

A COMPARISON OF A GRADED MULTISTAGE EXERCISE TREADMILL TEST
WITH CORONARY CINEARTERIOGRAPHY

BY

FRANK DAMIEN REARDON
B.Sc. UNIVERSITY OF OTTAWA 1971

THESIS

SUBMITTED TO THE SCHOOL OF GRADUATE STUDIES
IN PARTIAL FULFILLMENT OF THE REQUIREMENTS OF THE DEGREE
OF MASTER OF SCIENCE
IN
KINANTHROPOLOGY

SCHOOL OF PHYSICAL EDUCATION AND RECREATION
UNIVERSITY OF OTTAWA
1974



UMI Number: EC55721

INFORMATION TO USERS

The quality of this reproduction is dependent upon the quality of the copy submitted. Broken or indistinct print, colored or poor quality illustrations and photographs, print bleed-through, substandard margins, and improper alignment can adversely affect reproduction.

In the unlikely event that the author did not send a complete manuscript and there are missing pages, these will be noted. Also, if unauthorized copyright material had to be removed, a note will indicate the deletion.

UMI[®]

UMI Microform EC55721
Copyright 2011 by ProQuest LLC
All rights reserved. This microform edition is protected against
unauthorized copying under Title 17, United States Code.

ProQuest LLC
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106-1346

DEDICATION

To Diane for all her loving inspiration

ACKNOWLEDGEMENTS

My most sincere appreciation to my advisor, Dr. Maurice Jetté, Chairman, Department of Kinanthropology, for "les sages conseils et l'aide judicieuse" in the production of this thesis.

I wish also to thank Dr. Howard Wenger and Dr. Kim Tan for their collaboration, the members of the examination committee and the patients that were the subjects of this study.

A special thank you to Mrs. Marilyn Wahl for her assistance in the typing of the text.

ABSTRACT

This study was undertaken to compare the results of an electrocardiographic exercise treadmill test with the results of arteriographic studies of coronary heart disease in coronary patients.

It has been previously shown that most patients with established coronary occlusive disease, demonstrate ischemic myocardial changes, manifested in the repolarization phase of the ECG during maximal and near maximal exercise. Further, these manifestations of the hypoxic condition are associated with the ST-T complex. Attempts to quantify various aspects of ST-segment aberrations during exertion have shown that J-point depression with a horizontal or down-sloping ST-segment, and ST-segment depression, are associated with coronary heart disease and the extent of myocardial ischemia. A QX-interval of length greater than 50 percent of the QT-interval, typifies myocardial ischemia.

Eleven patients between the ages of 36 and 65 were diagnosed as having coronary heart disease by angiography. These patients were subjected to a Naughton multistage exercise treadmill test. The patients' angiograms were classified by a system based on the amount of occlusion of the major coronary arteries. The electrocardiogram was recorded at the end of each minute of exercise and recovery. Exercise was

terminated when a criterion heart rate associated with other adverse signs was attained, dyspnea, muscle fatigue, or other physical limitations to exercise became obvious, or aberrations of the ECG including ST-depression of 1mm, premature ventricular beats or undue tachycardia were noticed. The ECG's were analyzed and judged positive if the ST-segment depression exceeded 1.0 mm, J-point depression of ≥ 1 mm associated with a slope of $\leq 1\text{mV/sec}$, or a QX/QT ratio ≥ 0.5 .

The exercise stress test demonstrated a true positive fraction of 91 percent (10 of 11 patients tested) and a false negative fraction of 9 percent (1 of 11 patients tested).

TABLE OF CONTENTS

CHAPTER	PAGE
I. THE PROBLEM	1
Introduction	1
Statement of the Problem	3
Hypothesis	4
Scope of the Study	4
Limitations	5
Definitions and Abbreviations	5
II. REVIEW OF THE LITERATURE	7
Introduction	7
Fundamental Physiological Concepts	8
Pathophysiology of the Myocardium	8
The Exercise ECG	13
The Coronary Arteriogram	18
History of Exercise Testing	19
Master 2-Step Test, the Graded Multistage Exercise Test and the Naughton Test	21
Parameters of the Exercise ECG	29
QX/QT Ratio	29
ST-segment Slope, J-Point Depression	32
ST-segment Depression	33
Exercise Testing and Coronary Arteriography	38
Summary	45

CHAPTER	PAGE
III. METHODOLOGY	48
Introduction	48
Subjects	48
Medication	52
Classification of the Arteriograms	52
Test Session Protocol	52
Exercise Test Description	54
Criteria for Terminating the Exercise Test	56
Equipment	57
Exercise ECG Variables	58
Presentation of Data and Statistical Analysis	61
IV. RESULTS AND DISCUSSION	63
Introduction	63
Results	63
Exercise Stress Test Data	63
Correlations of the Exercise ECG with the Angiographic Results	67
Discussion	77
V. SUMMARY CONCLUSIONS AND RECOMMENDATIONS . . .	88
Summary	88
Conclusions	89
Recommendations	89
REFERENCES	91
APPENDIX A: TABLE OF SUBMAXIMAL CRITERION HEART RATES	100
B: TABLE OF CONTRAINDICATIONS TO EXERCISE .	102
C: EXERCISE TEST PROTOCOL	106

LIST OF TABLES

TABLE		PAGE
1.	Subject Anthropometric Data	49
2.	Results of Angiography	51
3.	Results of Exercise Stress Test	64
4.	Results of Exercise ECG	65
5.	Correlations of ECG Parameters with Angiographic Results	69

LIST OF FIGURES

FIGURE		PAGE
1.	Theory of Current of Rest	15
2.	Theory of Current of Activity	16
3.	Schematic Diagram of Abnormal ECG	59
4.	Stage of (+) ECG Response and CHD Rating . .	68
5.	Stage of (+) Response J/slope and CHD rating	71
6.	Stage of (+) Response ST-segment and CHD Raging	72
7.	Stage of (+) Response QX/QT Ratio and CHD Rating	73
8.	Maximum Value QX/QT and CHD Rating	74
9.	Maximum Value J/slope and CHD Rating	75
10.	Maximum Value ST-segment and CHD Rating . . .	76

CHAPTER I

THE PROBLEM

Introduction

The use of exercise stress testing for the evaluation of cardiovascular efficiency has been accepted since Master (1929) proposed the single phase, submaximal exercise test. At that time the diagnosis was based upon the subjects' blood pressure and pulse rate response to the exercise. In 1941 Master improved this test by making it a two-step test and by recording the electrocardiogram during the recovery phase. The electrocardiogram was shown to be a more sensitive indicator of ischemia than the previous parameters measured. Since then the latter test has been used almost universally and norms and correction factors for age, weight and sex have been well established. Recently, exercise stress testing has become more refined with advances in technology and the incorporation of the ergometer and motor driven treadmill. This type of testing has been shown to be quite a reliable and reproducible method of assessing cardiovascular adaptation to varying levels of stress in cardiac patients. The major advantage of such a multiphase test is that it has demonstrated a higher true positive fraction than the Master 2-step test, in detecting coronary disease.

Coronary arteriography dates back to 1933 when Peter Rousthoi demonstrated opacification of coronary arteries in living, intact, experimental animals. He was, however, discouraged from extending his investigations to include human subjects. Radner, in 1945, was the first to attempt this technique on man. His results were not very successful, and it was not until 1948 that Jönsson was able to obtain a reasonable image of the coronary arteries of living man. The quality of his films and those of many others was the limiting factor to their success. In the following years more concentrated effort in this field produced far superior results than had ever been attained.

In the past decade, with advances in angiographic technique, extensive insight into the etiology of many coronary diseases, and myocardial disorders, has been gained. Today selective coronary arteriography is a standard procedure in almost all pre-operational evaluations of coronary patients. It is widely accepted as being the best "invasive" technique for localizing and quantifying the effect of coronary heart disease.

While both of these techniques find application in detection and evaluation of coronary artery disease, the interpretation of the information derived from them is quite different. The electrocardiographic exercise stress test is a "non-invasive" method which is used primarily to predict the presence and extent of myocardial ischemia. It is relatively

inexpensive, easy to administer, and involves comparatively little trauma for the patient. On the other hand, coronary angiography, an "invasive" technique, is indispensable for the assessment of the location and extent of coronary occlusive disease. This method is time consuming, technically more involved, and has a higher mortality rate associated with it than does exercise stress testing. These techniques are, in a sense, complementary in that the data from both describes the presence and extent of myocardial ischemia and, simultaneously, the presence and extent of coronary occlusive disease.

The area of interest of this study, which was a part of a more extensive project, was the comparison of the results of a graded multistage exercise test and coronary angiography. Specific parameters of the exercise electrocardiogram were measured and compared to a rating of the coronary artery disease by angiography.

Statement of the Problem

The principal aim of this study was to compare the results of a graded multistage exercise electrocardiographic test, to the results of coronary arteriography, in coronary patients aged 36 to 62 years.

Rationale:

Various authors including; Bellet and Roman (1967), Ascoop and Simoons (1967), and Martin and McConahay (1972) have demonstrated that the graded multistage exercise treadmill

test is superior to the Master 2-step test in detecting coronary insufficiency. This is based on the fact that the multistage test shows a higher true positive fraction; i.e. this test is in accord with previous information.

It has also been shown by other researchers such as McHenry et al (1970) Likoff et al (1966) McHenry (1972), Bartel et al (1974) and Martin and McConahay (1972), that there is a high positive correlation between the extent of coronary heart disease and positive electrocardiographic response to an exercise stress test.

Hypothesis

It was believed that a large percentage of the patients having angiographic evidence of coronary heart disease would show a positive electrocardiographic stress test by at least one of the ECG parameters measured.

Scope of the Study

This project was designed to compare the results of an exercise ECG recorded during and after a Naughton Stress test to the results of coronary angiographic studies. The subjects used in this study were candidates selected for revascularization surgery by the Department of Cardio-Thoracic Surgery and ranged in age from 36 to 62 years. For the purposes of this study the extent of the disease was rated on a scale from 1 to 15 on the basis of the angiogram. The patients were then subjected to exercise stress testing, prior

to surgery. From the ECG recorded from electrodes placed in the CM_5 position at the end of each minute of exercise and recovery, 3 parameters were measured: J-point depression and slope of the ST-segment; ST-segment depression; and QX/QT ratio. The criteria for a positive test were: J-point depression of 1mm or more associated with a slope of less than +1 mV/sec; an ST-segment depression of 1 mm or more; and a QX/QT ratio of 0.5 or greater. The results of the exercise ECG were compared to the angiographic results to determine sensitivity of the exercise test expressed as a true positive fraction. The stage at which any parameter became positive was correlated with the rated extent of CHD. Correlations were also calculated for the stage at which each individual parameter became positive and the rated extent of the disease.

Limitations

The applications of the findings of this project are limited by the context in which the study was carried out. That is, the size and nature of the population, the equipment used, and laboratory conditions tend to make the results very specific.

Definitions and Abbreviations

Graded Multistage Exercise Stress Test (GXT):

The test used in this study, namely that proposed by Naughton (Fox and Naughton 1971).

J-point:

The point at which the QRS complex ends and the ST-segment begins.

J-point depression:

The depression or negative deviation of this point from an established baseline.

QX/QT ratio:

The ratio of the length of the interval from the beginning of the QRS complex to the point where the ST-segment returns to base-line, to the length of the interval from QRS onset to the end of the T-wave.

Sensitivity: $\frac{\# \text{ true (+)}}{\# \text{ true (+)} + \# \text{ False (-)}}$

LAD:

Left anterior descending coronary artery

RCA:

Right Coronary artery.

M/CA:

Marginal circumflex or the circumflex artery.

LCA:

Left Coronary artery.

CHD:

Coronary Heart Disease

CHAPTER II

REVIEW OF THE LITERATURE

Introduction

The principal objective of this project was to compare the results of an exercise stress test with the results of an angiographic procedure in the evaluation of coronary heart disease patients. In order to attain this end, a Naughton exercise stress test was employed. The ECG parameters measured as criteria for positive response to this exercise test included the J-point depression and slope of the ST-segment, the amount of ST-segment depression, and the QX/QT ratio. The findings of the exercise test ECG were then compared with the findings of the coronary angiograms.

In the following review of the literature, the following topics are reviewed:

1. Fundamental physiological concepts of exercise testing;
2. History;
3. Master 2-step test, graded multistage exercise test, and the Naughton test;
4. Parameters of the exercise electrocardiogram;
 - (a) QX/QT ratio
 - (b) ST-segment slope, J-point depression
 - (c) ST-segment depression

5. Exercise stress testing and coronary arteriography.

Fundamental Physiological Concepts

Pathophysiology of the Myocardium:

As long as the cardiac muscle cell membrane remains undisturbed, a resting membrane potential exists. Any factor that increases the sodium permeability of the membrane is likely to elicit an action potential or biphasic changes in membrane potential; depolarization and subsequent repolarization. The first event in an action potential is the increase in membrane permeability to sodium. The exact mechanism by which this takes place is not totally understood and many theories have been postulated. It is thought that calcium ions bound to structural proteins of the sodium "channels" are intimately involved in this process. During an action potential sodium conductance may increase by a factor of up to 1000. As the sodium ions diffuse to the inside of the membrane they carry positive charge as well, causing a reversal potential. The excess positive charge limits further influx of positively charged sodium ions. The reverse process, perhaps involving the rebinding of calcium in the sodium channels in turn tends to decrease influx of sodium. Sodium conductance is thus reduced to resting values.

The potassium conductance does not change significantly during the first half of the action potential but during the latter stages the conductance may reach 30 to 40

times the resting value. Again the exact mechanism is not yet clear. The return of the resting membrane potential is caused almost entirely by diffusion of potassium ions outward through the membrane. It has been known that when sodium conductance has returned to resting levels, the potassium conductance is 30 times its resting level. Thus potassium ions rapidly diffuse outward through the membrane. The plateau phase of the cardiac muscle cell action potential is thought to be due to a depletion of the calcium concentration in the immediate extracellular fluid. This decreases membrane potassium permeability. Sufficient calcium ions diffuse from surrounding extracellular fluid to restore membrane potassium permeability and the repolarization process.

Thus it can be seen that the cell membrane behaves as a capacitor due to the alignment of charged species on either side of the membrane. Thus the membrane lipid fraction behaves as a dielectric. The depolarization and repolarization processes can be thought of as discharge and recharge of membrane capacitance. It can be shown that any muscle cells deprived of the energy source, ATP, will eventually become electrically and mechanically inactive. The ATP in cardiac muscle is normally produced by aerobic metabolism. Thus this system functions adequately only in the presence of oxygen. This oxygen is transported to the metabolizing muscle cell site by oxygen transport molecules, myoglobin and hemoglobin. On a larger scale, the blood vessels, from artery to capillary

are vital to the distribution of oxygenated hemoglobin to the functioning myocardium. Thus, it follows that a decrease in the flow of blood to the heart muscle will impair the electrical and mechanical function of the cardiac muscle cell.

The electrocardiograph is used to describe qualitatively and quantitatively the electrical activity of the heart. Therefore, changes in blood flow to areas of the cardiac muscle are indirectly indicated in the electrocardiogram, under some conditions (Case, et al., 1966). Compromised blood flow and lesser O₂ delivery may cause ischemic ECG changes. These ischemic changes are most easily identified during the repolarization phase of the ECG. During an ischemic episode the electrical conduction characteristics of the myocardium are altered. This may produce aberrations in the depolarization phase of the electrocardiogram. For this reason wave forms associated with the depolarization phase - P and QRS complexes - may appear abnormal during ischemia. These changes are not as easily quantified as those which appear in the repolarization phase of the ECG. Abnormal repolarization of the myocardium is consistently demonstrated in the ST, T and U complexes of the electrocardiogram.

In many cases of coronary heart disease, development of collateral circulation may compensate for an arterial restriction resulting in an apparently normal ECG at rest. Often in this situation abnormalities of diagnostic and prognostic importance may be induced during effort.

Physical exercise is easily performed and involves many of the body systems. During exercise an adult may increase his resting oxygen intake ($\dot{V}O_2$), of about 300 ml. per minute, by a factor of 10. As the metabolic substrate requirements of the working muscle (including the heart) increase, the oxygen/substrate transport system must provide parallel increases in blood flow to the muscle. This system also has a role in the removal of metabolites. Pulmonary function also increases in proportion to workload.

The major determinants of myocardial oxygen consumption are heart rate, time integral of ventricular systolic pressure, velocity of contraction and cardiac mass. The coronary circulation may be adequate to meet oxygen requirements of the myocardium at rest, even in patients with significant occlusive disease. However, the efficiency is impaired when energy demands on the muscle exceed the supply. This may occur with an increase in one or all of the above mentioned determinants of myocardial oxygen consumption during physical exercise, emotional stress, or other experimentally induced stress conditions. This is exemplified by the infusion of isoproterenol, angiotension, or the inhalation of gas mixtures of low oxygen tension.

The myocardium extracts about seventy percent of the oxygen in the arterial blood during passage through the coronary circulation. Therefore, the increased oxygen demand of the heart muscle, must be met, almost totally, by an increase in

blood flow rate. If these demands are not met, metabolic electrophysiologic and hemodynamic derangements may occur. These derangements can include: (1) abnormal myocardial lactate production due to anaerobic metabolism; (2) ST-T changes in the ECG, significant dysrhythmias and disturbances in the atrioventricular and intraventricular conduction; (3) abnormally low cardiac output, when pulmonary arterial oxygen saturation is reduced to thirty percent by severe exercise. High filling pressures (left ventricular end-diastolic pressure) have been reported (Blake, 1972) and are probably due to changes in compliance of the ventricular wall. These symptoms are often displayed by patients with coronary heart disease during physical exertion. The relatively severe or total occlusion of one or more coronary arteries may give rise to this imbalance of energy supply and demand in specific areas of the myocardium.

Generally there are many factors that have a direct or indirect influence on the cardiovascular responses to physical exertion. These factors include the state of the myocardium (contractibility - previous infarcts etc.), age, sex, and "physical fitness" of the subject. The type of activity is a major factor as well. Some activities involve increases in intrathoracic pressure. This inhibits to some extent, the venous return and the coronary circulation. For example, lifting weights, or isometric exercise in which the individual forces against a closed glottis by contracting the intercostal and diaphragm muscles.

In addition the position of the subject during exercise (upright opposed to supine) will profoundly affect the hemodynamic response. Cardiac output and stroke volume are both normally lower when exercise is performed in the sitting or standing positions compared to exercise performed supine. The changes which also occur at rest are a result of the redistribution of blood from the thorax to the legs, which causes a decrease in venous return, and heart and stroke volume. When exercise is performed in a supine position a more profound increase in stroke volume occurs, resulting from the increased diastolic filling of the ventricles, as blood from the legs is redistributed to the thorax.

The Exercise ECG:

The manifestations of the ischemic myocardial condition in the electrocardiogram, as mentioned earlier, occur primarily in the repolarization phase. Specifically, these changes are associated with the ST-segment and T-wave complexes. The hallmark electrocardiographic changes occurring with myocardial ischemia are transitory ST-segment depression and T-wave changes.

ST-segment depression is thought to be produced by "currents of injury" created in the myocardium by a hypoxic condition (Goldman 1970). Two basic theories have been advanced in speculation to explain the phenomenon. These are the "Injury Current of Rest" theory and the "Injury Current

of Activity" theory. The "Injury Current of Rest" theory assumes that injured muscle, as in myocardial ischemia or infarction, is electrically negative to the surrounding healthy muscle. Figure 1(a) represents normal resting muscle and the corresponding recordings in electrodes placed in positions E. Figure 1(b) shows the relatively negative injured tissue and the subsequent recordings in resting muscle. Figures 1(c) and 1(d) show the recording deflections from baseline upon the initiation of depolarization and an advancing negative front. Figure 1(e) shows the tracing in the separate electrodes after one complete depolarization-repolarization cycle. Thus, the phenomena of ST-depression and ST-elevation.

The "Injury Current of Activity" theory assumes that the injured muscle does not become electrically negative as normal muscle does when stimulated. Thus the injured muscle, in Figure 2, during stimulation will have a lesser negative charge and thus will appear positive to the electrode facing it. This results in ST-segment elevation in this electrode. An electrode overlying the uninjured area however will necessarily record an ST-segment depression.

There is evidence that these mechanisms are not totally correct in their assumptions, at least in relation to myocardial ischemia. Eckmecki, Prinzmetal et al (1967) worked with intramural leads and demonstrated that ST-segment deviation produced by reduction in coronary flow occurred only in the epicardial half of the myocardium. Moderate myocardial ischemia produces

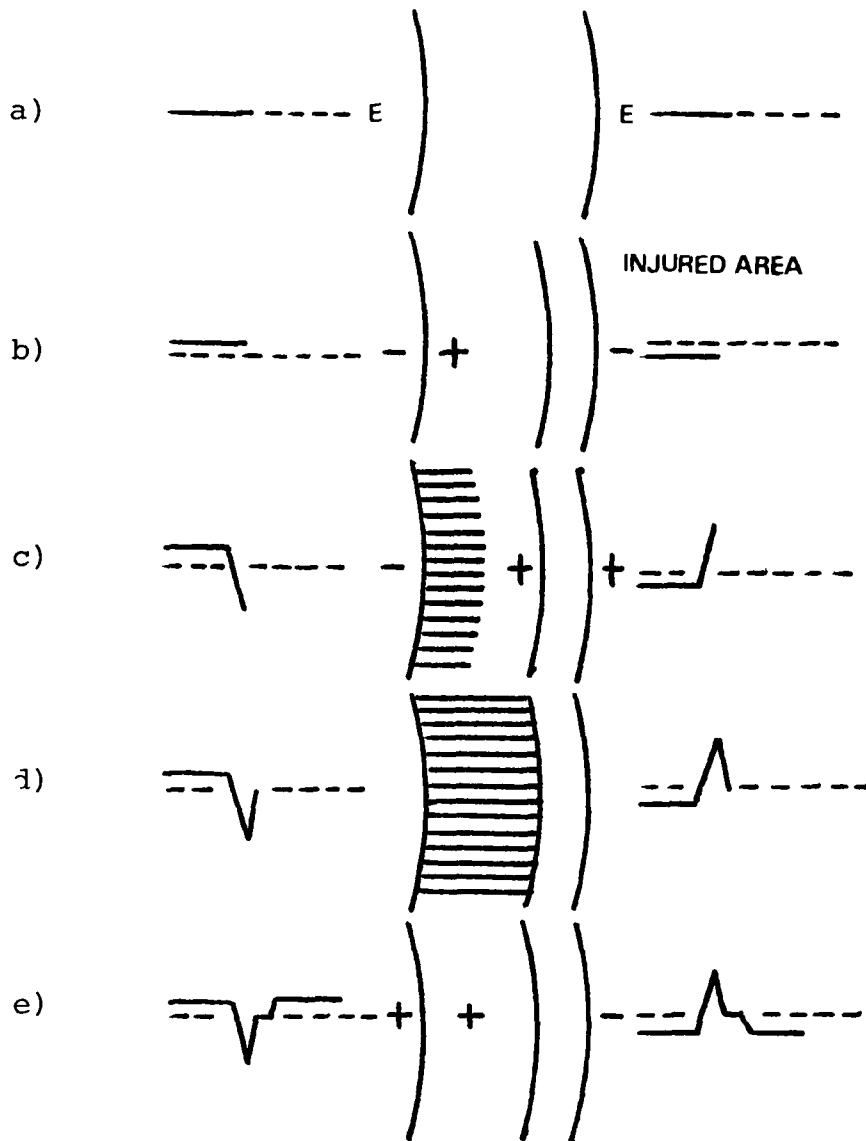


FIGURE 1. Theory of Injury Current of Rest

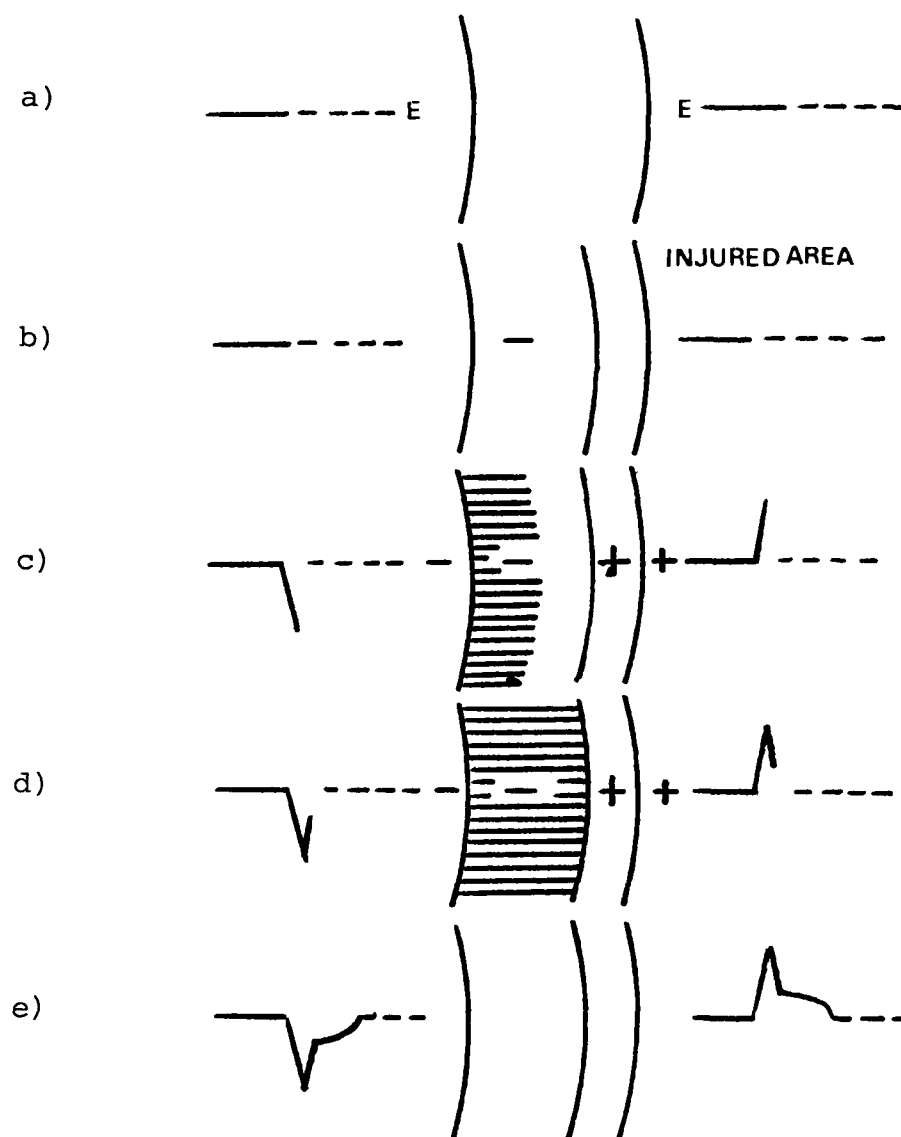


FIGURE 2. Theory of Injury Current of Activity

ST-segment depression in an epicardial lead, and major myocardial ischemia produces ST-segment elevation. Thus, ST-elevation usually implies severe ischemia; this idea was supported by the work of Linhart (1974a) and Fortuin (1970).

As a result of ST-segment depression, the T-wave may be dragged downward, producing the appearance of T-wave inversion. In addition, true T-wave inversion may occur in those leads which record ST-segment depression. This T-wave inversion is usually slight to moderate in degree. Occasionally one may see very deep T-wave inversion simulating that seen in myocardial infarction.

The normal heart, free of infarction, hypertrophy and conduction blocks etc., will not show adverse ST-segment changes in contour, depression or QX/QT ratio in the CM_5 lead during exercise (Doan, 1966). The abnormal heart, in the coronary patient, may show one or all three of these changes either during exercise or shortly thereafter. This is so in the majority of cases even when the resting 12-lead ECG is normal.

The use of exercise stress tests for the diagnosis of coronary insufficiency is based on the fact that a degree of insufficiency, the severity of which may not produce the anginal pain syndrome, may, in most cases, produce electrocardiographic changes characteristic of subendocardial injury. The electrocardiogram is more sensitive, in general, to coronary insufficiency than is the pain mechanism. The deep

layer of the myocardium, the subendocardium, is the first area to be affected by inadequate blood flow, since it is the furthest from the source. Changes in the ST-segment listed above are characteristic of injury to this area.

The Coronary Arteriogram:

Angiocardiology is one of the most valuable techniques available to the cardiologist and cardiac surgeon, for it enables an accurate, direct assessment of the anatomy and the function of the heart in many forms of heart disease. Like all invasive techniques, it is essentially complementary to clinical examination, phonocardiography and electrocardiography. The basic principle involves the injection of contrast medium into the vessel (atria, ventricles or arteries) to be studied, then the taking of a series of rapid X-ray exposures to follow the course of the opaque material, throughout a defined cycle. In the case of selective coronary arteriography the contrast medium is injected through a catheter manipulated into the appropriate coronary orifice under fluroscopic control.

Satisfactory angiography requires that three conditions be met: (1) rapid injection of contrast medium; (2) rapid exposure and high quality images; (3) safety of the patient.

If these conditions are met, diagnosis of coronary heart disease can be made with some certainty, and location of the obstructions is made easy. Many studies comparing methods of diagnosis of coronary heart disease use the coronary arteriogram

as the basis for comparison. The most widely used technique employed for this type of study is that method proposed by Sones (1960). Briefly the technique involves the insertion of the Sones catheter into the right brachial artery by open arteriotomy, passing into the ascending aorta, and manipulation into the appropriate coronary artery orifice under fluoroscopic control. Injections of 3 to 5 mls. of 90% Hypaque, diluted to 70%, are made into the artery. Starting with the patient in the 60° left anterior oblique position, then at various intermediate positions between and including the 20° right anterior oblique position multiple injections (up to 12) are made. At the end of the arterial study a ventricular function study is performed. Seldom do serious complications arise and the mortality rate is less than one percent for this procedure.

History

One of the first attempts at establishing a procedure to evaluate coronary circulation during stress, was by Master (1929). The physiological parameters measured then were, blood pressure and pulse rate. Normative values for changes in these parameters at given times during the test were set down. The underlying principle of the test, as for many exercise tests today, was to effect an increase in myocardial oxygen demand to such an extent that it can be met by increased coronary flow in the majority of healthy subjects, but not in

the case of the subjects with latent coronary insufficiency. Subsequently, it was found that the electrocardiogram could be used safely in conjunction with the exercise test, and indeed proved to be a better indicator of active and latent myocardial ischemia (Master, 1941). Because of its simplicity, availability, and prescribed adjustments for age, sex and body weight, the test was widely accepted. This test has been used clinically the world over for the past thirty years. Master and Rosenfeld (1967) recently emphasized the importance of standardization of the quantitative aspects of electrocardiographic response to exercise, the safety of the procedure and optimal criteria of horizontal ST-depression of 0.5 mm. or more. Friedberg et al., (1962) had reported the specificity for true negative responses as seventy-nine percent and the sensitivity of true positive responses as seventy-three percent for the Master step test. The optimum criterion was 0.75 mm ST-segment depression.

Master was one of the pioneers in the field of exercise electrocardiography, and his contributions in the area of diagnostic medicine have directed the short history of the study of myocardial ischemia through electrocardiography. The basic principles he proposed as the basis for his test have withstood the test of time, and are still being used universally as fundamental guidelines to exercise testing in general. These ideas have evolved somewhat from the form of the original proposal, in terms of practical application, and one still

finds widespread use of a modification of the original Master step test. The norms that he and many other investigators established through use of this test are still being used as a basis of comparison of more modern techniques.

Master Step Test, Graded Multistage Exercise Test and the Naughton Test

Recently (Bruce, 1969) the primary objectives of stress testing in screening for cardiovascular disease have been re-stated:

- (1) identification of pathophysiological risk factors for chronic disease,
- (2) quantitative assessment of functional aerobic capacity,
- (3) prediction of prognosis.

In light of these refined objectives the Master test is no longer considered to be suitable. Exceptions to the use of the Master test have been taken recently, on the grounds that it is too rigid and sometimes misleading (Goldberg, 1970). The reasons for this are plain; (1) the use of body weight to adjust the workload may not have a physiological basis (Rowell, 1969); (2) since the electrocardiogram is recorded after exercise, the information present during exercise can be missed; (3) the diagnostic yield is lower than that obtained with strenuous exercise (Linhart, 1974); (4) no steady state is attained.

Ascoop and Simoons et al., (1972) consolidated many ideas on this subject by comparing the diagnostic value of the Master test and a graded multistage test. They found that the graded multistage test better discriminated pathologic and normal coronary arterial systems than did the Master test. This was shown by the higher true positive fraction of the graded multistage test.

Martin and McConahay (1972) state that the treadmill test permits increasingly strenuous exercise to a level dependent upon each patient's capacity, in a mode familiar to all patients; that is upright walking on a flat surface.

They go on to say, as others have mentioned, that because the test is performed under continuous electrocardiographic surveillance the diagnostic sensitivity and safety of the patient is improved over previous tests.

Bruce and McDonough (1969) differentiated multistage tests as being either maximal or submaximal, in view of the exertion required to finish the test. A submaximal test is one which utilizes some arbitrary fixed limit of submaximal exertion, defined by the amount of work performed, or heart rate attained. These limits are applied to all persons tested regardless of their capacity. The maximal exertion test, on the other hand, does not have universally defined limits. After appropriate preliminary workloads, the patient performs until he attains an individually defined limit of capacity.

The value of the multistage exercise test electrocardiogram has been well documented. Recently attempts have been made to improve the accuracy of the exercise test as a diagnostic and prognostic tool. Much of the research is centered upon a more strenuous test, the graded multistage continuous exercise treadmill test; the assets of which have been described earlier.

Bruce and Hornsten (1969) in making recommendations for choice of test procedure suggest that the treadmill provides the advantages of involuntary, regulated workloads, against gravity rather than resistance. The energy expenditures are as a result more reproducible and hence more predictable at submaximal loads and slightly higher at maximal loads. They have used this multistage principle of uninterrupted submaximal and maximal workloads on a treadmill for several years, for both cardiac and normal testing. They employ several workloads of three minutes duration, increasing speed and treadmill elevation until a self-determined end point of limiting symptoms or adverse signs occur. The principle of the test is that it allows adequate time for the physiologic adjustments to be made before the workload is increased.

If duration of exertion under standardized conditions of the multistage test is displayed as a cumulative percentage distribution curve, several points emerge. First, about fifty percent of normals and patients with angina pectoris and/or previous myocardial infarction are physically well trained

and exhibit longer durations, thereby skewing the distribution curves to the right. Secondly, the mean difference in total duration of exercise between representative samples of the two groups, normals and patients, significantly vary by as much as two stages or 5.9 minutes. Since the workload was increased serially, the actual difference between groups, if they were working at the same workload, would be considerably longer. Thirdly, all of the normals, but only twenty-five percent of the patients, completed one-half of the third stage or 450 seconds of exercise. Fourthly, the performance of any patient could be readily interpreted on a percentile basis in relation to the appropriate spectrum; for example, a patient who completes 180 seconds of stage one, falls into the twenty-fifth percentile.

The treadmill test is thought to be the best form of multistage testing because, when compared with other forms of exertion, the treadmill test best attains predictable workloads with the least variance (Bruce & McDonough, 1969). This is so because the energy expenditure is controlled involuntarily. More recent improvements include continuous electrocardiographic monitoring with two or more leads, (Bellet, 1964) a more strenuous procedure, (Kattus, 1963) as well as computer applications for beat to beat analysis of heart rate, and ST-segment depression (McHenry, 1970).

Bellet and Roman (1967) worked with two groups of subjects; sixty normal male and female students, aged seventeen

to twenty years, and 150 middle aged subjects of both sexes. The latter group contained subjects with various types of atypical chest pain, hypertension or diabetes mellitus or all three, but showed no electrocardiographic evidence of myocardial infarction or ischemia in the resting twelve-lead electrocardiogram. The purpose of the study was to determine whether maximum exercise would produce an ischemic type of electrocardiographic change in young, presumably normal subjects. Also they wanted to know if more strenuous exercise than the Master step test increases significantly the yield of true positive results. This part of the study was conducted on the middle age group in which the possibility of coronary heart disease was very high.

The multistage maximal test was similar to that described by Doan et al., (1965) consisting of successive three minute periods of treadmill exercise of gradually increasing severity. Similar indices were also used for description of a positive test and for termination of exercise; ischemic ST-segment depression of greater than or equal to one mm. (0.1 mv), or the appearance of multiple premature ventricular contractions within the first five minutes of recovery. Negative responses were those which did not show these characteristics.

In twelve percent of the ninety-three patients with negative master step tests, the maximal exercise test resulted in the appearance of positive ischemic changes in the electrocardiogram. These findings further confirmed the work of

Sheffield et al., (1965) who obtained an additional twenty to twenty-five percent more positive tests with the maximal test in a similar study.

Bellet and Roman (1967) also demonstrated, as did Doan et al., (1965) and Sheffield et al., (1965) an absence of positive electrocardiographic findings (by the aforementioned criteria) in young adult male subjects even after strenuous exercise. The subjects were assumed to be normal and have good coronary circulation.

They concluded that in the comparison of the Master step test and the multistage maximal test, because there was an additional yield of true positive responses and because more strenuous exercise did not elicit abnormal changes in normal individuals, the performance of greater work levels is an asset to the exercise test.

In 1969 Ellestad et al., proposed a standard maximal stress test for the treadmill. Recording the ECG from leads in the CM_5 position, they had their patients attempt a test of increasingly vigorous, uninterrupted levels of exertion, as follows: At a fixed grade of ten percent, the patients exercised for three minutes at 1.7 mph; two minutes at three mph; two minutes at five mph. Termination of the exercise occurred when the patient became exhausted, showed a significant blood pressure drop, demonstrated progressive ST-segment depression, or developed anginal pain. If none of these symptoms occurred the patient was urged to continue until he

reached 95 percent of the predicted maximum heart rate, based on Astrand's scale.

Smokler et al., (1973) found that highly reproducible performances are found in duplicate tests after the initial test had been taken. They used a near maximal treadmill exercise tolerance test. The end point was what they rated as 3 - angina or moderately severe angina. The initial test usually results in a poorer performance than subsequent tests.

The high reproducibility of treadmill testing tends to support the idea that multistage treadmill testing is the method of choice.

Comparative studies with graded tests indicate that the Master test is no longer sufficient to induce reliable ischemic indices specific to coronary heart disease of the precision required today. It is for this reason that a multistage exercise treadmill test has been suggested as the most reliable in the screening and evaluation of patients that have coronary heart disease. There is still much controversy over whether a maximal treadmill test is superior to a submaximal test (Bruce and Konsumi, 1973), (Kattus et al., 1971).

Spangler, (1970) who has been using a submaximal test in his laboratory, suggests that a maximal test yields a higher true positive ST-segment response compared to the submaximal test. Smokler (1973) on the other hand, suggests that in terms of experimental mortality (i.e. the number of subjects not returning for further testing) a near maximal test is best.

In 1967 Naughton demonstrated that the same principles which are used in testing the physical fitness of the person in optimal physical condition can be used to assess individuals with clinically demonstrable evidence of heart disease. The test proposed, required an energy output of up to seven times the resting metabolic rate. Clearly such an energy expenditure was considerably less than maximal reserves possessed by a healthy well trained individual, but, was sufficient to evaluate the sedentary person and the patient with heart disease. The test had all the advantages of previous multi-stage treadmill tests, with the added advantage that it could be applied to coronary patients. This test protocol was still being used in 1966. Naughton at that time demonstrated, using this test, that patients, recovered from myocardial infarct, can develop a cardiovascular response, following physical conditioning, consistent with that observed to occur in presumably healthy men.

The contraindications to exercise, criteria for exercise termination and most of the pertinent information pertaining to the test, which is still used, were listed in 1971 (Fox, 1971). In prescribing exercise regimes for patients and normals (Naughton, 1972), Naughton et al., suggest that the maximum stress test (Bruce and McDonough 1969) provides data of great value, but that sufficiently useful information can be obtained by stopping exercise when the heart rate reaches eighty to ninety percent of the age adjusted,

predicted maximal heart rate. These are listed in the Appendix A. This particular test is considered by many to be the most suitable in its application to coronary subjects (Hellerstein, 1973).

Parameters of the Exercise ECG

QX/QT Ratio:

In 1958, Lepeschkin and Surawicz (1958) undertook the study of a large number of persons without detectable evidence of cardiac or coronary artery insufficiency. The purpose was to compare criteria for an abnormal Master test, and to establish new criteria that might differentiate true positive from false positive electrocardiographic response to exercise. A measurement that proved to be of great value was the interval from the beginning of the QRS complex to the point of intersection of the ST-segment with a baseline, drawn from the points of origin of two consecutive QRS onsets. This horizontal distance was expressed as a percentage of the horizontal distance measured from the beginning of the QRS complex to the end of the T-wave or QT-interval. It must be emphasized that the baseline used in this measurement is at best an approximation. The T-U junction is regarded as the nearest approach to the correct end of the QT-interval.

Blake (1972) states that this method of describing ST-segment changes quantitatively, is the best approach that has been proposed so far; in addition it is a method that

Master accepts. Some depression is necessary for there to be a QX interval at all, and depression of a duration of more than fifty percent of the value of the QT-interval is defined as flattening.

Criteria combining the magnitude of the ST-segment depression, length of depressed segment, and time of disappearance of the depression, allow a better differentiation of true positive and false positive tests, than any one of these parameters taken alone. Thirty-five percent of Lipeschkin's normal group showed all three of the following features: (1) greatest ST-segment depression amounting to 0.75 mm. or more; (2) return of the depressed ST-segment during the second half of the QT-interval; (3) true depression of the ST-segment exceeding 0.5 mm persisting for two or more minutes.

On the other hand, ninety-three percent of the sample with coronary artery disease showed all these features.

Master and Rosenfeld (1967) revised the Master step criteria for a positive test as follows: (1) any ST-segment depression greater than or equal to two mm; (2) a J-point depression with a QX/QT value of 0.5 or more or with a Q:T of 1.08 or more, or both; (3) appearance of ischemic ST-segment depression, defined as horizontal or sagging ST-segment.

Values less than these were considered to be negative tests.

Simonson (1963) notes the use of the Q:T ratio (actual QT-interval to the corrected QT-interval) derived from

Bazett's (1920) formula (1) is entirely empirical.

$$QT_c = K(R - R'') \quad (1)$$

where QT_c is the corrected QT-interval

K is a constant equivalent to 0.4,

$R-R''$ is the interval between successive R

waves. Simonson adds that this formula does not accurately represent the relationship between heart rate and the QT interval. The Q:T changes depend upon resting heart rate, absolute heart rate during exercise, rate of increase of heart rate during exercise, and heart rate decrease after exercise.

Because of the many factors involved, including also considerable variation in measurement, a rather large variation in Q:T must be expected.

Much of the experimentation of recent years concerning characterization of a positive electrocardiographic response involved the various anomalies of the ST-segment. The depression of this segment or, less often, the elevation, must, it seems, be defined in at least two dimensions; that of time and that of spatial orientation. The method of time definition described by Lepschkin and Surawicz involves the length of time that the ST-segment remains depressed in relation to the total time of the repolarization phase of the electrocardiogram. The physiological basis of ST-depression has been described earlier as a delay in the repolarization of the myocardium, due ultimately to an insufficiency of coronary blood flow to one or

many points of the ventricles. Quite obviously this value will vary as heart rate varies. Thus it was thought that a correction factor based on heart rate was required in order to allow for this variation. However, it seems quite unreasonable in this application, if it is assumed that the heart rate as such will intrinsically affect the total electrical cycle in a constant proportion, and therefore the need for empirical correction is theoretically unnecessary. This fact was pointed out by Simonson and he is of the opinion, as is Blake, that the QX/QT measurement, without corrected QT intervals, is valid in quantifying the ST-segment.

ST-segment slope, J-Point depression:

Lester et al., (1967) studied the relative electrocardiographic responses of older males to a near maximal Master step test and the multistage maximal treadmill test of Doan et al. The criterion measures used in this study were cardiac cycle length, J-point depression, and slope of the ST-segment. The method of calculation of these various parameters was as follows:

Determination of the ST-segment slope required construction of a baseline through three consecutive PQ-points. A tangent was then drawn to the first 0.08 secs. of the ST-segment and the slope in mV/sec, derived according to the relation -

$$dV/dt = d/\overline{BC}$$

where D is equivalent to the vertical distance in cm. from the baseline to the intersection of the ST-segment tangent.

- \bar{BC} is equivalent to chart travel in cm from B to the intersection with line D divided by chart speed in cm/sec. (see Figure 3)

The magnitude of J-point depression was measured directly as the vertical displacement of the J-point from the baseline. On no occasion was a single beat measured, but only complexes typical of those occurring over a period of several seconds, were evaluated. A flat or sagging ST-segment with a J-point depression of one mm or more was the only criterion used to establish a definitely positive response. Subjects with ST-segments appearing ischemic to inspection, but with slightly upward ST-segment slope by measurement, were classified as doubtful positive response.

ST-segment:

ST-segment depression as it is commonly used, refers to the point of maximum deviation of the ST-segment from the baseline. In many cases this is synonymous with the J-point depression, as is the case when the ST-segment slope is positive. This measurement of absolute depression of the ST-segment has been used in conjunction with exercise stress testing, since Master first proposed it. For many years the criterion magnitude of deviation for a positive test was taken to be 0.5 mm (Master, 1967). It has been suggested by various

investigators that a depression of 0.75, 1.0, 1.5 or 2.0 mm must be present before a depression was considered significant. Quite recently, values of up to 5.0 mm depression induced by a maximal stress test are considered to be safe (Linhart, 1974a,b). Robb and Marks (1964) found the amount of ST-segment depression after an exercise test correlated with the ultimate survivorship in 2,224 male life insurance applicants. The mortality ratio increased 2.5% to 15.8% as the magnitude of the ST-segment depression rose from less than one to two mm or more.

Doan et al., (1965) observed a greater frequency of transient ST-segment depression of one mm or more after maximal exercise, than that when compared to submaximal exercise.

Ascoop and Simoons (1971) used as their criteria a J-point depression of one mm or more associated with a horizontal or downsloping ST-segment over a time of eighty msec. These same criteria were used by Demany et al., (1967) Likoff et al., (1966) and Mason et al., (1967). Spangler et al., (1970), using a submaximal test, stated the criteria for a positive response as an ST-segment depression of one mm or more over a period of eighty msec., or an ST-J depression of 0.5 mm to 0.9 mm with an associated horizontal or downsloping ST-segment. Bruce and McDonough (1969) state that excessive ST-segment depression in one or more leads is usually evidence for and indicative of myocardial ischemia. They

concede that the classical response to exercise is a horizontal or downsloping ST-segment.

Recently, attempts have been made to classify electrocardiographic response to exercise. Kattus et al., (1971) suggest a system wherein response is categorized in one of three grades: a grade 3 response was one in which the ST-segment is depressed by several mm during exercise or recovery, and having a horizontal or downsloping configuration. A grade 2 response occurred when the ST-segment was depressed only during or at the end of exercise with almost immediate return to normal in post exercise recovery period. A grade 1 response shows horizontal or downsloping ST-segment seen only in post exercise recovery.

The test used was a graded exercise treadmill test and the value of grading the response is immediately seen because it tends to set a standard by which uniformity of testing can be carried out.

More recently, McHenry et al., (1972) developed a system which they termed the ST-index. This is accomplished through the use of an ST-segment analyser in which a beat-to-beat analysis is maintained. The index is computed by giving equal weight to the ST-segment slope and ST-segment depression, then adding the differences.

Bruce et al., (1966) classified the electrocardiographic response of their subjects in relation to the myocardial ischemia induced by exercise:

(1) Normal response, not indicative of ischemia, when ST-segment and J-point depression exhibited less than one mm of depression in consecutive beats.

(2) Borderline response, possibly but not definitely indicative of mild ischemia, when ST-segment junction was depressed at least 1.5 mm with every beat and/or there was marked respiratory variation of ST-segment depression of variable degree, from beat-to-beat.

(3) Abnormal response, probably consistent with myocardial ischemia, (in the absence of any digitalis therapy), when there was ST-segment depression of at least one mm. on consecutive beats throughout several respiratory cycles.

Linhart and Turnoff (1974b) very recently have suggested the use of maximal testing in the screening of cardiac patients. They suggest that the greater the stress applied, the more likely will be the possibility of separating the normal from the abnormal subject. The treadmill test in this case is the Bruce maximal test. The criteria they look for is an ST-depression of five mm or more, incurred at an arbitrarily defined maximal performance. They state that it has been their experience that it is safe to proceed to this level of ST-segment depression. They also suggest some guidelines in the discrimination of positive and negative exercise electrocardiographic response:

(1) functional depression alone does not indicate a positive response. It has been shown that J-point depression

is a normal physiologic response and is proportional to the degree of stress and the increase of heart rate.

(2) isolated T-wave inversion with exercise is not an indication of coronary artery disease.

(3) reversal of T-wave polarity from negative to positive is most common in patients without coronary artery disease.

(4) atrial and ventricular arrhythmias occur in five to ten percent of all exercise studies (most in the recovery phase) and it has been shown that only twenty-five percent have CHD.

(5) the ECG leads V_5 and V_6 have been shown to record only ninety percent of all ST-segment changes.

The controversy over test criteria for a positive electrocardiographic response has been going on since the beginning of exercise testing. It has been fairly well established that the ischemic ST-segment depression occurs very often during exercise in patients with CHD. As well, the incidence and extent of the depression may be directly related to the extent of the arterial disease; i.e. the number of arteries as well as the extent of the stenosis (Martin et al., 1972). Thus, the greater is the chance that ST-segment depression will occur during an exercise stress test. It is for this reason that the actual cut-off point for a positive test is still controversial. The literature relates both extremes, from 0.5 mm depression of ST-segment to five mm.

depression. The general concensus of opinion, and a large extent of the research today, centers on a positive test cut-off point of one mm ST-segment depression. (Bartel, 1974, Martin, 1972, McHenry, 1970). One contraindication to continued exercise, commonly accepted, is an ST-segment depression of greater than two mm.

Exercise Stress Testing, Coronary Arteriography

In 1972, Martin and McConahay (1972) attempted a study comparing the results of coronary angiography and maximal treadmill exercise testing. The aims of their study involved: (1) assessing prospectively the diagnostic usefulness of maximal treadmill exercise electrocardiography in evaluation of patients with coronary artery disease; (2) to evaluate the sensitivity and specificity of certain criteria used in the interpretation of the exercise electrocardiogram.

Sensitivity is defined as the number of true positive results divided by the sum of the number of true positives and false negative results. This is multiplied by one hundred and expressed as percent. Specificity is the number of true negative results divided by the sum of the number of true negatives and false positive results. Again this is expressed as a percentage; i.e., $\times 100$.

Patients who had been subjected to coronary arteriography participated in a maximal treadmill exercise test. Disease of a major coronary artery was considered to be functionally significant if its most severe narrowing exceeded fifty percent

of the arterial luminal diameter. On the other hand, patients were subjected to the exercise protocol until the occurrence of symptoms of excessive fatigue, dyspnea, angina, dizziness or ischemic ST-segment depression exceeding two mm. ST-segment depression was so termed when the ST-segment subtended an angle of at least ninety degrees to the ascending limb of the R-wave for at least eighty msec. The maximal extent of such ST-segment depression below the baseline as established by the P-R-segment was recorded for each level.

The results showed that sixty-three percent of the patients had arteriographic evidence of CHD. Twenty-three percent had one-vessel disease, eighteen percent had two-vessel disease and twenty-two percent had three vessel disease. Of the thirty-seven patients with no CHD, eleven percent were false positive if criterion ST-segment depression was set at one mm. If 0.5 mm depression was the cut-off, forty-three percent would show false positive in exercise test. Similarly there were no false positives when 1.5 mm was the criterion.

When a positive test was judged at one mm depression, sixty-five percent of the patients with single vessel disease, thirty-three percent of those with two vessel disease and fourteen percent with triple vessel disease, showed false negative in the exercise test. On the whole, sixteen percent of the patients were falsely negative if criterion were 0.5 mm ST-segment depression and thirty-eight percent at one mm. and fifty-two percent at 1.5 mm.

Areskag et al., (1967) compared a bicycle multistage test with coronary arteriography, using the criterion of greater than fifty percent occlusion in one or more vessels as significant CHD. The exercise test was negative if ST-segment elevation was less than one mm. or there was less than 1.5 mm of J-point depression. In this test they demonstrated by the exercise electrocardiogram only five percent false negative.

Using a similar arrangement, Likoff et al., (1966) showed very contrasting results. Positive electrocardiographic response was an ST-segment depression of one mm. or more. Each patient was classified according to the extent of one mm. or more. Each patient was classified according to the extent of his disease. Class one had luminal irregularities with no obstruction of the coronary arteries. Class two had fifty percent occlusion of one or more arteries. Class three had total occlusion of at least one coronary artery.

Class one showed fifty-two percent false negative, class two fifty percent and class three twenty-five percent false negative response to the exercise test.

McHenry et al., (1970) conducted similar experiments using a treadmill exercise protocol. In 1970, he showed in eighty-four percent of his patients known to have CHD by arteriography, a true positive response to the exercise test. In patients with fifty percent occlusion of one vessel, twelve percent demonstrated a false negative response to

exercise. Interestingly enough, McHenry points out that in five of the six patients with single vessel disease, the affected vessel was the RCA. In patients with established two and three vessel disease, ninety-four percent were true positive. The conclusions they drew from this study were that there is an increase in the true positive exercise stress test with increasing extent of the disease.

The 1972 study (McHenry 1972) was undertaken to show a correlation of the location and the extent of obstructive CHD and the ST-segment response to exercise. Again, all patients were shown to have greater than seventy-five percent occlusion of one or more vessels and displayed a normal resting twelve lead electrocardiogram. These patients were subjected to a multistage graded exercise test. An ST-segment depression of one mm. constituted a positive test when associated with an ST-slope of less than + 0.50 mV/sec. The study was biased in a sense that all patients actually had greater than ninety percent occlusion in one or more major arteries. However, it was shown that eighty-two percent had a positive response to the exercise test. Also sixty-three percent of those with one vessel disease, ninety-one percent of those with two-vessel disease and one hundred percent of those with triple vessel disease showed a true positive response.

Bartel et al., (1974) compared also the results of multistage exercise electrocardiography with findings of coronary arteriography. This study included patients suspected

of having CHD. A positive exercise test was indicated if there was depression of the ST-segment of more than one mm. for eighty msec, or more. The arteriograms were classified according to the number of arteries showing more than seventy percent occlusion. The results showed a very low false positive of eight percent. They also showed, as others had, (Ascoop, 1972, Martin 1972) that a decreasing false negative occurs with increasing number of vessels involved in the disease. Sixty percent false negative in patients with single vessel disease and thirty-four and twenty-four percent false negative in two and three vessel disease groups.

Linhart et al., (1974b) designed a study to demonstrate the applicability and limitations of the exercise electrocardiogram taken during a Bruce test. This was achieved by classifying the patients into groups. Group one were those with a normal resting electrocardiogram. Group two had abnormal electrocardiograms at rest and group three had abnormal resting electrocardiograms plus the fact that they were on active drug therapy. These groups were subjected to the exercise stress test and coronary arteriography. The results were expressed in terms of sensitivity and specificity of the exercise test. The specificity was highest in group one (one hundred percent) and group two (seventy-nine percent). Group three had a specificity of sixty-three percent. The sensitivity followed the same order at respective values, eighty-five, seventy-six and fifty-five percent.

This study demonstrated that the maximal graded exercise test was less effective as a diagnostic tool in the presence of an abnormal resting electrocardiogram due to right or left bundle branch block, left ventricular hypertrophy, rheumatic heart disease, hypokalemia, Wolff-Parkinson-White syndrome, and autonomic disorders. It was even less effective when given in conjunction with meals, smoking, digitalis and various other pharmacological agents, combined with the abnormal electrocardiogram.

Elevated ST-segment is frequently recognized as an electrocardiographic abnormality in cases of acute transmural myocardial infarction and less often in cases of transient ischemia. Fortuin et al., (1970) designed a study such that those showing ST-segment elevation during exercises were given coronary arteriograms. The idea was to predict the extent of occlusion of specific coronary arteries that would produce ST-elevation. They found that eight of the twelve patients showed ST-elevation in the anterior precordial leads during exercise and the arteriogram showed total or near total occlusion of LAD. Four of the twelve showed ST-segment elevation in standard leads II and III. These patients had total or almost total occlusion of the RCA. The conclusions drawn from this study were that ST-segment elevation during exercise is indicative of severe ischemia. The lesions which cause this ischemia can be localized by multilead electrocardiography.

The use of the arteriogram as a basis of comparison of the exercise electrocardiogram has only recently been popular in this field. As the classification of the exercise electrocardiogram is still quite subjective in the absence of universal standards, so too, the criteria for the evaluation of arteriograms is still quite personal. The review of the recent studies in this area brings to light a few general principles. It has been shown repeatedly that there is a high correlation between the occurrence of positive response to the exercise test and the extent of CHD. The false negative fraction varies almost inversely as the false positive fraction when the criterion level of ST-segment depression is varied. The false negative fraction also decreases with the amount of CHD and therefore ischemia. These facts seem to be true generally regardless of the type exercise protocol used. Cohen (1966) demonstrated this phenomenon using a Master step test. Areskag et al., (1967) and Likoff et al., (1966) similarly documented these effects using a bicycle ergometer multistage protocol, as McConahay et al., (1971) did later with the multistage treadmill protocol. Attempts have been made to account for the few cases in which ST-segment elevation occurs during exercise. Further, attempts have also been made to delimit the use and applicability of the exercise electrocardiogram in multistage treadmill testing protocol.

Summary

As research in any given area proceeds, various newer and better methods, standards and equipment are integrated into the research protocol until a satisfactory solution to the problem has been attained. Such is the case in the area of exercise testing. It has been the purpose of this brief overview of related literature, to point out several major advances in this area of stress testing.

Firstly, it was indicated that the Master step test was no longer sufficient to evaluate coronary heart disease with the precision required today. Further it was indicated that a graded multistage exercise test is superior in this regard. The exercise treadmill test is for many reasons the method of choice. However, the type of treadmill protocol has not been established with such clarity, but the implication is that a maximal or near maximal test is preferred. The Naughton test is one of the better tests for the testing of cardiac patients because it involves all the good points of treadmill exercise testing without being too uncomfortable to the patient.

The ST-segment of the exercise electrocardiogram is the most susceptible portion of the tracing to change in the ischemic condition of the myocardium produced by exercise. Again the absolute values or indications of positivity have not been firmly established. Until such time as the standards are set, it is necessary to evaluate as many variables as possible, to describe the various dimensions of the ST-segment response to exercise. The most popular variables to date are

the QX/QT ratio, slope of ST-segment and J-point depression, and absolute ST-segment depression. In employing these parameters, the time aspect, amplitude of deviation, and spatial orientation of the depression are quantified. The accepted criterion values of these parameters are a J-point depression of one mm associated with a slope of less than plus one mV/sec., a QX/QT value of greater than 0.5 and an absolute depression of greater than one mm.

Many authors describe the ST-segment as a depression of the ST-segment alone. In doing this they refer to the maximum deviation of this segment from an established baseline. Criterion values of one mm for a positive test are used. This information alone without a further qualification is insufficient information, just as the slope or the J-point depression alone are insufficient without an indication of maximum deviation or the time element involved. Thus, by the use of various parameters, one can effectively describe the numerous aspects of ST-segment depression, quite objectively.

As was pointed out, the coronary arteriogram is very popular as a basis of comparison in establishing the validity of an exercise test. Many aspects of the exercise test criteria as well have been discussed by various researchers, in relation to the extent of the disease. In fact, attempts have been made to classify the electrocardiograph response relative to classification of arteriographic findings. This idea of classification, especially of the arteriogram has been

shown to be very advantageous in the description of the electrocardiogram response to exercise.

CHAPTER III

METHODOLOGY

Introduction

It was previously indicated that this study was part of a project involving post-operational rehabilitation of cardiac patients. Therefore, included in the major project was pre and post-surgery stress testing as well as pre and post-rehabilitation evaluation. The exercise electrocardiographical testing, the subject of this study, was only one of the parameters measured in the total evaluation involved in the major project. The primary concern of this dissertation was to compare the results of an exercise stress test with the results of an angiographic procedure in the evaluation of coronary heart disease patients. A complete documentation of the methodology of the major project is available at the University of Ottawa Cardiac Stress Testing Unit (1972).

Subjects

The eleven subjects used in this study were referred to the Cardiac Stress Testing Unit by the Department of Cardio-thoracic Surgery as possible candidates (i.e. physically capable) for a post-operational rehabilitation program. The anthropometric data for each subject, including age, height, weight and an estimation of percent body fat are listed in Table 1. These patients, ages between 36 and 62 years with

Subject	Age (yrs)	Height (in)	Weight (lbs)	% Fat
EB	61	65.5	144.0	15.0
LC	58	67.0	166.0	15.8
SC	57	64.0	138.2	16.4
RD	64	71.5	150.0	15.2
RG	42	67.5	170.0	17.6
RG ₁	37	66.5	144.0	11.2
LK	45	65.5	156.2	19.8
WL	40	70.2	129.5	12.0
JM	39	70.0	171.0	16.7
WM	45	67.5	184.0	17.2
JR	44	69.0	173.0	16.4

TABLE 1 Subject Anthropometric Data

a mean age of 48.6, had a history of coronary occlusive disease and/or myocardial infarction, angina pectoris etc. Coronary angiographic studies were completed prior to the day of exercise stress testing. Subsequent to both of these procedures, the patients underwent revascularization surgery. A complete breakdown of the angiographic findings was done and is summarized in Table 2 for all patients included in this study. The subjects, listed in the extreme left-hand column by their initials, all suffered from coronary occlusive disease of one degree or another. In the adjacent column is listed the total number of major coronary arteries affected by the disease. The large heading "Selective Coronary Arteriography" is sub-divided six times, and lists the three major vessels with its respective disease rating for each patient. Also included in this table is a brief summary of the results of ventriculographic studies. The column on the extreme right lists the total heart disease rating of the patient. This value is obtained by summing the ratings of the individual arteries involved in the disease.

Subjects not able to partake in the exercise test due to undefined stress, were asked to return for re-examination at a later date. There were no mortalities in this particular study during the testing period. Extreme care was taken to note any contraindications to exercise testing listed in Appendix B. No patients were refused the exercise test on this basis.

Subject	No. Vessels Involved	Selective Coronary Arteriography						Left Ventriculography	Rating Sum
		RCA	Rating	LAD	Rating	M/CA	Rating		
EB	3	X	5	X	5	X	3	Akinesia Apex Region	13
SC	3	X	5	X	3	X	5	Good Contractility	13
LC	3	X	3	X	5	X	4	Hypokinesia Ant. Lat. Wall	12
WN	3	X	5	X	4	X	3	Hypokinesia Ant. Lat. Wall	12
JM	3	X	4	X	2	X	3	Normal Contractility	9
RG ₁	2	X	1	X	3	X	5	Hypokinesia Ant. Lat. Wall	9
JR	2	X	5	X	2			Normal Contractility	7
LK	2	X	3	X	3			Good Contractility	6
RD	2	X	3	X	3			Hypokinesia Apex Region	6
WL	2			X	3	X	2	Good Contractility	5
RG	2	X	1	X	3			Hypokinesia Distal 1/3	4

TABLE 2 Results of Angiography

Medication:

Subjects were advised to refrain from the use of medications for following periods of time prior to exercise testing:

β -blocking Agents (Inderal) - 2 weeks

Digitalis glycosides - 1 week

Nitroglycerin - day of testing

Nitrong (slow release nitroglycerin) - 24 hours

Classification of the Arteriograms

The arteriographic findings for each patient included in the study were classified according to the following scheme. Each vessel shown to be involved in the disease by coronary arteriography was rated according to the amount of stenosis or occlusion present, on a scale of 1 to 5. The rating system was:

0 for normal arteries

1 for 50% diameter stenosis (mild or insignificant disease)

2 for 50 to 75% diameter stenosis (moderate disease)

3 for 75-90% diameter stenosis (severe disease)

4 for 90 to 100% diameter stenosis (sub-total occlusion)

5 for 100% occlusion.

Test Session Protocol

All testing sessions were scheduled in the morning between 09:00 and 11:00. Testing within this time tends to

reduce the influence of various factors such as circadian rhythms, meals, anxiety and stress. Written instructions were provided to the patients pertaining to location of the test, sleep, dress, pre-test meal, smoking, drugs etc.

The subjects arrived at the lab and changed into appropriate clothing including shorts and soft soled shoes. They were then directed to a separate quiet room to rest for 15 minutes before a twelve-lead electrocardiogram was recorded. Subsequently the patients were subjected to various other tests not primarily concerned with this study. These included, pulmonary function tests, bone density measurements, and a short consultation with physical and social therapists. Also a blood analysis and anthropometric measures were done.

The subjects were then directed to the test area and the exercise ECG electrodes put in place. The patient was then seated and after the blood pressure cuff was attached to his left arm, a sitting and standing blood pressure recording were done; a phonocardiogram and pulse recording equipment were attached and recorded simultaneously with the ECG for later analysis of systolic time intervals. The cardiometer and oscilloscope were then activated, commencing the continuous monitoring of the patient. A short explanation of the procedure for mounting and dismounting the treadmill followed, after which the "warm-up" stage of the treadmill test began. After the prescribed time of repose the subject started stage one of the exercise test. During the last ten seconds of each

minute on the treadmill and during the 6 minutes of recovery, the ECG was recorded. If abnormalities were evident a permanent record was made continuously from the time of their onset. (In conjunction with other evaluations, the patient was required to breath into a mouthpiece during the third minute of each stage, and samples of expired gas were taken and later analyzed.) The blood pressure during exercise was recorded every second minute during exercise and recovery.

When the test was terminated for any reason, the patients completed the "tapering-off" stage, were seated, and further measurements of blood pressure, ECG, and systolic time intervals were carried out, as prescribed, during the six minutes of recovery.

Exercise Test Description

Each of the subjects was required to perform the following series of exercise intensities on the treadmill, until a self-determined maximal exertion or end point occurred or adverse signs contraindicating the continuation of exercise became apparent.

The graded multistage exercise test (GXT) chosen for this project was one based on that proposed by Naughton (Fox, 1971). It includes the following levels of exercise: (Appendix C).

An initial workload at an energy requirement of 1.6 METS⁽¹⁾ was performed at a speed of 1.5 mph and zero percent

¹A metabolic unit (MET) is defined as the equivalent of fifty Kcal/m²/hr or the metabolic rate of a man seated performing a sedentary task.

grade. This, as were all stages, was continued for three minutes. This stage was considered to be a warm-up period; the patient was allowed to adapt himself to walking on the treadmill. This warm-up is followed by a recovery phase of three minutes. During stage one of the test the speed of the treadmill is increased to 2 mph. This stage and the following stages continued for 3 minutes at 2 mph before the next stage is begun. Stage one corresponds to an energy output of 2 METS. The next level of energy output was 3 METS at an elevation of 3.5 percent. Stages three, four, five and six, each 3 minutes in duration and executed at 2 mph, required the following energy expenditures respectively; 4, 5, 6, and 7 METS, and correspond to elevations of 7, 10.5, 14 and 17.5 percent. If a test requires greater intensity, the treadmill is lowered to a slope of 12.5 percent, the speed increased to 3 mph, and the elevation increased by 2.5 percent increments every 3 minutes, to a maximum of 22.5 percent. Each new workload increases the energy expenditure by approximately 1 MET. There is no practical value in testing beyond 12 MET's (Fox, 1971). During this test, each workload is maintained for 3 minutes, to allow the subject to achieve a steady-state; it also allowed time for test parameters to be recorded.

The test was terminated if the patient exhibited any of the symptoms listed below, or attained his criterion heart rate in conjunction with other adverse signs (Appendix C).

The exercise test was never terminated on the basis of heart rate alone. When the patient stopped for one reason or another, the final attained level was followed by a "tapering-off" period of walking at 1.5 mph. and 0 percent grade for 1 minute. The basis of this is the prevention of hypotension and arrhythmias (Fox, 1971). The patients were then seated in a semi-reclining chair, and monitored for an additional six minutes.

Criteria for terminating the Exercise Test:

The exercise stress test was immediately halted by the physician and/or the examiner, on the basis of any or a combination of any of the following contraindications became apparent. The same physician and examiner were present at all times during the testing of the patient for all the subjects tested. The contraindications during exercise were the following:

- (1) The patient attained a pre-determined heart rate (Appendix C), in association with other adverse signs.
- (2) The patient complained of increasing chest pain, severe dyspnea, or severe fatigue.
- (3) Onset of paroxysmal supra-ventricular or ventricular arrhythmias.
- (4) Development of ischemic ST-T wave changes (ST-segment depression of two mm or more, positive T-waves becoming flat, or negative T-waves becoming positive).

(5) Onset of ventricular premature beats appearing before the end of the T-wave.

(6) Conduction disturbances other than slight atrioventricular block became apparent.

(7) The subject showed clinical signs of impending emergency situation, including pallor, cold moist skin, cyanosis, staggering, confusion in response to enquiries, the facies of cerebrovascular insufficiency, and head nodding.

(8) The patient's systolic and pulse pressure failed to increase.

Equipment

The graded multistage exercise test was carried out using a Quinton Instruments motor driven model 18.49C treadmill fitted with a programmed Quinton Exercise Control unit model 643, and an Exercise Cardiometer with digital display, Quinton model 609. The resting twelve lead, exercise and recovery ECG was recorded on a Cambridge VS4 portable electrocardiograph, calibrated daily to one mV per cm deflection, and paper speed of twenty-five mm/sec. The ECG was recorded from CM₅ leads. (Upper manubrium sterni and V₅ approximation). The electrodes were self-adhesive, Red Dot disposable type. Throughout the exercise test and recovery period, the subjects were monitored using a Hewlett-Packard 760 monitor scope and Sanborn 768-100 Gating amplifier. The patient's blood pressure, recorded before, during and after

exercise was registered using a standard sphygmomanometer attached to the subjects' left arm, at heart level. Emergency equipment and personnel trained in their use and administration, were kept near at hand. This included an AC-DC defibrillator, O₂ administration equipment, anti-arrhythmic drugs etc.

Exercise ECG Variables

The parameters of the ECG evaluated for this study included: the ratio QX/QT; J-point depression and ST-segment slope; and ST-segment depression.

J-point:

The J-point depression or amplitude of deviation from the baseline of the point at which the QRS complex ends and the RS-T segment begins, is measured in millimeters (1mm.= 0.1 mv.). The baseline is the isoelectric TP-segment, defined as the line from the termination of the T-wave to the beginning of the P-wave.

The ischemic flattening and increasing negativity of the slope of the ST-segment of typical myocardial ischemia is also very important in the evaluation of exercise ECG. This holds true more now since positive sloping of the ST-segment, associated with J-point depression is not considered as a positive test. Thus, it becomes important to measure not only ST-segment depression but also slope. The quantitative method of Lester et al., (1967) was used in this study (Figure 3).

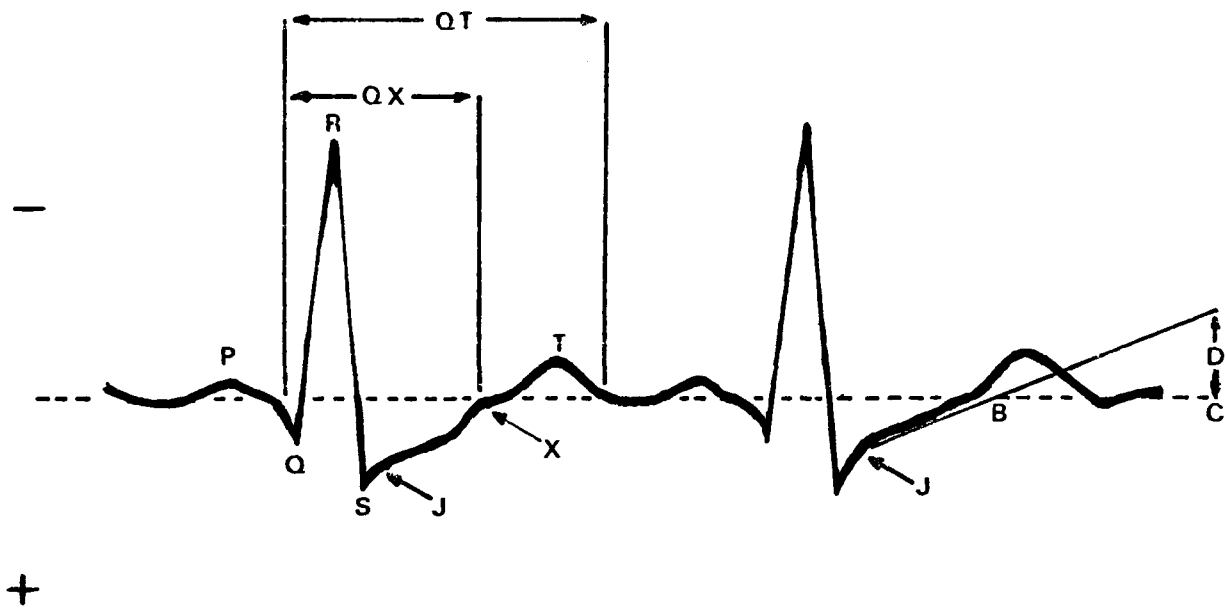


Figure 3. Schematic diagram of abnormal exercise ECG showing measurement of the parameters.

A baseline was constructed by joining two consecutive QRS onsets. A tangent was then drawn to the first 80 msec (2mm) of the ST-segment. The amount of deviation of the tangent from the baseline in a ten mm distance (0.4 secs) was measured. The slope is calculated by dividing the vertical deviation in mV by the horizontal distance, 0.4 secs. Three or more consecutive ST-segments were thus measured and the mean value recorded.

In this study a positive response was indicated by a J-point depression of one mm or more associated with a slope of less than 1.0 mV/sec.

QX/QT Ratio

The ratio, QX/QT and the method of its calculation, was taken from Lepeschkin (1958) (Figure 3). The first step in the calculation was to construct a line through the origin of two contiguous QRS complexes; this is considered a baseline. The QX interval is then measured from the QRS onset to the point where the ST-segment returns to the baseline. The QT-interval is taken as the horizontal distance from the beginning of the QRS complex to the end of the T-wave. The ratio was calculated by dividing the value of the QX-interval in mm by the QT interval in mm.

When the ratio of these two intervals was greater than 0.50 the ECG response of this parameter was said to be positive.

ST-segment depression:

The ST-segment depression was measured as the maximum deviation of the ST-segment as defined, in mm. A positive test by ST-segment depression was a depression of 1 mm.

All measurements for each parameter were made with Helios Vernier calipers on three beats. The values were averaged and the mean recorded. The calipers were calibrated to 0.1 mm. The ECG recordings analyzed were those of the last ten seconds of every third minute. When the test was prematurely terminated, the last ten seconds of the final recording was analyzed. The beats from the last ten seconds of each third minute of recovery were analyzed. The contraindications for exercise testing are also listed in the appendix.

Presentation of Data and Statistical Analysis

In keeping with the aims of the study the results are presented in the form of three tables. The first two tables contain data collected from the anthropometric and angiographic studies.

The data from the exercise test electrocardiogram is also presented in tabular form. One chart lists the subjects and the stage at which a positive response was obtained from each parameter. Another chart lists the maximum value observed of each parameter and the stage at which it was reached.

Various other information drawn from these charts are given including mean scores for individual parameters, true positive

fraction and correlations of the various parameters.

The coefficients of correlation were calculated by the method described by Freund (1967). The judgement of whether the value is significant or not was from the table of Fisher and Yates in Freund (1967).

CHAPTER IV

RESULTS AND DISCUSSION

Introduction

This study was conceived in order to compare the results of a graded multistage exercise ECG test with the results of coronary arteriography in coronary patients. The results of the study will be presented under the following headings:

1. Exercise stress test data;
2. Correlations of the exercise electrocardiogram with the coronary angiogram.

Following the presentation of the data is a discussion of the implications and relevance of these findings in relation to previous work in this field.

Results

Exercise stress test data:

The true positive fraction calculated for the exercise ECG treadmill test, based on the angiographic results was 91% (10/11). The false negative fraction was 9% (1/11).

The data obtained from the exercise stress test is shown in Tables 3 and 4. Table 3 lists the subjects by their initials, on the left hand side of the chart. The adjacent column to the right "CAG Rating", lists the extent of the

Subject	CAG Rating	Test Stage of (+) Response		
		J/Slope 1mm/ 1mV/sec.	ST 1 mm	QX/QT 0.50
EB	13	2	2	1
SC	13	5	5	2
LC	12	1	1	1
WN	12	3	1	2
RG ₁	9	3	3	4
JM	9	2	2	1
JR	7	2	2	1
LK	6	2	1	0
RD	6	5	5	5
WL	5	-	-	-
RG	4	6	6	6

TABLE 3 Results Exercise Stress Test
 0 - (+) response during rest.
 - no (+) response during test.

Subject	Test Completed Mins	J/Slope		ST		QX/QT	
		Max Value	Stage	Max Value	Stage	Max Value	Stage
EB	12.4	2.46/-0.20	4	2.56	4	0.65	4
SC	15.0	1.6/0.0	5	1.46	5	0.73	5
LC	1.7	1.76/0.00	1	1.76	1	0.63	1
WN	12.0	1.20/-0.33	4	2.00	4	0.69	4
RG ₁	16.5	1.93/0.10	6	2.00	6	0.73	6
JM	9.0	2.00/0.00	3	2.00	3	0.70	3
JR	9.0	1.63/-0.06	3	1.68	3	0.68	3
LK	14.5	2.16/0.00	5	2.16	5	0.77	5
RD	18.0	1.76/0.10	6	1.90	6	0.60	6
WL	18.0	0.00/-0.26	R	0.69	R	0.46	R
RG	18.0	1.66/0.42	Rec1	1.66	Rec 1	0.63	Rec1

TABLE 4 Results of Exercise -- ECG

R - max-value occurred at rest

Rec - 1st min. of recovery.

coronary artery disease as rated by the angiographic evidence. Under the title "Test Stage of (+) Response" are the subdivisions for each of the ECG parameters measured. Listed in the respective column for each patient is the stage of the corresponding parameter. Table 4 lists the subjects by their initials in the extreme left hand column and in the adjacent column the number of minutes of the exercise test that each completed. The major headings; J/slope, ST depression and QX/QT ratio, are sub-divided to list the maximum value recorded for each parameter during the test, and the stage at which it was recorded.

It can be seen that 4 of the subjects completed between 15 and 18 minutes of exercise; 3 subjects stopped exercise between 12 and 16 minutes of the test, 2 subjects stopped at 9 minutes, 1 at 12 minutes, and 1 subject stopped between 1 and 3 minutes of the test. On the average patients completed 13 minutes of exercise. Three patients finished 6 stages or 18 minutes and 1 patient failed to complete the first 3 minutes of the test.

For 5 of the patients the ratio of QX/QT, was the earliest indication of ischemia. This parameter appeared positive within the first 2 stages in this group. Of these patients 4 had 3-vessel disease and 2 had 2-vessel disease with an average rating of 10.0.

The ST-segment was the first positive indication of ischemia in 4 of the patients, 1 of which had 3-vessel

disease and 2 had two-vessel disease. On the average this appeared in the third stage.

The J-point/slope parameter appeared once first and twice at the same time as the ST-segment depression. One patient did not have positive response of any parameter in the whole test or in the recovery period.

The maximum values attained for each parameter occurred near the termination except in one case, when the maximum value occurred during rest. It appeared before exercise and was never a positive indication for any parameter.

In all cases, except for two subjects, the maximum value of deviation for each parameter was found to occur later in the exercise test than the positive indication for this parameter, i.e., the magnitude of deviation became greater as exercise continued. (In one patient there was no positive indication of any parameter in the exercise test. The other patient didn't finish the first stage of exercise.

Correlations of the exercise electrocardiogram with the angiographic results:

The correlation between the stage at which any of the three ECG parameters measured became positive, and the rated extent of coronary heart disease was found to be -0.54 . This correlation coefficient was not significant at the $\alpha = 0.5$ level. The regression diagram is illustrated in Figure 4.

Table 5 lists the correlations of the stage at which various parameters became positive and the rating of extent

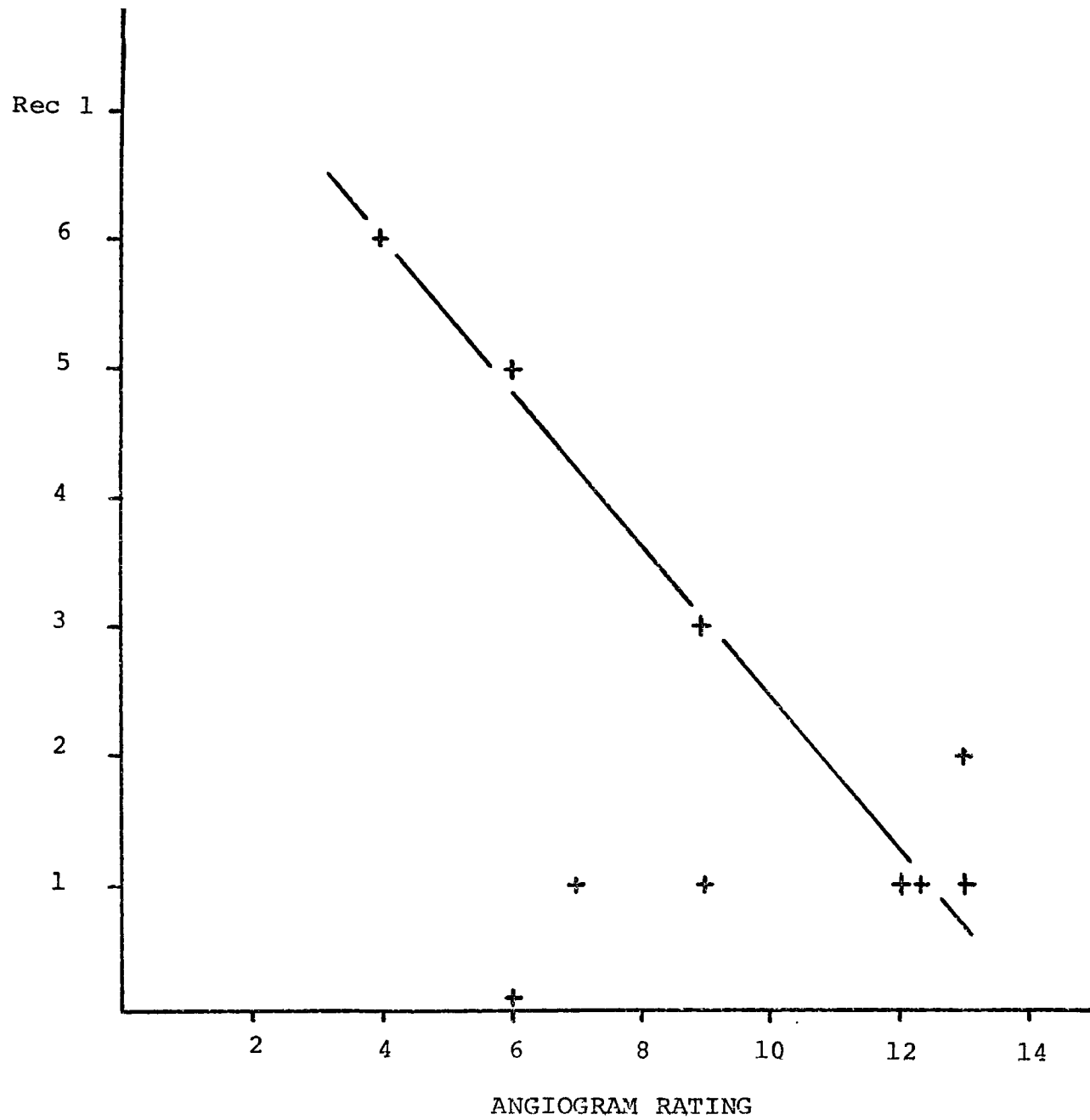


FIGURE 4 Stage of (+) ECG Response and CHD Rating.

Parameters	J/Slope	ST	QX/QT
Stage of (+) Response and Angiogram Rating	-0.13	-0.13	-0.53
Maximum Response and Angiogram Rating	+0.30	+0.04	+0.37

TABLE 5 Correlations of parameters measured with
angiographic results

of CHD. Also listed in this figure are the correlation for the maximum response of each of the parameters with the rating of the extent of CHD.

There is a correlation of -0.13 between the time of J-point/slope positivity and the extent of the disease. The correlation for the ST-segment depression and the magnitude of the disease rating is also -0.13 . The results are plotted and shown in Figures 5 and 6. These correlations are not significant. There is no significant ($\alpha = 0.1$ level) correlation (0.53) between the QX/QT ratio time of positivity and the extent of CHD rating (Figure 7).

Also shown in this chart are the correlations of the maximum response of each parameter, with the rating of the extent of the disease. For the J-point/slope parameter the coefficient is $+0.30$; for ST-segment it is $+0.04$; and for the QX/QT ratio this value is $+0.37$. These values are not significant ($\alpha = 0.05$). The results are plotted and shown in Figures 8, 9 and 10.

There was seemingly no relationship between the mechanical state of the left ventricle and the time of exercise of each patient. Five patients showed normal contractility and six showed impairment of the contractile properties of the ventricle.

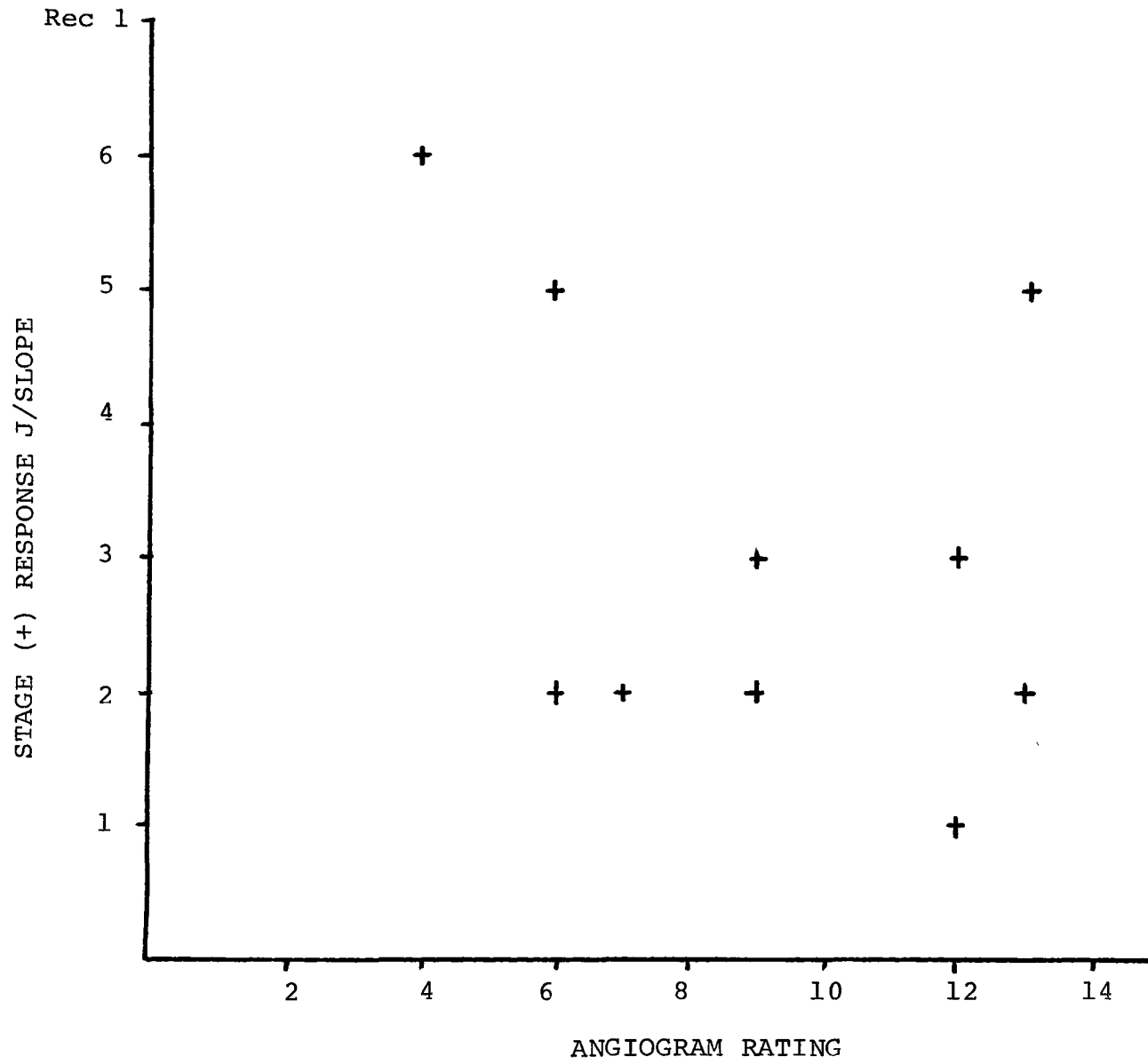


FIGURE 5 J/slope response and CHD rating

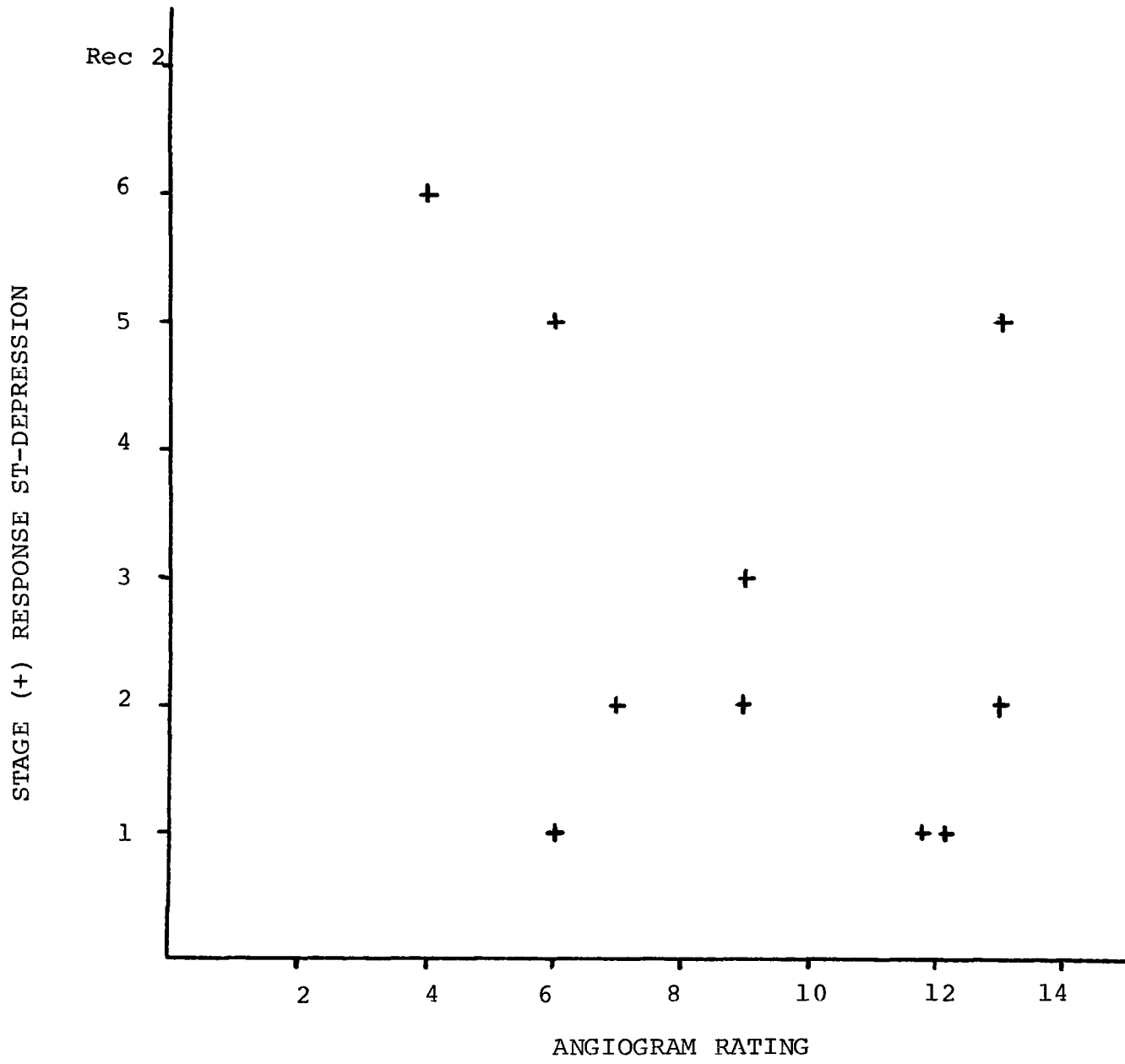


FIGURE 6 ST-segment response and CHD rating

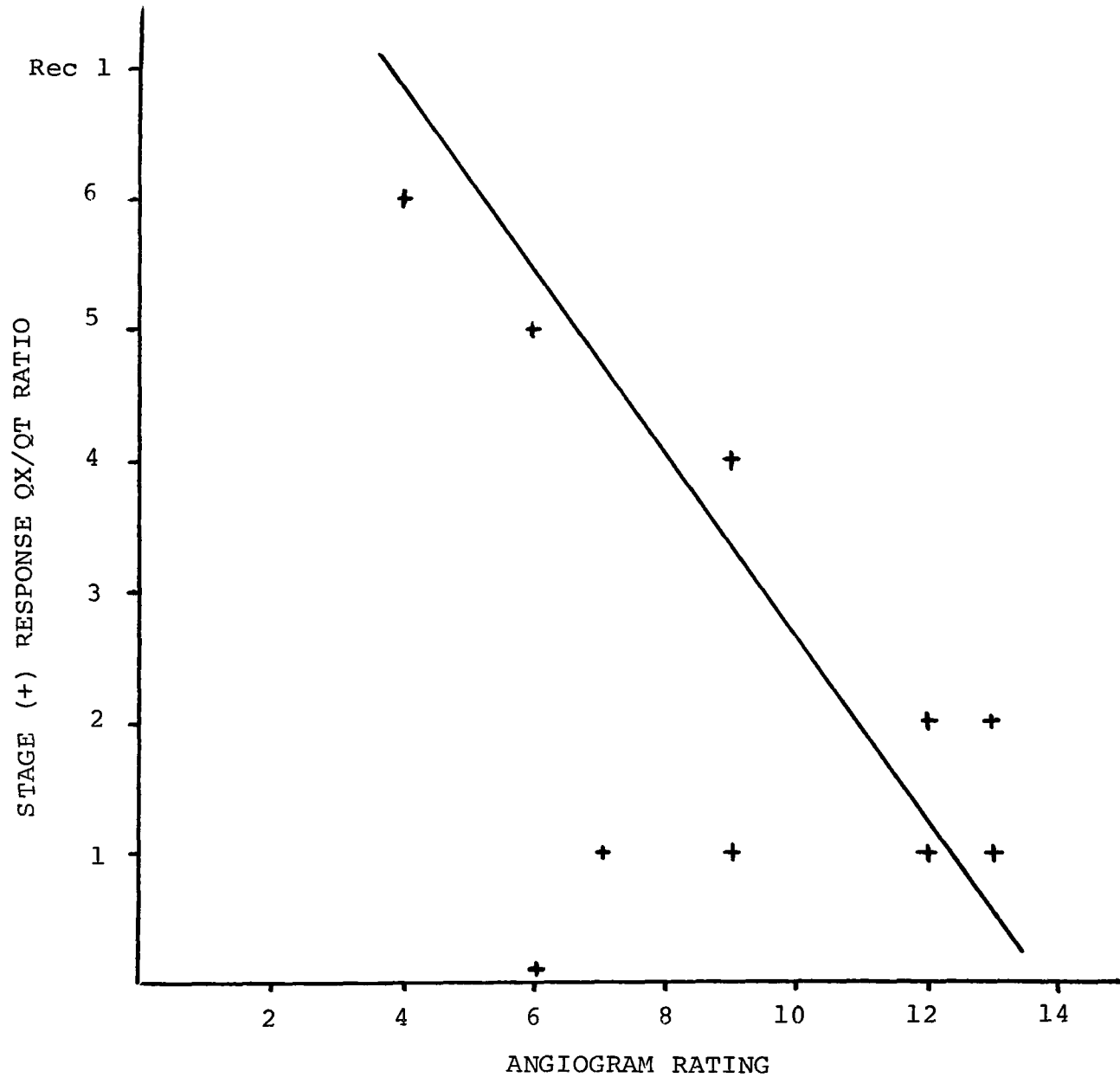


FIGURE 7 OX/QT Response and angiogram rating

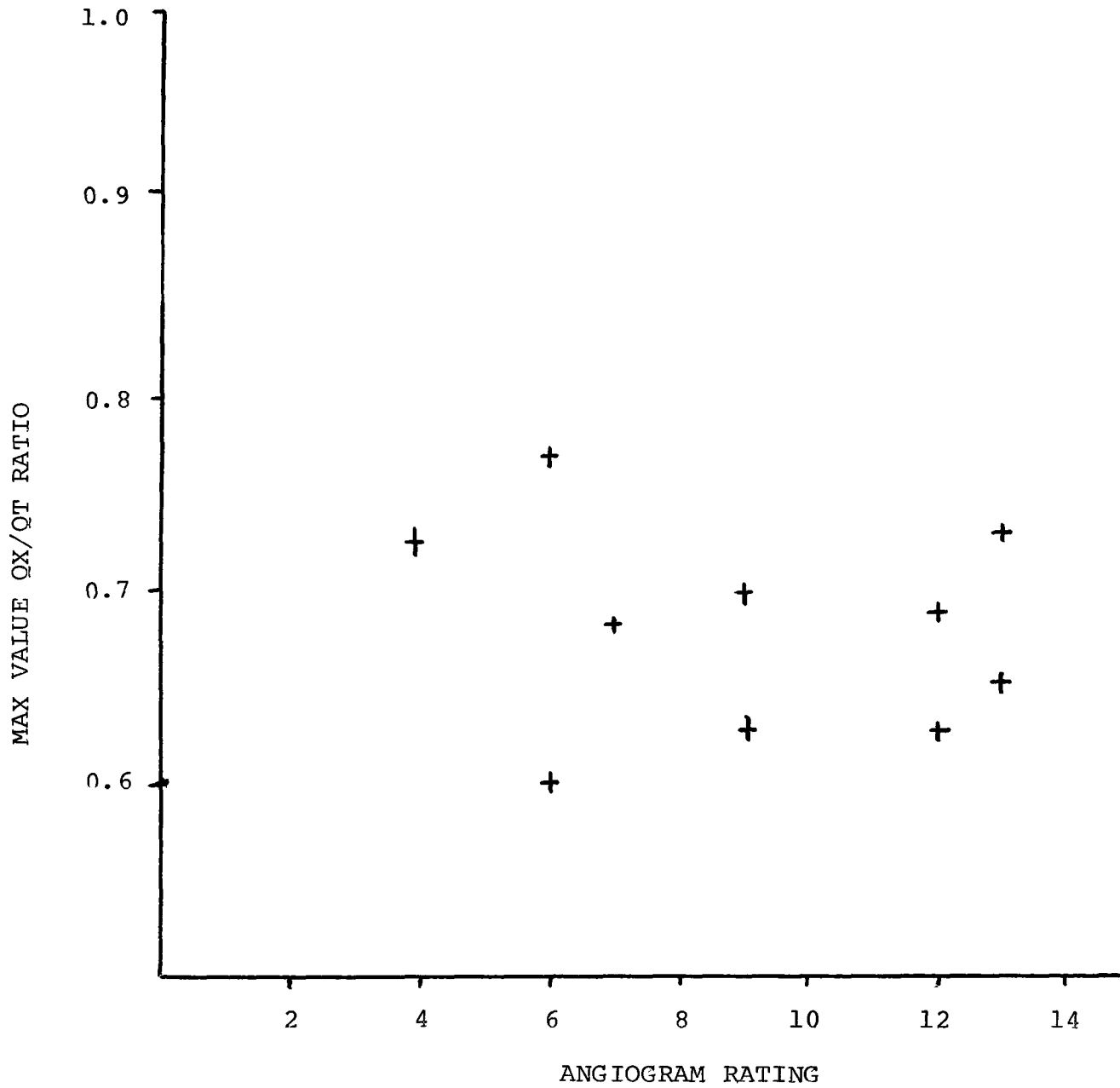


FIGURE 8 Maximum Value QX/QT and CHD rating

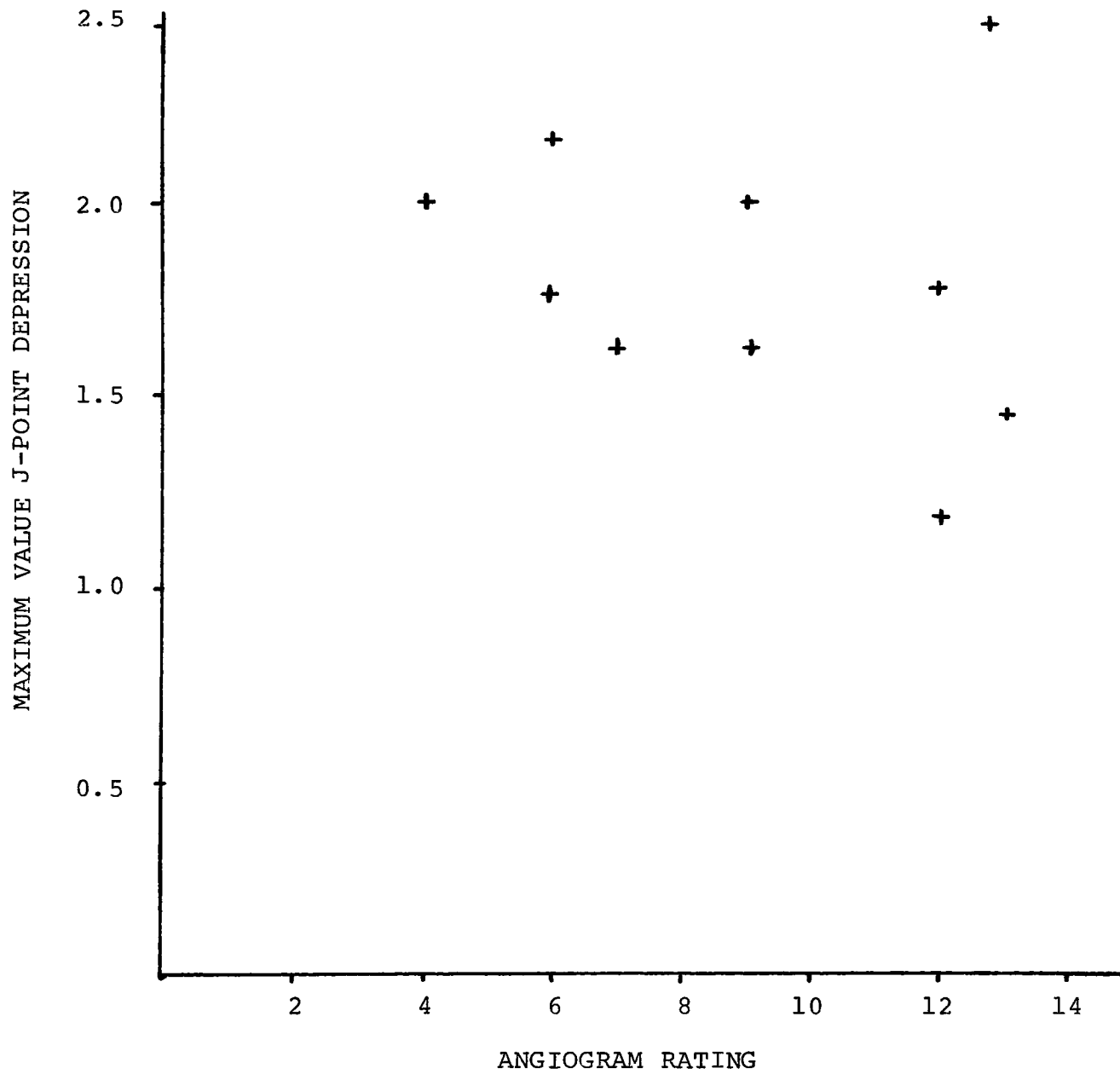


FIGURE 9 Maximum Value J/slope and CHD rating

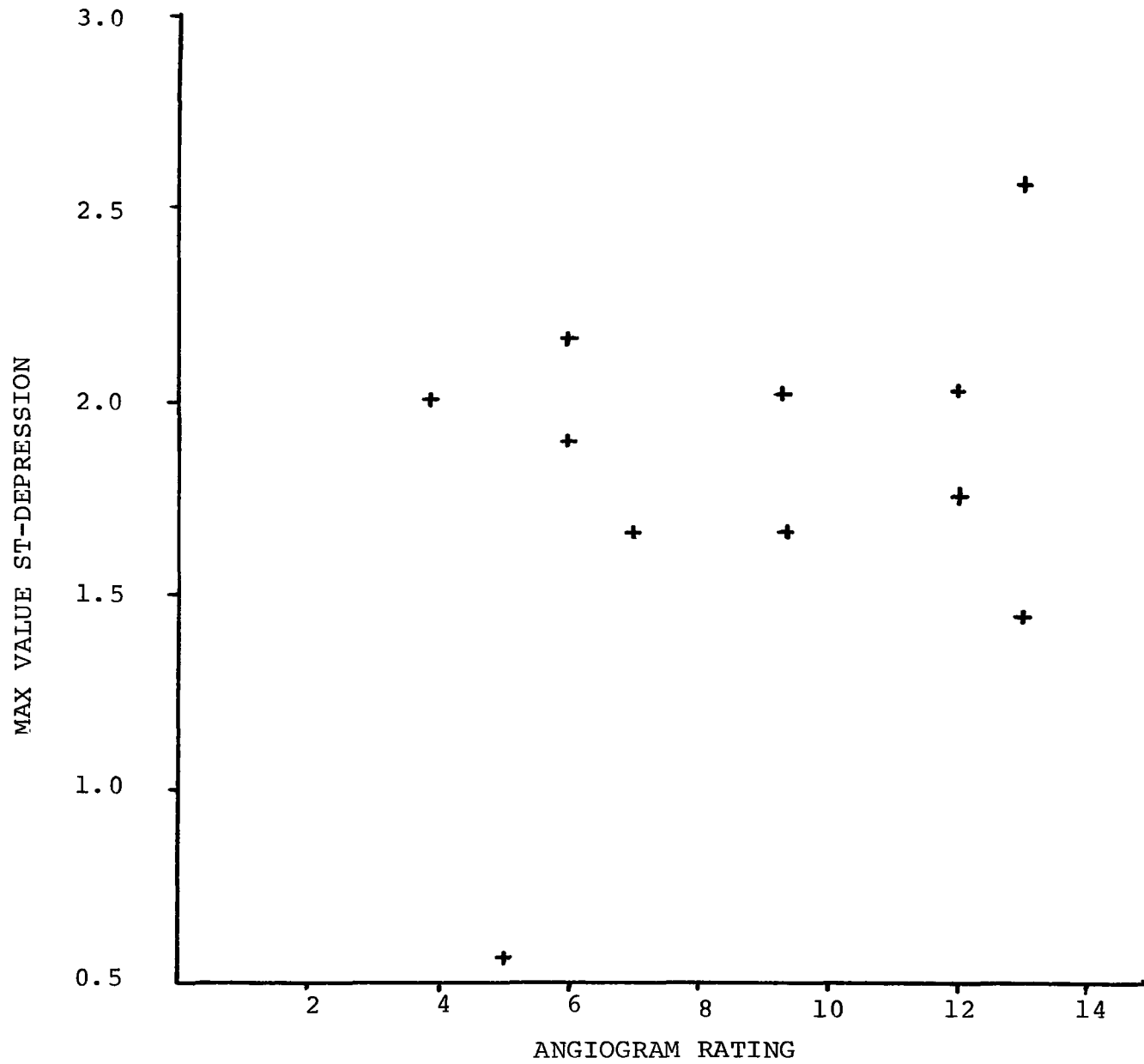


FIGURE 10 Maximum Value ST/segment Depression and CHD rating

Discussion

The correlations of exercise stress testing with coronary angiography has been well reviewed in the literature. Throughout these studies it has been consistently demonstrated that there is an increase in true positive results of stress testing the more severe is the disease (McHenry 1972). By the same token it has been demonstrated that there is a decrease in the number of false positive responses to the exercise program the more severe the disease of the patients tested (Bartel, 1974). When the criteria for judging the extent of significance of the heart disease, or the criteria for a positive exercise test are altered, it is noted that the number of true positive exercise tests and false negative exercise tests are profoundly affected (McHenry 1972, Martin et al., 1972). The conditions under which the test is administered also effects the outcome of the test (Linhart, 1974); as well the physical fitness of the patients influences these various fractions (Bruce Hornsten, 1969).

In most of the papers reviewed, the extent of the occlusive disease was gauged by the number of vessels involved. A criterion value, arbitrarily set, served as indicator of significant occlusive disease. Systems of classification such as these do not describe specifically the extent of the disease and therefore the observations made above are basically true, but a system of standardization is required so that there is some homogeneity of results and data.

Not listed in many of the above studies is the amount of collateral circulation that has developed in these patients. This fact is very important when it comes to evaluating stress tests and stress test parameters.

The most important relationship that has been proposed (Ascoop 1971) (Sheffield, 1972) is that, based on angiographic findings, the exercise stress test is a reliable method of screening for coronary heart disease. The results of this study are in agreement. From the data that was collected it can be stated that this exercise test and ECG criteria bear a significant relationship with the results of coronary arteriography in the prediction of CHD.

The sensitivity or true positive result of the exercise test was 10/11. That is to say that 10 of the 11 subjects known to have coronary occlusive disease showed a positive test when subjected to the exercise program. A very important coefficient or factor involved in this type of evaluation is the number of false negative results. The importance of the number of false negative tests is not that it is a statistically undesirable entity, but that in practical applications of such a test, the safety of the patients is involved. The false negative fraction for this study was 1/11. Martin et al., (1972) using criterion similar to those used for our study, showed a seemingly higher false negative fraction in comparison (38 percent). The difference in these apparently totally opposed results may

stem from the difference in basic design of each study. Their subjects were taken from a heterogenous group of normals and patients with varying degrees of occlusive disease. His sample was as follows: 37 percent with no evidence of disease; 23 percent with single vessel disease; 18 percent with double vessel disease; and 22 percent with triple vessel disease. All of the patients in our sample had by their classification double or triple vessel disease. It was previously established that as the extent of the disease increased the false negative result decreased. Since on the average our patients had more extensive disease than did the patients of their sample we would expect, on this basis alone, a significantly lower false negative occurrence in our study.

McHenry (1970) demonstrated a true positive result somewhat lower than the value reported for this study. It was 88 percent of the group. Again, as before his patients included those with a single vessel disease. For this reason the 12 percent false negative they recorded was somewhat larger than the value for this study. This reasoning is further supported by another result of their studies which showed a 94 percent true positive fraction in those patients with double and triple vessel disease. This value is much closer to the true positive figure that was recorded for this study.

This comparison of results and the explanation of the inconsistency of the results, clearly demonstrates the effect

of one of the previously mentioned limitations to this study, that is the group size and composition. As the results stand the image that is projected of the exercise stress test is only semi-complete. If the population studied had included a wider variety of subjects, normals and as well patients with varying degrees of occlusive disease, we could derive the fraction of false positive indications by the exercise test. The only fact we know, as it stands, is that 10 of 11 of the patients tested showed positive results on the exercise test. It cannot be said with certainty that normals would not respond as did the coronary patients with occlusive disease. By the same token a larger number of subjects could have confirmed these coefficients that were found.

Nonetheless the study was successful in demonstrating a high true positive fraction for the exercise test based on angiographic evaluations. Thus, it can be said on the basis of these and on the work of others that exercise is a valid technique for the detection of CHD.

Using the data collected in this study, an attempt was made to draw certain correlations between the ECG variables measured and the extent of coronary heart disease as rated by the system. The results are depicted in Figures 4 to 10. These plots were made from the data contained in Tables 3 and 4. The statistical correlation coefficients are in Table 4.

Figure 4 shows the relationship between the stage of the exercise program at which any of the three parameters became positive and the extent of coronary heart disease as rated by the suggested system. The coefficient of correlation was found to be -0.54 which is not significant at $\alpha = 0.05$ level. This result did not confirm the results of previous studies as expected. The probable explanation for this is that the rating of the angiograms does not indicate the extent of collateral circulation. As such this angiogram rating is really not a reliable means of describing the oxygen delivery to the tissue.

The correlation of the stage at which the QX/QT value became positive and the rated extent of the occlusive disease, was shown to be -0.53 (not significant $\alpha = 0.05$). This result is depicted in Figure 7. For the reason stated earlier, this result is contrary to what was expected. This was a reasonable supposition to make if it is assumed that the QX/QT is indeed the most sensitive of the parameters measured to ischemia. This was also shown in this study as the QX/QT ratio was the first to respond in many cases. The greater the extent of the disease, supposedly the greater the expected ischemia during exercise.

The correlation coefficient of the other two parameters measured were both -0.13 . This value is insignificant and this fact is shown in Figures 5 and 6 by the non-linearity of the points. The points are dispersed and the average line is very indefinite.

On the basis of this information it can be stated that in this study although no significant correlation with rated angiographic results was found for any of the parameters measured, the QX/QT value appears to correlate better than the J-point/slope parameter and ST-segment depression parameter with the extent of coronary heart disease.

The data collected for this study also confirmed previous ideas that as the exercise program continued and required higher energy output, the greater was the deviation from normal of the individual parameter. This was found to be true in 9 of the 11 patients for all parameters. What is signified is that as the ischemia produced by exertion became more prominent, the greater the deviation from normal were the evaluations of the ST-segment. If for example a patient showed a positive criterion for all three parameters at stage 2 then there was a high probability, 82 percent, that these values increased in magnitude with increased workload, i.e. at a later stage in the program. This idea and finding is consistent with the basic physiologic principles which are the basis of exercise testing.

The method of classification of the angiographic results suggested in the method of this study, while quite sufficient to describe the disease in separate vessels, was found not to be specific in describing the disease of the heart in general. The idea of presenting a method of standardizing the criteria for evaluating angiographic

results in place of very subjective descriptions, has been attempted before (Cohen, 1966). Defining a disease as being single or double or triple vessel disease is no longer sufficient. Some criterion to the extent of occlusion of the individual vessels must be made. The system presented for this study tends to define, even more specifically, the extent of the disease as well as the distribution. However, if these values are summed after classification of each vessel, the original sought after effect of describing the extent and distribution of the disease, is lost. It yields an index of the extent of the disease but no longer states the distribution. This becomes especially important if the angiographic scale is being used to describe the results of an exercise stress test, more so if the patients' success is described by the stage of exercise he is able to complete. For example, let us discuss the cases of two hypothetical subjects who are both rated a total of six for CHD. One subject has complete occlusion of LAD and scores 5 plus 1 for less than 50 percent stenosis of M/CA. The other patient scores 2 for LAD, 2 for RCA and 2 for M/CA. These cases describe a concentrated disease and very diffuse disease. If the amount of ischemia is directly proportional to the blood supply to the area, and the ischemic response of the ECG is in proportion with the stress on the cardiovascular system then the subject with complete occlusion of one artery will show ischemia at a lower workload than the individual with diffuse disease. The patient with narrowing of all arteries

will still be capable of supporting levels of work up to a certain limit before he becomes symptomatic. Up to a point the circulation that remains is sufficient to maintain the additional demand of the exercise test. The patient with complete occlusion is unable to support any or very little increase in workload before an ischemic condition becomes evident.

Thus, one patient is forced to cease the exercise test before the other, even though they have been rated equally by angiographic results. The results would then indicate that the exercise test isn't consistent in the rating of coronary patients, when physiologically in fact the patients aren't equal.

This argument doesn't apply at the extreme ends of the distribution curve, to those patients with a severe disease or those patients with minimal disease. Unless a system is devised, which allows for the development of collateral compensation as well as the relative extent of the disease in each artery, expressed in one number, it will remain very difficult to correlate reliably the relationship between the extent of the disease and any other parameter. Such an evaluation of collateral circulation could possibly explain the results of J.R. J.M. L.K. This is one explanation of why the correlation coefficients found in this study were so low. The fact that the number and composition of individuals of the group was limited would tend to decrease these values.

A similar method could be devised for the grouping of the three ECG variables measured into one rating describing the ECG response in general to the work stress. An attempt was made at establishing such a system in the following manner: For the value of the J/slope parameter a single rating was given to the response according to the formula:

$$\text{J/slope Response} = \text{J value of depression} - 2 (\text{slope value})$$

(It may be noted that the weighting of the slope value by a factor of 2 gives it equal proportions to the J - depression).

For this and the other two parameters measured, a range of the response of the group to each parameter was established by subtracting the value of the least response from the value of maximum response. The individual response was then gauged in relation to the response of others in the group. This was done by subtracting the least value of response in the group from the individual response value, dividing by the range and multiplying by 100, to yield an individual response rating:

$$\text{Individual Response Rating} = \frac{\text{Subject Response} - \text{least group response}}{\text{Range}} \times 100$$

These values were calculated for each parameter and summed for each subject. Upon dividing the resultant number by 3 yielded the ECG-index, based on 100.

There was no significant correlation ($\alpha = 0.10$) between the ECG-index at termination of exercise and the

angiographic rating. Also there was no significant difference ($\alpha = 0.10$) between the time that the subjects exercised and the extent of the coronary heart disease rated by the ECG-index. There is a significant ($\alpha = 0.10$) correlation between the rate of change of ECG-index with increasing work intensity and the angiographic rating. This value is 0.68. This finding implies that in subjects with coronary heart disease there is an increasing rate of ECG response the more severe is the disease.

If a criterion value of 66% is set for ECG response it is found that only 3 patients with serious disease (CAG rating 7) show a positive response and 2 without serious disease show a positive response.

The use of such classification systems of the response are invaluable to this area of study. As it stands the ECG-index gives equal weight to each parameter; however if the weighting system was changed this index might prove to be more applicable. Much information is required before such coefficients can be established. This study is the first attempt at such an index. An improvement could be made on the angiogram rating to include an evaluation of collateral circulation.

It was found that the exercise test protocol and the criteria used in it were sufficient to detect CHD in the patients. There was a relationship between the angiographic evidence for ischemic heart disease and the exercise stress

ECG. None of the patients were able to complete the full test. The test allowed for, in addition to the first six stages, another 4 stages at increasing workloads. On the average the patients finished thirteen minutes of the exercise. Three subjects finished 6 stages and one was unable to complete the first stage. A good test is one in which the patients that are to be tested find it neither too easy nor too difficult. This test seemed to fit very well this criterion. Many authors advocate the use of more stressful exercise in the belief that maximal exercise can be brought on earlier and thus receive a higher true positive result. The controversy as to whether this is necessary or not continues. The results of this test compared very favourably with these stress test results. Naughton (1966) and Fox (1971) have been using this basic test in their laboratories successfully for a great number of patients.

CHAPTER V

SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

Summary

This study was designed to compare the results of an exercise ECG recorded during and after a Naughton stress test to the results of coronary angiographic studies. The subjects used in this study were candidates selected for revascularization surgery by the Department of Cardio-thoracic surgery, and ranged in age from 36 to 62 years. The extent of the coronary occlusive disease was rated on a scale from 1 to 15 as evidenced by angiographic studies. Prior to surgery the patients were subjected to exercise testing. From the ECG recorded using CM_5 leads at the end of each minute of exercise and recovery, three parameters were measured: J-point depression and slope of the ST-segment; ST-segment depression; and the QX/QT ratio. The criteria for a positive test were: J-point depression of 1 mm or more associated with a slope of ≤ 1 mV/sec; an ST-segment depression of ≥ 1 mm; and a QX/QT ratio of 0.5 or greater. The results of the exercise ECG were compared to the angiographic findings to determine the sensitivity of the exercise test expressed as a true positive fraction. The stage of exercise at which any parameter became positive was examined with the rated extent of CHD.

The sensitivity of the exercise ECG test was found to be 91% (10/11). A false negative fraction of 9% (1/11) was also found. Of the correlations calculated none were significant ($\alpha = 0.1$ level).

Conclusions

Within the scope of this study, the following may be concluded:

1. The exercise stress test and the criterion electrocardiographic evaluations used in this protocol are a valid method of diagnosis of coronary heart disease. A method of rating ECG response to exercise is suggested.

2. There is a high true positive result and low false negative response to this exercise test based on angiography.

There is significant correlation between the rate of change of ECG-index with increasing work intensity and the angiographic rating.

Recommendations

The general structure of this study was found to be conducive to demonstrating the desired relationships. However, in light of the experience of having done a study, a few changes are recommended if such an investigation were again to be attempted. These changes centre mainly on the methodology.

First it would be of greater advantage to use a larger and more heterogeneous group of subjects than was used for this study. This group would preferably have normal subjects and patients representing all levels of disease included. In this way all aspects of the exercise protocol can be tested, including true positive, false negative, true negative and false positive fractions. A minimum of 100 subjects is thought to be sufficient to make generalizations from the results of the study.

The parameters that were used for the evaluation of the ECG were quite adequate and satisfactory. However, a much more reliable index could be used if all three of these aspects were incorporated into a single number describing at the same time orientation, depression and time of the ST-segment depression. This could be accomplished mathematically as was shown earlier, by employing a formula that allows for grouping of the parameters as to their relevance and sensitivity to myocardial ischemia. In turn this could be improved by weighting each parameter. Thus, standard values and scales could be used to describe a patient's reaction to exercise stress. Before the actual mathematical formulation could be presented much testing would be required to define each constant and coefficient. This idea is supported by previous studies that demonstrate the effects of shifting the criterion ECG values (Martin et al., 1972).

REFERENCES

REFERENCES

- American Heart Association, The Committee on Exercise. Exercise Testing and Training of Apparently Healthy Individuals: A Handbook for Physicians. Am. Heart Association, New York: 1972.
- Areskag, N., Bjork, M., Bjork, V., Hallen, H., Strom, Q. Physical work capacity: ECG reaction to work test and coronary angiogram in coronary heart disease. Acta Med. Scand. 472:9, 1967.
- Ascoop, C., Simoons, M. "Electrocardiography during exercise in patients with coronary sclerosis and normal ECG at rest. Comparison with findings from coronary arteries." Quantitation in Cardiography - Edit. Snellen Hempker Hugenholtz Van Bommel. 1971.
- Ascoop, C., Simoons, M., Egmond, W., Brischker. Exercise test history, and screen applied levels in patients with chest pain v. normal electrocardiogram at rest: comparison to findings at coronary arteriography. Am. Heart J. 82:609, 1971.
- Astrand, P. D., Rodahl, K. Textbook of Work Physiology. McGraw-Hill Book Co. Inc., New York: 1970.
- Bartel, A., Behar, V., Peter, R., Orgain E., Kong, Y. Graded exercise stress test in angiographically documented artery disease. Circ. XLIX:348, 1974.
- Bazett, H. An analysis of the time relations of electrocardiograms. Heart 7:353, 1920.
- Bellet, J., Muller, O., LaVan, D., Nichols, G., Herring, A. Radio-electrocardiography during exercise in patients with anginal syndrome. Use of multiple leads. Circ. 29:355, 1964.
- Bellet, S., Roman. L. Comparison of the double 2-step test and the maximal Exercise treadmill test. Circ. 36:238, 1967.
- Blake, T. Introduction to Electrocardiology 2nd edition. Appleton-Century-Crofts Meredith Corp. N.Y.: 1972.
- Bousfield, G., Angina Pectoris: Variations in electrocardiograms during paroxysms. Lancet 2:457, 1918.

- Bruce, R., Hornsten, T. Exercise stress testing in evaluation of patients with ischemic heart disease. *Prog. Cardio-vasc. Dis.* 11(5), 1967.
- Bruce R. A., McDonough, J. P. Stress testing in screening for Cardiovascular Disease. *Bull. N.Y. Acad. Med.* 45 1288, 1969.
- Bruce, R., Kusumi, F., Hosmer, D. Maximal oxygen intake and monographic assessment of functional aerobic impairment in vascular disease. *Am. Heart J.* 85:546. 1973.
- Bruce, R. A., Mazzarella, J. A., Jordan, J. W., Green, E. E. Quantitation of QRS and ST-segment responses to exercise. *Am. Heart J.* Vol. 71, No. 4, 1966.
- Case, R., Roselle H., Cramptom, R. Relations of ST depression to metabolic and hemodynamic events. *Cardiologica* 48:33, 1966.
- Cleland, W., Goodwin, J., McDonald, L., Ross, D. *Medical and Surgical Cardiology.* Blackwell Scientific Publications Oxford and Edinburgh, 1967.
- Cohen, L., Elliott, W. Klein. Coronary heart disease: Clinical cinearteriographic and metabolic correlations. *Am. J. Cardiol.* 17:153, 1966.
- Demany, M., Tambe, A., Zimmerman, H. Correlation between coronary arteriography and the post-exercise electrocardiogram. *Am. J. Cardiol.* 19:526, 1967.
- Dimond E. *The Exercise Electrocardiogram in Office Practice.* Charles C. Thomas Publishers, Springfield Illinois, U.S.A., 1961.
- Doan, A. E., Peterson, D. R. J. R. Blackmon, Bruce, R. A. Myocardial ischemia after maximal exercise in healthy Men: A method for detecting potential CHD? *Am. Heart J.* 69:11, 1965.
- Doan, A. E., Peterson, D. R., Blackmon, J. Bruce, R. A. Myocardial ischemia after maximal exercise in healthy Men: One year follow-up physically healthy and unhealthy men. *Am. J. Cardiol.* 17:9, 1966.
- Dubin, D. *Rapid Interpretation of EKG's.* 2nd Edition. Cover Publishing Co., Tampa, Florida, 1972.
- Eckmecki, A., Prinzmetal et al. Clinical and experimental difference between ischemia with ST-elevation and ischemia with ST-depression. *Am. J. Cardiol.* 7:142, 1961.

- Ellestad, M., Allen, W. Wan. M. Kemp, G. Maximal treadmill stress testing for cardiovascular evaluation. *Circ.* 39:517, 1967.
- Fortuin, N., Friesinger, G. Exercise induced ST-segment elevation: Clinical electrocardiographic and arteriographic studies in 12 patients. *Am. J. Med.* 49:459, 1970.
- Fox, S., Haskell, W. Physical activity and the prevention of coronary heart disease. *Bull. N.Y. Acad. Med.* 44:1028, 1968.
- Fox, S.M., Naughton, J., Gorman, P. Physical activity and cardiovascular health. 1. Prevention of coronary heart disease and possible mechanisms. *Mod. Concepts Cardiovasc. Dis.* 41:17-30, 1972.
- Fox, S. M., Naughton, J. P., Haskell, W. L. Physical Activity and the prevention of CHD. *Am. Clin. Res.* 3:404, 1971.
- Freund, J. *Modern Elementary Statistics*. Prentice-Hall Englewood Cliffs, N.J. 3rd Edit. 1967.
- Friedberg. C., Jaffe, H., Pordy, L., Chesky, K. Two-step exercise program. *Circ.* 26:1254, 1962.
- Gangong, W. *Medical Physiology*. Lange Medical Publications, Los Altos, California, 1971.
- Goldberg, A. N., Morran, J. T., Resnekov, L. Multistage electrocardiographic exercise tests - Principles and clinical applications. *Am. J. Cardiol.* 26:84, 1970.
- Goldman, M. J. *Principles of Clinical Electrocardiography*. Lange Medical Publications, Los Altos, California, 1970.
- Gutman, R. A., Alexander, E. R., Li, Y. B, C. B. Nin. Watten, R., J. Ting, M. Bruce, R. A. Delay of St-depression after maximal exercise by walking for 2 minutes. *Circ.* 42:229, 1970.
- Guyton, A. *Textbook of medical physiology*. 4th edition. W. B. Saunders Co., Philadelphia, 1971.
- Hellerstein, H. K. Exercise therapy in coronary disease. *Bull. N. Y. Acad. Med.* 44:1028, 1968.
- Hellerstein, H., Naughton, J. edit. *Exercise Testing and Exercise Training in Coronary Heart Disease*. N.Y. Academic Press, 1973.

- JUDKINS, M. P. Selective coronary arteriography. *Radiology*, 89:815, 1967.
- Kasser, I., Bruce, R. Comparative effects of aging and coronary heart disease on submaximal and maximal exercise. *Circ.* 39:757, 1967.
- Kattus, A., MacAlpin, R., Longmire, W. et al. Coronary angiograms in the study of angina petoris. *Am. J. Med.* 34:19, 1963.
- Kattus, A., Jorgensen, C., Worden, R., Alvaro, A. ST-segment depression with near maximal exercise in detection of pre-clinical coronary heart disease. *Circ.* 44:585, 1971.
- Katz, A. M. Effects of interrupted coronary flow upon myocardial metabolism and contractibility. *Prog. Cardiovasc. Dis.* 10(5):450, 1968.
- Kellerman, J. J. problems of exercise testing. *Chest.* 59:124 (138), 1971.
- Lee, G., Wilson, W., Amphatz, K., Tuna N. Correlation of vectocardiogram and electrocardiogram with coronary arteriogram. *Circ.* 38:189, 1968.
- Lepeschkin, E., Surawicz, B. Characteristics of true positive and false positive results of EKG in Master 2-step tests. *New Eng. J. Med.* 258:511, 1958.
- Lester, F. M., Sheffield, L. T., Reeves, T. J. Electrocardiographic changes in clinically normal older men following near maximal and maximal exercise. *Circ.* 35:5, 1967.
- Likoff, W., Kasparian, H., Segal. B. et al. Coronary arteriography. Correlation with electrocardiographic response to measured exercise. *Am. J. Cardiol.* 18:160, 1966.
- Linhart, J., Turnoff, H. Maximum treadmill exercise test in patients with abnormal control electrocardiograms. *Circ.* XLIX:667, 1974(a).
- Linhart, J., Turnoff, H. Pitfalls in diagnostic evaluation using exercise stress testing. *Chest*, 65:4, (1974b).
- MacAlpin, R. N., Kattus, A. A. Adaptation to exercise in angina pectoris. The electrocardiogram during treadmill walking and coronary angiographic findings. *Circ.* 53:183, 201, 1966.

- Martin, C., McConahay, D. Maximal treadmill exercise electrocardiography. Correlations with coronary arteriography and Cardiac Hemodynamics. *Circ.* 46:956, 1972.
- Mason, R. E., Likar, I., Biern, R., Ross, R. Multiple lead exercise electrocardiography. Experience in 107 normal subjects and 67 patients with angina pectoris and comparison with coronary cinearteriography in 34 patients. *Circ.* 36:517, 1967.
- Master, A. M., Friedman, R., Dack, S. The electrocardiogram after standard exercise as a function test of the heart. *Am. Heart J.* 24:777, 1942.
- Master, A. M., Rosenfeld, Exercise EKG's as an estimation of cardiac functional Dis. *Chest.* 51:347, 1967.
- Master, A., Oppenheimer, E. A Simple exercise tolerance test for circulatory efficiency with standard tables for normal individuals. *Am. J. Med. Sci.* 177:223, 1927.
- Master, A., Jaffe, H. The electrocardiographic changes after exercise in angina pectoris. *J. Mt. Sinai Hosp. N. Y.:* 7:627, 1941.
- Master, A. M. ST-elevation. *Am. Heart J.* 80:434, 1970.
- Master, A. M. Rosenfeld, I. Two step exercise test: current status after 25 years. *Mod Conc. Cardiovascular Dis.* 36:19, 1967.
- McConahay, D., McCallister, B., Hallerman, F., Smith, R. Comparison quantitative analysis of the electrocardiogram and vectorcardiogram. Correlations with the coronary arteriogram. *Circ.* 42:245, 1970.
- McConahay, D., McCallister, B., Smith R. Post-exercise electrocardiography: correlations with coronary arteriography and left ventricular hemodynamics. *Am. J. Cardio-* 28:1, 1971.
- McHenry, P., Lisa, C., Knoebel. S. Correlation of treadmill exercise electrocardiogram with arteriographic location of coronary disease. *Am. J. Cardiol.* 26:649, 1970.
- McHenry, P., Phillips, J., Knoebel, S. Correlation of computer-quantitates treadmill exercise ECG with arteriographic location of CHD. *Am. J. Cardiol.* 30:747, 1972.

- Naughton, J. Rehabilitation for patients with coronary heart Disease. Paper presented at the Post Graduate Course on Physiology and Psychology of Exercise Stress Testing and Training of Coronary Disease Patients and Coronary Prone Subjects. Arlie, Virginia, 1972.
- Naughton, J., Sevelius, G., Balke, B. Physiological responses of normal and pathological subjects to a modified work capacity Test. *J. Sports Med.* 3:201, 1963.
- Neely, J., Rovetto, J., Whitmer, J., Morgan, H. Effects of ischemia on function and metabolism of the isolated working rat heart. *Am. J. Physiol.* 225(3): 651, 1973.
- Robb, G. P., Marks, H. M. Latent coronary heart disease: determination of its presence and severity by the exercise electrocardiogram. *Am. J. Cardiol.* 13:603-618, 1964.
- Roitman, D., Jones, W. B., Sheffield, L. T. Comparison of submaximal exercise EKG test with coronary cine cardiogram. *Ann. Intern. Med.* 72:641, 1970.
- Rowell, L., Taylor, H., Simonson, E. et al. The physiological fallacy of adjusting for body weight in performance of the Master 2-step test. *Am. Heart J.* 70:461, 1965.
- Rushmer, R. *Cardiovascular Dynamics*, W. B. Saunders Co., Toronto, Can. 1970.
- Sandler, G. Comparison of radiocardiography and conventional electrocardiography in the exercise tolerance test. *Brit. Heart J.* 27:719, 1967.
- Sheffield, L. T. Quantitative approach to exercise testing for ischemic heart disease. In: *Quantitation in cardiology* Edit. Snellen, H. Hemker, H. Hugenholtz, P. Van Bommel, J. The Williams & Wilsen Co., Baltimore, 1972.
- Sheffield, L., Holt, J., Reeves, T. Exercise graded by heart rate in electrocardiographic testing for angina pectoris. *Circ.* 32:622, 1965.
- Sheffield, L. T., Reeves, T. J. Graded Exercise in diagnosis of angina Pectoris. *Mod. Conc. Cardiovasc. Dis.* 34:1, 1965.
- Simonson, E. Edit. *Physiology of Work Capacity and fatigue*. Charles C. Thomas Publishers, Springfield, Illinois, U.S.A., 1971.

- Simonson, E. The use of the electrocardiogram in exercise tests. *Am. Heart J.* 66:552, 1963.
- Smokler, P., MacAlpin, R., Alvaro, A., Kattus, A. Reproducibility of a multistage near maximal treadmill test for exercise tolerance in angina pectoris. *Circ.* 48:346, 1973.
- Sones, F. Cinecardioangiography, in *Clinical Cardio pulmonary Physiology*, 2nd edit. Gordon B. ed., New York, Grune and Stratton Inc. 1960, pp. 130-144.
- Spangler, R., Hroman, M., Miller, S., Rotenberg, D., Birnholz, J., Simmons, P., Westura, E., Fox, S. A submaximal exercise electrocardiographic test as a method of detecting occult ischemic heart disease. *Am. Heart J.* 80:752, 1970.
- University of Ottawa Cardiac Unit Rehabilitation Services, Exercise Testing Programme. Kin-72-4020-1, University of Ottawa, Dept. of Kinanthropology, Oct. 21, 1972.
- Van Herpem, G., Birschke, A., Hanssem, F. The correlation between the coronary arteriogram and other diagnostic parameters. 11th Int. Sym. on Vectorcardiography N.Y. 1970, North Holland Publishing Co.
- Wolf, E., Tzivoni, D., Stern, S. Comparison of exercise tests and 24 Hr. ambulatory electrocardiographic monitoring in detection of ST-T changes. *Brit. Heart J.* 36:90-95, 1974.
- World Health Organization Technical Report Series. Exercise tests in relation to the cardiovascular function. *Wld. Hlth. Org. Techn. Rep. Ser.* 388, 1968.

APPENDICES

APPENDIX A

SUBMAXIMAL CRITERION HEART RATES

SUBMAXIMAL CRITERION HEART RATES

Age	Heart Rate (b/min)
20-29	170
30-39	160
40-49	150
50-59	140
60-69	130

APPENDIX B

CONTRAINDICATIONS TO EXERCISE

CONTRAINDICATIONS AND CAUSES FOR SPECIAL CARE. (1)

CONTRAINDICATIONS TO EXERCISE AND EXERCISE TESTING

I. ABSOLUTE CONTRAINDICATIONS

1. Manifest circulatory insufficiency ("congestive heart failure")
2. Acute myocardial infarction.
3. Active myocarditis.
4. Rapidly increasing angina pectoris.
5. Recent embolism, either systemic or pulmonary.
6. Dissecting aneurysm.
7. Acute infectious diseases.
8. Thrombophlebitis.
9. Ventricular tachycardia and other dangerous dysrhythmias (multifocal ventricular activity).
10. Severe aortic stenosis.

II. RELATIVE CONTRAINDICATIONS*

1. Uncontrolled or high-rate supraventricular dysrhythmias.
2. Repetitive or frequent ventricular ectopic activity.
3. Untreated severe systematic or pulmonary hypertension.
4. Ventricular aneurysm.

(1) Fox, S.M., J.P. Naughton, and W.L. Haskell, "Physical Activity and the Prevention of Coronary Heart Disease", Annals of Clinical Research, 3: 404-432, 1971.

* In the practice of medicine the value of testing often exceeds the risk in patients with these relative contraindications.

5. Moderate aortic stenosis.
6. Uncontrolled metabolic diseases (diabetes, thyrotoxicosis, myxedema).
7. Severe myocardial obstructive syndromes (Subaortic stenosis).
8. Marked cardiac enlargement.
9. Toximias of pregnancy.

III. CONDITIONS REQUIRING SPECIAL CONSIDERATION AND/OR PRECAUTIONS

1. Conduction disturbances
 - a) Complete atrioventricular block
 - b) Left bundle branch block
 - c) Wolff-Parkinson-White syndrome
2. Fixed rate pacemakers.
3. Controlled dysrhythmias.
4. Electrolyte disturbances.
5. Certain medications
 - a) Digitalis
 - b) B-Blocking and drugs of related action.
6. Clinically severe hypertension (diastolic over 110, grade III retinopathy).
7. Angina pectoris and other manifestations of coronary insufficiency.
8. Cyanotic heart disease.
9. Intermittent or fixed right-to-left shunts.
10. Severe anemia.

11. Marked obesity.
12. Renal, hepatic and other metabolic insufficiency.
13. Overt psycho-neurotic disturbances requiring therapy.
14. Neuromuscular, musculoskeletal and arthritic disorders which would prevent activity.

APPENDIX C

EXERCISE TEST PROTOCOL

KIN-72-4020-1
OCTOBER, 1972

UNIVERSITY OF OTTAWA - CARDIAC UNIT

EXERCISE TESTING SESSION

TREADMILL TEST PROTOCOL*

-
1. Ensure that the patient has complied with all the preliminary instructions issued to him, i.e. sleep, food, drugs, etc.
 2. Patient will read and sign the consent form if he has not already done so. The test should have been previously authorized by the patient's physician and the form duly signed.
 3. Ensure that all recordings forms are ready. Enter all required data, including age and target heart rate.
 4. Pre-exercise 12 lead EKG. Patient should be made to relax for at least 5 min., prior to the recording.
 5. Draw 10 ml of venous blood (if so indicated by the test supervisor).
 6. Attach the electrodes for the exercise test - CM5 position: top of sternum, bottom of sternum (xiphoid process), V₅ position (on rib prominence).
 7. Direct patient to treadmill.
 8. Sit patient on semi-reclining chair on treadmill. Strap phonocardiogram to the patient so that good quality heart sounds are obtained. Place the transducer on the carotid artery. Ensure that the written record indicates a good upstroke and diastolic notch. Take a simultaneous recording for 10 seconds.
 9. Connect patient to EKG control panel.
 10. Attach blood pressure cuff to the left arm and take a sitting and resting blood pressure measurement. Record standing EKG.

11. Initiate subject to treadmill walking. Set treadmill at 1.5 mph, 0% grade. Once subject is comfortable, have him walk for a three minute period.
12. Rest for 3 minutes. Set clock.
13. Test will begin on the command of the test supervisor.

<u>Serial</u>	<u>MPH</u>	<u>% GRADE</u>	<u>MIN</u>
1	2	0	1
2	2	3.5	4
3	2	7.0	7
4	2	10.5	10
5	2	14.0	13
6	2	17.5	16
If required			
7	3	12.5	1
8	3	15.0	4
9	3	17.5	7
10	3	20.0	10
11	3	22.5	13

During exercise, take ECG each minute of test for 5 secs: ie. between the 55th and 60th secs. If arrhythmias occur, run ECG continuously and mark on paper the speed, grade and time on the ECG write-out.

At every minute, record heart rate (b/min) from digital read out. Record blood pressures at every 2nd minute.

14. At end of test, slow-down the treadmill to 1.5 mph and decrease elevation to 0% grade. Have patient walk for 2 minutes. Take recordings as for actual test.
15. When exercise test ends, have patient sit on semi-reclining chair on treadmill. Record pre-ejection intervals. These should be taken at exactly 15 seconds after the patient stops exercising.
16. Draw 10 ml of venous (if so indicated in para. 6 above).
17. During recovery, record EKG and heart rate every minute for six minutes. Take blood pressure readings at the 2nd, 4th and 6th minute of the recovery.
18. At 6th minute of recovery, record pre-ejection intervals.
19. Disconnect patient, remove electrodes and blood pressure cuff.

* Modified from Naughton, J. Rehabilitation for Patients with Coronary Heart Disease. Paper presented at the Post Graduate Course on Physiology and Psychology of Exercise Testing and Training of Coronary Disease Patients and Coronary Prone Subjects, Airlie, Virginia, April 1972.