Use of the exercise maximal ST segment/heart rate slope in assessing the results of coronary angioplasty

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SUMMARY A new exercise test was used to assess the effects of coronary angioplasty in 22 patients. Twenty five angioplasty procedures were performed and the exercise maximal ST segment/heart rate slope was measured before and after operation on 23 occasions; in two patients treated for unstable angina the slope was measured only after the two procedures. Successful angioplasty (23 of the 25 procedures) resulted in a significant reduction of the maximal ST/HR slope, usually falling by the equivalent of single vessel disease according to previously published criteria. When angioplasty produced little angiographic change (two of the 25 procedures) the maximal ST/HR slope was not significantly altered. A second, and successful, angioplasty for these two patients led to a significant reduction of the maximal ST/HR slope.

Twelve patients were restudied by coronary angiography and exercise testing approximately six months after angioplasty. Of these, six had experienced recurrent chest pain, and the exercise test successfully identified the three who had restenoses and the three who did not.

Thus the maximal ST/HR slope was useful as a non-invasive and accurate method for following the progress of individual patients after coronary angioplasty.

Since the first successful percutaneous dilatation of a coronary artery in 1977 there have been encouraging reports^{1,2} of the technical feasibility of angioplasty and of its success in relieving angina pectoris. Early experience^{1,2} concentrated on the immediate haemodynamic and angiographic results, but subsequent reports³⁻⁵ have dealt with the problems of the longer term evaluation of the effects of angioplasty. Methods of evaluation have involved exercise testing, the obtaining of maximal ST segment depression, rate-pressure product, and workload, thallium-201 radioisotope scanning for myocardial uptake, and technetium-99m gated pool cardiac scintigraphy. These methods are insufficiently sensitive to replace coronary angiography as the investigation of choice for assessing the clinical significance of recurrent symptoms in individual patients.

A new exercise test, using the maximal ST segment/heart rate slope, in 230 patients with chest

pain was able correctly to predict the number of major coronary arteries significantly obstructed.⁶ The present study shows that with occasional exceptions this index of ischaemia has been reliable in the follow up of patients who have undergone angioplasty; preliminary reports of this investigation have already been given.^{7,8}

Patients and methods

Between April 1981 and May 1983, 22 patients with angina pectoris inadequately controlled by drug treatment underwent coronary angioplasty on 25 occasions and were investigated by exercise testing. During this time 10 other patients had coronary angioplasty in Leeds but did not take part in this exercise study. The reasons for their exclusion are as follows: uncontrolled hypertension (one patient), respiratory and orthopaedic problems rendering the bicycle exercise difficult or painful (five patients), and distance of the patient's home from Leeds making regular follow up awkward (one patient). The remaining three patients performed the exercise test before

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attempted angioplasty but did not repeat the test subsequently. Two of the three required emergency aortocoronary bypass grafting for uncontrollable occlusion of the vessels undergoing dilatation, and there was evidence in both cases for acute myocardial infarction. The final patient had an unsuccessful but uncomplicated attempt at angioplasty and proceeded to aortocoronary bypass grafting. This patient declined to have further exercise tests. Data from these 10 patients are not included in this report. There were no deaths.

Of the 22 patients studied, 17 were men and five women; their mean age was 48 (range 33-7-58-5) years and the mean duration of their anginal symptoms 25 (range 2-80) weeks. Four patients had previously experienced documented acute myocardial infarctions (three transmural inferior and one subendocardial anterior), the time intervals between these four events and the angioplasty being 2, 8, 12, and 127 months respectively. Discrete and severe proximal coronary stenoses were located in the left anterior descending artery in 18 patients and in the right coronary artery in four. Four patients had multiple vessel disease (three double and one triple vessel disease). In each of these patients the only artery considered suitable for bypass grafting was that which underwent dilatation. Three patients had a second angioplasty, two after an unsuccessful primary dilatation and one for a restenosis at the site of the original dilatation. For 23 of the angioplasty procedures patients were exercised both before and after the operation. Two patients who presented with angina at rest were studied only after the angioplasty operation.

ANGIOPLASTY

Coronary angioplasty was performed according to the method of Grüntzig,¹ with the patients prepared for open heart surgery and with full cardiac surgical standby facilities. Coronary angiography was performed with multiple views of both arteries using caudocranial and craniocaudal angulation before and immediately after dilatation.

The angioplasty was considered to have been successful if it resulted in a 30% or greater increase in luminal diameter. Treatment with nifedipine 10 mg three times daily, dipyridamole 100 mg three times daily, and aspirin 300 mg once daily was started before the preoperative exercise test and continued until the conclusion of the study. Six months after the angioplasty left ventricular and coronary angiography were repeated using the original radiological projections in each case and intracoronary glyceryl trinitrate in effective doses.⁹

MEASUREMENT OF ANGIOGRAPHIC NARROWING

The films were reviewed simultaneously by two

angiographers (NPS and DRS). The diameter of the affected vessel was measured in the narrowest part of the stenosis using calipers and was related to the diameter of the apparently "normal" vessel proximal to the stenosis. These measurements were performed in every projection used to determine the most severe degree of narrowing of the coronary artery, which was expressed as the percentage reduction in diameter. A significant stenosis was considered to be present when the vessel diameter was reduced by 75% or more.

The following radiological projections were used to examine the left coronary artery in every patient studied: 20° right anterior oblique; left lateral; 50°-60° left anterior oblique with 25° craniocaudal angulation; 30° right anterior oblique with 30° caudocranial angulation; 30° right anterior oblique with 30° craniocaudal angulation; and 30° true caudal. For the right coronary artery every patient was examined using the following three projections: 30° left anterior oblique with 30° caudocranial angulation; 30° right anterior oblique with 30° caudocranial angulation; and right lateral. Where the anatomy of the vessels, or of the stenosis, required further clarification extra views were taken, which were repeated after the angioplasty and six months later in those patients who were restudied.

EXERCISE TESTING

The new exercise test^{10,11} was performed immediately before angioplasty (usually the day before) and between three and seven days afterwards. It was then repeated at the time of a further coronary angiogram performed six months later. The purpose of the exercise test was to determine the maximal ST segment/heart rate slope (ST/HR slope), which is an index of the severity of coronary artery disease,⁶ and to examine the changes in this value in each patient after angioplasty. Although the exercise test and the calculation of the maximal ST/HR slope have recently been reported in detail,^{10,11} a brief description is given here:

The electrocardiogram is recorded at a paper speed of 25 mm in 13 leads (12 standard and one bipolar CM5) using an ink jet recorder (Mingograph 62; Siemens) during the steady state of each stage of upright bicycle exercise. During a period of preliminary exercise the workload is adjusted such that each increment is associated with a rise in heart rate of approximately 10 beats/min. The heart rate and the mean ST segment depression are meticulously measured over at least 10 consecutive beats in all 13 leads at each stage of exercise using a magnifying glass fitted with a graticule. A line joining adjacent PR segments is used as the reference zero for the measurement of ST segment displacement. Thus a relation between increasing heart rate and progressive ST segment depression may be obtained. In some of the leads the linear regression of ST segment depression on heart rate achieves statistical significance, and the slopes of these lines are con-

Fig. 1 Angiographic narrowing in 22 patients before and after 25 angioplasty procedures and in 12 of these patients six months later. Continuous lines indicate the changes seen after 22 primary attempts at angioplasty. There are 19 continuous lines since the data from three pairs of patients are identical and are therefore represented by three lines. The data points from three patients who subsequently had a second angioplasty are marked A (case 1), B (case 2), and C (case 3) followed by (1). Broken lines indicate the changes after second angioplasty procedures in two patients, cases 1 and 2, whose first angioplasty attempts had been unsuccessful. The data points are marked by A(2) and B(2). The broken line indicates the change seen after the second angioplasty in case 3 whose restenosis was noted at six months. The data points are marked C(2).

sidered. The steepest of these lines of regression is the maximal ST/HR slope which is expressed in units of mm. beats⁻¹. min. 10⁻³.

In patients presenting with chest pain, the maximal ST/HR slope has been shown correctly to identify the number of major coronary arteries significantly narrowed.^{10 11} This has allowed the description of four distinct ranges of the maximal ST/HR slope in patients with triple, double, single, and no significant vessel disease respectively. The maximal ST/HR slope is measured with a very small variability (tolerance limits $\pm 1.9\%$)¹⁰ and is unchanged in patients taking

beta blocking drugs in therapeutic doses.¹²

The exercise tests were analysed by members of the team unaware of any angiographic findings.

Results

Twenty five angioplasty procedures in 22 patients were investigated by exercise testing. First attempts at angioplasty were successful on 21 occasions and produced very little angiographic change on another two occasions. These two patients had second and successful angioplasty procedures some six weeks after the first attempts. Thus overall there were 23 successful dilatations and two failures according to our angiographic criteria.

IMPROVEMENT IN ANGIOGRAPHIC NARROWING

Fig. 1 showed the changes in the degree of reduction in vessel diameter associated with 25 angioplasty procedures in the 22 patients and in 12 of these when restudied by coronary angiography six months later. The changes are striking except for those in two patients (cases 1 and 2), who showed no significant angiographic improvement. Both these patients had second and successful angioplasties, and the changes in vessel diameter are shown in Fig. 1. Overall, for the 25 procedures in the 22 patients the mean reduction in vessel diameter before angioplasty was 91.5% (range 70–99%) and immediately after angioplasty 40% (range 10–99%). This change was statistically significant ($p < 0.0005$; paired t test).

Twelve of the 22 patients underwent further coronary angiography six months after their angioplasty. From Fig. 1 it is clear that three of these patients had significant restenosis, and in one of the patients the vessel which had been dilated had become totally occluded. Of the two patients with patent but restenosed vessels, one (case 3) also showed appreciable progression in the severity of another lesion in the main lateral branch of a non-dominant circumflex artery. This patient elected to have a second angioplasty, and his restenosed anterior descending artery was successfully redilated. No attempt was made to dilate the lateral circumflex stenosis, which for technical reasons was unsuitable for angioplasty. Otherwise, for the nine other patients who have been restudied at six months, there was no significant difference between the degree of reduction in vessel diameter immediately after angioplasty (mean 34.5%, range 15–50%) and that seen six months later (mean 30%, range 0–60%) ($p > 0.20$; paired t test).

EFFECT OF ANGIOPLASTY ON THE MAXIMAL ST/HR SLOPE

The exercise test was performed both before and after angioplasty on 23 occasions and only after angioplasty

Fig. 2 The maximal ST/HR slope obtained before and after 25 coronary angioplasty procedures in 22 patients and in 12 of these patients at the time of a further coronary angiogram six months later. The limits of the ranges of the maximal ST/HR slopes previously shown in 230 patients are indicated; N, no significant vessel disease; 1VD, single vessel disease; 2VD, double vessel disease; and 3VD, triple vessel disease. Long continuous lines indicate the changes observed after the first attempts at angioplasty. There are 17 continuous lines representing 20 procedures since identical results in two and three patients respectively are represented by single lines. The three patients (cases 1, 2, and 3) who had a second angioplasty are marked A, B, and C followed by (1) at the appropriate points on the figure. Short continuous lines in the range of no significant vessel disease indicate the results from two patients with unstable angina who had no preoperative exercise test. Broken lines indicate the changes after second angioplasty procedures because of an unsuccessful primary attempt and are marked A(2) (case 1) and B(2) (case 2). The dotted line indicates the change after a second angioplasty for a restenosis shown at six months and is marked C(2) (case 3).

in two patients presenting with unstable angina. The change in the maximal ST/HR slope associated with these 23 procedures and the results after angioplasty in the other two patients are shown in Fig. 2. In addition, the results of exercise testing at the time of a further coronary angiogram performed six months

later are shown for 12 of the patients. All but two of the procedures were associated with a significant fall in the maximal ST/HR slope. The two exceptions are the results for the two patients (cases 1 and 2), in whom angioplasty was unsuccessful and produced virtually no angiographic alteration. Whereas unsuccessful angioplasty produced insignificant changes in the slope, in the same patients successful angioplasty significantly reduced both the slopes.

In general, when angioplasty was successful the maximal ST/HR slope was reduced from a value in the region appropriate to the patient's angiographic status before the dilatation to a value in the region appropriate to one less vessel disease. Thus the patient with triple vessel disease had an improvement in the maximal ST/HR slope from a value appropriate to triple vessel disease to a value appropriate to double vessel disease. Likewise, the patients with double vessel disease improved their maximal ST/HR slopes from the value of double vessel disease to that of single vessel disease. Angioplasty, which was effective in the patients with single vessel disease, was associated with an improvement in the maximal ST/HR slope by the equivalent of single vessel disease in all but three patients. The results from the two patients with unstable angina, after successful angioplasty, fell within the range of values for patients with no significant disease. Of the three exceptions to this pattern one patient with single vessel disease had a slope appropriate for double vessel disease and which improved after angioplasty to a value appropriate for single vessel disease, a result which has been confirmed by further outpatient exercise tests. Two patients with single vessel disease who had angioplasties which were immediately successful did not show improvement of their maximal ST/HR slopes out of the range of values for single vessel disease. One of these patients had an initial angiographic improvement from 99% to 65% vessel narrowing and was subsequently shown to have a complete occlusion of that artery six months later. It is quite possible that this artery became occluded early in the patient's post-operative course. The second patient had proved and documented variant angina associated with localised atherosclerotic disease of the proximal left anterior descending artery. Angioplasty was completely successful, improving the narrowing from 75% to 15%, and at six months the original area of disease was no longer apparent. The maximal ST/HR slope improved from 21 mm. beats⁻¹. min. 10⁻³ (upper limit of the range for single vessel disease) before the dilatation to 14 mm. beats⁻¹. min. 10⁻³ (lower part of the range for single vessel disease) immediately afterwards. At the time of the further coronary angiogram six months later the slope was still within the range of values for single vessel disease. As has been stated, all

the exercise tests were performed in this patient using the same drug protocol, which did not include beta blocking drugs. The angiography at six months was performed with and without intracoronary nitroglycerine, but no significant difference in the appearance of the previously treated vessel was apparent. An ergonovine test was not performed.

Overall, for the 23 procedures the mean maximal ST/HR slope before angioplasty was $25.68 \text{ mm. beats}^{-1} \cdot \text{min.} \cdot 10^{-3}$ (range 14.0–71.0) and after all 25 procedures $12.24 \text{ mm. beats}^{-1} \cdot \text{min.} \cdot 10^{-3}$ (range 6.0–34); the differences by a paired *t* test are statistically significant ($p < 0.05$).

During the first six months after angioplasty, six of the patients whose dilatations had been successful had a recurrence of their symptoms. All six patients had single vessel disease, and all were reinvestigated by exercise testing and coronary angiography. In three of the symptomatic patients the maximal ST/HR slope and subsequent coronary angiography showed no significant change from the results obtained immediately after angioplasty. In the other three patients with angina, there were significant changes. As described earlier, one patient had a totally occluded vessel and two others had clinically important restenoses. One of these patients (case 3) had an improvement in the maximal ST/HR slope from single vessel disease to no significant disease after his original angioplasty (Fig. 2). The ST/HR slope calculated at the time of coronary angiography six months later suggested the presence of double vessel disease, and the angiograms showed not only a significant restenosis at the site of the angioplasty but also progression of disease in another major vessel. After successful redilatation of the recurrent stenosis (Fig. 2) the slope was reduced to a value in the range for single vessel disease. The other patient with a restenosis was one of the two men who presented with unstable angina, and his maximal ST/HR slope increased from the value for no significant disease to that of single vessel disease. He elected to have aortocoronary bypass grafting rather than a second angioplasty. None of the four patients with double or triple vessel disease experienced any further symptoms. Therefore, in each of the three patients with significant angiographic deterioration at six months the exercise test was strongly suggestive of the deterioration, and in two of the cases the maximal ST/HR slope was significantly increased when compared with the results obtained after the initial angioplasty.

DIAGNOSTIC ACCURACY OF THE MAXIMAL ST/HR SLOPE

There were three occasions when a comparison of the maximal ST/HR slope and coronary angiogram could be made—that is immediately before angioplasty,

immediately after angioplasty, and at six months after angioplasty. Fifty seven comparisons were made comprising 20 before angioplasty (three patients (cases 1, 2 and 3) had repeated attempts), 25 immediately after angioplasty, and 12 six months later. Of the 57 comparisons, 52 showed agreement. Thus, there were five occasions when comparison of the ST/HR slope and coronary angiograms showed disagreement. Two of these five comparisons were in a patient with variant angina. As has been stated, angioplasty was successful but the ST/HR slope remained within the range of values for single vessel disease and the coronary angiograms six months later showed no abnormality at the site of the dilatation. We have no certain explanation for the persistence of ischaemia, but it may well be related to that patient's known propensity for coronary vasospasm. Disagreements between the exercise results and the coronary angiographic findings were also seen before and after successful dilatation of a proximal left anterior descending stenosis in another patient with single vessel disease. The ST/HR slope before the procedure suggested double vessel disease, whereas three days after dilatation the ST/HR slope suggested single vessel disease. No explanation for the overestimation of ischaemia in this case is available from the angiographic or clinical evidence, although the improvement in the ST/HR slope was of such magnitude that any restenosis might be expected to produce an easily detectable change. The fifth disagreement occurred after a marginally successful angioplasty in which a stenosis was dilated from 99% to 65% diameter reduction. This patient's ST/HR slope showed only slight improvement, and six months later the vessel in question was found to be occluded at the site of original stenosis. It is quite possible that at the time of the exercise test a few days after the angioplasty the degree of narrowing in the dilated vessel was already increasing.

Thus in patients with recurrent angina the maximal ST/HR slope correctly predicted the occlusion and the two restenoses before the repeat angiograms at six months. It was unchanged in the three other patients with less severe recurrent symptoms, and the angiograms confirmed that there had been no restenosis in those three cases.

Discussion

The proper postoperative management of patients after coronary angioplasty requires a non-invasive assessment of ischaemia. The emergence of an objective and quantitative exercise index of ischaemia, the maximal ST/HR slope, has allowed us (a) to compare the index with initial and subsequent angiographic appearances of the coronary vessels and (b) to interpret the clinical significance of recurrent symptoms.

Such a non-invasive technique has not been available before. Grüntzig *et al.*'s original account¹ of the results of angioplasty used several inadequate means of assessing the effects of coronary angioplasty. They used submaximal bicycle exercise testing and measured improvement by means of a symptomatic classification and by the use of steady state working capacity as a percentage of that predicted after adjustment for age, sex, and height.¹ Hirzel and his co-workers³ recognised that it was necessary to use a method to test "the functional capacity of the vessel" and used thallium-201 myocardial scintigraphy. None of his patients so studied had a history of myocardial infarction and all had single vessel disease, which made interpretation of their tests much easier. Even in these patients the sensitivity of the thallium scanning test was only 88%, and the authors accept that the technique is at best only semiquantitative. The appearance or reappearance of regional perfusion defects after angioplasty in single vessel disease may be useful in the diagnosis of restenoses but is unlikely to be applicable in patients who have experienced sizeable myocardial infarctions or who have more than single vessel disease. These limitations suggest that thallium scanning is not appropriate for repeated studies in individual patients. The cost of radionuclide scanning has recently been compared with that of exercise testing and of coronary angiography.¹³ At 1980 prices, an exercise test was costed at US \$100, a thallium scan at US \$350, and a coronary angiogram at US \$2000. Under these circumstances the yield of information does not seem to justify the expense of thallium scanning.

The use of exercise electrocardiography to determine absolute values of ST segment depression also has well known limitations. These limitations in terms of sensitivity and specificity have been the subject of a wide ranging review.⁶ At present, most patients who are candidates for angioplasty have single vessel disease, and false negative results are more likely in this group of patients than in patients with more extensive coronary artery disease. The lack of adequate sensitivity and specificity means that conventional exercise testing is not suitable for the accurate assessment of changes in myocardial ischaemia in these patients having coronary artery dilatation.

An approach which combines treadmill exercise testing with thallium 201 scanning has been described by Scholl *et al.*⁴ Preoperatively in their 54 patients the exercise test, recording from 15 leads (12 standard plus bipolar leads CM5, CC5, and ML), was abnormal in 32 (59%) of the patients. The thallium scan was abnormal in 36 (67%). Of the 10 patients who had both negative exercise tests and negative thallium scans, seven failed to reach their target heart rates. When these seven patients are excluded from the

analysis, the sensitivities of the exercise test and the scintigram were 67% and 80% respectively. Post-operatively, in asymptomatic patients abnormal exercise tests or thallium scans or both were observed in three sets of patients: (a) those having partial or probable restenoses; (b) those with more than single vessel disease; and (c) four patients in whom no obvious explanation was apparent. Thus despite extensive investigation these authors had no non-invasive alternative to the coronary angiogram for diagnosing restenosis or progressive disease after angioplasty.

The maximal ST/HR slope had been shown⁶ with a confidence of 99% to be able statistically to predict the presence or absence of significant coronary artery disease (defined here as one or more major proximal coronary arteries with a 75% or greater luminal diameter narrowing) in at least 98% of patients with angina. Many patients presenting with symptomatic coronary artery disease are able to perform a submaximal bicycle exercise test enabling calculation of the slope. There are no indeterminate results and the test is equally applicable to patients undergoing treatment with beta blocking agents. The presence of discrete ranges of values of the maximal ST/HR slope for patients with no significant disease, and with single, double, and triple vessel disease offers an index of ischaemia against which the performance of manoeuvres taken to alleviate myocardial ischaemia can be measured. In our group of patients, angiographically successful angioplasty was associated with an improvement in the maximal ST/HR slope usually by the equivalent of single vessel disease. Inadequate vessel dilatation resulted in only slight, and insignificant, changes in the slope. Thus in 22 patients having 25 procedures there were 57 comparisons of the coronary angiogram and the maximal ST/HR slope; there was agreement on 52 occasions.

The new exercise test was helpful in interpreting recurrent symptoms. Six of the 22 patients had recurrent symptoms after angioplasty. The recurrence of angina suggested that a restenosis might have taken place. The exercise test detected the three patients who had had occlusion or restenosis of the vessels which had been dilated. One of these patients had a significant progression of disease elsewhere, and the test detected this too. In another three patients it refuted the diagnosis of any restenosis where no significant deterioration in the vessel dilated was observed at subsequent coronary angiography. These observations showed the value of the coronary angiogram six months after angioplasty and emphasise the somewhat unreliable relation between symptoms and the degree of coronary luminal narrowing. No recurrence of angina has been reported by the four patients who originally had double or triple vessel disease. These four patients with multiple vessel disease all

continued to have more than 1 mm horizontal ST segment depression in some leads at submaximal heart rates after successful angioplasty. In such patients the accurate interpretation of recurrent symptoms would seem impossible without resorting to repeated coronary angiography. We found, however, that successful dilatation reduced the maximal ST/HR slope by the equivalent of single vessel disease and that a restenosis was associated with a return of the maximal ST/HR slope to values appropriate for the original degree of coronary disease or worse. These findings indicate that the maximal ST/HR slope may be valuable in interpreting the clinical significance of recurrent angina after coronary angioplasty, although the numbers examined so far are too small to draw a definite conclusion.

In conclusion, in this study angioplasty was successful in 23 of 25 attempts. There was a pronounced improvement in angiographic narrowing and in symptoms. One late occlusion and two restenoses were found, and both were associated with recurrent angina. Three other patients experienced some recurrence of angina but were found not to have had restenoses. This new exercise test, the maximal ST/HR slope, correctly predicted the state of the vessels in 52 of 57 coronary angiograms. The five disagreements between the exercise test and the coronary angiograms occurred in three patients. Possible explanations are available in one case in which the vessel treated was subsequently discovered to be occluded and in a second patient with variant angina. No explanation for the overestimation of ischaemia is available in the third patient. The success of angioplasty in relieving symptoms in those patients with multiple vessel disease suggests that more patients may be considered suitable for the procedure. Likewise, the clearly apparent improvement in the maximal ST segment/heart rate slope after angioplasty suggests that this new exercise test may be useful for the evaluation and follow up of such patients.

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