Journal of Cardiology 21: 565–578, 1991

Observer accuracy and confirmation of the important role of abnormal ST/T time course behavior in the evaluation of stress electrocardiograms

Clifford W. BARLOW
John B. BARLOW
Evan R. SOICHER*
Brian M. FRIEDMAN
Ronald M. JARDINE
Jeffrey KING
Dirk P. MYBURGH*
David H. G. SMITH*

Summary

Routine exercise electrocardiography has been criticized for yielding too many so-called "false-positive" results. Recent studies in our institution indicate that evaluation of the time course behavior of ST segment and T wave (ST/T) changes after cessation of exercise differentiates ischemic from non-ischemic ("false-positive") stress electrocardiograms (SEs). Our method of assessing time course behavior is clarified. The principal aim of this study was to determine the accuracy of experienced observers in making this differentiation. Records of consecutive patients undergoing coronary arteriography over a 2 year period were reviewed and 30 with SEs judged positive for ischemia by the widely accepted ST/T configurational criteria alone were selected at random for the investigation. Sixteen subjects had normal coronary angiograms and had therefore previously been regarded as having false-positive SEs. Fourteen patients had at least one significantly (>70%) stenosed coronary artery which

Department of Cardiology, University of the Witwatersrand, and the Johannesburg Hospital, Johannesburg; and *the Institute of Aviation Medicine, Pretoria
Address for reprints: J.B. Barlow, M.D., F.R.C.P., Department of Cardiology, University of the Witwatersrand, York Road, Parktown 2193, South Africa

Presented in part in a lecture delivered by J.B. Barlow at the University of Tokyo, July 23, 1990
Received for publication September 4, 1991; accepted September 7, 1991 (Ref. No. E-91-3)

was our yardstick for ruling that true myocardial ischemia, due to epicardial coronary artery disease (CAD), was present. Five observers, familiar with post-exercise ST/T time course patterns, independently and " blindly " analyzed all 30 configurationally abnormal SEs. Observers were informed only of the patient's age and sex; they were thus unaware of symptoms, exercise variables, coronary anatomy and the number of patients in the 2 groups. The observer consensus for ischemia of SEs using time course analysis was: total test accuracy 87%, sensitivity 79%, specificity 94%, positive predictive value 92% and negative predictive value 83%. Because all 30 patients had ST/T abnormalities, results of the sample for ischemia based on configurational criteria alone were sensitivity 100%, specificity 0% and positive predictive value 47%. We concluded that time course analysis plays a crucial role in evaluating SEs and that exercise electrocardiography remains a safe, cost-effective and reliable method of screening many asymptomatic, as well as symptomatic, subjects for CAD.

Key words
Exercise electrocardiography　　False positives　　ST/T time course behavior

Introduction

Exercise stress testing is a safe, non-invasive and easy investigation to perform[1,2]. It is important in the evaluation of chest pain[3~5], arrhythmias[6~8], effort tolerance, and in the detection of ischemia post-infarction[3,7]. It also contributes to the choice of therapeutic modality and the benefit derived from such therapy. Many exercise variables, in addition to the electrocardiographic changes, are of importance in analyzing stress tests[1,7,9]. These include duration and amount of exercise completed, blood pressure and heart rate response, and development of symptoms[10,11]. More complicated ST segment/heart rate relationships[12,13] and computer derived treadmill scores[14] have been developed to improve stress test accuracy. Radionuclide testing[15,16], exercise echocardiography[17,18] and pharmacological techniques[19~22] may also improve the evaluation of stress testing but increase the cost and complicate the investigation.

In the contemporary clinical setting, evaluation of the patient's exercise variables and the ST segment and T wave (ST/T) electrocardiographic changes are the primary markers used to assess whether a stress test indicates ischemia or not[5]. Exercise variables may often be unremarkable, in which case the configuration and extent of the ST/T changes have generally determined whether or not the stress electrocardiogram (SE) is evaluated as ischemic[1,2,5].

A number of coronary angiographic studies in patients developing ST segment depression following stress testing have suggested that this test has a poor positive predictive value for demonstrating coronary artery disease (CAD)[7,23~26]. Moreover, Bayesian analysis indicates that a limited test accuracy is likely when standard electrocardiographic criteria are applied[27]. In an attempt to improve the accuracy of the exercise stress test, analysis of the time course behavior of abnormal ST/T configurational changes after cessation of exercise[28,29] has received our attention[1,30,31]. We have delineated the various non-ischemic time course behavior patterns and contrasted them to the importantly different and less complex ischemic responses. Our ongoing experience has confirmed that by applying time course analysis, the sensitivity for diagnosing ischemia improves[30,31].

The principal aim of this study was to evaluate how accurately " blinded " observers, familiar with the analysis of post-exercise abnormal ST/T time course patterns, could differentiate ischemic from non-ischemic " false-positive " SEs. All SEs studied had previously been judged positive for ischemia on generally accepted ST/T configurational changes[5]. We emphasize that, throughout this study, we equate and correlate the terms " ischemia " and " non-ischemia " (false-positive) with the presence or absence of epicardial coronary artery disease as

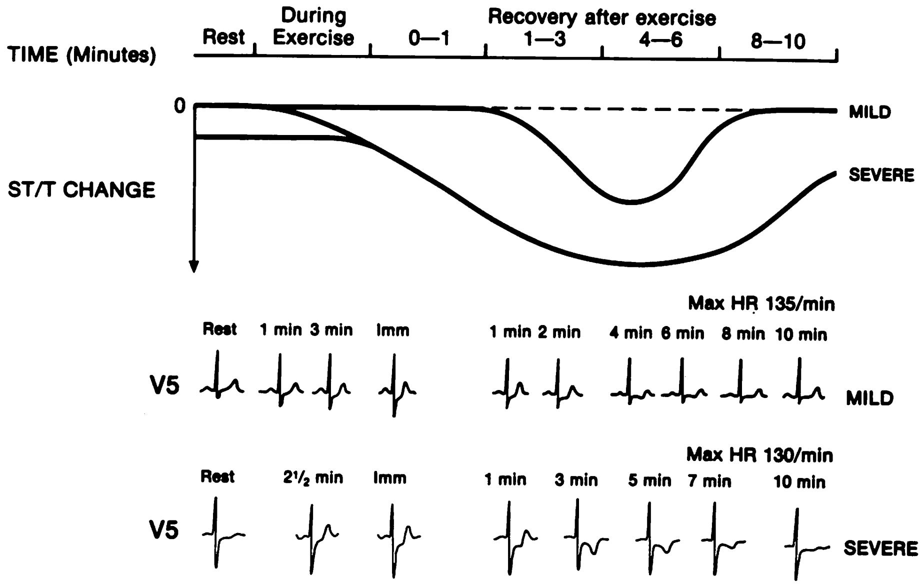


Fig. 1. Graphic representation of mild (onset about 2 min after exercise, offset about 8 min after exercise—upper curved line) **and severe** (lower curved line) **ischemic ST/T time course behavior patterns.**

In this and subsequent illustrations, the extent of ST/T configurational changes at rest, during and after exercise, are demonstrated by the vertical distances at relevant times of the curved lines below the baseline marked " O " and reflecting normal ST/T. The lower ECG recording shows lead V_5 from the stress ECG of a 54-year-old man with severe myocardial ischemia (triple vessel disease on coronary arteriography) and should thus be correlated with the lower curved line. At rest the tracing is marginally abnormal. Immediately post-exercise, the ST segment is very depressed and nearly horizontal (early onset). The ST/T are worse at one min because the ST is horizontal. From 3-7 min after exercise, although the ST segment is less depressed, especially at 7 min, the ST/T changes are assessed as most severe because the ST segments are downsloping (see text). At 10 min, the ST/T remain slightly more abnormal than at rest (late offset). The upper ECG tracing (mild) reflects the stress test of a 46-year-old woman with an 80% stenosis of her circumflex coronary artery and should be correlated with the upper curved line (mild). The ST segment is normal at rest, depressed but still upsloping, immediately and one min post-exercise. The ST segment is horizontal and definitely abnormal at 2 min (late onset) and the ST/T return to normal at 8 min (early offset) after effort. The ST changes are judged worst for ischemia at 4 and 6 min post-exercise because, albeit not depressed, they are downsloping. The T waves are biphasic but remain predominantly upright. Maximal heart rates (Max HR) shown in this and subsequent stress test examples were usually recorded immediately after exercise.

demonstrated on selective coronary angiography. We do not address nor do we attempt to exclude the possibility that the ST/T abnormalities with a non-ischemic time course pattern may in some instances reflect true myocardial ischemia resulting from abnormal function of the coronary microvasculature[32]—a somewhat ill-defined entity variously called Syndrome X[33] and microvascular angina[34]. Prior to elucidating the methodology, it is relevant to clarify time course analysis and the various time course patterns.

Description of time course patterns

Time course analysis depends essentially[1] on

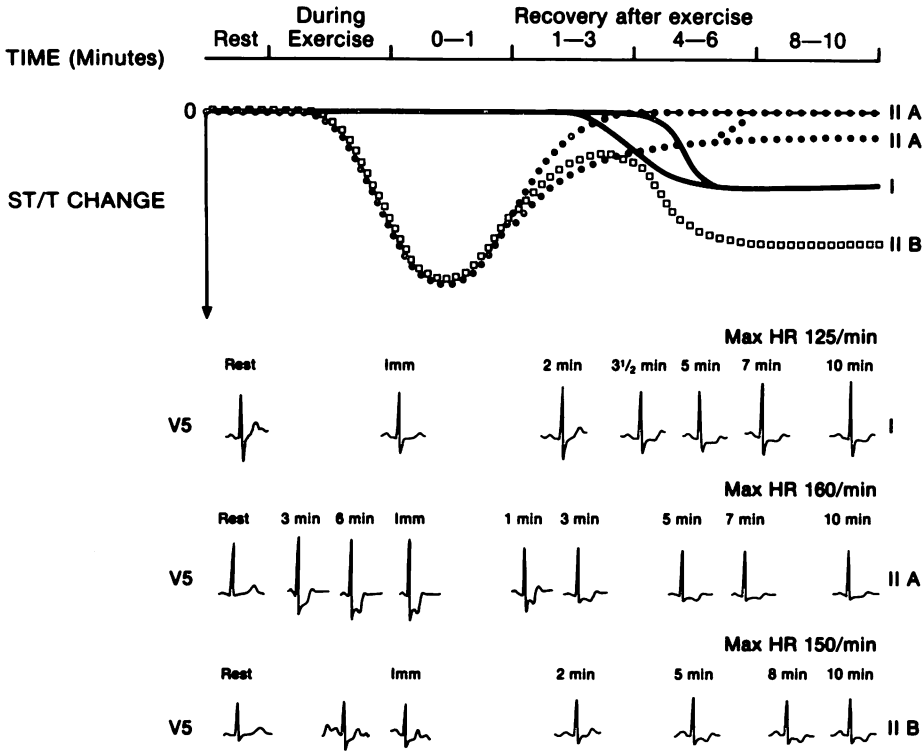


Fig. 2. Schematic representation (as described in Fig. 1) **of Types I and II non-ischemic time course patterns.**

Examples of V_5 from stress ECGs of 3 patients with these non-ischemic time courses are demonstrated. Type I remains normal or is only mildly abnormal until the 3 to 10 min post-exercise period. Type II improves one (see ECG IIB) to 3 (see ECG IIA) min after exercise but may later deteriorate again (IIB). The late onset, late offset of the Type I patient and the early onset, early offset of the 2 Type II SEs differ dramatically from ischemic time course. Predictably, coronary arteriography was normal in all cases.

a comparative evaluation of the ST/T configurations before exercise with those ST/T changes that may supervene or become more abnormal during the 10 min post-exercise period (**Fig. 1**). Although observations during exercise on ST/T are now widely practised with treadmill stress testing, assessment of time course behavior patterns relates solely to the post-exercise phase. When the ST/T changes occur during exercise, these are invariably recorded unaltered in the immediate post-exercise tracing. The ST/T configurational alterations are evaluated on the assumption that if they reflect ischemia at a specific time, the appearances should be graded in accordance with the electrocardiographic severity of the ischemia. Thus an upsloping ST segment occurring immediately after exercise reflects, if ischemic at all, relatively mild ischemia whereas a horizontal ST segment, especially when depressed below the isoelectric line, would indicate more advanced ischemia. A downsloping ST segment, which is often associated with a partially or completely inverted T wave, reflects greater " ECG ischemia " even if there is no or less ST segment depression than when the ST segment was horizontal (**Fig. 1**). The fact that the ECG evidence of verified myocardial ischemia does not always correlate with the ex-

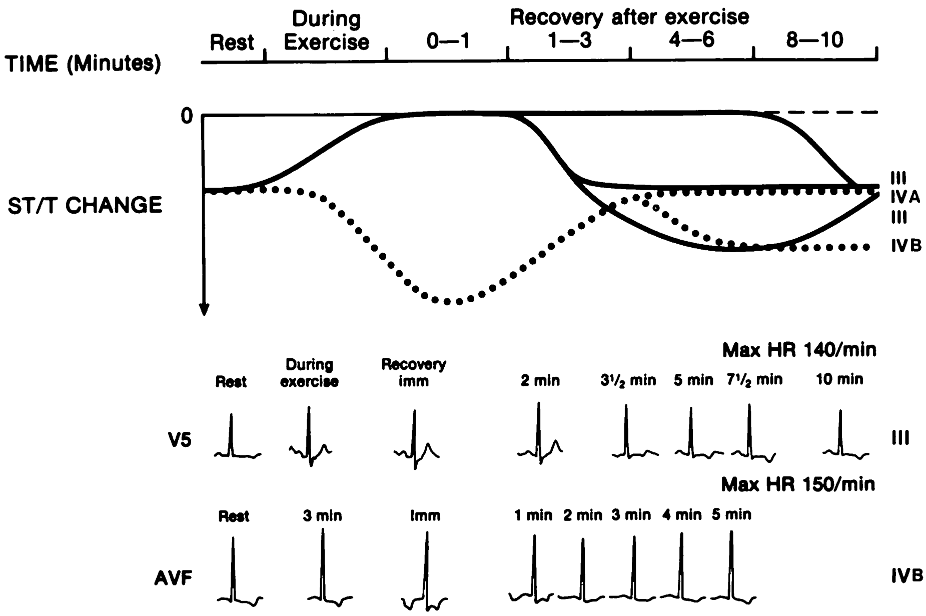


Fig. 3. Schematic representation (as described in Fig. 1) **of Types III and IV non-ischemic time course patterns.**

ECGs are, by definition, "abnormal" at rest. Examples from stress ECGs of patients with Types III and IVB are shown below. Lead aVF of the Type IVB patient improves at 2 min post-exercise but deteriorates again at 4 and 5 min (see text). Selective coronary arteriography in both patients was normal.

tent of anatomical CAD[5,22] is not pertinent to the assessment of time course behavior patterns.

Evaluated in this manner, the SE time course patterns of the ST/T changes that denote true myocardial ischemia are late onset, early offset when the ECG evidence of ischemia is mild and early onset, late offset when it is severe (**Fig. 1**). Most cardiologists are aware that early onset ST/T changes occurring soon after starting exercise, and thus prominent in the immediate post-exercise recording, persist for at least 8 min into the recovery phase and reflect severe ischemia[3,14]. Relatively mild ischemic ST/T changes, on the other hand, whether due to modest coronary artery stenosis, inadequate exercise completed or stress testing undertaken during therapy with a β-receptor blocking agent, may only appear in the recovery phase and do not last as long (**Fig. 1**). Non-ischemic time course patterns are more variable but importantly different. Other workers have also observed[28,29,35,36] that the ST/T time course interpretation is contributory in analyzing SEs but the 4 different types, arbitrarily labelled I–IV, were delineated[1], practised[30,37] and slightly modified[31] in our laboratories. Patients with normal resting ECGs would belong to Type I or II (**Fig. 2**), whereas those having the ST/T changes at rest would be classified as Type III or IV (**Fig. 3**).

Non-ischemic time course patterns may seem complex but there are, in fact, only 2 principal non-ischemic responses during the 10 min recovery phase. Types II and IV changes are early in onset and early in offset. The ST/T abnormalities are thus worst during and, most importantly re time course analysis, immediately after exercise (i.e., early onset), improve one to 3 min after exercise (i.e., early offset) but in both Types II (**Fig. 2**) and IV (**Fig. 3**) the

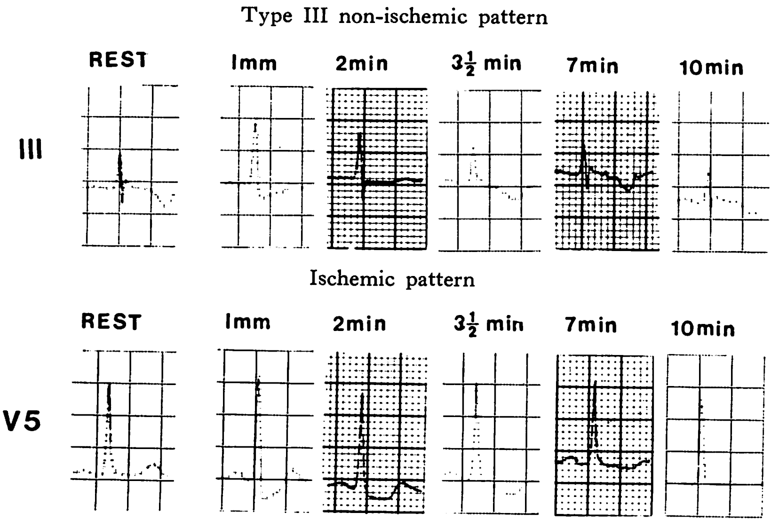


Fig. 4. Resting and post-exercise ECGs of a 53-year-old man (see patient 1, Table 4) **who showed a Type III non-ischemic pattern with normalization of inverted T waves immediately after effort in standard lead 3 but an ischemic pattern in V_5.**

He had typical angina with a billowing mitral leaflet clinically. Coronary arteriography showed significant 2 vessel coronary artery disease.

ST/T may become more abnormal again during the 4 to 10 min post-exercise period. Types I (**Fig. 2**) and III (**Fig. 3**) have late onset, late offset ST/T changes during the post-exercise phase but Type III, which is abnormal at rest, has the additional easily identifiable feature of normalizing during and therefore also immediately after effort (**Figs. 3, 4**).

Methods

Selection of stress electrocardiograms

Records of more than 2,000 consecutive patients undergoing coronary arteriography at our institutions over a 2 year period ending December, 1988, were obtained by 2 " selectors " (CWB and ERS). Following exclusion of patients with technically unacceptable SEs (e.g. ST/T configuration distorted by artefact or tracings not recorded for 10 min after cessation of exercise), unstable angina[7], previous myocardial infarction, systemic hypertension (blood pressure exceeding 150/100 mmHg), hemodynamically important valve disease, Wolff-Parkinson-White (WPW) syndrome, complete right or left bundle branch block as well as those patients on β-blocker, digitalis or diuretic therapy at the time of the exercise test, the selectors isolated 143 SEs which were positive for ischemia on ST/T configurational criteria alone. Cases of so-called " mitral valve prolapse "[1,6,29,37], provided associated mitral regurgitation was minimal, were not excluded. Configurational abnormalities comprised horizontal or downsloping ST segment depression at least one mm below the isoelectric line and 0.08 sec beyond the J point. Irrespective of whether or not the previously attending clinician had favored a diagnosis of CAD in these 143 patients, the apparently positive SEs had been a principal indication for subsequent coronary arteriography.

In order to test the accuracy of " blinded " observers in assessing SEs positive for ischemia on configurational criteria, 30 SEs randomly chosen by the 2 selectors from the series of 143 were considered a sufficient number. The selectors alone decided on the numbers that they would include the 2 groups, true or " false " positive for ischemia, using significant arteriographic CAD as the yardstick. Any combination ranging from no true positives and 30 false positives to 30 true positives and no false positives was therefore permissible. The selectors elected to extract at random 16 patients with normal coronary arteriograms and 14 with significant CAD. Luminal narrowing in one or more coronary arteries of $\geq 70\%$ was judged significant whereas luminal narrowing $\leq 20\%$ was deemed normal. No patients with $>20\%$ but $<70\%$ stenosis were included because the presence of true myocardial ischemia would have been uncertain in such instances.

The stress test

Exercise testing was performed on a treadmill using the standard Bruce protocol. A 12-lead electrocardiogram was recorded in the supine position prior to commencement of exercise. During exercise 3 leads, usually II, V_2 and V_5, were monitored continuously and recorded intermittently. Maximum heart rate was sought as the end point but exercise was sometimes terminated according to standard indications, such as breathlessness, fatigue, severe chest pain or marked ST segment depression. Twelve-lead ECGs were recorded in the supine position immediately and at 2 min intervals, or even more frequently, until 10 min after exercise or longer if the ST/T configurational changes had not yet returned to the resting state. None of the patients selected for the study received nitrate therapy during or after stress testing in order to avoid possible interference with time course behavior patterns.

The observer panel

Five observers, all familiar with the analysis of time course patterns, assessed the 30 SEs selected. The observers made their evaluations without consultation and were not only unaware of the relative number of true and " false " positives in the sample but were also blinded to all clinical details except the age and sex of the patients. Although the precise number in each group had been predetermined by the 2 " selectors " prior to random selection from the series of 143 SEs, the patients were coincidentally

Table 1. Clinical and morphological data of the 30 patients whose SEs were randomly chosen from the series isolated

	" False-positive " group	True positive group
Number of patients	16	14
Male : female	12 : 4	11 : 3
Average age (years)	50.4	53.5
Symptoms		
Typical angina	4	11
Atypical chest pain	10	2
Asymptomatic	2	1
Coronary arteriography*		
Normal coronaries	16	0
Single vessel CAD	0	10
Two or more vessel CAD	0	4

* CAD (coronary artery disease) was considered significant if there was $>70\%$ narrowing of a coronary artery.

closely matched for age and sex distribution (**Table 1**). The patients with CAD had, not surprisingly, had a higher incidence of typical anginal symptoms. The observers were required to differentiate the ischemic from the non-ischemic SEs based solely on time course analysis of the ST/T changes. The time course pattern was classified (i.e., Types I, II, III or IV) in all non-ischemic cases. The majority opinion (i.e., that of at least 3 observers) was taken as consensus when observers disagreed.

When all the observers' written opinions were available, results were analyzed by the 2 selectors. A 6th investigator (JBB), not included on the panel because he had first delineated time course patterns[1] and from whom all information except age and sex of the patients was also withheld, independently reported on some of the SEs and later, with the selectors, reviewed discordant findings of the observer panel.

Results

Nine of the patients in the " false-positive "

Table 2. Non-ischemic time course patterns in patients with normal coronary arteries

Type I	5
Type II	5
Type III	4
Type IV	2
Total number	16

Table 3. Results of observers in predicting ischemia

	Observer consensus (%)
Test accuracy	87
Sensitivity	79
Specificity	94
Positive predictive value	92
Negative predictive value	83

group had late onset, late offset (Types I and III) patterns while 7 had early onset, early offset (Types II and IV) time course behavior (**Table 2**). The consensus results are summarized in **Table 3**. Observer consensus correctly diagnosed 26 of the 30 SEs to achieve a total test accuracy of 87%. Eleven of the 14 patients with significant CAD were correctly assessed, resulting in a sensitivity of 79% for ischemia. This comprised 8 of 10 patients with single vessel CAD and 3 of 4 with multiple vessel CAD. Fifteen of 16 patients with non-ischemic time courses were correctly evaluated, thus attaining a 94% specificity in excluding ischemia. There was complete consensus as to the particular non-ischemic time course pattern involved in these 15 instances.

Clinical, electrocardiographic and arteriographic findings of the 4 patients in whom the observer consensus was apparently incorrect and the proposed reasons for error are shown in **Table 4**.

Discussion

A prevalent challenge to the clinician in daily practice is evaluation for the presence of CAD. While it is generally accepted[2,5] that SEs contribute meaningfully to the diagnosis and prognostic assessment of CAD in symptomatic patients, their poor predictive value for demonstrable CAD in asymptomatic and low risk subjects has been emphasized because of the allegedly high prevalence of "false-positive" results[23~27]. Although the importance of clinical assessment and exercise variables have been underlined[1,7,9], it has largely remained the configuration and extent of ST/T changes that determine whether or not the test is considered abnormal[5]. Configurational criteria, principally comprising a horizontal or downsloping ST segment 0.08 sec from the J point and ST depression at least one mm below the isoelectric line, are invariably provided in all studies. However, methods of measuring ST depression are not uniform[31] and are infrequently clarified. Moreover, the actual SEs, especially "false-positive" SEs, are seldom illustrated.

It is our ongoing clinical experience[30,31] that evaluation of the post-exercise time course behavior of ST/T configurational alterations leads to a marked improvement in the diagnostic yield of SEs. In this study we attempt to clarify our previously described[1,37] method of interpreting time course patterns and illustrate examples of the 4 non-ischemic as well as the ischemic patterns. In order to validate the reliability of time course assessment in improving SE interpretation, 2 selectors analyzed the observations and conclusions of 5 independent observers familiar with post-exercise ST/T behavior patterns. Majority consensus of the observer panel was judged relevant in this context rather than an analysis of individual observer accuracy. The observer consensus was good considering the methods involved in this investigation. The observers were unaware of any clinical details or exercise variables save the age and sex of each patient and, from the SE, the heart rate attained. They were also unaware of the numbers that the selectors had allocated to the ischemic and non-ischemic groups. All 30 SEs had previously been judged positive on

Table 4. Clinical, electrocardiographic and arteriographic features of the 4 incorrectly assessed patients

Pt no.	Age sex	Arteriographic findings	Relevant clinical data	Stress electrocardiogram (selectors' opinions)	Observers' findings	Reviewer's (JBB) "blind" opinion	Conclusion-reviewer's analysis of his and the observers' SE assessments
1	53 M	Significant 2 vessel disease	Typical angina Nonejection systolic click	Anterior leads: ischemic time course Inferior leads: type III non-ischemic time course	Non-ischemic type III	Ischemic because of anterior changes Two time course patterns	Ischemic SE Observer error caused by 2 time course patterns (Fig. 4)
2	56 M	Significant 1 vessel disease	Typical angina	Develops aberrant conduction in immediate post-exercise tracing. Ischemic time course	Non-ischemic type II	Ischemic when normally conducted complexes are analyzed	Ischemic SE Four observers erred in interpreting aberrantly conducted complexes (Fig. 5)
3	51 M	Significant 1 vessel disease	Typical angina	V_3 and V_4: ischemic time course II, III, aVF, V_5 and V_6: type III non-ischemic time course	Non-ischemic type III	Ischemic because of anterior changes Two time course patterns	Ischemic SE Observer error caused by 2 time course patterns
4	59 M	Normal coronary arteries	Atypical chest pain	V_3 and V_4: type III non-ischemic time course with severe configurational changes	Ischemic	Type III non-ischemic	Non-ischemic SE Observer error possibly due to severe ST/T configurational changes

Pt=patient; SE=stress electrocardiogram; ST/T=ST segment and T wave.

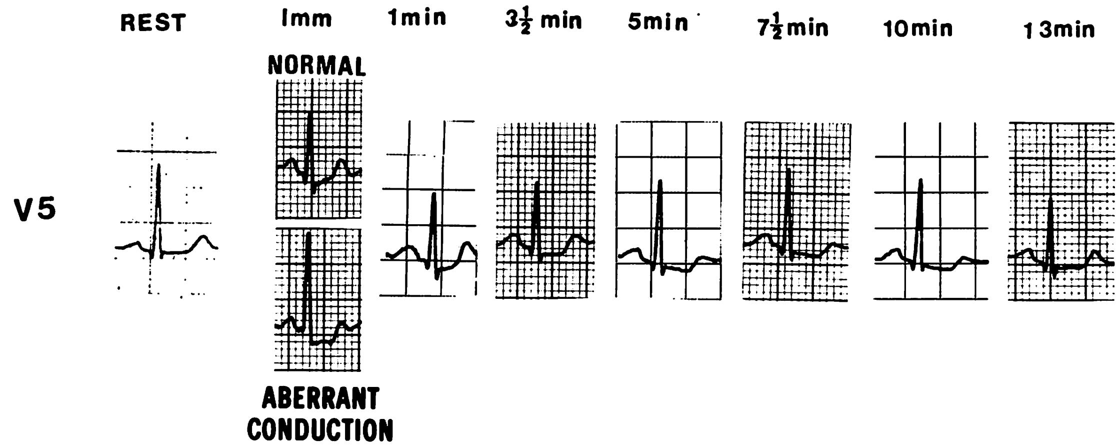
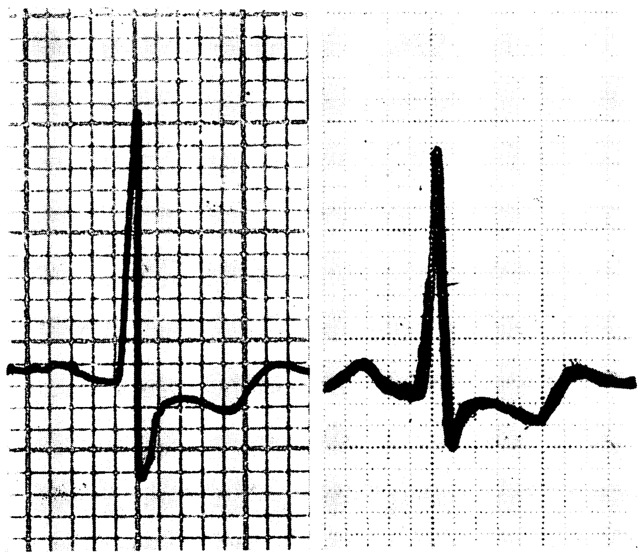


Fig. 5. Resting and post-exercise ECGs of the 56-year-old man (see patient 2, Table 4) **with typical angina and developed intermittent aberrant conduction in some of the beats of the immediate post-exercise tracing.**

Interpreting the normally conducted complex in the immediate post-exercise tracing reveals a fairly mild ischemic pattern with relatively late onset at $3^1/_2$ min and early offset at $7^1/_2$ min. When considering the aberrant complex immediately post-exercise the time course may be incorrectly interpreted as a Type IIB non-ischemic pattern. The one min tracing would then be interpreted as showing " less ischemia " (early offset) because the ST segment is upsloping, than the aberrantly conducted beat but with deterioration again at 5 min when the ST becomes downsloping. This man had significant single vessel coronary artery disease.

conventional ST/T configurational criteria alone. Using these configurational criteria, the sensitivity for the sample had therefore been 100% since all 14 patients with CAD were detected. The positive predictive value, however, had been only 47% because the 16 patients with normal coronary arteriograms had also, but incorrectly, been considered ischemic. For the same reason, the specificity for the sample using only conventional configurational criteria had been 0% because no non-ischemic patients were excluded. The additional analysis of ST/T time course behavior retained a good sensitivity (79%) while considerably improving both the specificity (94%) and positive predictive values (92%).

As shown in **Table 1**, 11 of 14 patients with CAD had typical angina compared with 4 of 16 with normal coronary arteries. Indeed, all 3 patients whom the consensus incorrectly evaluated as non-ischemic but who had CAD, had presented with typical angina (**Table 4**). This might well have influenced and assisted the attending physician in clinical practice regardless of the exercise response. Review of the 4 SEs in which observer consensus was incorrect, suggested that observer error affected by dual time course patterns (**Fig. 4**), temporary aberrant conduction (**Fig. 5**) or unusually severe ST/T configurational abnormalities played a role in the misdiagnosis (**Table 4**). These unusual SEs were a consequence of random selection and were, we submit, particularly difficult for " blinded " assessment. All 4 were, however, correctly interpreted by the reviewer not on the panel (**Table 4**). The specificity (94%) and positive predictive values (92%) of the observers were high. This strengthens our hypothesis[1] that normal epicardial coronaries are seldom, if ever, associated with an SE which is ischemic in both configuration and time course. In other words, while readily conceding that we have been subject to observer error in this study and also during our overall practice of applying time



(A) (B)

Fig. 6. Lead V_5 recorded in 2 patients 5 min after exercise demonstrating similar ST/T configuration.

Example A represents an ischemic patient with triple vessel disease. Example B is from a patient whose stress ECG followed a Type IIB non-ischemic time course pattern and whose coronary arteriogram was normal.

course behavior[1], we have yet to detect, either in our own experience or in a published illustration, a definite "false-positive" SE in which the time course pattern and other factors could be fully evaluated.

It may be impossible to assess whether the ST/T changes reflect ischemia on configuration alone[1] (**Fig. 6**). By analyzing the relative severity of ST/T changes at frequent intervals for at least 10 min after cessation of exercise, the crucial time course pattern of an SE can be established. We contend that patients with one of the 4 non-ischemic patterns may often be managed in similar manner to those with ST segments that remain normal after exercise. The clinical presentation and so-called exercise variables[9] remain highly contributory in evaluating an exercise treadmill test. A patient with a non-ischemic time course pattern may require radionuclide studies[16], other non-invasive tests[20] or coronary arteriography, if clinically indicated, for the same reasons that patients require further investigation when the ST segments remain normal but a completely "false negative" SE is suspected. We consider, however, that in asymptomatic subjects, or those with atypical symptoms, a non-ischemic time course response should be regarded as normal and thus CAD as highly improbable. We dispute the philosophy[23~26,38,39] that a high prevalence of "false positives" in such subjects makes stress testing unreliable or even contraindicated.

This study depended on the demonstration of significant CAD on angiography as evidence of myocardial ischemia. Conduction disturbances, notably WPW syndrome, and hemodynamically significant aortic or mitral valve disease, as well as other causes of left ventricular hypertrophy and dysfunction, such as systemic hypertension and hypertrophic cardiomyopathy, may cause the ST/T configurational changes before or after exercise that mimic, or may sometimes in fact reflect, myocardial ischemia despite normal epicardial coronary vessels. Patients with these conditions were excluded from this study but the time course behavior patterns of those ST/T abnormalities require investigation. Our preliminary observations on WPW syndrome and hypertrophic cardiomyopathy[40] suggest that a non-ischemic time course behavior pattern supervenes. We are also aware that true myocardial ischemia may not be present in patients with CAD where collateral circulation is adequate[3]. Nonethelese demonstrable significant CAD on coronary arteriography remains principal standard[20] for confirming a diagnosis of myocardial ischemia in both clinical and research practices.

Abnormal or non-specific ST/T changes are associated with a number of conditions in which the epicardial coronary arteries are angiographically normal. These include so-called syndrome X[33] or microvascular angina[32,34], hyperventilation[41], vasoregulatory T-wave changes[41,42], athlete's heart syndrome[6,43] and mitral valve prolapse[1,6,29]. The possible causal mechanisms of ST/T changes in these cases are not relevant to this study. Moreover, the hemodynamic alterations and pathophysiological factors that supervene 3 or 4 min after exercise when ischemic ST/T changes are maximal in patients with CAD have also not, to our knowledge, been clarified. A steal phenomenon[19] at this time, shifting flow from stenosed vessels supplying ischemic or potentially ischemic myocardium to non-ischemic myocardium through dilated normal coronary arteries, is probably an important factor. The post-exercise early onset, late offset or late onset, early offset time course pattern of myocardial ischemia is constant in our experience provided that patients with unstable angina or ECG evidence of previous myocardial infarction are excluded, that coronary spasm does not supervene and that glyceryl trinitrate is not given during or shortly after exercise. The late onset, late offset (Types I and III) or early onset, early offset (Types II and IV) non-ischemic patterns are also remarkably constant. We reiterate, however, that the ST/T changes must be interpreted as we have outlined if time course behavior patterns are to be optimally applied. Importantly, this includes judging no ST depression with a downsloping ST segment as worse "ECG ischemia" than significant ST depression with a horizontal or, of course, upsloping ST segment. Observations on ST depression alone[44,45] or not confined to the post-exercise period[45] will provide disparate results and will seldom differentiate true from "false-positive" SEs.

Conclusion

The exercise stress test remains an easy, cost effective and practical method for detecting ischemic heart disease. Multivariate analysis of history, clinical examination, exercise and electrocardiographic variables remains crucial in interpreting whether a stress test is positive for ischemia or not. All of these factors are observer dependent and thus require clinical acumen. We have confirmed that time course behavior patterns of the post-exercise ST/T configuration lends increased predictive value to the exercise test. As with assessment of clinical signs and more sophisticated invasive and non-invasive investigations, observer accuracy will vary among individuals depending on expertise, experience and the criteria applied. The results of this study, with 5 different observers each analyzing the same 30 SEs, indicate that many so-called "false positives" will be detected as true negatives for ischemia when time course analysis is added to the evaluation of post-exercise ST/T configurational alterations. Computerization of our method of assessing time course analysis should decrease, if not eliminate, observer error and thus further enhance the accuracy of stress test interpretation.

Addendum

After this paper was prepared for publication, Ellestad et al (Am Heart J 123: 904–908, 1992) in a study of 462 subjects concluded that "time course of ST depression. . . adds significantly to the information gained during exercise testing". As with others[44,45], however, their time course observations were made on ST depression alone and not ST/T configurational changes as practised by us. It is thus not surprising that Ellestad et al still encountered a large number of " false positives ".

References

1) Barlow JB: The " false-positive " exercise electrocardiogram: Value of time course patterns in assessment of depressed ST segments and inverted T waves. Am Heart J **110**: 1328–1336, 1985
2) Fisch C: Evolution of the clinical electrocardiogram. J Am Coll Cardiol **14**: 1127–1138, 1989
3) Goldschlager N, Sox HC: The diagnostic and prognostic value of the treadmill exercise test in the evaluation of chest pain, in patients with recent myocardial infarction, and in asymptomatic individuals. Am Heart J **116**: 523-535, 1988
4) McNeer JF, Margolis JR, Lee KL, Kisslo JA, Peter RH, Kong Y, Behar VS, Wallace AG, McCants CB, Rosati RA: The role of the exercise test in the evaluation of patients for ischemic heart disease. Circulation **57**: 64–70, 1978
5) Detrano R, Gianrossi R, Froelicher VF: The diagnostic accuracy of the exercise electrocardiogram: A meta-analysis of 22 years of research. Prog Cardiovasc Dis **32**: 173–206, 1989
6) Barlow JB, Pocock WA: Mitral valve prolapse, the athlete's heart, physical activity and sudden death. International J Sports Cardiol **1**: 9–24, 1984
7) Detrano R, Froelicher VF: Exercise testing: Uses and limitations considering recent studies. Prog Cardiovasc Dis **31**: 173–204, 1988
8) Podrid PJ, Venditti FJ, Levine PA, Klein MD: The role of exercise testing in evaluation of arrhythmias. Am J Cardiol **62**: 24H–33H, 1988
9) Ellestad MH, Savitz S, Bergdall D, Teske J: The false positive stress test: Multivariate analysis of 215 subjects with hemodynamic angiographic and clinical data. Am J Cardiol **40**: 681–685, 1977
10) Sheffield LT, Reeves TJ, Blackburn H, Ellestad MH, Froelicher VF, Roitman D, Kansal S: The exercise test in perspective. Circulation **55**: 681–683, 1977
11) Wiens RD, Lafia P, Marder CM, Evans RG, Kennedy HL: Chronotropic incompetence in clinical exercise testing. Am J Cardiol **54**: 74–78, 1984
12) Okin PM, Ameisen O, Kligfield P: Recovery-phase patterns of ST segment depression in the heart rate domain. Circulation **80**: 533–541, 1989
13) Mary DASG, Elamin MS, Smith DR, Linden RJ: Value of ST segment/heart rate relation during exercise as index of severity of coronary artery disease. Br Heart J **47**: 201–202, 1982
14) Hollenberg M, Zoltick JM, Go M, Yaney SF, Daniels W, Davis RC Jr, Bedynek JL: Comparison of a quantitative treadmill exercise score with standard electrocardiographic criteria in screening asymptomatic young men for coronary artery disease. N Engl J Med **313**: 600–606, 1985
15) Kaul S, Lilly DR, Gascho JA, Watson DD, Gibson RS, Oliner CA, Ryan JM, Beller GA: Prognostic utility of the exercise thallium-201 test in ambulatory patients with chest pain: Comparison with cardiac catheterization. Circulation **77**: 745–758, 1988
16) Johnson SH, Bigelow C, Lee KL, Pryor DB, Jones RH: Prediction of death and myocardial infarction by radionuclide angiocardiography in patients with suspected coronary artery disease. Am J Cardiol **67**: 919–926, 1991
17) Wann LS, Faris JV, Childress RH, Dillon JC, Weyman AE, Feigenbaum H: Exercise cross-sectional echocardiography in ischemic heart disease. Circulation **60**: 1300–1308, 1979
18) Ryan T, Vasey CG, Presti CF, O'Donnell JA, Feigenbaum H, Armstrong WF: Exercise echocardiography: Detection of coronary artery disease in patients with normal left ventricular wall motion at rest. J Am Coll Cardiol **11**: 993–999, 1988
19) L'Abbate A: Pathophysiological basis for noninvasive functional evaluation of coronary stenosis. Circulation **83** (Suppl): III-2–III-7, 1991
20) Simonetti I, Rezai K, Rossen JD, Winniford MD, Talman CL, Hollenberg M, Kirchner PT, Marcus ML: Physiological assessment of sensitivity of noninvasive testing for coronary artery disease. Circulation **83** (Suppl): III-43–III-49, 1991
21) Picano E, Lattanzi F, L'Abbata A: Present application, practical aspects and future issues on dipyridamole echocardiography. Circulation **83** (Suppl): III-111–III-115, 1991
22) Beer SG, Heo J, Iskandrian AS: Dipyridamole thallium imaging. Am J Cardiol **67**: 18D–26D, 1991
23) Froelicher VF, Thompson AJ, Wolthuis R, Fuchs R, Balusek R, Longo MR, Triebwasser JH, Lancaster MC: Angiographic findings in asymptomatic aircrew with electrocardiographic abnormalities. Am J Cardiol **39**: 32–38, 1977
24) Piepgrass SR, Uhl GS, Hickman JR, Hopkirk

JAC, Plowman K: Limitations of the exercise test in the detection of coronary artery disease in apparently healthy men. Aviat Space Environ Med **53**: 379–382, 1982

25) Fisch C, De Sanch RW, Dodge HT, Reeves TJ, Weinberg SL: Guidelines for exercise testing. J Am Coll Cardiol **8**: 725–738, 1986
26) Coplan NL, Fuster V: Limitations of the exercise test as a screen for acute cardiac events in asymptomatic patients. Am Heart J **119**: 987–990, 1990
27) Rifkin DR, Hood WB Jr: Bayesian analysis of electrocardiographic exercise stress testing. N Engl J Med **297**: 681–686, 1977
28) Lozner EC, Morganroth J: New criteria to enhance the predictability of coronary artery disease by exercise testing in asymptomatic subjects. Circulation **56**: 799–802, 1977
29) Malcolm AD, Ahuja SP: The electrocardiographic response to exercise in 44 patients with mitral leaflet prolapse. Eur J Cardiol **8**: 359–363, 1978
30) Neutel JM, Barlow CW, Barlow JB, King J, Myburgh DP: The importance of time course behaviour of ST segment and T wave changes following exercise: A reliable aid towards eliminating " false positives ". S Afr Med J **78**: 637–641, 1990
31) Barlow CW, Soicher ER, Barlow JB, Friedman BM, Myburgh DP: Post-exercise time-course analysis of ST segment and T wave changes: An important contribution to the role of stress electrocardiography in aircrew. Aviat Space Environ Med **62**: 165–171, 1991
32) Epstein SE, Cannon RO, Bonow RO: Exercise testing in patients with microvascular angina. Circulation **83** (Suppl): III-73–III-76, 1991
33) Kaski JC, Crea F, Nihoyamopoulos P, Haskett D, Maseri A: Transient myocardial ischemia during daily life in patients with syndrome X. Am J Cardiol **58**: 1242–1247, 1986
34) Cannon RO III, Schenke WH, Quyyumi A, Bonow RO, Epstein SE: Comparison of exercise testing with studies of coronary flow reserve in patients with microvascular angina. Circulation **83** (Suppl): III-77–III-81, 1991
35) Lachterman B, Lehmann KG, Abrahamson D, Froelicher VF: " Recovery only " ST-segment depression and the predictive accuracy of the exercise test. Ann Intern Med **112**: 11–16, 1990
36) Bajaj R, Wasir HS: Value of analysis of the evolution of the pattern of the ST segment in exercise electrocardiograms. Int J Cardiol **29**: 323–326, 1990
37) Barlow JB, Pocock WA: Mitral leaflet billowing and prolapse. *in* Barlow JB: Perspectives on the mitral valve. FA Davis, Philadelphia, 1987, pp 45–111
38) Chamberlain DA: Routine and exercise electrocardiography in aircrew: Technique, interpretation and recommendations. Eur Heart J **5** (Suppl): A-55–A-60, 1984
39) Petch MC: Misleading exercise electrocardiograms. Br Med J **295**: 620–621, 1987
40) Neutel JM, Barlow JB, King J, Myburgh DP: Importance of stress testing in apical hypertrophic cardiomyopathy. Br Heart J **59**: 615, 1988 (abstr)
41) McHenry PL, Richmond HW, Weisenberger BL, Rodway JS, Perry GF, Jordan JW: Evaluation of abnormal exercise electrocardiogram in apparently healthy subjects: Labile repolarization (ST-T) abnormalities as a cause of false positive responses. Am J Cardiol **47**: 1152–1160, 1981
42) Friesenger GC, Biern RO, Likar I, Mason RE: Exercise electrocardiography and vasoregulatory abnormalities. Am J Cardiol **30**: 733–740, 1972
43) Zeppilli P, Pirrami MM, Sassara M, Fenici R: T wave abnormalities in top-ranking athletes: Effects of isoproterenol, atropine, and physical exercise. Am Heart J **100**: 213–222, 1980
44) Kong B, Heo J, Iskandrian AS: The duration of ST segment depression as an indicator of the pathophysiology of myocardial ischemia. Am Heart J **118**: 195–197, 1989
45) Pupita G, Kaski JC, Galassi AR, Gavrielides S, Crea F, Maseri A: Similar time course of ST depression during and after exercise in patients with coronary artery disease and syndrome X. Am Heart J **120**: 848–854, 1990