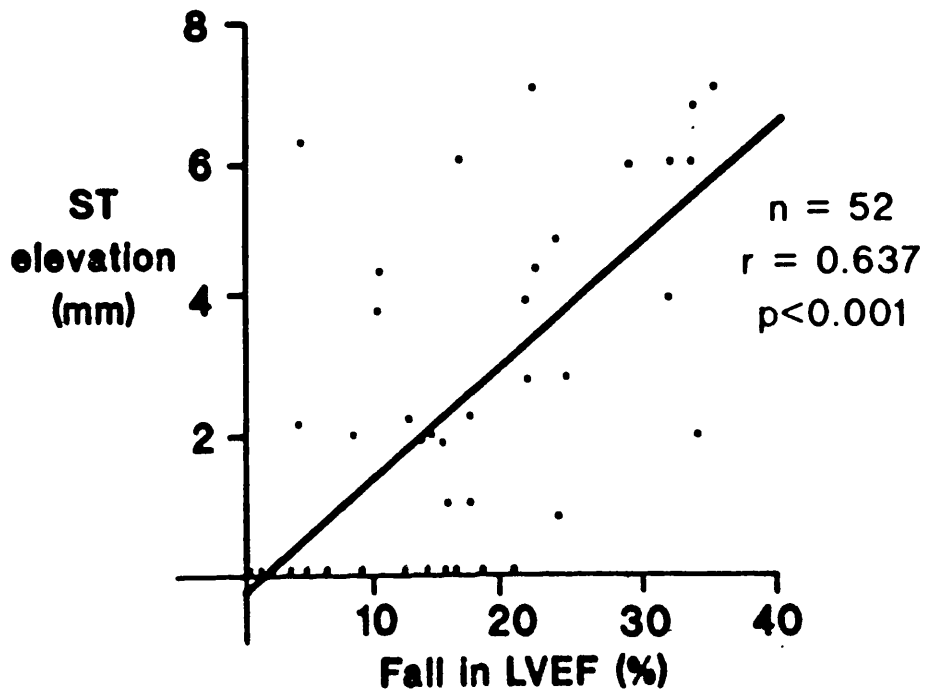
Fig. 9.

Relationship between the fall in left ventricular ejection fraction (LVEF) and the magnitude of ST segment elevation during balloon inflation.

DISCUSSION

EFFECT OF BALLOON INFLATION ON GLOBAL LV FUNCTION

Before PTCA in the 52 patients studied mean LVEF was within normal limits and regional wall motion of the 5 segments analysed was also within the range derived from 10 normal subjects. The limitations of using such a control group are discussed later.

During PTCA the mean fall in LVEF was from 73% to 57%. This is similar to the experience of other workers. Serruys (21) noted a fall from 62% to 48% after 50 seconds of balloon occlusion. The fall in LVEF in the present study (16%) is similar to the decrease that he reported (14%).

Doorey (22) noted a similar fall from 66% to 44% in the absence of nitrate. Following the administration of nitrate LVEF during PTCA fell to a lesser degree from 66% to 49%. Bertrand (23) noted a fall from 73% to 45% which is in keeping with the present findings.

All the studies referred to above examined only LAD balloon inflation. In the 35 patients in the present series who underwent LAD PTCA, LVEF fell from 74% to 55%.

Previous studies have not examined global LV performance in patients undergoing RCA or LCX PTCA. This study shows that reduction in LVEF is significantly more pronounced during LAD PTCA (19%) than during either right (10%) or cirumflex (8%) inflation. This would be compatible with our knowledge of the coronary circulation, the LAD supplying the majority of

the anterior LV wall, septum and apex. Although in all the right coronary angioplasties examined, the RCA was the dominant artery, giving rise to a posterior descending branch, the mass of myocardium supplied is less than that subtended by the LAD. The size of the circumflex circulation in patients is variable. In some patients the system may be quite small particularly if there are many inferior left ventricular branches arising from the right coronary artery or large diagonal branches arising from the LAD. The 30 degrees RAO projection that was used may be another factor accounting for the small decrease in ejection fraction during circumflex inflation. This does not profile the lateral surface of the ventricle and therefore may not be the most sensitive projection in which to detect wall motion abnormalities consequent on circumflex artery occlusion. This is discussed more fully later and in Chapter 11.

EFFECTS OF BALLOON OCCLUSION ON REGIONAL WALL MOTION

In this study it was found that balloon inflation in the LAD predictably produced deterioration in anterobasal, anterior and apical segments. These findings are in keeping with those of other workers. Doorey (22) also demonstrated inferoapical dysfunction and noted that only antero- and inferobasal segmental shortening failed to decrease significantly. Wohlgelernter (17) similarly showed inferoapical dysfunction in addition to apical and septal changes.
The present study also showed a significant increase in

inferobasal contraction in this group. The mechanism of such enhanced inferobasal contraction is uncertain and discussed further in Chapter 8. This augmentation was not observed by Wohlgelernter (17) or Alam (16).However, in Doorey's study (22) infero- apical and mid inferior segment shortening increased during LAD PTCA after the administration of nitroglycerin, in comparison to that during PTCA without nitroglycerin. Although inferobasal contraction was also greater during LAD PTCA with nitroglycerin, it was not significantly so.

All patients in the present study routinely received a nitrate as part of their pre-medication and therefore the specific role of nitrates in improving segmental function remote from the primary ischaemic territory was not assessed. This study has shown that both inferior and apical contraction deteriorated during RCA PTCA. Few workers have examined the effects of balloon inflation during right coronary PTCA. Alam's study (16) demonstrated that during RCA PTCA abnormal wall motion was most noticeable posteriorly while Hauser (15) demonstrated deterioration in inferior contraction. Visser (18) studied only 2 patients during right coronary occlusion but showed that the degree of abnormality, expressed as a wall motion score, was less than that during LAD inflation. Furthermore, although LV size index increased from 170mm to 196mm during LAD PTCA these changes were less pronounced during RCA PTCA. This suggests that RCA balloon occlusion may result in a less detrimental effect on global and regional LV performance than LAD

inflation.   The results of the present study support this view in that LVEF fell to a greater extent during LAD PTCA than during RCA PTCA.

The specific effect of circumflex occlusion on regional LV performance has only been reported by Alam (16) and Hauser (15). Alam observed the effect of both LAD and circumflex occlusion in one patient who developed reduced systolic excursion of both septum and posterior walls. Hauser showed no change in wall motion on 2-Dimensional echocardiography during circumflex occlusion in one patient. He considered that this may have been due to the fact that this patient underwent only a 30 second inflation. However, any wall motion abnormality would probably have occurred by this stage. The present data on 8 patients showing no significant change in any segments during circumflex inflation, suggests that it is more likely that LV segments rendered ischaemic by circumflex occlusion are less amenable to either echocardiographic or ventriculographic assessment. As individual LV segments contribute to global contraction, this would also account for LVEF during circumflex PTCA falling only to 61%, significantly less than during LAD PTCA. As discussed later, abnormal wall motion during circumflex PTCA may have been detected using an LAO projection which better profiles the lateral LV wall compared with RAO.

The effects of diagonal balloon occlusion on segmental wall motion have not been previously described. Only 2 patients were assessed in this study and both demonstrated anterior and apical dysfunction. Interestingly, inferobasal

contraction increased but in view of the small number of patients in this group these changes were not significant.

ECG CHANGES

During PTCA 12 lead ECG monitoring demonstrated ST segment alteration in 33 of 52 patients (63%). In Hauser's (15) study only 8 of 18 patients (44%) developed ST change during LAD PTCA although this was incorporating a 6 limb lead ECG system together with lead V5. In contrast, 10 of 12 patients (83%) in Alam's study developed ST change (16). Wohlgelernter (17), using a 12 lead system in 14 patients recorded ST change in 9 (64%), but confirmed that this was more frequent than with using only a 3 lead system. Visser's (18) study of 15 patients showed ST change in only 4 (27%) although again, only limb leads were used.

Faletra (19) similarly reported a low incidence of ST change in only 2 of 9 (22%) patients while Khaja (20) showed ST alteration in 9 of 15 (60%) patients. Doorey's study of 10 patients revealed ST change in 7 (70%) but only 3 leads were monitored (22).

The incidence of ST change in this study is similar to other reported series. It has confirmed that the left ventricle can become ischaemic in the absence of significant ECG change. However, the magnitude of global LV ischaemia as manifest by a fall in LVEF correlated significantly with the degree of ST segment elevation and to a lesser extent with ST segment depression. This suggests that ST alteration is an

index of the degree of LV ischaemia during PTCA rather than its presence.

Recent work by Friedman (44) has suggested that the ability of the ECG to detect ischaemia during PTCA may be enhanced by using intracoronary ECG. Thus, unipolar ECGs are recorded via the tip of the guidewire positioned distal to the coronary stenosis being treated. He has shown that in 25 patients undergoing 29 dilatations ST segment elevation or peaking of the T wave occurred in 21 instances on intracoronary monitoring. However, monitoring three surface ECG leads detected ST change in only 9 instances. In all these 9 cases the intracoronary ECG also detected ST change but at an earlier stage and reflected to a greater degree. This work is open to criticism as only a 3 or at most 4 lead system was used to monitor the surface ECG and these leads were chosen as to reflect "likely areas of reversible ischaemia" during PTCA. Thus 6 patients undergoing LAD PTCA were only monitored with leads 1, AVL and V6 which may detect lateral but not anterior LV ischaemia. A 12 lead ECG system was used in the present study. The use of special electrodes that did not interfere with fluoroscopy was clearly important in this regard.

Methods

All the 52 patients reported in this section had normal LV contraction as suggested by diagnostic cine left ventriculography before the PTCA procedure. They were therefore selected for this study as being most likely to

demonstrate a wall motion abnormality during balloon occlusion. Reviewing the data in Table 2. it can be seen that mean segmental shortening for all patients before PTCA was within a normal range. This range was derived from 10 other patients who underwent intravenous digital left ventriculography as part of a separate study. They had been shown to have normal coronary arteries and normal LV contraction with cineangiography and it was felt acceptable to use this group as a reference range for our method of wall motion analysis. It is appreciated that such a group cannot be regarded as entirely 'normal' as they had previously presented with a symptom suggesting cardiac pathology in order to justify invasive cardiac investigation. Any study using such a group suffers from this limitation and the present study is no exception. However it should be noted the main results of this work relate to the change in LV performance within patients, each acting as his own control. Thus the requirement for a truely valid control group for comparison is lessened.

Ideally, to examine LV changes during PTCA a control ventriculogram should be performed immediately prior to the study inflation. In these studies, this was undertaken prior to the procedure and therefore between 1 and 7 balloon inflations may have occurred before the study inflation. This was considered acceptable as a control study immediately before inflation would necessitate the withdrawl of the deflated balloon. This would be required in order to ensure

that it did not impede anterograde coronary flow and produce LV ischaemic changes in the baseline study. The balloon would then have to be repositioned for the study inflation. Such recrossing of partially dilated lesions can prejudice the outcome of PTCA and this was therefore considered unwarranted.

Patients were not studied during the same balloon inflation. Although most studies were planned for the third inflation, this protocol could not be adhered to in all cases for practical reasons e.g unsatisfactory balloon positioning. In any event, the effect of ballon inflation on LV performance did not appear to be influenced by the number of preceeding inflations as the fall in LV ejection fraction was no different between patients studied during the 3rd, 4th or subsequent inflations.

Left ventriculography was performed after at least 20 seconds as all previous studies had documented LV abnormalities by that time (14-19). In addition this allowed time to adjust the position of the image intensifier for the required projection.

The majority of the patients studied were taking anti-anginal medication. In addition, they were given a long acting nitrate and calcium antagonist as premedication for the PTCA procedure and such agents may well have modified the ischaemic consequences of balloon occlusion. However, it was considered unacceptable to withold such treatment particularly as the outcome of the procedure may have been jeopardised. Despite the presence of these agents ischaemic

abnormalities were still documented during PTCA and as any
drug effect would also have been operating during the
baseline study patients would still be acting as their own
controls.

The effect of contrast medium on ECG analysis is important.
For this reason ST changes were measured immediately prior to
contrast injection for ventriclography and nonionic medium
was used in order to minimise any unwanted ECG effects
(34,35). In addition, a check was made that the ECG had
returned to baseline before the next balloon inflation in
order to ensure that any selective coronary injections of
contrast did not interfere with ECG analysis.

The 30 degrees RAO projection that was used in this study
confers important constraints on the interpretation of the
results. Whereas anteroapical wall motion was impaired during
LAD PTCA and inferoapical contraction modified during RCA
dilatation, no specific wall motion abnormality was seen in
the group of 8 patients undergoing LCX inflation. In practice
it is recognised that occlusion of the main circumflex artery
does produce wall motion abnormality. In a RAO projection
anteroapical or inferoapical dysfunction may be apparent but
posterior or lateral abnormalities are better appreciated with
LAO or left lateral ventriculography. As the London Chest
Hospital was not equipped with biplane angiographic
facilities, rather than perform 2 ventriculograms in
different projections during PTCA, we confined ourselves to
only one view. As a result significant wall motion change

during LCX PTCA was not apparent and as the fractional shortening of individual LV segments contributes to global ejection fraction this too appeared to be modified to a lesser degree than that during LAD or RCA PTCA. It would be inappropriate to conclude from these data that LCX occlusion cannot produce marked impairment of LV performance and this remains a limitation of this study. However, it should be appreciated that in those subgroups specifically compared with respect to changes in regional wall motion, only those patients undergoing LAD PTCA were examined.

CHAPTER FOUR

PROTECTIVE ROLE OF COLLATERAL VESSELS DURING PTCA

Introduction

In the early 1900's it was observed pathologically that the extent of myocardial damage associated with coronary occlusion was not entirely determined by the muscle mass apparently dependent on that artery (45,46). Thus the existence of a coronary collateral circulation in man was proposed. Fulton's (47) work using stereoarteriography in the 1960's further demonstrated the existence of collateral vessels. His association between the degree of collateralisation and the magnitude of myocardial damage suggested the functional importance of the collateral circulation in man.

It would be easy to draw the conclusion that collateral vessels protect the myocardium from threatened ischaemia. Fulton's observations however are accompanied by the reservation that it was not possible to determine whether collaterals were already present at the time of coronary occlusion or whether they had developed subsequently. Thus, prospective studies had to await a method of examining the coronary circulation in life with selective coronary arteriography.

Oldham (48) studied the distribution of bypass graft flow perioperatively with labelled macroaggregates and showed that the area of myocardium perfused was independent of the presence or absence of angiographically demonstrable

collateral vessels. Clearly this work has to be viewed with the appreciation that the patients studied were undergoing coronary artery surgery and therefore that their collateral circulation was possibly inadequate. In any event, their conclusion echoed that of Gorlin in 1976: "coronary collaterals in man are more an indication of severe regional ischaemia (present or potential) than a sign of biological 'compensation' for a perfusion deficit" (49).

The question of whether collateral vessels in patients with single vessel disease exert a protective effect during exercise testing, was addressed by Tubau (50). Exercise duration and both the development and magnitude of ST segment depression was no different in those with, compared to those without angiographically demonstrable collaterals. However perfusion defects on Thallium scintigraphy were more frequent, and the number of myocardial segments involved was greater, in patients without collaterals, suggesting that these vessels may well have a protective function.

These findings are supported by those of Kolibash (51), although he demonstrated marked variation. While in some patients collaterals were highly effective in maintaining myocardial perfusion, in others they appeared to be of no significance.

PTCA is a technique which involves the rapid occlusion of a coronary artery with a balloon. Hill (52) was thus able to study the rate of development and physiological significance of collateral vessels during balloon coronary occlusion using

contralateral coronary arterial injections. He showed that collaterals can be demonstrated during the first and subsequent balloon inflations even though they were not demonstrable prior to PTCA. The degree of myocardial ischaemia during balloon inflation as manifest by angina, ST segment alteration or elevation in pulmonary artery wedge pressure, decreased with repeated inflations in only one of six patients. However, this did not correlate with the ability to visualise the distal arterial segment filling via collaterals. He concluded that the acute development of collaterals was possible but that their physiological role during threatened ischaemia was inconsistent.

This conclusion is not entirely valid as he was demonstrating the acute visualisation of collaterals rather than their development. These vessels may only be demonstrated angiographically when the degree of proximal narrowing is great enough to reduce anterograde flow sufficiently and thus allow distal filling by collaterals.

The presence of collaterals has also been demonstrated in patients without significant fixed coronary obstruction who occluded a coronary artery as a result of either spontaneous, or ergonovine induced spasm (53). Contralateral contrast injection demonstrated the transient appearance of collaterals which disappeared when the spastic artery became patent. This suggests that collaterals may develop without the stimulus of a persistent pressure gradient between coronary systems.

Elayada (54) attempted to relate the degree of collateral

circulation with the extent of LV wall motion abnormality in the subtended territory. He confirmed the popular view that collateral vessels could not be visualised angiographically unless there was proximal total or 'near-total' occlusion. Furthermore there was no difference in regional LV function between patients with good, poor or absent collaterals. His conclusions have to be tempered in the same way as those of Fulton i.e. his study was retrospective and cannot address the question of whether collaterals had been present at the time of coronary occlusion.

Predictably, collaterals have been shown to disappear after successful PTCA (55), again supporting the view that their appearance is dependent on the presence of a major proximal stenosis and therefore a pressure difference between coronary systems.

The haemodynamic contribution of collaterals to the coronary circulation was assessed by Probst (56) who measured the pressure distal to the inflated angioplasty balloon during PTCA. This 'occlusion pressure' correlated with the extent of the collateral supply and remained constant through successive inflations. Probst did not examine the degree of myocardial ischaemia during balloon inflation and relate this to either the occlusion pressure or the degree of collateral filling.

The latter question was addressed by Yamagishi (57) during coronary artery spasm. Those patients without collateral vessels demonstrated during episodes of ergonovine induced

spasm had a higher pulmonary artery diastolic pressure compared to those with collaterals. In addition great cardiac vein flow decreased further and ST segment elevation was more frequent during coronary spasm in patients without visible collaterals.

Freedman (58) supported the view that collaterals are only visualised when coronary luminal narrowing was in excess of 90%. He noted that in patients with totally obstructed arteries the presence of collateral vessels was more frequently associated with non Q wave infarction than Q wave infarction. He suggested that collateral flow may protect from Q wave infarction but observed that the presence of collaterals did not prevent execise induced ischaemia as judged by Thallium imaging. Once again, such a conclusion is not entirely valid as the state of the coronary circulation was not apparent at the time of coronary occlusion. An infarct substantial enough to produce Q waves may equally well have damaged the collateral circulation in addition to myocardium.

A prospective study was undertaken by Nestico (59) who followed patients with single vessel disease for a mean of 82 months. He noted that the incidence of cardiac events - albeit low at 6.4% - was no different between those with collaterals and those without.

Recent studies by Rentrop (60) and Cohen (61) have shed important light on the demonstration of collateral vessels and their functional significance during PTCA. They showed that during balloon inflation the degree of collateral

filling of the distal arterial segment, increased. Furthermore, the extent of the collateral circulation correlated inversely with both the hypocontractile perimeter of the LV demonstrated with echocardiography and the sum of ST segment elevation consequent on balloon occlusion. Angina during balloon inflation also occurred more frequently in patients with poor collaterals than in those with a more extensive collateral system.

Many of the observations of the collateral circulation in man have been undertaken after coronary occlusion, and any resulting myocardial damage, has occurred. Therefore inferences cannot be drawn concerning any potentially protective role. PTCA allows a prospective examination of the collateral circulation to be undertaken, and therefore their functional significance to be determined. Using intravenous digital subtraction ventriculography the present study has assessed the degree to which collateral vessels may protect the myocardium during episodes of threatened ischaemia resulting from balloon inflation.

Patients and Methods

Diagnostic coronary arteriograms undertaken before PTCA were reviewed by 2 observers in order to quantify the degree of any collateral circulation. Selective arteriograms were performed in multiple projections and incorporated 3 to 5 ml injections of contrast injected by hand over a period of 1 to 3 seconds. Cine recording was continued after each injection

until it was apparent that there was no further vessel opacification. Collateral supply was then graded according to a previously published method (61) which expresses the degree of collateral filling of the distal arterial segment as a numerical score: No collateral vessels visible = 0; collateral vessels visible = 1; opacification of < 50% distal arterial segment = 2; opacification > 50% distal arterial segment = 3.

Results

Of all the 52 patients studied 17 had demonstrable collateral supply to the arterial segment distal to the target stenosis prior to PTCA (mean collateral grade = 1.8) .

Global LV Performance

There was no difference in control LVEF between the 35 patients without and the 17 patients with collateral vessels (71% vs 76%, NS). During balloon inflation LVEF fell in both groups to 54% and 63% respectively, (p< 0.001 for both groups). LVEF during inflation was significantly lower in the group without collaterals (p< 0.02).

There was an inverse correlation between the degree of the collateral supply and both ST elevation (r=-0.397, p< 0.005) and ST depression (r = -0.297, p<0.025) during PTCA.

Regional LV Performance (27 patients)

In order to examine the effect of collateral vessels on

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regional LV wall motion only those patients with single vessel disease undergoing LAD PTCA were studied (Patient Nos. 1,3,5,7,10,12,17,18,22,25-28,31-34,39,40,42-45,49-52 on Table 1). In all cases the target stenosis was proximal to the first diagonal branch. There were 27 such patients of whom 15 had no angiographically demonstrable collaterals, (Group 1) while the remaining 12 patients had some degree of collateral supply (mean collateral grade = 1.7, Group 2). The severity of coronary obstruction was greater in group 2 than in group 1 (94% v 86%, p<0.05). Control LVEF was no different between these 2 groups (74% vs 78% respectively, NS).

During balloon inflation LVEF fell to 50% in Group 1 (p< 0.001) but only to 66% in Group 2 (p< 0.001). The magnitude of this fall was significantly less in Group 2 compared with Group 1 (12% vs 23%, p < 0.01). In these patients there was an inverse correlation between the fall in LVEF and the extent of collateral supply, (r = -0.446, p < 0.01, Fig.10).

Tables 6 - 8. summarise LV segmental wall motion before and during PTCA and compares the 15 patients without collateral vessels (Group 1) with the 12 in whom collateral vessels could be demonstrated angiographically (Group 2). As can be seen there were significant differences between groups. Apical regional shortening during PTCA was lower in those patients without collaterals (11%) than in those with (26%, p< 0.05, Table 8.), and a significant fall in anterobasal contraction was confined to Group 1. (Table 6.).
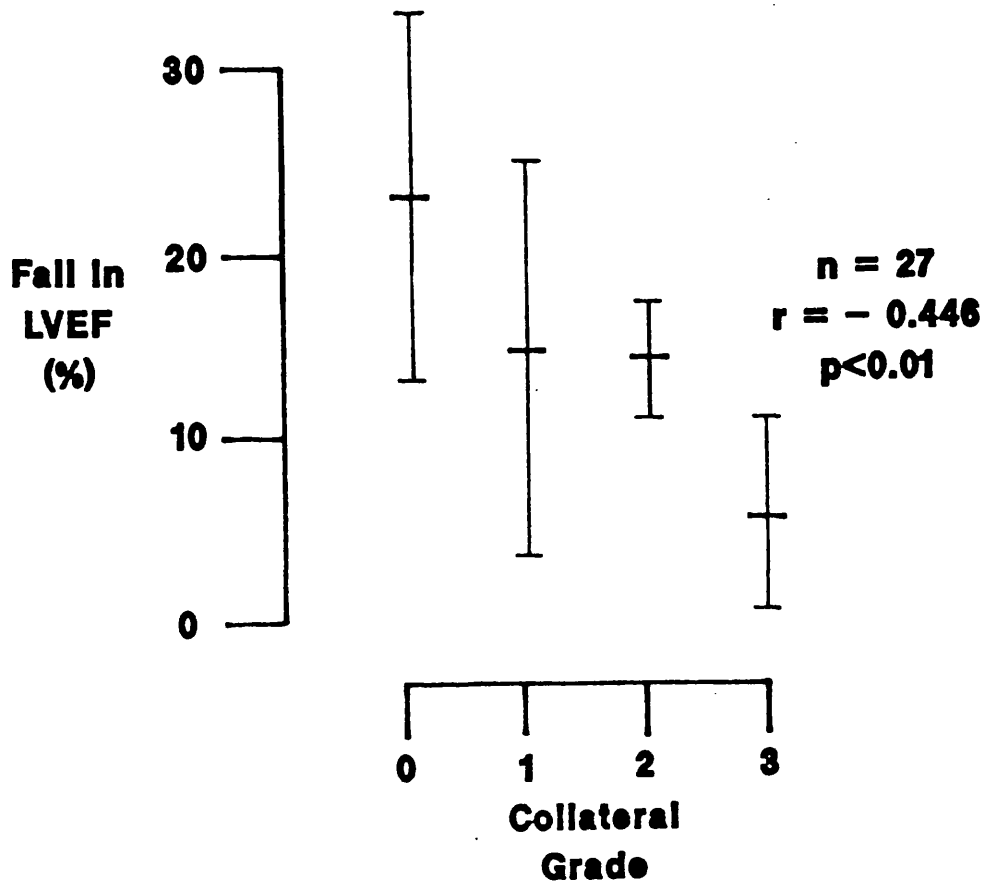
Fig. 10.

Relationship between the collateral supply and the fall in left ventricular ejection fraction (LVEF) in patients undergoing LAD balloon inflation. Horizontal bars = means (SD)

Table 6.

LV Regional Wall Motion Before and During PTCA

in Patients With and Without Collateral Supply

Values = mean regional shortening (%) (SD)

LV Segment	GROUP 1 (n=15) (no collaterals)			GROUP 2 (n=12) (with collaterals)		
	Pre-PTCA	During PTCA	p	Pre-PTCA	During PTCA	p
Anterobasal	37(9)	24(13)	<0.01	38(11)	33(17)	NS
Anterior	38(9)	12(11)	<0.001	42(11)	19(24)	<0.001
Apical	51(8)	11(14)	<0.001	55(12)	26(22)	<0.001
Inferior	48(13)	43(14)	NS	48(15)	53(13)	NS
Inferobasal	8(11)	23(17)	<0.01	5(14)	27(23)	<0.01

Table 7.

Reduction in % Regional Shortening Compared Between Patients
With and Without Collateral Supply

Values = mean % (SD) Negative values = increased contraction

LV Segment	Group 1 no collaterals (n=15)	Group 2 collaterals (n=12)	p
Anterobasal	13(15)	5(12)	NS
Anterior	26(13)	23(17)	NS
Apical	40(18)	29(20)	NS
Inferior	5(18)	-5(10)	NS
Inferobasal	-15(18)	-22(23)	NS

Table 8.

LV Segmental Wall Motion Before and During LAD PTCA in
Patients Without (Group 1) and With (Group 2) Collaterals
Values = mean% (SD)

	Pre-PTCA			During PTCA		
LV Segment	Group 1	Group 2	p	Group 1	Group 2	p
Anterobasal	37(9)	38(11)	NS	24(13)	33(17)	NS
Anterior	38(9)	42(11)	NS	12(11)	19(24)	NS
Apical	51(8)	55(12)	NS	11(14)	26(22)	<0.05
Inferior	48(13)	48(15)	NS	43(14)	53(13)	NS
Inferobasal	8(11)	5(14)	NS	23(17)	27(23)	NS

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ECG Changes

The degree of ST segment elevation during LAD balloon inflation was greater in Group 1 (4.9 mm) than in Group 2 (0.9 mm, p< 0.001). Similarly, the magnitude of ST segment depression was greater in Group 1 (1.4 mm) compared with Group 2 (0.4 mm, p< 0.02). In addition, there was an inverse correlation between the magnitude of both ST segment elevation and depression during PTCA, and the extent of the collateral circulation, (r=-0.680, p< 0.001, Fig. 11; r = -0.444, p< 0.01 respectively).
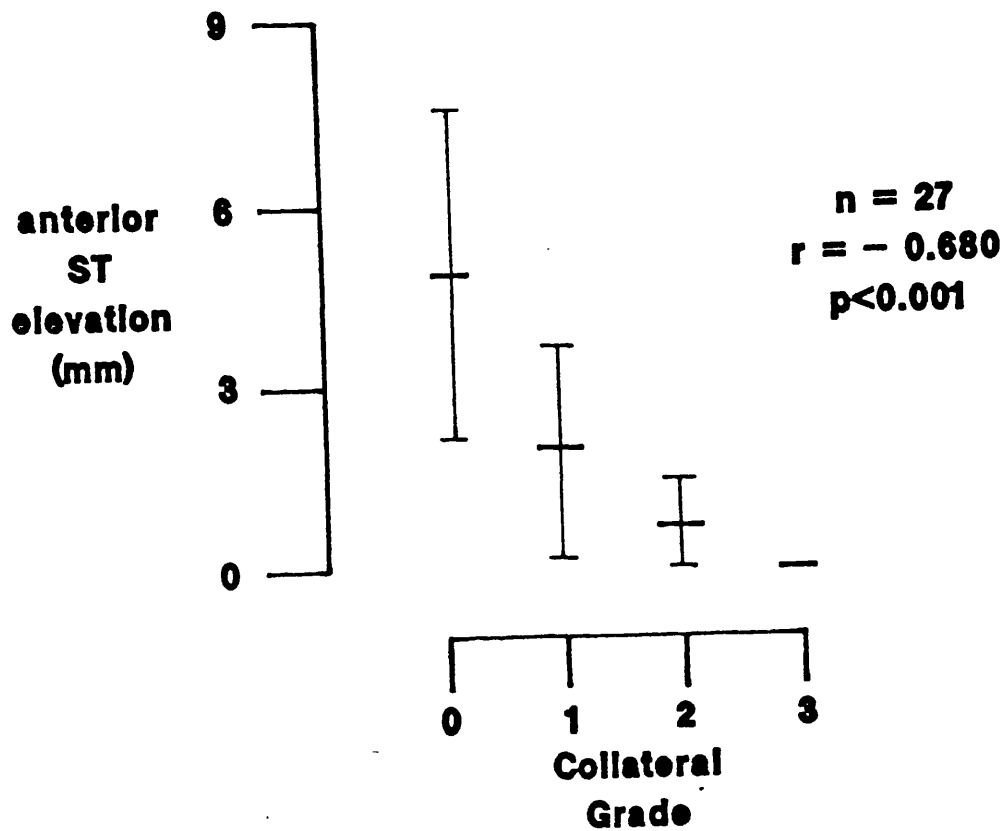
Fig. 11.

Relationship between the collateral supply and the degree of
ST segment elevation during LAD balloon inflation
Horizontal bars = means (SD)

Discussion

Previous studies addressing the potential protective role of collateral vessels have related the degree of left ventricular dysfunction following thrombotic coronary occlusion to the extent of the collateral circulation demonstrated subsequently. Although some workers have shown reduced left ventricular damage associated with the presence of an extensive collateral system (47), this is not the finding of others (54). Such retrospective studies have to be viewed with caution as the state of the coronary circulation at the time of vessel occlusion is unknown. PTCA has now allowed the development and functional role of these vessels to be further assessed.

Collateral vessels not apparent before PTCA can be demonstrated by contralateral coronary arteriography during balloon inflation (60), and those present before the procedure are no longer demonstrable after successful balloon dilatation (55).

In addition to their angiographic demonstration, their haemodynamic contribution has also been examined during PTCA (56). The pressure distal to the inflated angioplasty balloon has been shown to relate to the angiographic extent of the collateral supply.

The present study has assessed the functional role of the collateral circulation and has demonstrated that the manifestations of myocardial ischaemia consequent on balloon coronary occlusion are reduced in the presence of collateral vessels that fill the distal arterial segment. Furthermore,

the degree of ischaemia produced during PTCA correlated with the extent of the collateral supply.

These findings are in accord with other workers (61). Cohen examined the occurrence of anginal pain, together with both the degree of ST elevation and echocardiographic evidence of LV dysfunction, during balloon inflation. He related these findings to the collateral supply apparent during balloon coronary occlusion and demonstrated that these indices of myocardial ischaemia were reduced in the presence of collateral vessels.

The present study differs from that of Cohen's. Although a similar system was used to grade the collateral supply (60), collaterals were assessed before rather than during PTCA. As the ability to demonstrate collaterals angiographically is dependent in part on the degree of proximal arterial obstruction (58), this assessment of the collateral status may have been an underestimate. However, others (52) have shown that although collateral filling of a distal arterial segment may increase abruptly following balloon occlusion during PTCA, the protective effect of this apparent increase in flow is variable.

Even in the presence of an extensive collateral supply ventriculographic abnormalities were still apparent during PTCA. This finding is also shared by others who noted angina, ST elevation and LV dysfunction during balloon inflation despite the complete opacification of the index artery by collateral vessels (61). This suggests that even an abundant

collateral supply may be inadequate to completely protect potentially ischaemic myocardium. Previous studies have also shown that the presence of collaterals does not necessarily reduce the extent of exercise induced ischaemia (58) or the subsequent incidence of cardiac events (59). Furthermore as all the patients in the present study were limited by symptoms prior to PTCA, it might be predicted that their collateral circulation would not be entirely adequate.

Methods

The extent of the collateral circulation is usually assessed with selective coronary arteriography. This method may have limitations as a number of factors influence the appearance of collaterals following contralateral coronary contrast injection. As their opacification is at least partly dependent on a pressure gradient across coronary vascular beds, the pressure used for contrast injection, as well as the degree of proximal obstruction, are particularly relevent in determining their appearance. In addition, the presence of vasodilator drugs and the resolution of the angiographic equipment are also important.

In the patients studied, no attempt was made to standardise the pressure and flow rate of selective coronary contrast injections, the technique adopted being that used routinely for diagnostic studies. Vasodilators, in the form of a nitrate and a calcium channel blocker, were administered to all patients prior to PTCA in order to ameliorate ischaemia during the procedure and reduce any tendency to coronary

vasospasm. The specific effect of such drugs on the collateral circulation is unclear (62).

The role of the collateral circulation in patients with multivessel disease has not been spesifically addressed. The results in all 52 patients suggested that a collateral supply did confer benefit during PTCA and although the correlation was not close, this advantage did relate to the extent of collateralisation with repect to ST segment changes. When patients with only single vessel disease undergoing LAD PTCA were selected this relationship was closer despite fewer patients. This may relate to the whole group of 52 patients containing 15 with multivessel disease. The presence of additional coronary obstruction possibly in vessels supplying collaterals to the PTCA vessel, may have impaired any protective effect during balloon occlusion despite adequate collateral visualisation on the baseline arteriogram. Small patient numbers did not allow this interesting question to be addressed and this study therefore largely confined itself to only those patients without additional coronary disease.

Others have documented the degree of collateral filling during PTCA by contralateral coronary contrast injection during balloon inflation. We did not choose to do this as it would have required additional arterial access and thus increase the invasive nature of this study.

In conclusion, although the angiographic assessment of collateral vessels may have limitations, it does provide an indication of the quality of the collateral circulation and

this is supported by the results of the present study.

PTCA, by producing reversible, controlled coronary occlusion has allowed a prospective evaluation of the functional role of collateral vessels. ECG and left ventriculographic manifestations of ischaemia during balloon inflation are less pronounced in the presence of angiographically demonstrable collateral supply. This would support their protective role over myocardium at risk of ischaemia following coronary occlusion.

CHAPTER FIVE

EFFECT OF BALLOON INFLATION IN SINGLE AND MULTIVESSEL DISEASE

Introduction

The majority of previous studies that have examined the ischaemic consequences of balloon inflation during PTCA have been confined to patients with single vessel coronary disease. However, the expanding indications for PTCA has meant that an increasing proportion of patients treated with this technique have significant obstructive disease in more than one major coronary vessel. It is therefore relevant to this thesis to address the question of whether balloon occlusion during PTCA in patients with additional coronary disease imposes a greater ischaemic burden on the left ventricle than that in patients with only single vessel involvement.

In order to address this aspect the 52 patients described previously were examined.

Patients

Of the 52 patients described in Table 1. 37 had at least a 70% stenosis in a single vessel (SVD) while the remaining 15 patients had multivessel disease (MVD; 12 with 2VD, 3 with 3VD). The grade of the collateral supply to the arterial segment distal to the treated stenosis was similar in the 2 groups (mean collateral grade: 0.7 vs 0.3 respectively, NS).

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Results

Global LV Performance

Control LVEF in the 37 patients with single vessel disease was higher than that in the 15 patients with multivessel disease, (75% vs 68% respectively, p<0.02) During PTCA LVEF fell to 59% (p<0.001) in those with single vessel disease and to 51% (p< 0.001) in those with multivessel disease. Although LVEF during inflation was lower in those patients with multivessel disease, (p< 0.05), the magnitude of the fall in LVEF in each group was not different, (16% vs 17% respectively, NS).

ECG Changes

The magnitude of ST segment elevation produced by balloon inflation in the 37 patients with single vessel disease (2.4 mm) was no different to that in the remaining 15 patients with multivessel disease (2.3 mm, NS). Similarly, the degree of ST segment depression was not different between these two groups (0.8 mm vs 1.2 mm respectively, NS).

Regional LV Performance (35 Patients)

In order to examine regional LV performance only the patients undergoing LAD PTCA were assessed. There were 35 such patients of whom 27 had SVD (identified numerically in Chapter 4) and 8 MVD (Patient Nos. 4,13,19,20,24,36,47,48 in Table 1.) Baseline LVEF was also similar in the 2 subgroups (76% vs 70%, NS) as was the collateral grade (0.8 vs 0.6, NS). During balloon inflation in the LAD, LVEF fell to 57% in

those with SVD and to 48% in those with MVD. The magnitude of this fall was no different between subgroups (19% vs 22%, NS).

As seen from Tables 9 - 11 although changes in wall motion occurred during PTCA in both groups, there were no differences in regional LV contraction either before or during LAD balloon inflation between patients with single or multiple vessel disease.

Similarly, there was no difference between these 2 subgroups in the degree of either ST elevation, (3.2 mm vs 3.0 mm, NS) or ST depression (1.0 mm vs 1.0 mm respectively, NS) during LAD PTCA.

Table 9.

Changes in Regional Wall Motion During LAD PTCA in
Patients With Single (SVD) and Multivessel Disease (MVD)

Values = mean % shortening (SD)

LV Segment	SVD (n=27)			MVD (n=12)		
	Pre-PTCA	During PTCA	p	Pre-PTCA	During PTCA	p
Anterobasal	37(10)	28(15)	<0.002	36(11)	30(15)	NS
Anterior	40(10)	15(18)	<0.001	36(13)	8(16)	<0.002
Apical	53(10)	17(19)	<0.001	39(20)	3(13)	<0.01
Inferior	48(14)	47(14)	NS	47(7)	43(12)	NS
Inferobasal	7(12)	25(20)	<0.001	13(14)	24(7)	NS

Table 10.

Change in Segmental Shortening During PTCA. Comparison Between
Patients With Single (SVD) and Multivessel (MVD) Disease

Values = mean change % (SD).
Negative values = increased contraction

LV Segment	SVD (n=27)	MVD (n=8)	p
Anterobasal	10(14)	6(16)	NS
Anterior	25(15)	28(16)	NS
Apical	35(19)	36(22)	NS
Inferior	1(15)	3(16)	NS
Inferobasal	-18(20)	-11(14)	NS

Table 11.

Segmental Contraction Before and During LAD PTCA in patients

with Single Vessel (n = 27) and Multivessel Disease (n = 8)

Values = mean % shortening (SD)

(SVD = Single Vessel Disease, MVD = Multivessel Disease)

LV Segment	Pre-PTCA			During PTCA		
	SVD	MVD	p	SVD	MVD	p
Anterobasal	37(10)	36(11)	NS	28(15)	30(15)	NS
Anterior	40(10)	36(13)	NS	15(18)	8(16)	NS
Apical	53(10)	39(20)	NS	17(19)	3(13)	NS
Inferior	48(14)	47(7)	NS	47(14)	43(12)	NS
Inferobasal	7(12)	13(14)	NS	25(20)	24(7)	NS

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Discussion

Other studies have been concerned only with patients with single vessel disease with the exception of Visser's work (18) who included one with two vessel disease in his group of 15 patients. The present study has shown that up to 60 seconds of balloon inflation does not produce greater ischaemic manifestations in patients with multivessel disease compared with those with single vessel disease. The magnitude of ST segment change and fall in LVEF was no different between these two groups.

In order to assess the effect on regional wall motion, only those patients undergoing LAD PTCA were selected. In this group of 35 patients the degree of ST change and reduction in LVEF was no different in those with single compared with multivessel disease. Although anterior and apical wall motion to fall to a greater degree during LAD PTCA in the multivessel group, this difference was not significant.

It would be erroneous to suggest that multivessel disease does not impose a greater ischaemic burden on the left ventricle than single vessel disease in patients who sustain coronary occlusion. The outcome following a complication during angioplasty in multivessel disease is less favourable than that in patients with single vessel occlusion (63) and presumably reflects the consequences of coronary occlusion in the face of a reduced coronary reserve dependent on other vessels. Conceivably, assessment of left ventricular performance after 60 seconds of balloon occlusion may be inadequate to compare these two groups of patients in terms

of the consequences of protracted coronary occlusion.

Methods

Although it might have been anticipated that LV performance would have become more impaired during PTCA in patients with multivessel disease, this was not the case in this study. As suggested the maximum study inflation time was limited to 60 seconds and this may have been relevant. Another factor in patients with multivessel disease who sustain coronary occlusion must be the degree to which nonoccluded vessels can contribute to any collateral recruitment. We demonstrated that in patients undergoing LAD PTCA the degree of collateral supply was no different between patients with and without additional disease. However, as discussed in the previous chapter the protective ability of collateral vessels in patients with multivessel disease is unclear.

In order to address this question and ideal comparison would include patients undergoing LAD PTCA in whom collateral supply to the LAD itself is clearly supplied by either the right or circumflex arteries. Patients could be separated into those with additional RCA or LCX disease and those without, and the effect of such additional coronary obstruction in collateralising vessels would then be assessed.

Unfortunately, small patient numbers did not allow this specific comparison to be made. Of the 35 patients undergoing LAD PTCA only 8 had multivessel disease and only in 3 of these was the LAD collateralised.

CHAPTER SIX

THE EFFECT OF SHORT AND LONG BALLOON INFLATIONS

Introduction

The duration of individual balloon inflation during PTCA is
variable. It is usually dependent on the degree to which the
patient tolerates balloon occlusion but in the absence of
symptoms that require the balloon to be deflated, operators
tend to use ECG monitoring as a guide to the duration of each
dilatation. Thus, marked ST segment elevation or frequent
ventricular ectopics may indicate that balloon inflation
should be terminated.

A current hypothesis, presently being tested, is whether or
not prolonged balloon inflation modifies the incidence of
restenosis after successful PTCA and there is experimental
work to support this notion (11). As there may be a trend in
favour of more prolonged inflation times, it was relevent for
this study to examine to what extent left ventricular
ischaemic abnormalities progress during the course of
coronary balloon occlusion.

Patients

The 52 patients previously described in Table 1. were divided
into 2 groups. Twenty-eight patients underwent digital
subtraction ventriculography after 20 seconds of balloon
inflation and the remaining 24 patients after 60 seconds.
There was no difference in the collateral grade between these
two groups (collateral grade: 0.5 vs 0.7 respectively, NS)

Global LV Performance

Control LVEF in the 28 patients studied after 20 seconds of balloon occlusion (74%) was no different to that in the 24 patients studied after 60 seconds (71%, NS). During balloon inflation LVEF fell similarly in both groups to 58% and 56% respectively (NS), the magnitude of this fall being no different between groups (16% vs 15%, NS).

ECG Changes

There was no difference between the 28 patients studied after 20 seconds of balloon coronary occlusion and the 24 studied after 60 seconds in terms of the degree of ST segment elevation (2.9 vs 1.7 mm, NS) or of ST segment depression (0.9 vs 0.9 mm, NS) respectively.

Regional LV Performance (27 patients)

In order to compare the effect of 20 and 60 second balloon inflations on segmental LV contraction only patients with single vessel disease undergoing LAD PTCA were compared. There were 27 such patients of whom 17 were studied after 20 seconds and the remaining 10 after 60 seconds of balloon occlusion. The collateral grade was not different between these 2 groups (0.6 vs 1.0 respectively, NS).

In these 27 patients, as in the whole group, the magnitude of ST segment elevation or depression was independent of 20 or 60 second inflations. Thus, mean ST elevation was 3.8 mm in patients studied after 20 seconds and 2.1 mm after 60 seconds (NS). Similarly, the results for ST depression were 1.0 mm and 0.6 mm respectively (NS).

There was no difference in LVEF between these 2 groups before (74% vs 78%, NS) or during PTCA, (56% vs 59%, NS).

Tables 12 - 14 show segmental LV contraction before and during PTCA in the patients studied after 20 and 60 seconds as well as a comparison of the changes in wall motion between patient groups. There were two differences between these groups. Inferobasal contraction during balloon inflation was greater in the group studied after 60 seconds (37%) than in those studied after 20 seconds (17%, p< 0.01, Table 14.). In addition, a significant fall in anterobasal contraction was confined to Group 1 (Table 12.).

Table 12.

Segmental Contraction During LAD PTCA in Patients
After 20 and 60 seconds of Balloon Inflation

Values = mean % (SD)

| LV Segment | 20 secs (n=17) | | | 60 secs (n=10) | | |
	Pre-PTCA	During PTCA	p	Pre-PTCA	During PTCA	p
Anterobasal	38(10)	27(15)	<0.02	36(9)	29(17)	NS
Anterior	38(11)	17(18)	<0.001	42(8)	12(19)	<0.001
Apical	51(11)	19(19)	<0.001	56(9)	14(21)	<0.001
Inferior	45(14)	45(12)	NS	54(12)	51(18)	NS
Inferobasal	4(9)	17(15)	<0.01	11(17)	37(20)	<0.01

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Table 13.

Change in Segmental Contraction During LAD PTCA. Comparison
Between Patients Studied after 20 and 60 Second Inflations

Values = mean % (SD). Negative Values = Increased Shortening

LV Segment	20 secs (n=17)	60 secs (n=10)	p
Anterobasal	11(16)	7(10)	NS
Anterior	22(14)	30(16)	NS
Apical	31(20)	42(17)	NS
Inferior	0(15)	3(17)	NS
Inferobasal	-13(16)	-26(25)	NS

Table 14.

LV regional Wall Motion during LAD PTCA in patients studied
after 20 (17 pts) or 60 Seconds (10 pts) of Balloon Inflation

Values = Mean Regional Shortening % (SD)

LV Segment	Pre-PTCA			During PTCA		
	20	60	p	20	60	p
Anterobasal	38(10)	36(9)	NS	27(15)	29(17)	NS
Anterior	38(11)	42(8)	NS	17(18)	12(19)	NS
Apical	51(11)	56(9)	NS	19(19)	14(21)	NS
Inferior	45(14)	54(12)	NS	45(12)	51(18)	NS
Inferobasal	4(9)	11(17)	NS	17(15)	37(20)	<0.01

Discussion

This study was unable to demonstrate any difference in ischaemic manifestations in patients studied after 60 seconds of balloon inflation compared to those after only 20 seconds. This suggests that there is no progression in the degree of myocardial ischaemia up to 60 seconds. The left ventricle was examined after 20 seconds as all previous workers have shown that left ventricular asynergy occurs within 20 seconds of balloon occlusion.

Observations vary as to when left ventricular dysfunction begins. Visser (18) reported the onset of LV dysfunction after 8 seconds while Das (14) noted asynergy after only 5 seconds.

There remains some question as to whether left ventricular dysfunction continues to deteriorate up to 60 seconds. In this study no difference was found in either the degree of ST segment elevation or the fall in LVEF between those patients studied after 20 seconds and those after 60 seconds of inflation. This is in common with other workers. Visser (18) observed the degree of LV dyskinesis was not related to the duration of balloon inflation. Furthermore, Bertrand (23) demonstrated that LVEF fell from 73% to 46% after 30 seconds and to 45% after 50 seconds suggesting that LV function had not deteriorated in the intervening 20 seconds.

In contrast, Hauser (15) using 2-D echo noted the onset of dysnergy at 19 seconds and described a rapid deterioration of regional LV contraction to dyskinesia. Wohlgelernter (17) also

described a gradual decline in LV function having started to deteriorate at 12 seconds. By 40 seconds 71% of ventricles studied were severely hypokinetic, the remainder were either akinetic or dyskinetic. After 60 seconds 29% were hypokinetic while a much larger proportion were now akinetic or dyskinetic. Serruys work also suggests this (21). After 20 seconds of occlusion LVEF fell from 61% to 54% while after 50 seconds LVEF fell to 48%. Although this was significantly less than control it is not stated whether this was significantly less than that after 20 seconds.

In terms of regional wall motion patients with single vessel disease undergoing LAD PTCA were specifically studied and showed no further deterioration in wall motion beyond 20 seconds. However, an increase in inferobasal contraction was documented after 60 seconds which was not apparent after 20 seconds. The mechanism of augmented contraction of the non-ischaemic segment is unclear and discussed in more detail in Chapter 8. However, it is possible that, following coronary occlusion, some time must elapse before such enhanced contraction can be recruited.

Methods

In order to address the effect of short and long balloon inflation on LV performance 20 and 60 second balloon inflations were chosen. 20 seconds of balloon occlusion was selected to represent short inflations because it has been well established by others that LV dysfunction after

coronary occlusion is apparent by this time. 60 seconds was chosen as a long inflation time because the operators involved with these patients' treatment were reluctant to maintain balloon inflation for longer periods particularly if there was accompanying ECG or clinical evidence of myocardial ischaemia. Subsequent experience and newer data has meant that operators are now more prepared to perform longer inflations in the knowledge that any LV dysfunction produced is unlikely to be permanent. Thus, with present experience, a better comparison of short and long inflations might comprise 20 and perhaps 180 seconds of balloon occlusion.

The recruitment of collateral vessels over the course of longer coronary balloon occlusion may have been one factor in the lack of difference between patients undergoing 20 and 60 second inflations. The initial collateral grade in patients having LAD PTCA was not different between those who subsequently underwent 20 or 60 second inflations. Although the collateral supply may have altered during the course of longer inflations, the limitations to this study discussed in Chapter 4. meant that we were not able to examine the collateral circulation during balloon occlusion.

Ideally, a comparison of short and long inflations should be undertaken in the same patient and others have performed such studies. The protocol for the present study however allowed only 3 ventriculograms and as we also intended to examine LV performance after PTCA we were limited to only one study during balloon inflation.

CHAPTER SEVEN

EFFECT OF BALLOON INFLATION ON LV VOLUMES AND THEIR RELATIONSHIP TO ECG R WAVE AMPLITUDE

Introduction

In 1977 Bonoris (64) suggested that changes in R wave amplitude during exercise may enhance the diagnostic accuracy of the exercise ECG in the investigation of patients with suspected coronary disease. This hypothesis was derived from work by Brody (65) 20 years earlier in which he postulated that the intracavity blood mass would influence the QRS complex of the surface ECG.

During normal exercise, an increase in stroke volume is achieved by a reduction of LV end-systolic volume and is accompanied by a fall in R wave amplitude. In patients with coronary artery disease the ventricular myocardium becomes ischaemic on exercise with both contraction and relaxation being abnormal. LV end-systolic volume rises while end-diastolic volume remains unchanged or increases. This is thought to be reflected in R wave amplitude which increases in a similar fashion. Such a change, together with any accompanying ST segment alteration, may increase the sensitivity and specificity of the exercise test. Analysis of R wave amplitude has also been found to be valuable in patients with resting ST-T abnormalities in whom the interpretation of further ST-T changes with exercise is questionable (66).

Although some workers have found changes in R wave amplitude similarly useful (67) this is not a universal experience. Others have not found exercise induced changes in R wave amplitude to be of diagnostic value (68-70,71). Furthermore, Battler (72) demonstrated only a poor correlation between QRS amplitudes and LV volumes.

Work by David (73) also showed R wave amplitude to be a poor indicator of LV volume. In addition he has shown that changes in R wave amplitude during ischaemia are more closely correlated with alteration in intra-myocardial conduction (74).

Previous studies which have examined LV dimensions during PTCA have demonstrated increases in LV volumes during balloon inflation, however analysis of R wave amplitude has not been undertaken.

As PTCA induces transient and predictable alteration in LV dimensions, this study was designed to clarify the relationship between R wave amplitude and LV volumes during episodes of myocardial ischaemia induced by balloon inflation.

Patients

The first 30 patients (Nos.1 - 30 on Table 1.) who underwent intravenous DSA during PTCA were analysed in this study. The method with which LV volumes were calculated has been described in Chapter 2. Correction was made for magnification and body surface area and therefore the values expressed are

absolute volumes. The method with which ECG R wave amplitude was determined has also been described and was in accordance with other previously published methods (67).

Results

LV Volumes

The results are summarised in Table 15. Before PTCA LV end-diastolic volume was 140 ml. During balloon inflation this increased by 6% to 148 ml but this change was not significant. In contrast end-systolic volume increased by 73% from 44 ml before PTCA to 76 ml during coronary occlusion, ($p < 0.001$, Fig. 12).

R Wave Amplitude

Mean R wave amplitude in leads V4 to V6 was 10.1 mm before PTCA. During balloon inflation this decreased by 12% to 8.9 mm, ($p < 0.01$). There was a significant inverse correlation between the change in LV end-systolic volume and alteration in R wave amplitude ($r = -0.371$, $p < 0.05$).

Table 15.

LV Volumes and R Wave Amplitude Before and During PTCA

(30 patients)

Values = mean (SD)

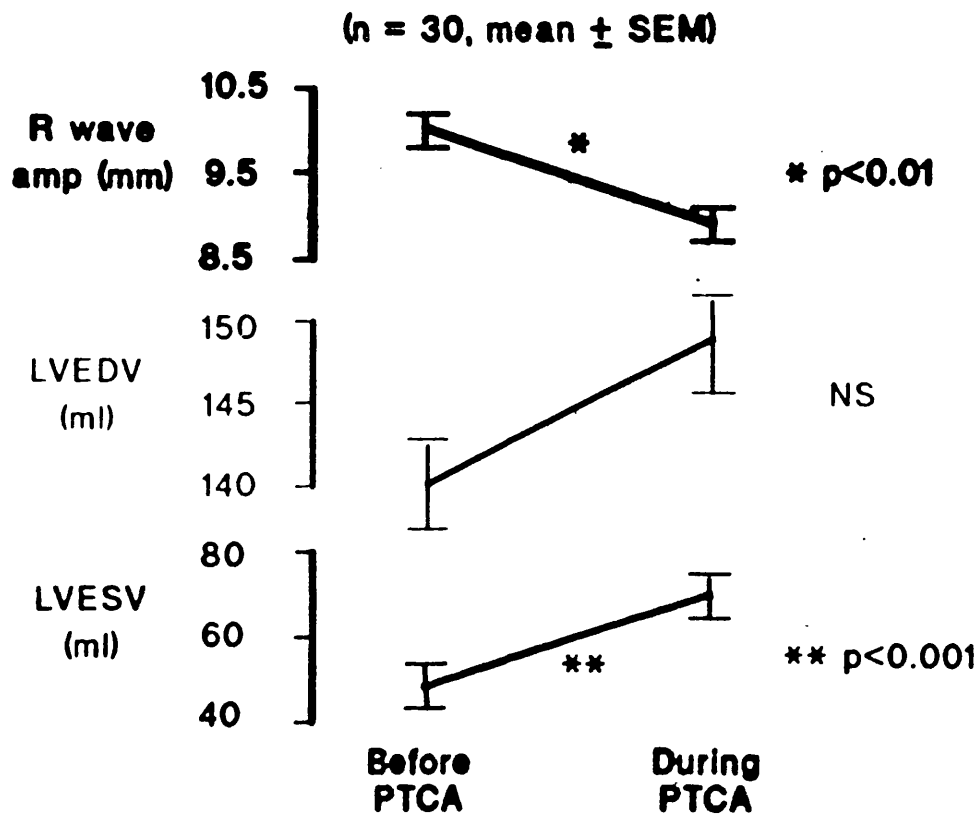|	Pre-PTCA	During PTCA	p
LV End-Diastolic Vol. (ml)	140(31)	148(38)	NS
LV End-Systolic Vol. (ml)	44(15)	76(33)	<0.001
R Wave Amplitude (mm)	10.1(3.5)	8.9(3.5)	<0.001

Fig. 12.

ECG R wave amplitude (mm), LV end-diastolic volume, EDV (ml) and LV end-systolic volume, ESV (ml) before and during balloon inflation

Discussion

Studies by Bertrand (23) and Serruys (21) both demonstrated a clear increase in LV end-systolic volume (ESV) during PTCA balloon inflation. Bertrand showed that LV ESV increased from 28ml m-2 pre-PTCA to 59ml m-2 after 50 seconds of balloon inflation, an increase of 111%. Serruys reported a more modest increase of 43% from 29 to 41ml m-2. The present study demonstrated an increase of 73% from 44 to 76ml in keeping with previous results.

Changes in end-diastolic volume (EDV) were less marked. Serruys showed an insignificant increase of 2% from 79 to 81ml m-2 while Bertrand's result did reach significance (97 to 107ml m-2), an increase of 10%. The results of the present study are in keeping with those of Serruys revealing an insignificant increase of 6% from 140 to 148ml. Visser (18) also examined left ventricular diastolic dimensions with apical 2-D echocardiographic views and showed that LV size index increased significantly (170mm to 196mm).

Doorey (22) also showed that end systolic volume increased by 73% from 30 to 52ml m-2 during balloon inflation but in the absence of nitroglycerin. When nitroglycerin was administered LV ESV increased to 37ml m-2, a change of only 23%. Similarly, in the absence of nitroglycerin, end diastolic volume increased, though insignificantly, from 87 to 93ml m-2. However, following the administration of nitroglycerin LVEDV decreased to 80ml m-2. This is in contrast to the results of the present study in which all patients were pretreated with a long acting nitrate

routinely. It is likely that this premedication continued to exert its effect during the PTCA procedure. However, examination of Doorey's results revealed that there was no control ventriculogram performed in the presence of nitroglycerin. Thus, left ventricular volumes during balloon inflation in the presence of nitroglycerin were compared to control volumes in its absence, and this may not have been a valid comparison.

R wave alteration during PTCA has not been previously documented. The present study has shown a significant reduction in R wave amplitude during balloon inflation of 12% from 10.1 to 8.9mm. These measurements were taken immediately prior to contrast injection in order to obviate any effect that contrast media may have produced on the QRS complex. Despite an increase in LV ESV and no significant change in LV EDV, R wave amplitude decreased. There was a weak but significant inverse correlation between change in systolic volume and R wave amplitude. These results indicate that the generation of the R wave is independent of changes in left ventricular volume.

This conclusion supports the work of others who similarly found no relationship between R wave amplitude and left ventricular volume (73). Furthermore, David has suggested that R wave decrease during transient coronary occlusion more closely follows changes in intramyocardial conduction (74). He showed a bi-phasic R wave response following circumflex coronary ligation in the dog. R wave fell to 18% below

control 30 seconds after coronary occlusion and subsequently increased to 52% above control after 150 seconds. In contrast, LV EDV increased progressively reaching a plateau at 130 seconds. This clear disparity emphasises the independance of R wave amplitude and left ventricular volume. At 20 and 60 seconds after occlusion R wave amplitude was still below control and this is in accord with the results of the present study following transient coronary occlusion in man during PTCA.

These results are also supported by recent work by Vancheri (75). By producing an acute reduction in LV volumes in normal subjects with intravenous frusemide, he showed that the QRS amplitude increased. This too is contrary to what may be expected if the Brody hypothesis was correct. It is postulated that a reduction in LV volume decreases the short-circuiting effect of the intracavity blood mass on the longitudinal components of the depolarisation wave front.

Methods

The method by which R wave height was measured in this study was similar to that used in previously published work (67). Clearly, a number of factors may modify the ECG R wave in addition to patient respiration and these should be taken into account when interpreting these results. However, many such factors, e.g. body habitus, are not relevant to this study which was specifically examining the change in R wave amplitude in the same patient following coronary balloon occlusion.

It is well recognised that angiographic contrast medium can modify the QRS complex and for this reason a number of precautions were taken when ECG recordings were made in our patients. Importantly, R wave amplitude was assessed using the 10 ECG complexes recorded immediately prior to each ventriculographic contrast injection and the time between any 2 studies was never less than 5 minutes. We were therefore confident that the contrast medium used for this purpose should not have interfered with ECG analysis.

Selective coronary arteriography is necessary during a PTCA procedure and this also has the capability of confounding R wave measurements. In order to avoid this the initial R wave measurement was made immediately before any arteriography had been undertaken and before the start of the PTCA procedure. Selective coronary arteriography would then be undertaken in order to ensure that the index stenosis had not occluded since the diagnostic angiogram and to provide reference frames to aid wire and balloon positioning.

In cases where arteriography was performed between balloon inflations and therefore possibly prior to a study inflation, the 12-lead ECG was allowed to return to baseline before the next inflation and at least 3 minutes elapsed before ECG analysis during that inflation.

A further safeguard in this respect was the use of non-ionic contrast medium (Omnipaque) for both coronary arteriography and left ventriculography and this should have minimised any effects on the QRS complex.

Rather than any increase in R wave amplitude, the reverse was

found and this reduction correlated with the increase in end-
-systolic volume. The mechanism of R wave reduction in these
patients is not clear. As this was measured from leads V4 to
V6 and the majority of patients were undergoing LAD PTCA, it
raises the possibility of brief anterior wall transmural
ischaemia as a cause of transient loss of praecordial R wave.
The weak correlation that was found between the reduction in
R wave and end-systolic volume would support this notion. The
greater the degree of anterior ischaemia produced by LAD
balloon inflation, the larger the end-systolic volume might
become and similarly praecordial R wave would fall to a
greater degree.

This question was not specifically addressed in our study. If
patients undergoing LAD PTCA were to be excluded the number
of patients in the study group would have been substantially
less. Furthermore, those patients undergoing LCX PTCA would
also need to be excluded for two reasons. Firstly, ECG lead
V6, which contributed to the calculation of R wave amplitude,
may itself be directly affected by circumflex occlusion as a
result of lateral myocardial ischaemia. Secondly, any changes
in LV volumes during LCX PTCA may have been underestimated
because of the 30 degrees RAO projection that was used as
discussed in Chapter 3. Thus, ideally only those patients
having right coronary artery dilatation would be suitable.

It would appear, therefore, that studies examining changes in
LV volume and their relationship to the ECG, may need to be
divided into those which use ischaemia as a method of
changing volumes (73,74) and those in which LV dimensions are

altered by modifying ventricular filling or loading

conditions (75).

CHAPTER EIGHT

SIGNIFICANCE OF "RECIPROCAL" ST DEPRESSION DURING PTCA

Introduction

During acute myocardial infarction ST segment depression is frequently seen in ECG leads remote from the infarct site as suggested by the location of ST elevation. It has long been a subject of discussion as to whether such changes are detecting additional ischaemia in a territory remote from the infarct area or whether they represent merely an ECG phenomenon, reflecting ST elevation over the opposite surface of the heart. The term "reciprocal" ST depression has therefore been coined (76).

Much of the work addressing this question has been undertaken in the context of acute inferior MI when ST elevation inferiorly is accompanied by ST depression across the praecordial leads. In a study by Salcedo (77) such changes, interpreted as demonstrating coexistent anterior wall ischaemia, were found to be predictive of the presence of additional LAD disease. Goldberg (78), however suggested that these changes were instead a sensitive and specific indicator of postero-lateral ischaemic dysfunction complicating inferior MI. Gibson (79) similarly found a greater degree of LV dysfunction in these patients due to infero-posterior infarction rather than anteroseptal ischaemic injury.

These findings are not the experience of all workers. Croft (80) did not find that praecordial ST depression predicted the

degree of LV dysfunction in individual patients with acute inferior MI, but more that it was related to the magnitude of inferior ST elevation. Gelman (81) showed that such ECG changes during the course of inferior infarction were associated with an adverse clinical course with a greater enzyme release and more frequent episodes of atrioventricular block. Heart failure was also more common especially if anterior ST depression was persistent (>48 hours), although the presence of these ECG findings alone did not relate to hospital mortality. During the follow-up period, however, reinfarction was more frequent in these patients.

During post infarction exercise testing, Jennings (82) was able to reproduce ST depression that had previously occurred during the acute phase of infarction in ECG leads remote from the infarct site. The long term outcome in these patients was less favourable than that in patients without such changes, suggesting that this ECG appearance reflects additional ischaemia rather than being a purely reciprocal phenomenon. PTCA, by producing controlled transmural myocardial ischaemia, has allowed this question to be further addressed. ST elevation during balloon inflation is frequently accompanied by ST depression in areas remote from the primary ischaemic territory. In a study by Brymer during LAD PTCA (83), inferior ST depression associated with anterior ST elevation was considered to be due to balloon occlusion of a particularly extensive LAD artery that coursed around the LV apex and supplied a proportion of the inferior surface. Thus

remote ST depression in patients with this coronary anatomy did indeed represent "ischaemia at a distance".

This is not necessarily the conclusion of others who have studied patients developing inferior ST depression during LAD PTCA (84). In these patients there was not a greater incidence of multivessel disease as one might expect if such remote changes did indeed represent ischaemia. Their conclusion was that these inferior changes were more likely to simply reflect coexistent anterior ST elevation and thus be merely reciprocal.

In the present study another manifestation of myocardial ischaemia during PTCA was examined; by documenting LV wall motion during balloon inflation the interpretation of ST depression, in sites remote from the occluded artery, should be clarified.

Patients

Of the previously described total patient population of 52, this study confined itself only to the 27 patients with single vessel disease who were to undergo LAD PTCA and identified previously in Chapter 4 and in Table 1. The ECG changes that they developed during LAD balloon inflation allowed them to be separated into 2 groups. Of the 27 patients, 13 developed inferior ST depression > 1 mm (Group 1) while the remaining 14 patients did not develop such inferior ST change (Group 2).

Results

During balloon inflation the magnitude of anterior ST segment elevation seen in Group 1 (mean = 5mm, range 1-9mm) was greater than that in Group 2 (mean = 1.5mm, range 1-6mm, p< 0.001). The degree of anterior ST elevation in all 27 patients correlated with the degree of inferior ST depression (r = 0.657, p< 0.001).

Global LV Performance

Resting LVEF was similar in both groups (Group 1 76%, Group 2 75%, NS). During balloon inflation LVEF fell in both groups to 52%, (p< 0.001) and 62%, (p< 0.001) respectively. The magnitude of this fall was greater in Group 1 (24%) than in Group 2 (13%, p< 0.02).

When all 27 patients were assessed the fall in LVEF during balloon inflation correlated with both the magnitude of ST segment elevation (r = 0.605, p< 0.001) and ST segment depression (r = 0.403, p< 0.05).

Regional LV Performance

Regional motion of the 5 LV segments examined in each of the 2 groups is shown in Tables 16 and 17. Before balloon inflation there were no differences in regional contraction between groups other than anterior segmental shortening which was lower in Group 1 than in Group 2 (36% vs 43%, p< 0.05).

During balloon inflation anterior and apical segmental contraction decreased in both groups (Group 1: 36% to 10%, p<0.001, 55% to 12%, p< 0.001; Group 2: 43% to 19%, p< 0.001,

51% to 22%, p< 0.001). Anterobasal contraction fell significantly only in Group 1 (38% to 21%, p< 0.002), the magnitude of this decrease being greater in Group 1 (18%) than in Group 2 (2%, p< 0.01). There was no change in inferior contraction in either group (Group 1: 52% to 49%, NS; Group 2: 44% to 46%, NS). In contrast, inferobasal contraction increased in both groups   (Group 1: 4% to 29%, p<0.01; Group 2: 9% to 20%, p< 0.02).

When all 27 patients were assesed, only the decrease in apical shortening correlated with the magnitude of anterior ST elevation (r = 0.396, p< 0.05).

Table 16.

Regional Wall Motion Before and During LAD PTCA in Patients With

(Group 1) and Without (Group 2) Inferior ST Segment Depression

Values = mean % (SD)

	GROUP 1 (13 pts)			GROUP 2 (14 pts)		
	Pre-	During		Pre-	During	
LV Segment	PTCA	PTCA	p	PTCA	PTCA	p
Anterobasal	38(10)	21(16)	<0.002	37(10)	35(12)	NS
Anterior	36(9)	10(10)	<0.001	43(10)	19(23)	<0.001
Apical	55(9)	12(15)	<0.001	51(12)	22(22)	<0.001
Inferior	52(9)	49(12)	NS	44(17)	46(17)	NS
Inferobasal	4(6)	29(21)	<0.01	9(16)	20(18)	<0.02

Table 17.

Changes in Regional Wall Motion During LAD PTCA.

Comparison Between Patients with and without Inferior ST

Segment Depression

Values = mean change (%) (SD).
Minus values = increased shortening

LV Segment	Group 1 ST depression (n=13)	Group 2 no ST depression (n=14)	p
Anterobasal	18(15)	2(8)	<0.01
Anterior	26(12)	24(18)	NS
Apical	43(19)	28(17)	NS
Inferior	4(17)	-2(14)	NS
Inferobasal	-25(23)	-12(16)	NS

Discussion

The results of the present study show that during LAD PTCA patients who develop inferior ST segment depression (>1 mm) associated with anterior ST segment elevation have a greater degree of anteroapical ischaemia. This is supported by such patients developing a greater degree of anterior ST segment elevation, a lower LVEF and additional anterobasal LV dysfunction in comparison with patients without inferior ECG change. Anterior and apical contraction during PTCA also deteriorated further in the group with inferior ST segment depression in comparison to those without, but this difference was not significant.

Despite the presence of inferior ST segment depression, inferobasal contraction was enhanced. This augmentation of inferobasal contraction also occurred in those patients who did not develop inferior ST depression and the magnitude of this increase was no different between those with and without inferior ECG change. It is therefore concluded that such inferior ST segment depression does not indicate inferior ischaemia but simply reflects a greater degree of anterior ischaemia.

Much previous work examining the question of reciprocal ST segment change has been undertaken in the context of acute infarction and in particular, in patients who develop anterior ST segment depression during acute inferior infarction (77-81).The emergence of coronary angioplasty has now enabled workers to examine similar ST segment alteration in the context of reversible controlled coronary occlusion.

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Two recent studies address this question.

Quyyumi (84) noted that the development of inferior ST segment depression during LAD PTCA was not a reliable indicator of the presence of additional coronary disease. He concluded that it was unlikely that such inferior changes represented ischaemia but that they were merely an electrical phenomenon.

Brymer (83) has put forward another explanation for the mechanism of ST segment depression over a territory remote from the primary ischaemic zone during PTCA in patients with single vessel coronary disease. He used the term "ischaemia at a distance" and based his explanation on balloon occlusion of unusually extensive LAD coronary arteries that supply a proportion of the inferior myocardial surface. He concluded therefore that such ST segment depression was more likely to be due to ischaemia rather than be purely reciprocal.

The present study does not support this view. The size of the LAD in these patients was not examined specifically. Some may have been extensive and supplying a portion of the inferior myocardium. If the inferior surface of the heart was rendered ischaemic during balloon inflation in such vessels, reduced inferior and inferobasal contraction might have been anticipated. However, in the present study, inferior contraction was preserved and inferobasal contraction enhanced.

The mechanism of augmented contraction of the non-ischaemic segment in this context is unclear. Recent work suggests that the Starling mechanism is not responsible (85). This is

supported by the data presented in Chapter 7. and other studies (21) which have shown that LV end-diastolic volume does not increase during PTCA. Another possibility is increased contractility secondary to sympathetic activation but the data from this study does not allow this aspect to be addressed.

It is more likely that mechanical interaction between the non-ischaemic and ischaemic regions results in inferior regional afterload reduction (85), and therefore augmented inferior contraction during LAD PTCA.

Methods

A possible criticism of these results is that in patients with 'reciprocal' ST depression, remote inferior ischaemia may have occurred but was not detected using our method of wall motion examination. Particularly, posterolateral LV dysfunction may not have been appreciated as discussed in Chapter 3. because of the 30 degrees RAO projection that was used for ventriculography. However, we have already shown in Chapter 3. that during inferior territory ischaemia resulting from RCA balloon occlusion, inferior wall motion is apparent and associated with inferior ST segment changes. This would therefore support the validity of our method of demonstrating inferior wall ischaemia if indeed it did occur.

Insufficient patient numbers did not allow examination of the converse situation i.e. anteroapical wall motion in patients with precordial ST depression during RCA PTCA. Only 8 patients underwent PTCA of the right coronary artery and in 3

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there was additional coronary disease. This involved the LAD in 2 patients.

The increase in inferobasal contraction that we have consistently observed may be considered to be a quirk resulting from our method of wall motion analysis. In mitigation of this criticism 2 factors should be considered. Firstly, during acquisition of the raw ventriculographic images in some patients it was apparent that there was hypercontractility of the inferior surface. Secondly, other workers using a different method of LV assessment (22) have also observed these changes suggesting that it would appear to be a real phenomenon.

The possible mechanisms of hyperfunction of the non-ischaemic segment mentioned above could not be specifically addressed in this study. Although the Starling mechanism is thought unlikely to be responsible it should not be dispensed with as a possible cause without further discussion.

One possibility is that increased diastolic stretch of the non-ischaemic segment does occur but that because this may be confined to a relatively small region of the ventricle, it is not reflected in a significant increase in overall LV end-diastolic volume. This may explain why we and others have shown only small increases in diastolic volume, often failing to reach statistical significance. Our method of wall motion analysis only addressed systolic shortening towards, or in some cases 'lengthening away' from, a point defined within the venticular cavity. Diastolic lengthening of individual segments could not be examined with our computer program.

It is concluded that inferior ECG changes in this context are purely a reciprocal ECG phenomenon and do not represent distant inferior ischaemia. It should be emphasised that these results cannot be applied to patients in whom the coronary anatomy is not known. This study was undertaken on a selected group of patients who were known to have single vessel LAD disease. It would be erroneous to extrapolate these results to patients presenting with acute anterior infarction in whom inferior ST segment depression accompanies anterior ST segment elevation. These data do indicate however that inferior ST segment depression can occur in the absence of inferior ischaemia.

CHAPTER NINE

LEFT VENTRICULAR PERFORMANCE DURING EARLY PTCA FOLLOWING SUCCESSFUL THROMBOLYTIC THERAPY FOR ACUTE INFARCTION

Introduction

The place of thrombolytic therapy in the early stages of acute myocardial infarction is now well established (86,87) and thrombolysis is now in widespread use. However reduction in mortality in myocardial infarction following treatment has not consistently been associated with improvement in left ventricular function. Furthermore, the dissolution of an occlusive coronary thrombus frequently leaves a high grade stenosis which has the propensity to reocclude and therefore jeopardise the long term outcome.

Some centres have chosen to electively dilate such stenoses with PTCA in the hope that the risk of reocclusion will be reduced. The results of PTCA in this setting are more favourable if the procedure is undertaken some weeks after presentation rather than during the acute stages of threatened infarction and thrombolysis (92).

Previous work has reported that during balloon inflation in this situation, evidence of myocardial ischaemia can still be demonstrated. The occurrence of chest pain or ST segment elevation suggests the presence of viable left ventricular muscle subtended by the treated artery and therefore that myocardial salvage had been achieved with thrombolytic therapy (93).

The institution in which the present study was undertaken was similarly evaluating the role of early PTCA in patients who had received thrombolytic therapy for acute M.I. This procedure was therefore used in an attempt to "reproduce" thrombotic coronary occlusion. By documenting the degree of left ventricular dysfunction during balloon coronary occlusion it was hoped to demonstrate to what extent myocardium had been salvaged.

Patients and Methods

Fifteen patients (Nos. 53 - 67 on Table 18. and in Appendix 1.) were studied of whom 12 were male. Their mean age was 56 years (range 38 - 76 years). All had presented with acute myocardial infarction with chest pain of at least 30 minutes duration and ST segment elevation (>2 mm in anterior ECG leads or >1 mm in inferior leads). Eight patients had presented with anterior infarction and the remaining 7 had presented with inferior infarction.

This selected sample formed part of a larger group all of whom had presented with acute myocardial infarction and had received 1.8 million units of Streptokinase within 6 hours of the onset of symptoms. They were maintained on intravenous heparin and transferred to the London Chest Hospital for early coronary arteriography.

Elective PTCA was undertaken to the infarct related vessel if it was patent but still contained a high grade (> 70%) stenosis and if there was only additional coronary disease in at most one other major vessel. All the patients studied were

Table 18.

CHARACTERISTICS OF PATIENTS STUDIED DURING PTCA AFTER THROMBOLYTIC THERAPY

No.	Sex	Age	MI Site	PTCA Vessel	Additional Disease	LVEF (%)	PRE-PTCA WALL MOTION (%)				
							AB	A	AP	I	IB
53	M	55	ANT	LAD		57	16	15	17	58	26
54	M	38	INF	RCA		79	32	47	58	46	-8
55	M	43	INF	RCA		75	27	25	43	59	25
56	F	52	ANT	LAD		64	25	23	35	55	18
57	M	57	INF	RCA		56	38	41	6	15	15
58	M	60	INF	RCA		72	33	41	55	36	-10
59	F	55	ANT	LAD	LCX	68	5	13	49	58	4
60	M	57	ANT	LAD		60	33	25	26	43	15
61	M	44	ANT	LAD		40	17	1	-2	39	22
62	M	59	ANT	LAD		60	40	23	6	64	40
63	M	76	INF	RCA	LAD	82	26	43	64	60	-14
64	M	52	ANT	LAD		39	26	6	5	29	19
65	F	71	ANT	LAD	LCX	43	-11	-17	16	42	15
66	M	56	INF	RCA	LCX	52	10	15	34	38	10
67	M	69	INF	RCA		60	24	36	31	36	2

in a stable condition without ongoing ischaemic symptoms. PTCA was undertaken to the LAD in 8 and the right coronary artery in 7 patients, 6 days (mean) after initial presentation (range 2-11 days).

During the PTCA procedure particular care was taken to avoid side branches during balloon inflation. Contrast injections were therefore employed in order to demonstrate that the inflated balloon was not obstructing important branches.

Results

ECG Changes

During balloon inflation 13 of the 15 patients developed ST segment elevation in leads overlying the myocardial territory subtended by the treated artery. The maximum degree of ST elevation was 3.1 m (range 1.5 - 5.5 mm). Importantly, 5 of these patients had pre-existing Q waves in the infarct territory.

Global LV performance

Before PTCA the mean LVEF was 60% (range 39% - 82%). During balloon inflation this fell to 47% (p<0.001, range 21% - 68%, Fig. 13).

Regional LV Performance

1. LAD PTCA (8 patients; Fig. 14, Table 19.)
In this subgroup LVEF fell from 54% to 40% (p<0.001)

As seen in the accompanying table a significant decrease in segmental contraction was confined to the apical segment (19% to 1%, p<0.01). As previously described during LAD balloon occlusion, there was in addition an increase in inferobasal contraction (19% to 24%, p<0.05).

2. Right Coronary PTCA (7 patients; Fig. 15, Table 20.)
In this subgroup LVEF fell from 68% to 55% (p<0.01). There was a significant fall in inferior contraction (41% to 16%, p<0.01).
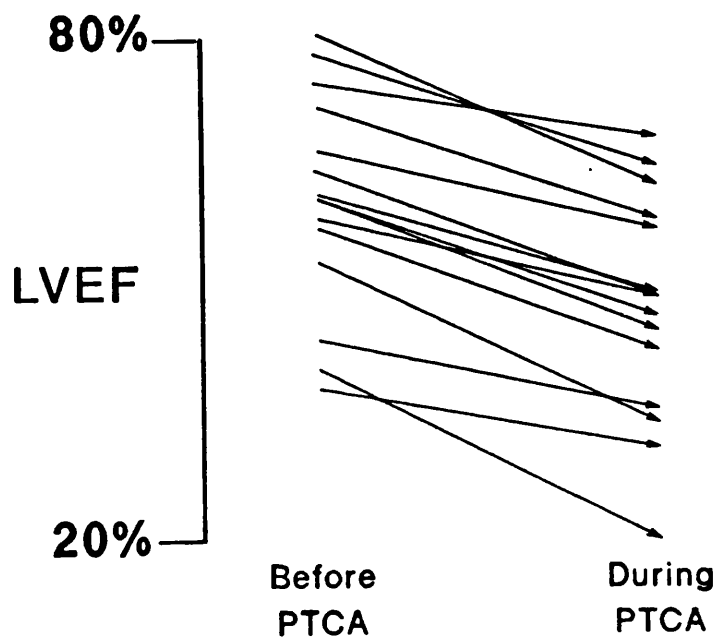
Fig. 13.

Individual results for 15 patients showing change in left ventricular ejection fraction (LVEF) before and during PTCA following thrombolytic therapy for acute infarction.
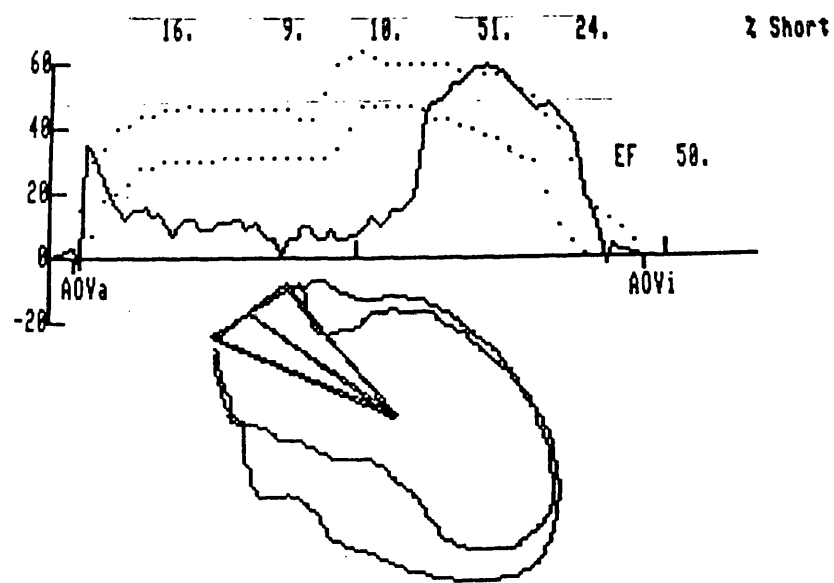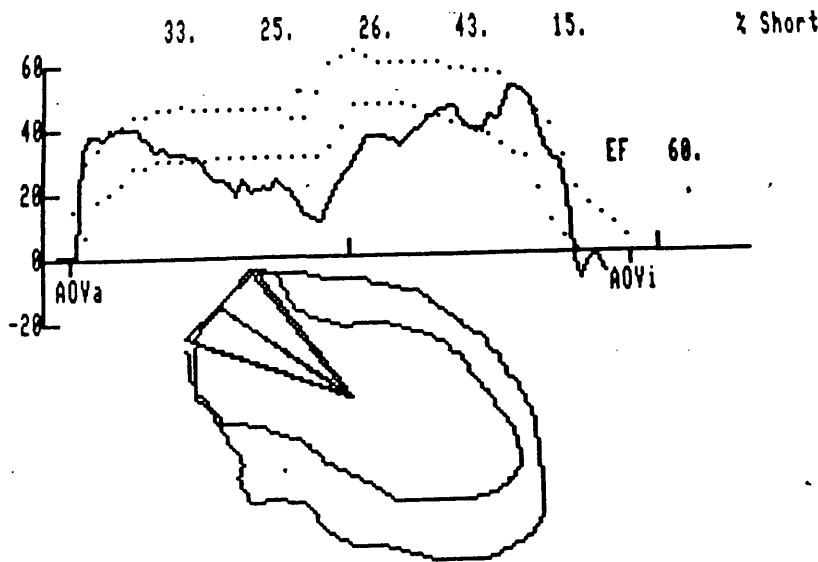
Fig. 14.

Example of LV wall motion analysis before (top) and during
(bottom) LAD balloon inflation following thrombolysis.
Ejection fraction (EF), anterior and apical shortening are
reduced prior to PTCA and fall further during balloon
inflation. Anterobasal shortening also deteriorates.Note
enhanced inferobasal contraction during PTCA.

Table 19.

LV Ejection Fraction (LVEF) and Segmental Wall Motion

During LAD PTCA after Thrombolysis

(n = 8) Values = means % (SD)

	Pre-PTCA	During PTCA	p
LV Ejection Fraction	54 (11)	40 (12)	< 0.001
LV Segments:			
Anterobasal	19 (16)	16 (14)	NS
Anterior	11 (14)	1 (10)	NS
Apical	19 (17)	1 (14)	< 0.01
Inferior	48 (12)	43 (16)	NS
Inferobasal	19 (10)	24 (8)	< 0.05
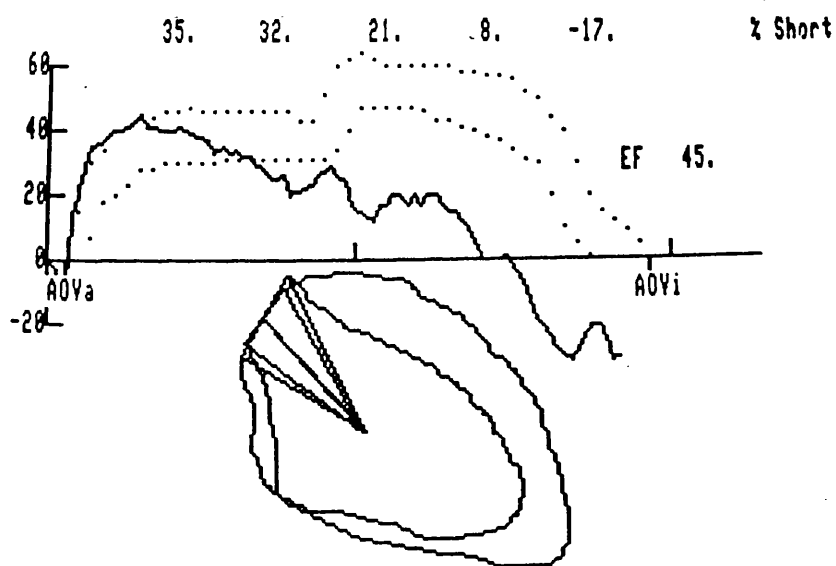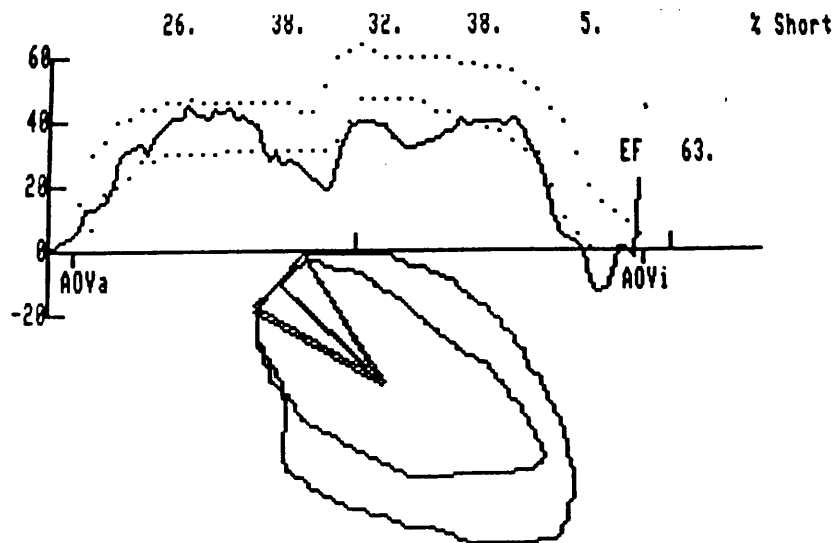
Fig. 15.

Example of LV wall motion analysis before (top) and during
(bottom) right coronary PTCA after thrombolysis. Ejection
fraction (EF), apical and inferior shortening are reduced
prior to PTCA and fall further during balloon inflation.
There is an additional deterioration in inferobasal
contraction while anterobasal contraction is enhanced.

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Table 20.

LV Ejection Fraction (LVEF) and Segmental Wall Motion

During Right Coronary Artery PTCA after Thrombolysis

(n = 7) Values = means % (SD)

	Pre-PTCA	During PTCA	p
LV Ejection Fraction	68 (12)	55 (11)	< 0.01
LV Segments:			
Anterobasal	27 (9)	33 (5)	NS
Anterior	35 (11)	35 (7)	NS
Apical	42 (19)	28 (15)	NS
Inferior	41 (15)	16 (15)	< 0.01
Inferobasal	3 (14)	-2 (9)	NS

Discussion

This study has shown that during PTCA balloon occlusion in patients previouly treated with a thrombolytic agent, LV dysfunction may still be demonstrable. This suggests that myocardium had been salvaged by the achievement of coronary patency in the early hours of acute infarction.

Although thrombolytic therapy has been shown to reduce mortality during acute myocardial infarction, improvement in either global or regional left ventricular function has not been a constant finding. This may relate to the lack of a reliable assessment of infarct size. Enzyme levels do not necessarily correlate with the extent of myocardial necrosis because of their "washout" following reperfusion (94-96). Electrocardiographic mapping is also limited as it can only be applied to anterior or lateral infarcts (97,98) and the height of the ST segment may be modified by other factors such as intraventricular conduction defects, pericarditis, chest wall thickness and intervening lung tissue (99). Measurements of regional left ventricular wall motion to assess infarct size are also unreliable. This is because of their inability to differentiate infarcted areas of myocardium from segments rendered ischaemic but still capable of functional recovery as myocardial "stunning" resolves (100,101).

Controlled coronary reocclusion during elective PTCA allowed an opportunity to assess myocardial ischaemia prospectively, a further deterioration in LV performance indicating the extent of myocardial salvage.

This group of patients studied were highly selected,

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comprising only those with patent infarct related vessels. The state of their coronary circulation at the time of presentation cannot be ascertained although it is presumed that an occlusive thrombus played a part in their symptoms and therefore, that treatment with streptokinase was responsible for subsequent coronary patency.

The purpose of the study was to use PTCA balloon inflation as a method of reproducing thrombotic occlusion. Clearly, there will be differences between the two processes which make this assumption unreliable. However, care was taken to avoid side branches during balloon inflation in an attempt to reocclude the artery at the same site.

To what extent the degree of deterioration of LV contraction during PTCA relates to the amount of myocardium salvaged, is unclear. The state of the collateral circulation at the time of thrombotic occlusion is unknown but it is likely that collateral vessels would have been more prominent during PTCA approximately one week later. As it has been shown that these vessels can confer myocardial protection during PTCA, one could postulate that this demonstration of LV salvage may be an underestimate of the amount of muscle that would have been damaged if coronary patency had not been achieved.

In the 15 patients studied LVEF was lower before PTCA in comparison with that in the 52 patients that contributed towards most of the data in this thesis (60% vs 73%). This reflects the fact that a degree of LV dysfunction had resulted from previous, albeit aborted, coronary occlusion.

Thus, anterobasal, anterior and apical wall motion was already reduced in those patients who presented with anterior infarction and similarly, inferobasal contraction was impaired in those with inferior infarction. Whether or not this regional dysfunction was permenant or only represented a transient phenomenon (100), is not clear but in any event further dysfunction could be demonstrated during balloon coronary occlusion. This was particularly apparent in the apical segment during LAD PTCA and in the inferior segment during right coronary occlusion.

As has been previously documented, augmented inferior contraction was apparent during LAD PTCA. The mechanism of this hyperfunction is unclear and discussed elsewhere (85,102). Importantly, both ST segment elevation and a further deterioration in LV contraction were apparent during balloon coronary occlusion even in patients with pre-existing Q waves overlying the infarct territory. This suggests that Q wave development may not necessarily indicate "completed" myocardial infarction.

Methods

Importantly, the patients studied did not have evidence of ongoing ischaemia. Were this the case, one might anticipate the development of further ischaemia during balloon inflation thus confirming the presence of still viable myocardium in the territory of the infarct vessel. In current practice, these patients would have been mobilised in hospital and probably have performend an exercise test before any plans

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were made regarding investigation and revascularisation. However, our policy at the time of this study was to assess the feasibility of early investigation in such patients with a view to PTCA if the coronary anatomy was appropriate.

It might be anticipated that the earlier thrombolytic therapy was administered with respect to the onset of symptoms, the greater the degree of myocardial salvage demonstrated using our method. We examined the relationship between the time elapsing before Streptokinase was given and the degree of LV dysfunction seen during PTCA but no significant correlation was found. This may relate to the small number of patients as well as to individual variability in the rate at which myocardial necrosis progresses following coronary occlusion.

CHAPTER TEN

LEFT VENTRICULAR PERFORMANCE AFTER PTCA

Introduction

Previous studies have documented that all ischaemic abnormalities consequent on balloon inflation during PTCA resolve completely after the procedure (14-18,21-23). However, anxiety exists concerning the effect of longer balloon occlusion on the left ventricle and the post-ischaemic dysfunction that may result (100).

This study therefore also addressed this subject and in selected patients examined LV performance after the PTCA procedure.

Patients

37 of the 52 patients underwent intravenous digital subtraction ventriculography after PTCA (Patient Nos. 1-10, 12-14,17,18,20-22,25,27-30,32-34,36-39,42,44,46-48,50 and 51 on Table 1. and in Appendix 1.) In all cases the accompanying ECG had returned to its control state and ventriculography was performed within 15 minutes of the final balloon inflation.

15 patients were not studied after PTCA. In 9 cases the procedure had become complicated by protracted coronary occlusion. This had resulted in a prolonged episode of myocardial ischaemia associated with marked ST segment elevation. It was felt inappropriate to study these patients

further. In 3 patients the PTCA procedure itself had become protracted and had already utilised a large volume of contrast medium. The addition of a third ventriculogram incorporating another 40 ml of contrast was deemed unwise. The 3 remaining patients not studied after PTCA were recruited into another study that required them to undergo ventriculography during another balloon inflation. Ethical approval for the present study did not extend to 4 ventriculograms and thus the post-PTCA study in these patients was waived.

Results, (Fig. 16, Table 21.)

Table 11. shows LVEF and regional wall motion before and after PTCA in the 37 patients studied. Both LVEF and regional wall motion returned to control values after the procedure.

EF   81.

% Short

24.   12.   15.   4ö.   23.   % Short

EF   52.

4ö.   43.   68.   61.   7.   % Short

EF   84.
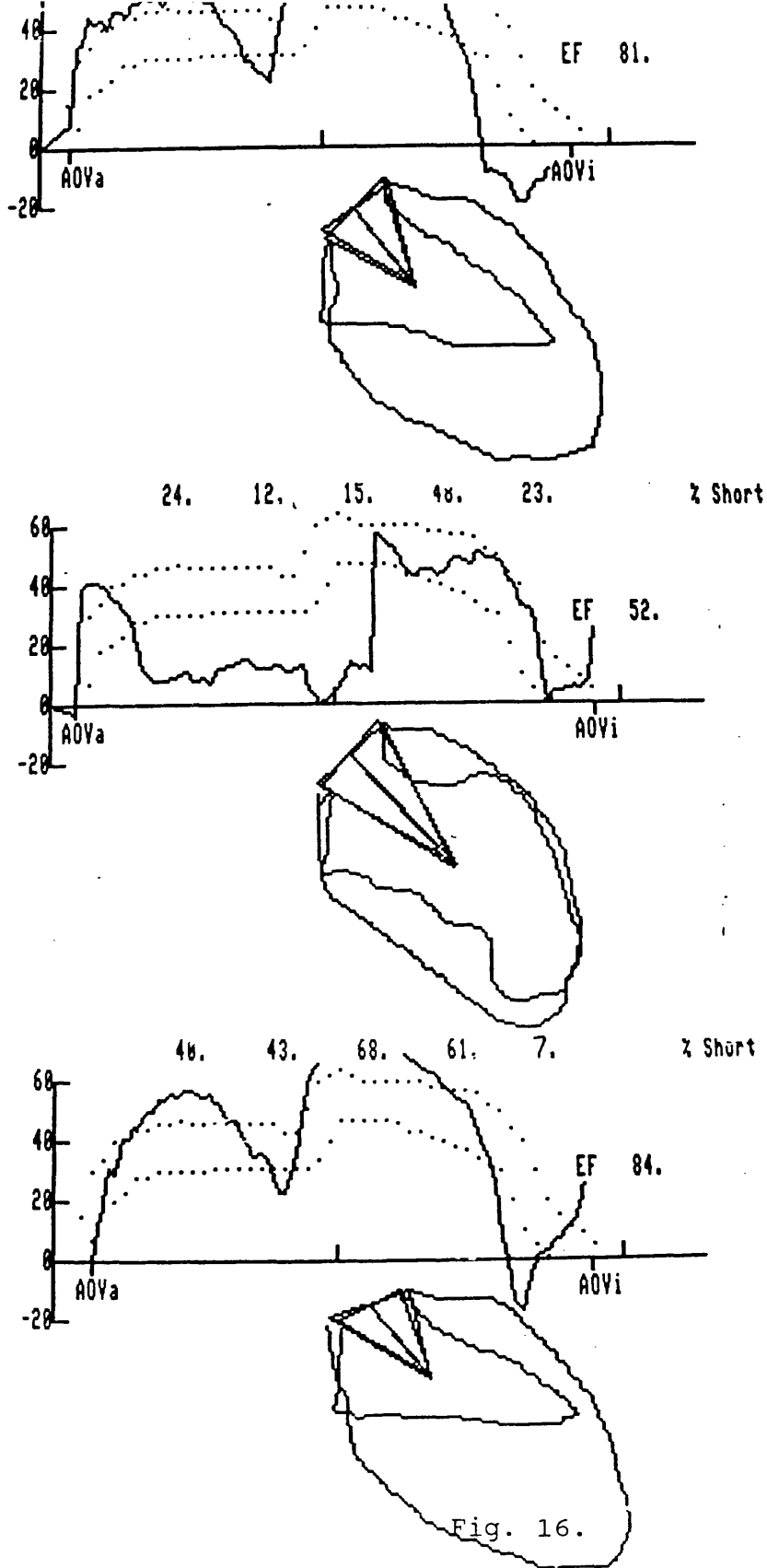
Fig. 16.

LV contraction before (top), during and after (bottom) LAD
PTCA. Despite marked abnormalities during balloon inflation
wall motion and EF returns to baseline after the procedure.

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Table 21.

LVEF and Segmental Wall Motion Before and After PTCA

(37 patients) Values = mean % (SD)

	Pre-PTCA	Post PTCA	p
LV Ejection Fraction	74(9)	73(8)	NS
LV Segments:			
Anterobasal	37(11)	35(10)	NS
Anterior	38(13)	36(16)	NS
Apical	48(16)	45(20)	NS
Inferior	49(13)	49(17)	NS
Inferobasal	8(15)	9(15)	NS

Discussion

This study found that ejection fraction and regional wall motion returned to control values after the angioplasty procedure. This has been the experience of others who have found no persistent dysfunction following long, numerous inflations (21).

Some workers have documented hypercontractility immediately after balloon deflation in segments that were dysfunctional during coronary occlusion (17,18). These changes are apparent up to 20 seconds after balloon deflation but rapidly normalise. This overshoot phenomenon in regional wall motion was not observed in the present study. All patients were studied within 15 minutes of the completion of the PTCA procedure but in no case was the third ventriculogram performed so soon after the final balloon deflation.

These results were based on a selected sample of patients who had undergone uncomplicated PTCA. Those patients in whom the procedure was unduly prolonged, or those in which protracted episodes of myocardial ischaemia developed, were excluded from this study. It might be anticipated that, in these patients, LV performance may still be impaired after PTCA compared to the baseline state, full recovery of function perhaps taking longer to be completed. However, these data support the view that uncomplicated PTCA, incorporating up to 60 second balloon inflations, does not produce sustained derrangement of left ventricular performance.

Methods

Left ventriculography was undertaken at the end of the PTCA procedure and therefore when the balloon catheter, guide wire and guiding catheter had been withdrawn. Ideally, this could have been performed immediately after a balloon inflation but this was felt to be impractical. In many cases a further balloon inflation was required to achieve a satisfactory PTCA result. To withdraw the balloon catheter temporarily, which would have been necessary in order to perform a final ventriculogram without the possibility of reduced coronary flow, only to recross the target lesion again, was considered unacceptable.

Instead, rather than examining the time to complete resolution of any wall motion abnormalities documented during balloon inflation, we chose to demonstrate that LV performance could return to its baseline state after repeated inflations. Unfortunately, this meant that we could not study any residual effects on LV contraction immediately after particularly protracted balloon inflations and nor could we assess any rebound hypercontractility of segments rendered ischaemic and hypocontractile during balloon inflation.

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DISCUSSION

METHODS

Intravenous Digital Subtraction Left Ventriculography

PTCA has allowed a unique opportunity to study the earliest manifestations of left ventricular ischaemia following coronary occlusion. In the present study, intravenous DSA provided a reliable assessment of LV performance during balloon inflation. The employment of this technique during PTCA has not been described by other workers (103).

Although respiratory motion can often degrade the results of mask subtraction, this did not prove to be a problem, even in acquisitions during balloon coronary occlusion.

A non-ionic contrast agent (Iohexol) was used which has distinct advantages. During intravenous DSA, passage of the contrast bolus through the pulmonary circulation can cause the patient to cough which may interfere with image analysis. This can be reduced using non-ionic contrast and did not occur in any of the 67 patients. The use of non-ionic contrast enabled 3 ventriculograms to be performed in the majority of patients. With conventional contrast agents such an amount of sodium, together with that required for the PTCA procedure itself, might impose a significant ionic load.

The relative lack of ectopic activity during intravenous DSA proved to be a distinct advantage, occurring in only 9 of 52 patients (17%). This is lower than the incidence reported by

Norris in a study of 26 patients (25) in whom 9 (35%) developed ectopic beats during intravenous ventriculography. This higher incidence may be explained by his use of an end-hole catheter (either a Cournand or a Zucker) to deliver the contrast bolus. This would direct the contrast jet in only one direction and thus tend to generate ectopic activity by increasing either atrial or ventricular excitability. For this reason a pigtail catheter was chosen for the present study from which contrast is ejected in many directions. Catheter recoil is therefore minimised and contrast mixing is improved. The incidence of complications was minimal with only one patient developing transient atrial fibrillation. Nine patients developed ectopic beats in this study. These were supraventricular in 5, presumably directly related to atrial contrast injection. This finding is in accord with Norris who also found atrial ectopics to be more frequent than those of ventricular origin.

One particular advantage of intravenous digital subtraction ventriculography was that it did not significantly increase the invasive nature of the PTCA procedure itself. A femoral venous sheath is routinely inserted during PTCA in order to provide a route for intravenous drugs or a temporary pacing catheter if required. The use of this sheath to insert a central venous pigtail catheter for right atrial contrast injection was preferable to cannulating another peripheral artery which would have been required if direct cine left ventriculography had been undertaken during PTCA.

Most studies comparing DSA with direct cine left ventriculography have used the Sandler Dodge formula for the derivation of LV volumes and LVEF (42) and this method was therefore chosen for the present study.

The assessment of regional LV function took account of the large degree of subjective variability that results in individual variation. For this reason a quantitative method was chosen (43) which does not rely on interobserver concordance. DSA is particularly suited to automated methods of wall motion analysis and therefore observer variation is minimised. Alteration in LV wall motion during PTCA forms the basis of many of the results in this study. Therefore the method used warrants further discussion, in order to justify its use in preference to other methods.

When attempting to quantify the extent of regional inward or outward motion a major problem is the fixing of a point to which movement can be related. Many workers have used the long axis of the LV constructed from a point on the aorto-mitral plane to the apex (104-108). However, this assumes that the same point on the apex can be located in successive frames. In patients with coronary disease, and particularly during LAD PTCA, the apex may be distorted (109). Furthermore, movement expressed perpendicular to a long axis may be valid for the body of the ventricle but is untrue for the apex and base which tend to move towards the LV centre.

Alternatively, rather than along perpendicular cords, other

workers have expressed inward motion along radial lines towards the midpoint of the long axis (110). Clearly, this does not exclude the unsound nature of using the long axis in the first instance, but the concept of expressing wall motion towards a ventriclar centre is attractive and subjective assessment of ventriculograms suggests that such motion is a better approximation to actual ventricular movement.

The only point inside the LV outline which can be defined independent of ventricular size and shape is the geometric centre of gravity (111). This study therefore used radii emanating from the centre of gravity of the end-systolic frame towards the ventricular outline in order to quantify regional wall motion.

This method has been previously described, and in normal subjects during synchronous contraction, it has been demonstrated that rotation of the centre of gravity about the aortic midpoint is minimal (average 0.24 degrees). In contrast, rotation of the long axis is greater averaging 3.08 degrees (43).

It is clear that an akinetic or dyskinetic area will tend to shift the centre of gravity towards that region possibly distorting wall motion analysis. A further method is therefore required which incorporates the fixing of a second point on the ventricular outline. This is achieved by translating end-systolic and end-diastolic images such that the centres of the aortic valve plane are superimposed. The centre of the AV plane is chosen because it is least sensitive to operator decisions as to the location of the

aortomitral or aortoventricular junction.

The limitation of this method in identifying left ventricular abnormalities during circumflex PTCA has been discussed in Chapter 3. Biplane angiography would have been an undoubted advantage although in order to quantify regional wall motion from a LAO projection another computer program would have been required. This is because although another end-systolic geometric centre of gravity could be identified, the identification of another fixed point to which to relate inward movement, would also be necessary.

This remains an important limitation of this study. However the main results relate to patients specifically selected because they were undergoing LAD PTCA. Therefore any ischaemic wall motion abnormalities that they produced during balloon inflation would have been identified from a 30 degrees RAO projection.

Alternatively, instead of biplane angiography, a digital subtraction system incorporating densitometry may have avoided some of the limitations involved with patients having LCX PTCA. This technique allows the change in pixel density during the cardiac cycle to be examined. As pixel density is proportional to the amount of contrast in the ventricular cavity, the change in pixel density in a region of interest from end-diastole to end-systole, will represent the fraction of the end-diastolic volume expelled i.e. ejection fraction. This avoids the need for accurate outlining of

ventricular images and can be used to examine the contribution towards global ejection fraction of specific ventricular regions.

In order to undertake wall motion analysis as described in this study the end-diastolic and end-systolic images needed to be selected and manually outlined. An R wave marker was able to identify the end-diastolic frames but choosing the end-systolic frames required operator input. Thus the frame with minimal LV dimensions was selected visually. Furthermore, as our system did not incorporate automated edge detection, the operator was also required to manually outline the ventricular endocardial contour. Ideally, this should have been performed with the operator blinded to whether any particular study was performed during, before or after PTCA but for practical reasons this was not possible. The presence of the inflated PTCA balloon in the coronary artery was clearly apparent in studies performed during PTCA (see Figs. 4 and 6) and therefore operator identification of these images was unavoidable.

CLINICAL IMPLICATIONS

The duration of balloon inflation during PTCA has become longer over the last decade from perhaps 10 to 20 seconds to 1 or 2 minutes. This has been the result of increased operator experience together with data demonstrating that the ischaemic consequences of balloon coronary occlusion are

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not of greater magnitude with longer inflation and, as with shorter inflations, are reversible. However there remain circumstances in which prolonged balloon inflation may be desirable.

Firstly, protracted inflation may be required in order to improve the immediate outcome of the procedure as might be indicated in the presence of substantial intimal dissection complicating PTCA (112). Secondly, prolonged pressure application has been shown to enhance the compression of atheromatous plaque and may have a beneficial effect on the development of restenosis (11).

While balloon inflation in excess of 1 to 2 minutes is envisaged, anxiety may be engendered concerning both the short (100) and longterm (113) effects of such sustained transmural myocardial ischaemia upon left ventricular function. Thus, monitoring of myocardial ischaemia during PTCA needs to be sufficiently reliable to detect ischaemic abnormalities. In addition, patients with already compromised left ventricular function e.g. following recent or previous infarction, may be particularly sensitive to further ischaemia during PTCA which may be undesirable and again emphasises the need for a reliable indicator of ventricular ischaemia.

Many centres rely on ECG changes as an objective indicator of ischaemia but monitoring of multiple lead systems is not universal. The data from this study and other work (15-20, 22), confirms that even with 12 lead ECG monitoring, left ventricular ischaemia may not be detected with ST segment

monitoring. Although the degree of ST segment change does relate to the magnitude of ventricular dysfunction during balloon occlusion, this correlation is not close and there remain some patients in whom LV mechanics may become substantially altered in the absence of significant ECG abnormality (103). Furthermore, other ECG abnormalities thought to be indicative of myocardial ischaemia e.g. remote ST segment depression and alteration of R wave amplitude, have also been shown to be unreliable (84,102,71-75).

Myocardial Protection during PTCA

With the advent of prolonged balloon inflation there has been increasing attention focussed on methods that may ameliorate the ischaemic consequences of balloon coronary occlusion. This was foreseen even the pioneering days of PTCA as evidenced by Gruentzig's description of his first PTCA procedure, in which mention was made of a roller pump which could be employed if important ischaemia developed during the procedure (114). Such methods comprise pharmacological agents administered either systemically or via the intracoronary route, or methods by which regional myocardial perfusion is maintained during balloon inflation. Finally, intra-aortic balloon counterpulsation may be used, particularly if left ventricular performance is already subtantially impaired.

Pharmacological Intervention

Systemic nitroglycerin has been shown to reduce the extent of

myocardial injury in patients with acute infarction (115,116).

In addition to a reduction in the degree of ST elevation,

limitation of infarct size has been suggested (117,118).The

mechanism by which its beneficial effects are achieved

includes an increase in regional myocardial blood flow to the

ischaemic zone and a presumed reduction in myocardial oxygen

consumption with both arterial and venous vasodilatation

(119).

A delay in the onset of both chest pain and ST segment

alteration during PTCA has been shown following an

intravenous bolus of nitroglycerin (0.2 mg). Although no

significant change in LV wall motion was noted, displacement

of the diastolic pressure volume relationship during balloon

inflation was less pronounced (22). All the patients

described in our studies were pretreated with long-acting

isosorbide dinitrate (20 mg) 2 hours before the PTCA

procedure.

Beta adrenergic blockade has also been employed during PTCA

following the demonstration of a reduction in ST segment

elevation during acute infarction (120). Propranolol (0.1 mg

per kg) was given intravenously during LAD PTCA in 16

patients (121). Signs of myocardial ischaemia were not

prevented in 6 despite a comparable reduction in heart rate

in both responders and nonresponders.

The degree of myocardial protection afforded by the systemic

administration of drugs may be limited by the varying degree

of penetration of agents into the ischaemic zone (122). Thus,

in 21 patients undergoing PTCA, either propranolol (0.5 - 2 mg, 11 patients) or saline (10 patients) was injected into the index artery after 2 control balloon inflations (123).In the propranolol group the development of ECG evidence of ischaemia was delayed in comparison with the control group. Furthermore, in contrast to the results of intravenous studies, intracoronary administration produced a more homogenous response allowing for longer balloon inflation. There was no change in heart rate or blood pressure suggesting a regional protective effect. The majority of the patients described in our studies had been taking a beta-adrenergic blocking agent on a regular basis and this was continued on the day of the PTCA.

Serruys evaluated the role of intracoronary nifedipine (0.2 mg) during PTCA and observed effects on both regional left ventricular wall motion and myocardial lactate production (124). Nifedipine exerted a negatively inotropic effect reducing systolic function to the same extent as seen after 45 seconds of balloon occlusion in the absence of the drug. However, this abnormality of systolic function was associated with a reduction in myocardial lactate production and thus a regional cardioplegic role for nifedipine was suggested.

Similar results have been reported with the use of intracoronary Nicardipine (0.2 mg) which has the advantage of not depressing myocardial contractility (125). Many of the patients described in our studies were taking a calcium channel blocker on a regular basis prior to PTCA. In addition all our patients received a calcium antagonist as well as a

long-acting nitrate as premedication 2 hours before the procedure. Despite the presence of these agents, together with a beta-blocker in many cases, ST segment changes and left ventricular wall motion abnormalities still occurred in many patients during balloon inflation. However, this study did not address the specific role of these agents in the prevention or reduction of myocardial ischaemia in this setting.

Myocardial Perfusion with Arterial Blood

Distal coronary hemoperfusion was initially evaluated in dogs during prolonged coronary occlusion, arterial blood being delivered via the central lumen of the balloon catheter with a roller pump and flow rates of approximately 55 ml min-1 (126) Although myocardial ischaemia was reduced there was a high incidence of haemolysis and thrombosis. Studies in human subjects during PTCA have demonstrated a reduction in ECG and echocardiographic evidence of ischaemia and thus has allowed prolonged balloon inflation (127,128).

Distal coronary haemoperfusion during balloon inflation has also been studied using a modified balloon catheter which allows blood to enter the central guide wire lumen through a series of holes in the catheter shaft proximal to the balloon (129). Erbel has used such a continuous perfusion balloon catheter and showed in vitro that at a perfusion pressure of 120 mmHg flow rates of 63 ml min-1 for normal saline and 43 ml min-1 for a plasma expander, could be achieved. In 11

patients undergoing PTCA, balloon dilatation time could be prolonged (39 to 81 seconds) and both the incidence and time to onset of ST segment elevation, were reduced. A similar experience has been reported by other workers (130,131).

After the main body of work in this thesis was completed, we obtained the Erbel Continuous Perfusion Catheter (CPC) and were able to assess its ability to ameliorate ischaemia during PTCA in a pilot study using the ventriculographic analysis method described.

Four patients undergoing LAD PTCA were studied before PTCA and during balloon inflations with the CPC catheter. Studies during PTCA were performed in random order either with the guide wire still in the balloon catheter or with the wire withdrawn and therefore allowing anterograde blood flow into the distal LAD. Mean ejection fraction fell from 76% before PTCA to 61% without continous perfusion but only to 67% with perfusion. These changes were not significant. Wall motion analysis suggested only minimal preservation of anterior and apical contraction when perfusion was allowed in comparison to the regional dysfunction seen with the guide wire still in situ and therefore without perfusion.

Our impression of this catheter was that it did seem able to produce a modest reduction of ischaemia during PTCA. However, further studies using this particular balloon catheter were halted largely because its diameter, which had to be large in order to allow continuous blood flow, meant that it was relatively inflexible. Newer developments of this system, such as the Stack balloon catheter (ACS), are now available and may

prove to be valuable in particular clinical settings.

A modified balloon catheter which allows rapid (40 msec) R wave triggered inflation and deflation (60 msec) during diastole, has also been investigated by Kuhl (132). In 8 dogs he showed that mean coronary flow during balloon dilatation varied according to the balloon occlusion time. Thus, during 5 minute dilatations, mean coronary flow was maintained up to inflation times of 30% of the RR interval and decreased by 50% if balloon inflation was 80% of the cardiac cycle. No ischaemic ECG changes occurred and no reactive hyperaemia was seen supporting the authors' contention that sufficient coronary flow had been supplied during balloon dilatation.

Myocardial Perfusion with Oxygenated Fluorocarbons

An alternative to the perfusion of blood is the use of oxygen carrying Flourocarbon emulsions. These organic compounds have low viscosity but high oxygen carrying capacity and one example (Fluosol DA 20%) has received much attention as a possible agent that might mitigate the ischaemic effects of balloon occlusion during PTCA. Anderson infused oxygenated Fluosol at a rate of 60 ml min-1 through the balloon catheter during PTCA in 34 patients (133). Compared with balloon inflations incorporating an infusion of Ringers lactate solution, the onset of angina was delayed (33 to 41 seconds) as was the onset of ST segment elevation.

Cleman (134) similarly studied 20 patients undergoing LAD PTCA and compared left ventricular wall motion abnormalities

echocardiographically during balloon inflations with Fluosol or Ringers solution. He demonstrated that LV wall motion was better preserved during balloon inflation incorporating Fluosol, but deteriorated when Ringers solution was infused. These studies and others (128) confirm that the ischaemic consequences of balloon occlusion are improved by oxygen delivery rather than by enhanced washout of metabolites. During the course of our studies we attempted to obtain samples of Fluosol in order to assess its protective ability using our method during PTCA. Unfortunately it had not then been licensed by the Food and Drugs Administration in the USA and therefore was unavailable in the UK.

Retroperfusion

The supply of arterial blood to the ischaemic zone during PTCA has also been attempted with retroperfusion through the coronary sinus. The concept of myocardial protection by arterialization of the cardiac venous system was first introduced as a surgical procedure (135). More recently, specifically designed catheters direct arterial blood into the coronary sinus while the sinus itself is occluded during diastole with an inflated balloon (136). In a canine model, infarct size was reduced by approximately 35% during retroperusion of arterial blood while perfusion with venous blood, or intermittent balloon occlusion of the coronary sinus without arterial blood delivery, did not afford protection. The efficacy and safety of this intervention in patients has yet to be fully determined. Farcot (137) used

retroperfusion in 6 patients during PTCA with only 3 of the 6
showing improvement of indices of myocardial ischaemia.
Weiner (138) has also reported the use of coronary sinus
retroperfusion during LAD PTCA in 3 patients. Femoral
arterial blood was infused during diastole through an ECG
triggered autoinflatable balloon catheter and resulted in a
delay to the onset of chest pain compared with that during
PTCA balloon inflation without retroperfusion (28 to 99
seconds). Similarly, the time to the development of
comparable degrees of ST elevation was subtantially prolonged
(60 to 137 seconds).

Intra-Aortic Balloon Counterpulsation (IABC)

The use of IABC in reducing ischaemia during PTCA has not
been fully evaluated. The feasibility of this intervention
during PTCA has been reported in 14 patients (139) but in these
cases there was either severe haemodynamic instability prior
to PTCA, or the procedure itself had become complicated by
acute vessel closure.
It has been suggested that IABC should be considered in
patients undergoing PTCA with a large area of myocardium at
risk or in those in whom LV performance is already reduced
(140). This may include patients with acute infarction or post
infarction angina, particularly if PTCA is to be undertaken
to a vessel subtending a territory remote from a previous
infarction. This technique may therefore allow prolonged
balloon inflation in these high risk groups.

It can be seen from our pooled results, and from the individual data in Appendix 1., that in some cases LV performance became markedly impaired with a large reduction in ejection fraction. However, in no patient did severe haemodynamic derrangement result and therefore we did not need to consider intra-aortic counterpulsation in this group of patients. One explaination for this may be that we selected patients with normal resting left ventricular function for this study in order that we were more likely to produce a wall motion abnormality during PTCA. If some patients had a degree of left ventricular dysfunction before PTCA, haemodynamic deterioration may have developed during balloon inflation.

CONCLUSIONS

Balloon inflation during PTCA has been shown to produce a marked deterioration in left ventricular performance after only 20 seconds. This ischaemic abnormality may be modified by the presence of collateral vessels and in some cases mitigated by augmented contraction of non-ischaemic segments. ECG monitoring may be unreliable in the detection of ischaemia in this setting. This is particularly relevant in patients with already impaired ventricular function who may not tolerate even brief episodes of balloon coronary occlusion. Furthermore, if protracted balloon inflation is shown reduce the incidence of restenosis after PTCA, the

reliable monitoring of periprocedural ischaemia becomes even more important.

It is also likely that interventions designed to ameliorate ischaemia during balloon inflation will require assessment. This may be more accurate using analysis of left ventricular ischaemic abnormalities rather than depending solely on ECG indices of myocardial ischaemia.

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Individual Results: Data on 67 Patients

Values are listed in order according to the following sequence:

Patient no., no. coronary arteries diseased, vessel undergoing PTCA (1=LAD,2=RCA,3=LCX), collateral grade, study inflation no., inflation duration (sec), ST elevation (mm), ST depression (mm), LVEF pre-PTCA (%), LVEF during PTCA (%), LVEF post PTCA (%), anterobasal, anterior, apical, inferior, inferobasal segmental shortening (%) respectively pre-, during, post PTCA.

(-1 indicates a missing value)

1,1, 1,0,9,60,4,2,78,46,76,30,35,55,65,11,17,11,4,45,59,36,19,68,
  1,8

2,1, 2,0,3,60,0,0,58,52,61,30,38,42,48,0,16,25,36,35,15,44,35,21,
  5,10

3,1, 1,0,3,60,4.6,0,76,54,61,37,50,51,44,0,30,11,-3,37,38,40,35,
  64,40,0

4,2, 1,0,3,60,2.1,1.9,71,54,75,33,35,41,55,15,16,-14,-20,35,32,
  33,40,50,55,0

5,1, 1,1,4,60,0,1,77,72,77,50,45,55,52,0,51,9,15,64,50,56,30,58,
  47,10

6,1, 3,0,3,60,0,0,55,53,62,15,5,0,60,50,0,-20,-25,55,50,10,0,10,
  62,45

7,1,1,1,5,60,2.3,0,78,67,77,35,40,48,59,38,31,42,12,62,60,41,38,
  60,60,10

8,2,2,0,5,60,2.3,1.6,55,51,61,35,21,11,40,30,25,21,-1,23,17,34,23,
  5,51,29

9,1,3,3,4,60,0,0,63,59,70,41,26,39,40,8,16,19,35,41,0,31,29,54,39,
  10

10,1,1,0,3,60,6,0,73,42,74,37,40,46,52,38,30,0,-8,15,35,41,56,43,
  39,30

11,2,3,0,4,60,0,0,66,50,-1,15,29,30,39,8,26,31,25,17,0,-1,-1,-1,
  -1,-1

12,1,1,3,3,60,0,0,82,69,77,20,43,63,69,0,14,19,35,68,0,41,37,61,
  50,0

13,2,1,0,6,60,0,0,51,32,57,11,21,40,45,0,21,0,10,30,18,-1,-1,-1,
  -1,-1

14,1,2,0,6,60,1,2,79,62,74,12,35,58,60,10,10,33,55,35,-15,33,14,
  48,60,0

15,3,3,0,4,60,0,0,71,65,-1,12,21,35,58,4,15,30,10,58,37,-1,-1,-1,
-1,-1

16,3,4,0,2,60,1,2,69,56,-1,15,26,29,50,7,23,0,-12,50,36,-1,-1,-1,
-1,-1

17,1,1,1,3,60,2,1,78,44,70,27,29,60,46,0,2,-5,-7,35,56,20,5,50,
53,0

18,1,1,2,3,60,0,0,74,58,73,47,45,68,36,-10,55,-7,15,52,35,33,31,
30,50,45

19,3,1,1,3,60,2.5,1.5,61,40,-1,40,17,0,42,25,20,-5,-2,33,35,-1,-1,
-1,-1,-1

20,2,1,1,3,60,2.7,2,70,48,69,45,37,26,36,20,20,-5,10,59,30,37,32,
20,60,30

21,2,2,0,4,60,2,3,83,77,89,42,41,68,61,0,29,50,56,42,-20,15,40,65,
68,-5

22,1,1,2,4,20,0,0,62,50,69,52,17,25,45,22,50,-20,-5,40,30,35,15,
10,61,26

23,2,2,0,3,20,2.5,1.5,61,40,-1,17,28,48,40,5,10,24,40,0,3,-1,-1,
-1,-1,-1

24,2,1,0,3,20,6,0,69,53,-1,28,30,61,43,9,39,28,20,51,25,43,20,20,
67,30

25,1,1,0,3,20,7,2,80,45,72,52,49,63,57,4,20,13,10,30,30,45,36,58,
55,0

26,1,1,0,4,20,0,0,58,44,-1,30,38,40,11,0,37,28,10,19,0,-1,-1,-1,
-1,-1

27,1,1,0,3,20,3,2.5,68,44,66,43,37,39,52,10,10,12,7,58,0,30,37,40,
54,0

28,1,1,0,3,20,9,1.5,75,37,66,20,14,65,57,0,0,-4,10,40,22,26,19,15,
51,0

29,2,3,0,3,20,2,2,58,45,56,25,11,21,58,10,14,-18,29,35,25,34,-5,4,
53,37

30,1,3,0,3,20,2,1,77,62,75,40,47,53,57,-10,35,33,30,29,26,35,33,
30,63,25

31,1,1,0,3,20,4.5,2,70,60,-1,50,32,58,42,5,35,17,15,40,40,-1,-1,
-1,-1,-1

32,1,1,0,3,20,9,2,78,47,76,30,25,59,65,10,53,22,-14,35,0,34,26,60,
64,0

33,1,1,1,3,20,5,3,85,61,80,37,41,67,60,0,10,15,26,62,52,20,18,67,
69,10

34,1,1,1,3,20,2,0,81,73,81,21,38,62,21,0,21,12,61,29,1,32,35,70,
15,0

35,1,3,0,3,20,0,0,81,75,-1,15,6,59,66,19,29,33,55,43,10,-1,-1,-1,
-1,-1

36,2,1,0,3,20,4,1,82,61,84,45,58,48,46,12,58,22,-10,50,20,30,56,
59,59,5

37,1,2,0,3,20,2,0,70,61,70,50,37,27,12,0,38,32,29,-4,-2,37,37,31,
21,1

38,1,3,0,3,20,0,0,83,80,83,51,55,59,38,-7,43,48,57,54,-7,40,51,
68,60,-32

39,1,1,1,3,20,0,0,79,78,81,51,56,48,34,-11,32,48,45,57,4,42,54,
50,48,4

40,1,1,3,3,20,0,0,73,63,-1,46,57,40,37,0,42,55,29,46,11,-1,-1,-1,
-1,-1

41,1,4,0,3,20,0,0,75,75,-1,45,50,45,33,2,42,28,23,23,15,-1,-1,-1,
-1,-1

42,1,1,0,4,20,6,3,81,52,84,44,42,59,55,-5,24,12,15,48,23,40,23,68,
61,7

43,1,1,0,3,20,8,3,75,72,-1,33,39,46,55,0,16,29,49,55,13,-1,-1,-1,
-1,-1

44,1,1,0,3,20,6,2,72,39,71,47,40,42,34,9,15,8,10,57,7,50,50,34,
30,5

45,1,1,0,3,20,4,0,71,61,-1,37,43,45,43,1,40,27,23,50,19,-1,-1,-1,
-1,-1

46,1,2,1,6,20,0,0,86,77,86,46,66,55,37,5,40,50,48,34,4,50,58,58,
44,6

47,2,1,0,3,60,7,2,81,47,83,41,47,61,54,-11,23,8,5,58,19,41,53,59,
52,-5

48,2,1,3,3,20,0,0,73,53,74,43,40,35,54,32,43,29,12,32,14,51,40,54,
48,-2

49,1,1,2,3,20,0,0,78,63,-1,33,48,55,53,0,42,13,25,52,17,-1,-1,-1,
-1,-1

50,1,1,0,3,60,2,2,71,57,66,36,38,44,43,14,17,-6,18,62,31,36,37,30,
41,15

51,1,1,3,3,60,0,0,90,85,88,39,56,68,70,20,41,46,60,69,9,22,50,67,
75,14

52,1,1,0,5,20,1,0,79,55,-1,31,43,49,48,23,19,-2,16,54,27,-1,-1,-1,
-1,-1

53,1,1,-1,-1,-1,2,-1,57,29,-1,16,15,17,58,26,0,-8,2,55,29,-1,
-1,-1,-1,-1

54,1,2,-1,-1,-1,2,-1,79,63,-1,32,47,58,46,-8,27,26,46,30,11,-1,
-1,-1,-1,-1

55,1,2,-1,-1,-1,1.5,-1,75,68,-1,27,25,43,59,25,41,44,40,35,6,-1,
-1,-1,-1,-1

56,1,1,-1,-1,-1,0,-1,64,49,-1,25,23,35,55,18,38,19,-2,36,21,-1,
-1,-1,-1,-1

57,1,2,-1,-1,-1,3,-1,56,49,-1,38,41,6,15,15,32,35,22,15,-3,-1,
-1,-1,-1,-1

58,1,2,-1,-1,-1,3,-1,72,59,-1,33,41,55,36,-10,32,29,37,24,0,-1,
-1,-1,-1,-1

59,2,1,-1,-1,-1,2,-1,68,57,-1,5,13,49,58,4,18,3,28,61,12,-1,-1,
-1,-1,-1

60,1,1,-1,-1,-1,0,-1,60,50,-1,33,25,26,43,15,16,9,10,51,24,-1,
-1,-1,-1,-1

61,1,1,-1,-1,-1,4.5,-1,40,32,-1,17,1,-2,39,22,10,2,-2,19,28,-1,
-1,-1,-1,-1

62,1,1,-1,-1,-1,3.5,-1,60,46,-1,40,23,6,64,40,36,-7,-22,62,38,-1,
-1,-1,-1,-1

63,2,2,-1,-1,-1,1.5,-1,82,63,-1,26,43,64,60,-14,34,45,32,16,-8,-1,
-1,-1,-1,-1

64,1,1,-1,-1,-1,5.5,-1,39,21,-1,26,6,5,29,19,5,-14,-7,31,19,-1,-1,
-1,-1,-1

65,2,1,-1,-1,-1,5,-1,43,37,-1,-11,-17,16,42,15,8,3,4,29,18,-1,-1,
-1,-1,-1

66,2,2,-1,-1,-1,4,-1,52,36,-1,10,15,34,38,10,26,31,1,-8,-2,-1,-1,
-1,-1,-1

67,1,2,-1,-1,-1,3,-1,60,48,-1,24,36,31,36,2,37,35,18,3,-17,-1,-1,
-1,-1,-1