DEVELOPMENT OF RATE RELATED EXERCISE-INDUCED MYOCARDIAL ISCHEMIA AND RISK OF SELECTED CORONARY DISEASE ENDPOINTS

by

Sharon Diane Bruce

Thesis submitted to the Faculty of the

Virginia Polytechnic Institute and State University

in partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE

in

Education

in

Health and Physical Education

APPROVED:

William G. Herbert, PhD, Chairman

Don R. Sebolt, PhD

Douglas Southard, PhD

May, 1993

Blacksburg, Virginia

ABSTRACT

The purpose of the study was to determine whether serial graded exercise test (GXT) responses, known to have prognostic importance, in the coronary artery disease population generally, can differentiate certain cardiovascular mobidity and mortality endpoints among physically active patients. Data were obtained in 1989 at three community-based cardiac rehabilitation programs from three serial GXT results in 23 paired cardiac event (CE) and non-event (NE) patients. A cardiac event was defined as having an myocardial infarction (MI), percutaneous translumial angioplasty (PTCA), coronary artery bypass grafting (CABG), and cardiac death. Comparisons were made just prior to each CE patients event. Statistical analyses were done on four exercise test variables: ST-segment depression (ST80) at peak exercise, heart rate adjusted ST-segment depression (ST/HR slope), exercise induced ventricular dysrhythmias (PVC), and exercise induced chest pain. Chi-square analyses showed no significant changes across the serial tests for any of the variables examined in either the CE or NE groups ($P>0.05$). Nevertheless, the CE group had significantly more ST-segment depression, ST/HR slope, and exercise chest pain in all GXT intervals in comparison to the NE group. These findings do not support the use of serial exercise GXTs for prognostic information for the physically active cardiac rehabilitation maintenance patients.

ACKNOWLEDGMENTS

I would like to thank my chairman, Dr. William G. Herbert for his patience, persistence and direction over these long years. Much thanks to the other committee members, Dr. Don Sebolt and Dr. Reed Humphrey for their advice and dedication, and Dr. Doug Southard, who became involved near the end of this long journey. Many thanks and love go to my parents, Marion and 'Dusty' Bruce, for their unyielding support and ever present love in reminding me to keep on working and not give up. And to my best graduate friend and research partner, Vernon Baker, many, many thanks for your local and long distance support and friendship. Also, thanks to my good friend, "Oh, Suzanna" Kurtz, for her continued educational support and laughter throughout this ordeal. And finally, thanks to Mrs. Joanne Miller who endlessly took my phone calls and request with good faith and a smile.

TABLE OF CONTENTS

		Page
LIST OF TABLES		vii
LIST OF FIGURES		viii
I.	INTRODUCTION	1
	Statement of the Problem	3
	Significance of the Study	4
	Research Hypothesis	5
	Delimitations	5
	Limitations	7
	Basic Assumptions	8
	Definitions and Symbols	9
II.	LITERATURE REVIEW	10
	Exercise Induced ST-Segment Displacement	10
	Exercise Induced Ventricular Dysrhythmias	14
	ST/HR Slope Index	17
	Delta ST/HR Index	19
	Summary	20
III.	JOURNAL MANUSCRIPT	22
	Abstract	23
	Introduction	24
	Methods	25
	Results	28
	Discussion	31
	References	35
IV.	SUMMARY OF THE STUDY	47
	Summary	47
	Conclusions	48
	Recommendations for Future Research	49
	Recommendations for Clinical Practice	50

BIBLIOGRAPHY.. 51

APPENDIX A: Detailed Methodology and Data Analysis.. 55

APPENDIX B: Data Collection Instructions............ 62

APPENDIX C: Data Collection Form.................... 67

APPENDIX D: Raw Data................................ 72

APPENDIX E: Statistical Analysis.................... 79

LIST OF TABLES

Table		Page
1:	Characteristics of Subjects	38
2:	Clinical History Variables	39
3:	Cardiovascular Medications According to Patient Groups.........................	40
4:	Physiologic and Exercise Performance Variables According to Patient Groups.....	41

LIST OF FIGURES

Figure Page

1: Study Design for Selection of 23 Pairs of Subject.......................... 37

2: Comparison of Exercise ST-Segment Shifts Within Serial GXTs for CE and NE Groups... 42

3: Delta ST/HR Index Across GXTs............. 43

4: Exercise-Induced Chest Discomfort Across Serial GXTs.............................. 44

5: Frequency of Occurence in GXTs for exercise-Induced Chest Discomfort......... 45

6: PVC Patterns in GXT3 During Exercise...... 46

CHAPTER I

INTRODUCTION

The Framingham Heart Study (1949) demonstrated that coronary heart disease (CHD) was a problem largely manifested by lifestyle. It demonstrated that CHD risk related lifestyles are associated with higher incidence of coronary artery disease (CAD) and sudden cardiac death. Of the current U.S. population of about 248 million, over 69 million - more than one in four Americans - suffer from some form of cardiovascular disease (American Heart Association Heart Facts, 1992). Of these 69 million, nearly 6 million have coronary heart disease.

Annually, 1.5 million individuals with CAD will have an acute myocardial infarction (MI), and more than 500,000 of these will die (Heart Facts, 1992). Statistics for the U.S. (1985) show that myocardial infarction is the leading cause of death in America. Many of these deaths may be premature in individuals with known CAD. Angina pectoris, a symptom of myocardial ischemia, another manisfestation of CAD. Estimates based on the Framingham Heart Study are that 3 million people in the U.S. suffer from angina and 350,000 new cases occur each year (Heart Facts, 1992).

Several invasive and non-invasive interventions can alleviate symptoms associated with CAD, myocardial ischemia, and the risk of a myocardial infarction. Utilization of coronary angiography, increased by ≥65% during 1979 to 1987, this procedure allows the physician to determine significant disease and whether surgical intervention may be necessary (Heart Facts, 1992). Patients also undergo >200,000 coronary artery bypass grafting (CABG) procedures annually in the U.S. (Dubach, Froelicher, Klein, & Detrano, 1988). Another invasive treatment, percutaneous transluminal coronary angioplasty (PTCA) is now gaining acceptaince as an alternative form of revascularization for selected CAD patient (Raizner, Hust, Lewis, Winters, Batty, & Roberts, 1985).

The medical decisions leading to the foregoing invasive procedures must be predicated upon cost-effective evaluation procedures. The procedure widely used for this purpose today in the United States to clinically assess early disease is the graded exercise test (GXT). The GXT is a multilevel exercise stress test measuring ECG repsonses and signs and symptoms, which can estimate functional capacity and detect adverse reactions to physical exercise with very little risk to the patient (Madsen & Gilpin, 1983). Thus, the GXT is a procedure which has proven very helpful in diagnosing suspicious chest pain for prognosis or stratifying patients according to risk for future cardiac events. Although CAD patients enrolled in supervised exercise maintenance program are generally thought to be at a low risk for cardiac events than non-exercising patients, assessing their maximal functional capacity, is nevertheless an advantage because peak physical performance inadvertantly influences prognosis (Mark, 1990). Patients with CAD generally demonstrate a reduction in maximal exercise capacity compared to non-diseased cohorts. The lower maximal stroke volume and heart rate also contribute to reduced cardiac output and maximal oxygen consumption. Furthermore, when disease is suspected, many patients voluntarily will restrict their physical activity causing a certain deconditioning. Thus, the administration of the GXT will help the physician to assess the patients exercise tolerance and potential for future cardiac endpoints.

Statement of the Problem

Limited research is available showing the predictive value of responses obtained from the graded exercise test on CAD and post-MI patients within a maintenance cardiac rehabilitation exercise program for late risk of rehospitalization due to a coronary event. Thus, the immediate problem continues to be one of identifying the salient indicators of risk and the response characteristics for their indicators beyond which probable risk is sufficient to prompt clinical intervention.

Need for the Study

Among other clinical indicators, exercise testing has been advocated to establish prognosis. Patients with a reduced functional capacity, as well as those with a normal functional capacity, should be stratified as high or low risk for a coronary event to aid the physician in decisions for medical interventions. Prognostic use of the GXT early after hospitalization due to a coronary event has been well documented (Krone, Gillespie, Weld, Miller & Moss, 1985). However, only a few investigators have assessed the utility of the clinical GXT to stratify the late risk of events for CAD patients enrolled in a maintenance exercise program. Therefore, the specific aim of this investigation was to determine if selected electrocardiographic and heart rate responses in GXTs can differentiate risk of cardiovascular events in individuals participating in a supervised exercise maintenance program.

Significance of the Study

Exercise testing has been useful in identifying those patients with a high probability of coronary artery disease. Various hemodynamic, electrocardiographic, and symptom responses to exercise testing have been examined alone, and in combination, to determine their relation to the extent of coronary disease. Thus, the physician's primary diagnostic goal is identification of patients who are at high risk for a cardiovascular event and in need of more definitive evaluation due to the severity of CAD. This identification of high risk patients will also assist cardiac rehabilitation specialist in determining the level of care needed for supervising exercising CAD patients. Therefore, there is a need to accurately identify GXT responses that may assist in determining late high risk patients in a supervised exercise maintenance program.

Research Hypothesis

The following null hypothesis was tested:

Ho: Coronary artery disease and post myocardial infarction patients participating in a supervised exercise maintenance program, do not differ from non-event patients in patterns for exercise electrocardiographic/heart rate responses obtained from the three serial GXTs with regard to rehospitalization due to a coronary event within 12 months following three serial graded exercise tests.

Delimitations

The following delimitations are inherent in the design of this study:

1. It is retrospective in nature, involving only three cardiac therapy centers;

   a. Virginia Polytechnic Institute & State University Blacksburg, VA

   b. Wake Forest University, Winston-Salem, NC

   c. Glen Frye Regional Hospital, Hickory, NC

2. A referring physician's diagnosis of CAD or post-MI from the patients medical history record was required prior to their entry into the medically supervised exercise program;

3. Data were restricted to GXT results, medical history records and lab data collected in conjunction with the GXTs of male patients with program entry diagnoses of CAD or MI;

4. The two group classification differentiated as cardiac event (CE) and non-event (NE) patients exclusively on the basis of the referring physician's primary diagnosis after rehospitalization (for CE patient, this was clinical endpoint). The CE patients were characterized as having been rehospitalized due to a coronary event within 12 months following three serial GXTs. None of the NE patients were rehospitalized for a coronary event within 12 months following three serial GXTs;

5. Each group was selected from a subject pool in accordance with the inclusion criteria: male, age 40-71 years, absence of digitalis therapy, body mass index $\leq$40, participation in the exercise program at least three months prior to the first GXT, three serial completed GXTs within 12 months, and the attainment of a near-maximal endpoint in each of the three GXTs;

6. The CE and NE patients were matched according to entry diagnoses, medications throughout the period bounded by the three serial GXTs, and the time span in which the GXTs were performed;

7. Near-maximal GXT criteria was based on the rating of

perceived exertion (RPE) and the respiratory exchange ratio (R);

8. Continuous participation for at least 3 months prior to the first serial GXT, and in the supervised exercise maintenance program a ≥50% attendance during the period bounded by the three serial GXTs was required.

Limitations

The following limitations may restrict the interpretation of the findings of this study:

1. Due to this being a retrospective patient medical chart study, it lacks some of the rigor in experimental control that would otherwise be associated with such factors as subject selection, control of testing procedures, and cardiologic admission criteria.

2. This investigator only reviewed clinically stable and physically active patients enrolled in a supervised exercise rehabilitation program. The results would, therefore, be limited in the generalizability to other populations;

3. Subjects were not excluded on the basis of medical, dietary or psychological treatment by their physician;

4. The criteria from which the CE and NE group were selected were limited to specific diagnostic variables and exercise cardiovascular responses in the GXTs under consideration;

5. Changes in patient treatment, ie., medication changes, changes in exercise program, inadequate patient adherence to individualized exercise prescriptions over the course of the serial GXT period no control over these factors may have altered functional responses and exertional signs/symptoms of cardiovascular dysfunction;

6. The small sample size of patients, thus limiting inferences that can be made about the patient group;

7. Coronary artery bypass surgery as an endpoint for the cardiac event group was based upon the individualized physician's decision for medical advisability of this procedure to be performed.

8. An interval between GXT3 and the cardiac event was not specified, e.g. 10 days post GXT3, thus allowing differences among the CE subjects event time frame;

Basic Assumptions

The following basic assumptions made regarding this investigation are:

1. The physician's referral information and primary cardiac diagnosis on each subject was accurate;

2. The GXT protocols were administered by competent technicians;

3. Data from the GXTs were measured and recorded accurately;

4. Each subject attained a maximal, symptom limited endpoint in their treadmill test;

5. Each subject adhered to their individualized exercise training program during the time which the three serial GXTs were administered;

6. This data is applicable only to patients who have maintained aerobic exercise in a thrice weekly organized program;

Definitions and Symbols

ST/HR Slope - linear regression analysis of the maximum heart rate related change in ST-segment depression during exercise. Expressed as uV/bt/min.

Delta ST/HR Slope - calculated by dividing the maximal additional ST-segment depression, corrected for any resting ST-segment depression in that lead on the upright preexercise resting ECG, by the exercise-induced change in HR from upright resting HR.

Dysrhythmias - documented from ECG as ventricular ectopic beats (PVCs), and graded by the Lown's classification. This grading system uses three level of ventricular premature depolarisation frequency and four complex features to assign patients to one of seven grades.

Post-MI - Post myocardial infarction

CABG - Coronary Artery Bypass Grafting Surgery

PTCA - Purcutaneous Transluminal Coronary Angiolplasty

ST-Dep (J80) - Magnitude of ST-depression visually measured and averaged in three consecutive complexes from a point 0.08 msec after the J point using the horizontal level of the PQ junction.

CAD - Coronary artery disease, as determined by physician's diagnosis through electrocardiographic studies and/or angiogram studies.

CHAPTER II

REVIEW OF THE LITERATURE

Exercise testing has been shown to be useful in predicting of subsequent coronary events in most populations, including patients with previous myocardial infarction (Theroux, Water, Halphien, Debaisieux, & Mizgala, 1979). Exercise testing also has become a routine and cost-effective non-invasive tool for the medical evaluation of coronary artery disease (CAD) and for risk stratification with post-MI patients. Researchers have evaluated these populations and examined prognostic value of the GXTs therein.

In this chapter several of the prognostic variables derived from GXTs will be examined specifically within the populations of CAD and MI patients. The relevant research on the ST-segment depression and ventricular dysrhythmias will be discussed as to their value for predicting mortality and cardiac events within the populations of CAD and MI patients. In addition, studies were reviewed in which the ST/HR slope has been examined as a potential index for increasing sensitivity for the exercise test and the detecting severity of CAD.

Exercise Induced ST-Segment Displacement

One of the earliest studies correlating ST segment depression with subsequent mortality from CAD patients was reported by McNeer, Margolis, Lee, Kisslo, Peter, Kong, Behar, Wallace, McCants and Rosati (1977). Exercise testing, following the Bruce protocol, was administered to 1170 patients; 574 had angiographically verified CAD involving at least one coronary artery. A positive exercise test response was considered when horizontal or down-sloping ST-segment depression of $\geq$0.1mV persisted for at least 0.08 sec in the absence of pre-existing ST-segment abnormalities. The exercise ST-segment response coupled with a failure to complete Stage 2 of the Bruce protocol was associated with an 85% survival rate in one year and a 63% survival rate at 4 years. Furthermore, 97% of patients who had a positive exercise test in Stage 1 or Stage 2 had significant CAD, and over 60% of these patients had three-vessel disease. Patients with a negative ST-segment response who achieved Stage IV or greater had less than a 15% prevalence of three vessel disease. In combination, the ST-segment depression and exercise duration, were found to improve the diagnostic value of the exercise test.

Weiner, McCabe, and Ryan (1983) presented results in agreement with McNeer et al. (1977); they found that an ST-segment depression $\geq$2mm in Stage I of the Bruce protocol coupled with the persistence of such responses throughout the test were effective in distinguishing high- vs. low-risk subgroups of CAD patients relative to predicting cardiac mortality. One hundred and ninety-nine patients, exercise tested according to the Bruce protocol one day prior to cardiac catherization, were followed annually for 4 years. A positive ischemic response was considered to be 0.1mV of ST-segment depression. The high-risk group was characterized by ≥0.2mV ST-segment depression lasting ≥5 min involving three or more leads, left ventricular dysfunction, S3 gallop, or cardiac enlargement. The high-risk group had a significantly greater percentage (20%) of cardiac mortality, than the low-risk groups (2%) with neither exercise ischemia nor left ventricular dysfunction. Therefore, a combination of clinical variables such as the ST-depression and time of appearance can expand the use of risk stratification in CAD patient management.

Among MI patients, the ST-segment depression has also been reported to increase the predictive value of the exercise test. Theroux, Waters, Halphen, DeBaisieux, and Mizgala (1979) reported that ST-segment depression was predictive of coronary events one year following an MI. Two hundred and ten post-MI patients were treadmill tested one day prior to hospital discharge. The one year mortality rates were 2.1% (3 of 146) in patients without exercise ST-segment changes, and 27% (17 of 64) in those with depression of the ST-segment ($p<0.001$). Sudden death occurred in 0.7% (1 of 146) of the patients who showed no ST-segment changes and in 16% (10 of 64) of the patients with ST-segment depression ($p<0.001$). Thus, the investigators concluded that pre-discharge exercise testing may predict mortality among MI patients with ST-segment changes in the subsequent year.

Murray, Salih, Tan, Derry, Murray and Littler (1988) followed 300 post-MI patients for a mean of 12 months, 158 (53%) of whom had ST-segment depression. Treadmill testing was administered a mean of 9 days post-infarction using a combination of protocols as described by Naughton et al. (1953). An ischemic response was considered ≥0.1mV at 0.08 sec from the J point of the QRS complex on three consecutive beats. Although not significant, 105 of the 158 (66%) patients with ST-segment depression had coronary events. Ten (6%) of the 158 patients with ST-segment depression died due to cardiac events during the follow-up period. The investigators found the ST-segment depression a sensitive prognostic indicator for coronary events when the GXT was adminstered early after infarction.

Kavanagh, Shephard, Chisholm, Qureshi and Kennedy (1979) calculated indexes of prognosis for 610 post MI patients participating in a vigorous exercise rehabilitation program for an average of 36.5 months. Serial exercise tests were administered every 6 months or as indicated by abnormal functional responses. Electrocardiographic changes were recorded from the CM5 lead during a progressive bicycle ergometer test protocol. An abnormal ischemic response was considered as horizontal or downsloping ST-segment ≥0.2mV. Each patient performed up to 75% of their predicted aerobic power. During the period of observation 23 deaths occurred due to cardiac disease. Twenty-one patients had nonfatal recurrent infarctions. Of the 23 cardiac deaths, 10 (43.5%) had ST-segment depression ≥0.2mV. Only eight (38.1%) of the 21 patients with nonfatal recurrent infarctions had an abnormal ST-segment response. The investigators suggested that patients with severe ST-segment changes show less benefit from an exercise program than those without ischemic responses.

Thus, investigators have shown that the ST-segment depression is an important prognostic indicator for recurrent cardiac events among CAD and post-MI patients at times both remote from and early after initial infarction. However, ST-segment displacement among CAD patients was found to have greater predictive value while considered in combination with other GXT variables such as time of appearance of the ST-segment and duration of exercise.

Exercise-Induced Ventricular Dysrhythmias

The predictive value of exercise-induced ventricular dysrhythmias is highly controversial (Sami, Chaitman, Fisher, Holmes, Fray & Alderman, 1984). In a retrospective study, Nair, Thomson, Aronow, Pagano, Ryschon and Sketch (1984) studied 186 angiographically verified CAD patients with normal (>50%) and abnormal (<50%) left ventricular ejection fraction (LVEF) to determine whether exercise-induced ventricular dysrhythmias predict mortality independent of LV function. All 186 patients performed a treadmill exercise test using the Bruce protocol. Exercise-induced ventricular premature impulses were considered complex if they occurred in pairs or runs, were multiform, or if they occurred at a frequency of >10 b min-1. There was no significant differences in the incidence of sudden death and cardiac death among CAD patients with a normal LVEF with and without exercise-induced ventricular dysrhythmias. The same result was found in CAD patients with an abnormal LVEF. Therefore, in CAD patients the value of exercise-induced ventricular dysrhythymias appeared not to be predictive of sudden death or cardiac mortality independent of LV function.

Another retrospective study by Sami et al. (1984), investigated the prognostic significance of exercise-induced ventricular dysrhythmias in patients with stable CAD. The patient population (1,486) was constituted from the Coronary Artery Surgery Study (CASS) registry. Each patient underwent a treadmill test according to the Bruce protocol. Patients were categorized into two groups: minimal ≤70% narrowing and significant CAD (≥70% diameter reduction in any major coronary artery or ≥50% narrowing in the left main artery). The overall 5 year mortality rate was relatively low and not significant. Of patients with exercise-induced ventricular dysrhythmias, the 5 year mortality rate was 12% versus patients without exercise-induced ventricular dysrhythmias at 10%. Moreover, there were no differences in mortality rates according to the two CAD group classifications..

As described in an earlier section of this chapter, Kavanagh et al. (1979), examined prognostic indicators of 610 physically acitve MI patients. During the follow-up period of 36 months, 21 nonfatal recurrent infarctions and 23 cardiac deaths occurred. Only one patient with a nonfatal recurrent MI revealed both unifocal and multifocal PVCs. Two patients who suffered fatal recurrences had demonstrated multifocal PVCs in previous exercise tests. Thus, the investigators concluded that multifocal PVCs may carry a somewhat higher risk (1.52 vs. 0.25) for cardiac death for patients in a conditioning program.

Madsen, Gilpin, Henning, Ahnue, LeWinter, Ceretto, Joswig, Collins, Pitt and Ross (1984) studied complex ventricular arrhythmias (CVA) during a 24-h ambulatory monitoring period in patients prior to their hospital discharge. The question was whether CVAs carried independent risk for sudden cardiac death. The study consisted of a subgroup of 434 patients who were discharged from the hospital following an acute MI. A one year follow-up period was observed. A linear discriminant analysis was used to evaluate the independent importance of prognostic variables within 1 year. The 6 month analysis indicated a very low predictive value when presence of complex ventricular arrhythmias was entered as an independent variable. However, at 1 year the complex ventricular arrhythmias did have prognostic value alone, but the predictive power increased when combined with other variables (64% vs. 77%), as S3 gallop, or left ventricular ejection fraction (LVEF).

Therefore, the presence of exercise-induced ventricular dysryhthmias in CAD and MI populations have shown weak, if any, correlation to sudden cardiac death or recurrent cardiac events. These investigators, however, report that ventricular dysrhythmias have significance for prediction of cardiac death when associated with other adverse factors with known prognostic value such as the ST-segment depression.

ST/HR Slope Index

Linear regression analysis of the maximum heart rate-related change in ST-segment depression during exercise (the ST-segment/heart rate slope) has been found to improve the diagnostic sensitivity of the exercise ECG for the identification of patients with coronary disease and the detection of three-vessel and left main coronary disease beyond that available with standard exercise test criteria (Okin, Kligfield, Ameisen, Goldberg, & Borer, 1988). To aid in the identification of three-vessel disease a standard for the ST/HR slope partition of 6 uV/bt/min has been used for several prospective testing studies (Finkelhor, Newhouse, Vrobel, Miron, & Bahler, 1986).

Ameisen, Okin, Devereux, Hochreiter, Miller, Zullo, Borer, and Kligfield (1985) treadmill tested 50 patients with stable angina, 45 acute MI patients and 17 normal subjects with a high prevalence of inadequate ECG responses to exercise using the standard or modified Bruce protocols. Of those with stable angina, 42 of the 46 (91%) CAD patients had ST/HR slope values ranging from 1.2 to 20.0 uV/bt/min (x=5.5 uV/bt/min). Fifteen of those with stable angina (36%), had ST/HR slope values greater than 6uV/bt/min. In acute MI patients, the range of ST/HR slope values was 0.0 to 30.4 uV/bt/min (x=3.8 uV/bt/min). Fifteen (36%) of the 42 acute MI patients had ST/HR values ≤1.1 uV/bt/min. Of the normal subjects, 16 (94%) had ST/HR slope values <1.1 uV/bt/min. Therefore, the investigators interpreted that with ischemic heart disease patients the ST/HR slope appears to be most predictive of CAD in patients with stable angina. In acute MI patients, the value of the ST/HR slope is limited due to the recent injury and wall motion abnormalities.

Okin et al. (1988) examined the ability of the ST/HR slope to identify three-vessel coronary artery disease. One hundred twenty-eight patients with stable angina were treadmill tested and underwent coronary angiography to verify the severity of disease. When the extent of CAD was defined by a 50% and 75% luminal obstruction, the ST/HR slope (≥6uV/bt/min) identified patients with three-vessel CAD with a sensitivity of 93% and 100%, respectively. The investigators found evidence that ST/HR slope values ≥6uV/bt/min could accurately distinguish three vessel disease and stratify patients according to risk. Thus, these investigators have shown it is possible to use the ST/HR slope to aid in medical diagnosis and non-invasive follow-up of patients with verified disease.

Delta ST/HR Index

The delta ST/HR index has also been shown to be a valuable screening method in detection of CAD (Kilgfield, Ameisen, & Okin, 1987). This methods divides the maximal ST segment change by the total change in HR from rest to peak exercise. Okin, Kligfield, Milner, Goldstein & Lindsay (1988) studied 62 asymptomatic subjects with abnormal exercise tests. They reported that a previously established delta ST/HR index value <1.6uV/bt/min correctly indentified 34 of 52 subjects (65%) who, despite abnormal exercise ECGs, had no rest or exercise radionuclide abnormalitites. A delta ST/HR index ≥1.6uV/bt/min detected 7 of 7 subjects with abnormal radionuclide abnormalities who had CAD at cardiac catherization. Okin, Chen & Kligfield (1990) studied 124 typical angina patients referred for angiography, who underwent exercise testing at the time of admission and had abnormal results. The delta ST/HR index had a 94% (116 of 124) sensitivity for the detection of CAD. These studies suggest that the delta ST/HR index can improve the usefulness of standard exercise ECG in screening for CAD.

ST/HR Slope and Beta-Blocking Agents

In contrast to the standard ST-segment criteria, the ST/HR slope is not markedly affected by the use of beta-blocking drugs, since a decrease in ST-segment depression is accompanied by a parallel decrease in heart rate response to exercise (Okin _et_ _al_. 1988). Okin _et_ _al._ (1985) found no difference in the mean ST/HR slope among patients with 1-, 2-, and 3-vessel disease, regardless of the presence or absence of beta-blockade. This finding is in agreement with Kardash _et_ _al_., who found no difference in the ST/HR slope in 21 patients tested with and without a beta-blockade (Okin et al. 1985). Herbert, Dubach, Lehmann, & Froelicher (1991) reported that the delta ST/HR index values on patients recieving beta-blockade therapy did not improve the diagnostic accuracy of an abnormal test result as compared with the standard ST-depression method.

Summary

The preceding sections have included evaluations of physically active, stable CAD and MI patients for risk stratification according to GXT prognostic indicators. In stable CAD patients, the ST-segment depression in conjunction with duration of exercise (failure to complete Stage 2 of Bruce) were found to improve the diagnostic value of the GXT (McNeer _et_ _al_. 1977). Furthermore, ST-segment depression and its time of appearance during exercise appear to be effective in identifing early and late risk of subsequent cardiac events (Weiner _et_ _al_. 1983).

In acute MI patients, an ischemic response during exercise was found to be predictive of certain future cardiac events. Futhermore, there seems to be increased likelihood of cardiac events was reported among stable MI patients participating in a long term conditioning program (Kavanagh et al. 1979).

Another GXT variable, ventricular dysryhthmias, was found to have little predictive value among CAD or MI patients. In CAD patients with normal or abnormal functional capacities, ventricular dysrhythmias were not predictive of sudden death or cardiac mortality (Sami et al. 1984). However, a small risk ratio was associated with unifocal (0.25) and multifocal (1.52) PVCs for cardiac death among physically active MI patients (Kavanagh et al. 1979).

The ST/HR slope was reported to improve the diagnostic sensitivity of the exercise ECG for the identification of patients with three vessel disease. CAD patients with stable angina were identified as having ischemic heart disease with greater accuracy than MI patients with stable angina (Ameisen et al. 1985). An ST/HR slope value of 6uV/bt/min was found to identify patients with three-vessel disease (75% luminal obstruction) with a sensitivity of 100%. Although, the extent of disease cannot be accurately distinguished by the ST/HR slope, the prognostic value of the index within severely diseased patients is substantial. The delta ST/HR index was also reported to improve the diagnostic screening value of patients with CAD, however, the detection of the severity of the disease was less likley.

Development of Rate Related Exercise-Induced Myocardial Ischemia and Risk of Selected Coronary Disease Endpoints

Sharon D. Bruce, William G. Herbert,
Don R. Sebolt, Reed H. Humphrey,
and Douglas Southard

Sharon D. Bruce, William G. Herbert,
Don R. Sebolt, Reed H. Humphrey and Douglas Southard
Laboratory for Sport, Exercise and Work Physiology
Department of HPER
VPI & SU
Blacksburg, Virginia 24061
703-231-6565

ABSTRACT

The purpose of the study was to determine whether serial graded exercise test (GXT) responses, known to have prognostic importance, in the coronary artery disease population generally, can differentiate certain cardiovascular mobidity and mortality endpoints among physically active patients. Data were obtained in 1989 at three community-based cardiac rehabilitation programs from three serial GXT results in 23 paired cardiac event (CE) and non-event (NE) patients. A cardiac event was defined as having an myocardial infarction (MI), percutaneous translumial angioplasty (PTCA), coronary artery bypass grafting (CABG), and cardiac death. Comparisons were made just prior to each CE patients event. Statistical analyses were done on four exercise test variables: ST-segment depression (ST80) at peak exercise, heart rate adjusted ST-segment depression (ST/HR slope), exercise induced ventricular dysrhythmias (PVC), and exercise induced chest pain. Chi-square analyses showed no significant changes across the serial tests for any of the variables examined in either the CE or NE groups ($P>0.05$). Nevertheless, the CE group had significantly more ST-segment depression, ST/HR slope, and exercise chest pain in all GXT intervals in comparison to the NE group. These findings do not support the use of serial exercise GXTs for prognostic information for the physically active cardiac rehabilitation maintenance patients.

CHAPTER III

JOURNAL MANUSCRIPT

Graded exercise testing (GXT) is a widely employed non-invasive procedure for supporting physician's decisions on the medical management for diagnosed coronary artery disease (CAD) and post-myocardial infarction (MI) patients. Use of the procedure has increased dramatically in recent years, rising from 500,000 in 1986 to upwards of 650,000 in 1988 (17).

Cardiac rehabilitation programs utilize serial exercise testing for a number of reasons, including identifying cardiovascular problem areas among their exercise maintenance patients. The most frequent uses of the GXT are to determine the likelihood of coronary artery disease (CAD), estimate prognosis and to determine functional capacity. Major professional clinical groups have taken different positions on the question of how frequently exercise testing should be repeated in cardiac rehabilitation programs. Such serial testing is believed by some (5) to assure continuing safety and apprpriateness of exercise. Other associations (1) have raised doubts about the medical value of serial testing in the setting of cardiac rehabilitation.

The physiological responses and symptoms obtained during the GXT provide the basis for prognostic assessment. However, limited research is available showing the predictive value of these indicators within the setting of stable CAD patients. This is particularly true for patients who are regularly following an organized exercise program and are part of a low-risk subset relative to rehospitalization due to a coronary events.

The purpose of this study, therefore, was to determine the value of the symptom-limited GXT in stable CAD and post-MI patients who were physically active for differentiating risk of selected cardiovascular endpoints. Risk was defined in terms of specific events occuring within close proximity to the last in a series of three GXTs. In this report, electrocardiographic, heart rate and exercise angina responses were examined.

METHODS

This retrospective study involved a group of 46 males diagnosed with CAD and/or who were post-myocardial infarction (MI) status. The mean age of this group was 56 years (range 40 to 71). All subjects were actively participating (50% attendance) in a supervised exercise maintenance program. Two subgroups were identified for comparisons. One was defined as a cardiac event (CE) group, consisting of patients rehospitalized due to a coronary heart disease related event. These included MI, bypass surgery, angiography, coronary angioplasty or cardiac death. None of those designated as non-event (NE) subjects had been rehospitalized for a coronary event during the period in which the matching CEs subjects had their events. Each cardiac event subject was matched with a non-event subject according to a similar initial diagnosis at the time of entry into the exercise program. Cardiovascular medications also were taken into consideration when matching CE and NE subjects.

Subjects and data were obtained from three community based cardiac rehabilitation centers in the Southwestern United States. Records of approximately 250 prospects who had been actively participating for at least 2 years were examined. Virginia Polytechnic Institute & State University contributed 9 pairs of subjects, Wake Forest University 13 pairs and Glen Frye Regional Hospital 2 pairs. Male prospects were excluded on the basis of the following criteria: age >71 years, digitalis therapy, obese (body mass index of >40), failure to attain a near-maximal end-point during the GXT (failure to attain respiratory exchange ratio of unity and/or RPE=17), less than 3 months participation in the supervised exercise program prior to GXT(1), and completion of fewer than three consecutive GXTs <12 months part.

Three serial GXTs had been conducted on all subjects and were administered less than 13 months apart. The average time of observation was 20.2 months. The average interval for the CE and NE groups between entry into the supervised exercise program and GXT(1) was 27.6 (±5.4) months and 19.0(±4.2) months, respectively. The average time interval for the CE group between GXT(1) and GXT(2) was 6.8(±0.7) months, compared to 7.4(±0.8) months for the NE group. The average interval between GXT(2) and GXT(3) for the CE and NE group was 7.8(±0.9) and 7.8(±1.0) months. Two way ANOVA with repeated measures across time was performed on these intervals. The F ratio for time and group main effects and for time x group interactions were non-significant ($p>0.05$). The average interval between GXT(3) and the cardiac event for the CE group was 4.8(±1.4) months.

Exercise Testing and Program Protocol

Symptom-limited exercise testing was performed on a treadmill using modified Balke or similar protocols, which increased in speed and grade every 2-3 minutes (1-3 METS). Test termination was determined by the attending physician upon appearance of significant clinical signs and symptoms or the patient's request to stop. A 12-lead ECG system was used to monitor continuously the electrocardiographic responses at rest and during exercise. The magnitude of ST depression was visually measured to the nearest 50mV (.1 mV=100 mV), and averaged in three consecutive complexes from a point 0.80 msec after the J point using the horizontal level of the PQ junction for three consecutive complexes as the reference isoelectric baseline. The heart rate adjusted change ST segment depression between standing rest and peak exercise was calculated as the delta ST/HR Index, as defined by Okin et al. (9). At maximal exercise all ECG leads were recorded and the precordial lead usually V5 which had the greatest magnitude of ST depression was utilized as the measure of ischemia. The pre-exercise baseline was then subtracted from the peak ST level in exercise. Any baseline ST elevation was disregarded in measurement of ST shifts. The ST shift was then divided by the heart rate elevation between the same two ECG recording points to calculate the delta ST/HR index.

Ischemic symptoms considered to be angina were measured according to a 1-4+ rating scale. Premature ventricular complexes were classifed by the attending physician as none, single or multiple. Blood pressure responses, signs and any additional symptoms were also recorded at each stage of exercise.

Typical exercise sessions in the supervised maintenance programs where these subject pairs had been participating consisted of a cardiovascular warm-up, an aerobic conditioning component, cool-down activity and flexibility/relaxation routines, performed as 50 min/sessions three times weekly.

STATISTICAL ANALYSIS

Descriptive statistics were computed for key characteristics of the two patient subgroups.In addition, dependent t-tests were used to compare CE and NE on those used for the matching criteria. Such comparisons served to demonstrate potential effects of factors that were thought to bias treadmill test results. For exercise responses, analysis of variance for ST Dep(80) and ST/HR Index and the Chi-square for chest discomfort and premature ventricular contractions, were used to evaluate responses between groups or serially across the three GXTs.

RESULTS

Two subject groups of 23 paired CE and NE subjects were utilized for comparison. The majority of subjects were post-MI (58%), followed by diagnosed CAD (33%), and the rest were post-CABG (9%). Matching of the NE to CE subjects at the time of GXT was based upon the following matching criteria: age, weight, diagnosis, selected cardiovascular medications, exercise tolerance (METpk) and exercise program participation dates. Among the 23 cardiac events subjects that occurred after the third GXT observation period, 8 were MIs (five of which resulted in death), 12 CABG, 2 PCTA, and 1 cardiac catherization.

Insert Figure 1

The characteristics of the two groups were evaluated from records obtained at the time of the first GXT (Table 1). No significant differences were found between the CE and NE groups for any of the descriptive characteristics, e.g., age, BMI, serum cholesterol, utilizing the dependent t-test.

Insert Table 1

Clinical history variables were compared between both groups. Table 2 shows that post-MI subjects were predominant within each group. Diagnosis of CAD, without prior MI was the next most prevalent subset (33%). Although, no statistical analysis was computed, both groups had similar numbers in regards to initial diagnosis.

Insert Table 2

The majority (92%) of subjects received cardiodynamic medications (Table 3), with B-blockers and/or nitrates most common in both groups. Groups were not significantly different on the number of medications and nearly one-half were receiving multiple cardiovascular agents. Similarly, the types and numbers of these medications were not significantly different between groups.

Insert Table 3

Comparisons of CE and NE at GXT1 showed no significant differences in terms of resting responses and exercise tolerance when utilizing the dependent t-tests to show how the groups were similar in comparison (See Table 4). During GXT1, the CE subgroup had significantly more ischemic ST segment depression in exercise than the NE subgroup, ($\bar{x}$=0.2mV vs. 0.1mV for CE vs. NE) whether or not adjustments for differences in chronotropic response of the heart were considered, ie., the delta ST/HR index (mean=4.6mV vs. 2.5mV). The CE subgroup also evidenced three fold more angina-type chest discomfort at GXT1, but this difference failed statistical significance according to the chi-square analysis.

Insert Table 4

Serial comparisons for inherent ST changes in both groups are illustrated by Figures 2 & 3. These results show a persistence of significantly ($p<0.001$) greater exercise induced ischemia in CE. However, ANOVA showed no significant variation in ischemic repsonses over the serial test period. Results for delta ST/HR Index were essentially the same as for the classical measure of ischemia ST depression ($p<0.005$).

Insert Figures 2 & 3

Comparisons between CE and NE generally demonstrate that more than twice as many CE patients ($p\leq0.10$) had exertional angina. However, the pattern of occurrence in CE over time, did not show a statistically significant increase in this response at GXT3 by repeated measures ANOVA (Table 4). Figures 4 & 5 show exertional PVC activity was generally rare in these medically managed patients and thus not statistically different between or across the three GXTs by repeated measures ANOVA.

Insert Figures 4,5 & 6

DISCUSSION

A concern in this study was the matching procedure for CE and NE subject pairs. It was not possible to match the subject pairs on any independent measure of disease severity, e.g., locus/magnitude of MI area, or CAD vessel lesions. This may have biased intergroup comparisions for the prognostic variables. The experimental observation period and scheduling for GXTs for matched pairs differed somewhat. Also, variablity in compliance to the exercise program may have influenced certain GXT responses. However, the matching procedure did demonstrate absence of selection biases for age, body size, primary CAD risk variables, diagnostic history or important cardiovascular medications.

Unfortunately, the inclusion of coronary artery bypass graft surgery (CABG) as a cardiovascular event endpoint creates a somewhat arbitrary measure of clinically critical progression in coronary artery disease. Further clinical data through invasive procedures such as angiography would enhance the measure of disease progression. Patients with signs or symptoms of myocardial ischemia (ST-depression/angina) on an exercise test are more likely to accept the treatment option of CABG and/or PTCA since the decision is heavily weighted by the physician's judgement

(6) and increasing access to the procedure in the United States today. Fifteen of 23 CE patients had surgical procedures as their cardaic event in this study. Despite the subjectivity that this adds to one definition of a critical cardiovascular disease event, the need to identify patients with the evolving disease process will increase in the 1990s. Surgery for coronary revascularization increasingly will be a more frequently indentified endpoint for many patients who participate in cardiovascular exercise maintenance programs.

Serial graded exercise testing at 3-6 months to evaluate CAD patients in rehabilitation programs is advocated by the American College of Sports Medicine (3), and the American Association for Cardiovascular and Pulmonary Rehabilitation (2). Serial tests are useful to update individual exercise prescriptions, as well as provide clinical information which may improve objectivity of stratification of exercising patients according to lower- and higher-risk subgroups. Practioners need to find ways to increase the prognostic ability of their evaluation protocols. Thus, this study addresses a clinically meaningful issue which can be considered a new concept in regards to the physically active patient population over a period of time.

In this study, there were no definitive changes cross time which would have shown that evolving problems might be detectable. This finding is comparable to the findings of the ACC/AHA which did not agree with serial GXTs. However, we did find CEs to have nearly twice as much exercise induced ischemia on ECGs as documented by ST-T changes, and more symptomatic manifestations of CAD during every exercise test. Exercise-induced ST-segment depression in patients with CAD has long been known as an indicator of poor prognosis (2%-6%) in early post-MI populations (7,9,11,13,14,). Sami et al. (11) found ST-segment depression of 0.2mV or more to be predictive of cardiac arrest or CABG among post-MI patients during a 2 year follow-up period. Markiewicz et al. (7) found similar results with ST depression (at least 0.1mV) predictive of later coronary events during a follow up that averaged 18 months. McNeer et al. (8) and Theroux et al. (14) also identifed exercise ST-segment response as markers of increased risk of early mortality.

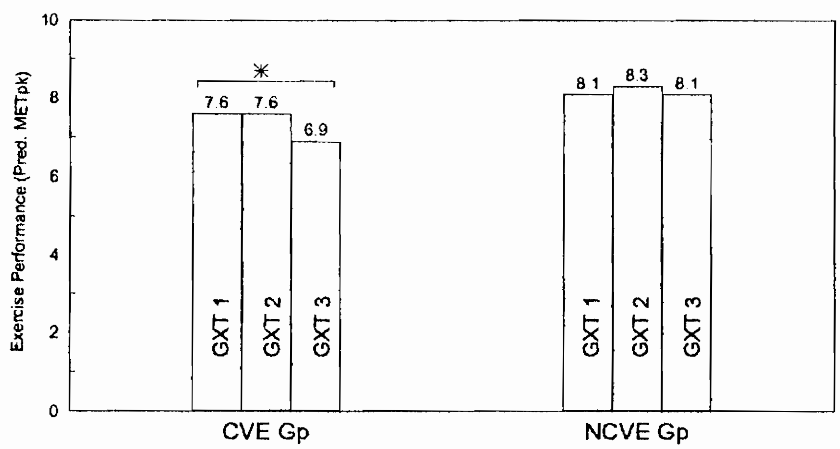
Examination of exercise-induced PVC patterns appeared to be nondescriminating in this study with respect to differentiating the endpoints. Premature ventricular complexes in exercise occurred with minimal frequency among patients in all GXTs regardless of group membership. This is not an uncommon finding in larger CAD population studies, particularly for groups that are being managed with anti-arrhythmic medications. Independently, exercise-induced PVCs are not predictive of cardiac events or mortality (10,13). Overall, the ST-segment depression and exercise induced chest discomfort within serial exercise testing appears to be useful in further stratfying the risk of possible future coronary events among exercising CAD patients. To enhance the information from serial GXTs future research could be performed with improvement of the time window regarding the cardiac event following GXT3. Setting a time frame, ie. 4 weeks, will allow a greater knowledge as to how frequently GXTs should be administered.

Hemodynamic Responses and Exercise Tolerance

	CVE Group	NCVE Group
Heart Rate (bt/min)	61 (8)	64 (10)
Systolic BP (mmHg)	124 (12)	124 (15)
Diastolic BP (mmHg)	80 (8)	80 (10)
Pk HR, GXT (bt/min)	131 (25)	138 (26)
Pk SBP, GXT (mmHg)	162 (27)	163 (20)
Pk DBP, GXT (mmHg)	83 (10)	84 (9)
Pred. METs, GXT	8.1 (2.3)	7.5 (2.1)

CVE Gp = Endpoints of PTCA, CABG, MI, Death
NCVE Gp = Comparison Gp of Matched Patients
Values are Means and (SD), * = P

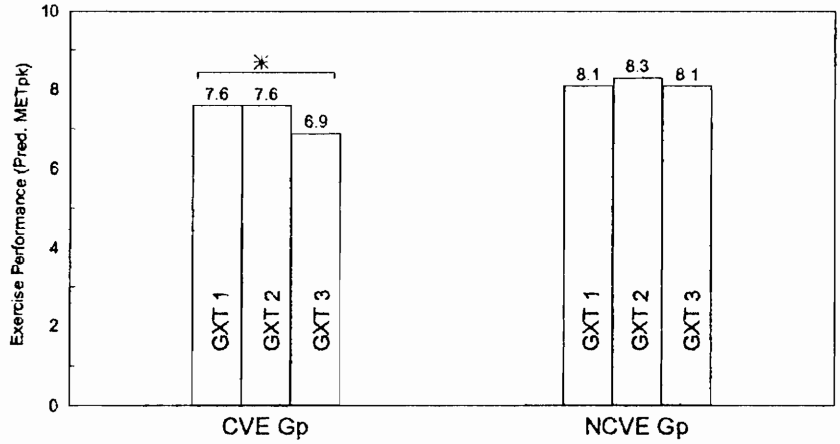
Results



Exercise Tolerance in Serial Functional GXTs

CVE Gp = PTCA, CABG, MI or Death
NCVE Gp = Pair-matched non-event patients
* = P

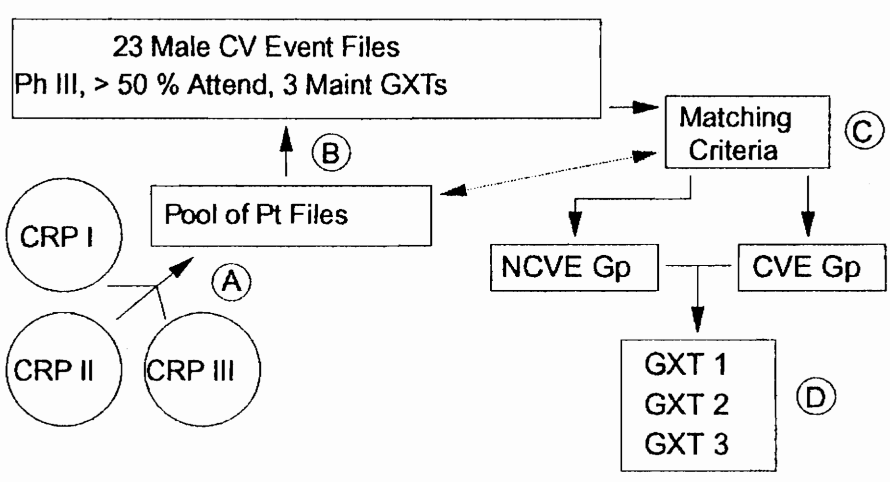
Results



Exercise Tolerance in Serial Functional GXTs

CVE Gp = PTCA, CABG, MI or Death
NCVE Gp = Pair-matched non-event patients
* = P

Study Design



REFERENCES

1. ACC/AHA Task Force on Assessment of Cardiovascular Procedures (1986) Report on Guidelines for Exercise Testing. Journal of American College of Cardiology. 8:725-738.

2. American Association for Cardiovascular and Pulmonary Rehabilitation. Guidelines for Cardiac Rehabilitation Programs. 1991.

3. American College of Sports Medicine. Guidelines for Graded Exercise Testing and Prescription. (1991) 4th ed., Philadelphia, Lea and Febiger.

4. American Heart Association (1990). Special Report on Exercise Standards. Circulation, 82:2286-2322.

5. Froelicher, E.S., & Perdue, S.T. (1991) Clinical, Epidemiologic, and Statistical Methods Used in Prognostic Studies of Survival After Myocardial Infarction. Journal of Cardiopulmonary Rehabilitation. 11:16-22.

6. Gore, J. (1988) Dramatic Increase in Diagnositc Testing for MI Patients Reported. The Exercise Standards and Malpractice Reporter. Volume 2: 28.

7. Markiewicz, W., Houston, N., DeBusk, R.F., (1977) Exercise Testing Soon After Myocardial Infarction. Circulation. 56:26-31.

8. McNeer, J.F., Margolis, J.R. Lee, K.L., Kisslo, J.A., Peter, R.H., Kong, Y., Behar, V.S., Wallace, A.G., McCants, C.B., & Rosati, R.A. (1977) The Role of the Exercise Test in the Evaluation of Patients for Ischemic Heart Disease. Circulation. 57:64-70.

9. Murray, D.P., Salih, M., Tan, L.B., Derry, S., Murray, R.G., and Littler, W.A. (1988) International Journal of Cardiology. 20:353-363.

10. Okin, P.M., Kligfield, P., Ameisen, O., Goldberg, H.L., and Borer, J.S. (1988) Identification of Anatomically Extensive Coronary Artery Disease by the Exercise ECG ST Segment/Heart Rate Slope. American Heart Journal. 115:1002-1012.

11. Sami, M., Kraemer, H., & DeBusk, R.F. (1979) The Prognostic Significance of Serial Exercise Testing After Myocardial Infarction. Circulation. 60:1238-1246.

12. Sami, M., Chaitman, B., Fisher, L., Holmes, D., Fray, D., and Alderman, E. (1984) Significance of Exercise-Induced Ventricular Arrhythmia in Stable Coronary Artery Disease: A Coronary Artery Surgery Study Project. American Journal of Cardiology. 54:1182-1188.

13. Schechtman, K.B., Capone, R.J., Kleiger, R.E., Gibson, R.S., Schwartz, D.J., Roberts, R., Young, P.M., Boden, W.E., and the Diltiazem Reinfarction Study Research Group. (1989) Circulation. 80:1148-1158.

14. Theroux, P., Waters, D.D., Halpien, C., Debaisieux, J.C., & Mizgala, H.F. (1979) Prognositc Value of Exercise Testing Soon After Myocardial Infarction. New England Journal of Medicine. 301:341-345.

15. Yang, J.C., Wesley, R.C., and Froelicher, V.F., Ventricular Tachycardia During Routine Treadmill Testing: Risks and Prognosis. Archives of Internal Medicine. (1991) 151:349-353.

16. Weiner, D.A., Levine, S.R., Klein, M.D., & Ryan, T.J. (1984) Ventricular Arrhythmias During Exercise Testing: Mechanism, Response to Coronary Bypass Surgery and Prognostic Significance. American Journal of Cardiology. 53:1553-1557.

17. Zoler, Mitchell L. (1990) Exercise Tests: Detecting Asymptomatic CAD. Medical World News, 24-30.

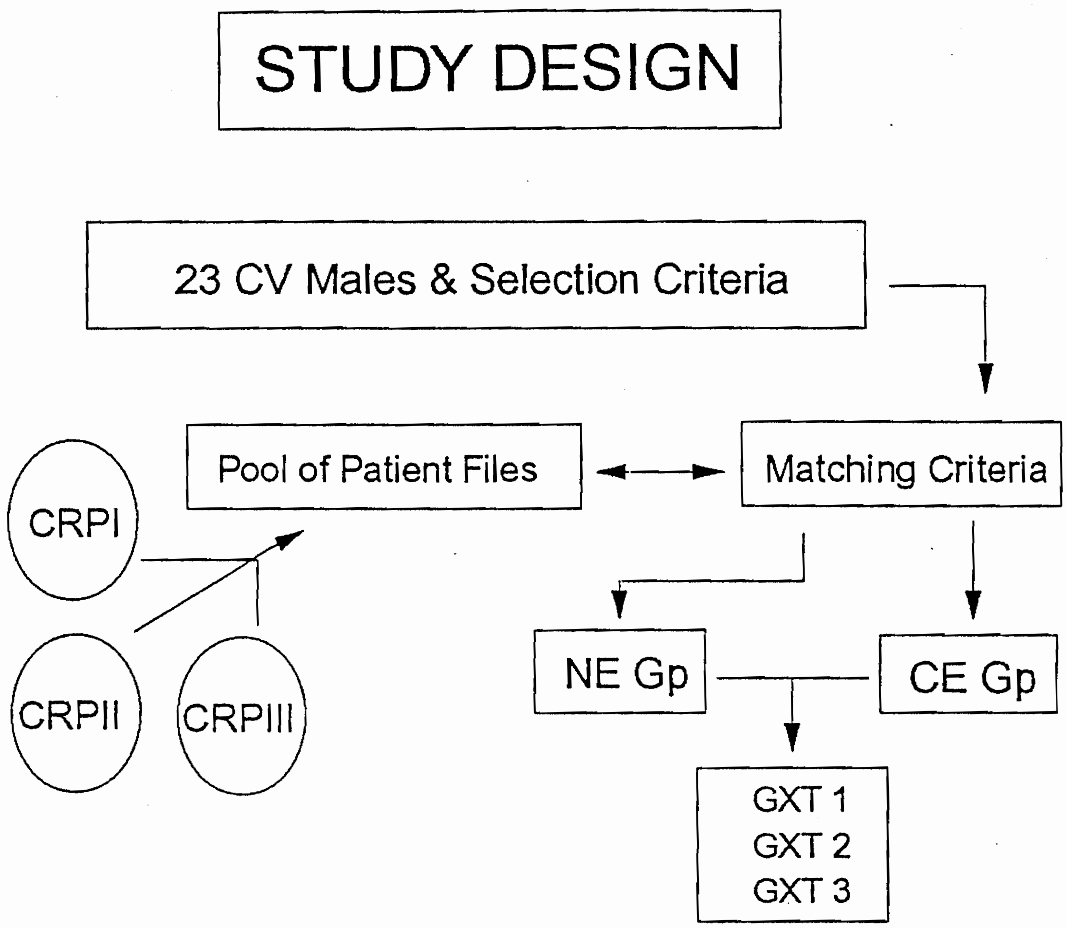


Figure 1: Study Design for Selection of 23 Paired Subjects

Table 1 Characteristics of Subjects

	CE	NE
Age (yr)	55 (7)	57 (6)
Ht (cm)	180 (7)	180 (7)
Wt (kg)	91.3 (9.6)	94.1 (9.7)
BMI	25.9 (3.3)	25.1 (2.5)
Serum Cholesterol (mg/dl)	233 (42)	212 (32)
Smoking History(%)	70	61

Values are means and (SD).

Table 2

Clinical History Variables

	CE	NE
Clinical History Variables:		
Myocardial Infarction	15(65)	12(52)
Clinical Q Waves:		
Anterior Q's [3]	3(20)	1(8)
Other Q's	12(80)	11(92)
Angina	2(9)	1(4)
CAD Related Surgery [1]	2(9)	2(9)
CAD [2]	4(18)	8(35)
Hypertension	8(35)	8(35)

Values are frequencies and (percentages)

[1] Coronary Artery Bypass Surgery

[2] Confirmed by Angiography

[3] Physician Diagnosed Anterior Q Wave MI's

Table 3

Cardiovascular Medications According to Patient Groups

	CE	N E
Patients w/ Mulitple Medications:		
Single	10(43)	9(39)
Multiple	11(48)	12(52)
None	2(8)	2(8)
Types of CV Medications:		
Beta Blockers	14(61)	9(39)
Nitrates	7(30)	11(49)
Calcium Channel Blockers	4(17)	3(13)
Diuretics	1(4)	2(8)
Other	1(4)	1(4)

Values are frequencies and (percentages)

Table 4
Physiologic and Exercise Performance Variables
According to Patient Groups

	CE	NE
Heart Rate (bt/min)	61(8)	64(10)
Systolic BP (mmHg)	124(12)	124(15)
Diastolic BP (mmHg)	80(8)	80(10)
Predicted METS	8.1(2.3)	7.5(2.1)

Mean values and (SD) selected from GXT(1)

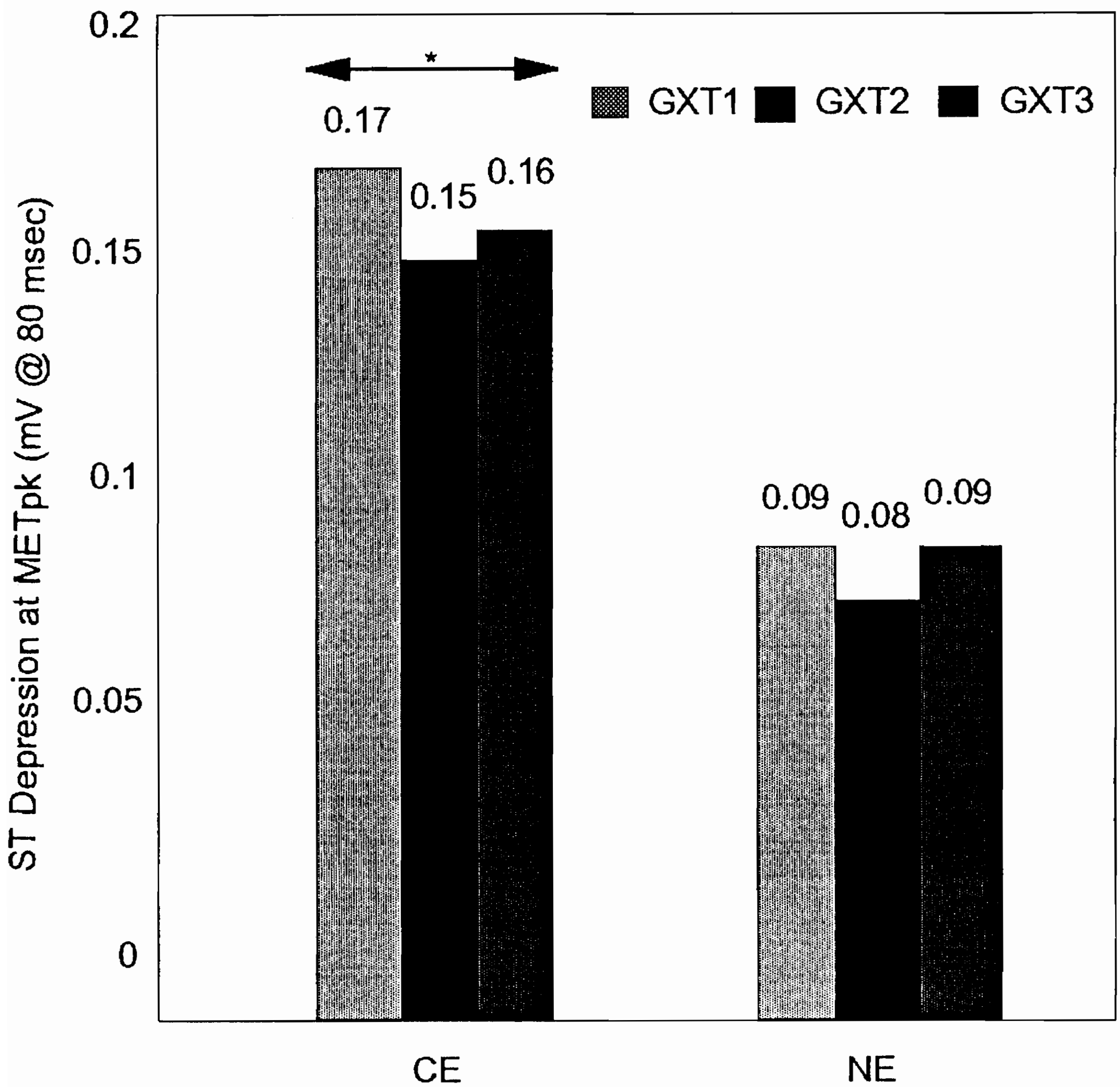


Figure 2

Exercise ST Segment Shifts Within Serial GXTs

Among CE and NE Groups, *p < 0.001 (F=13.87)

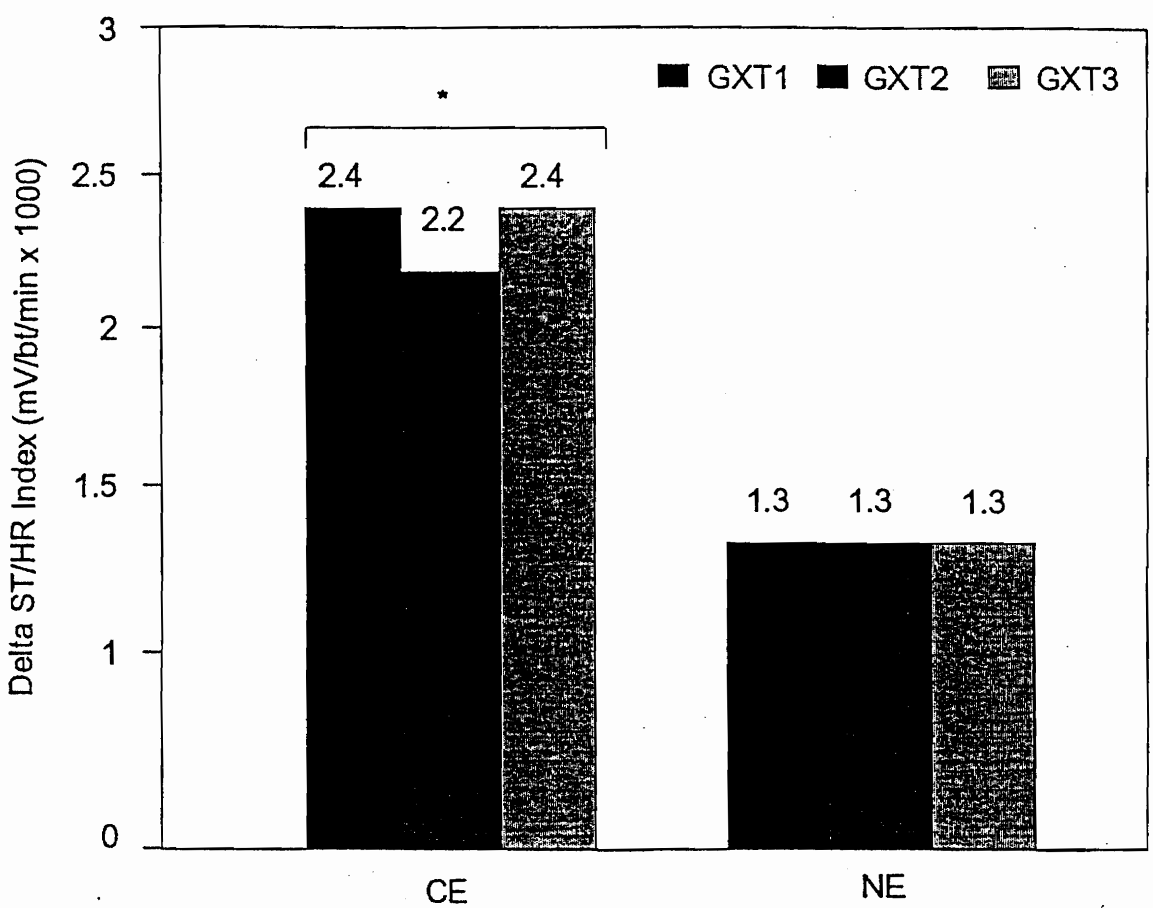


Figure 3: Delta ST/HR Index Across Serial GXTs *p<0.005 (F=8.30)

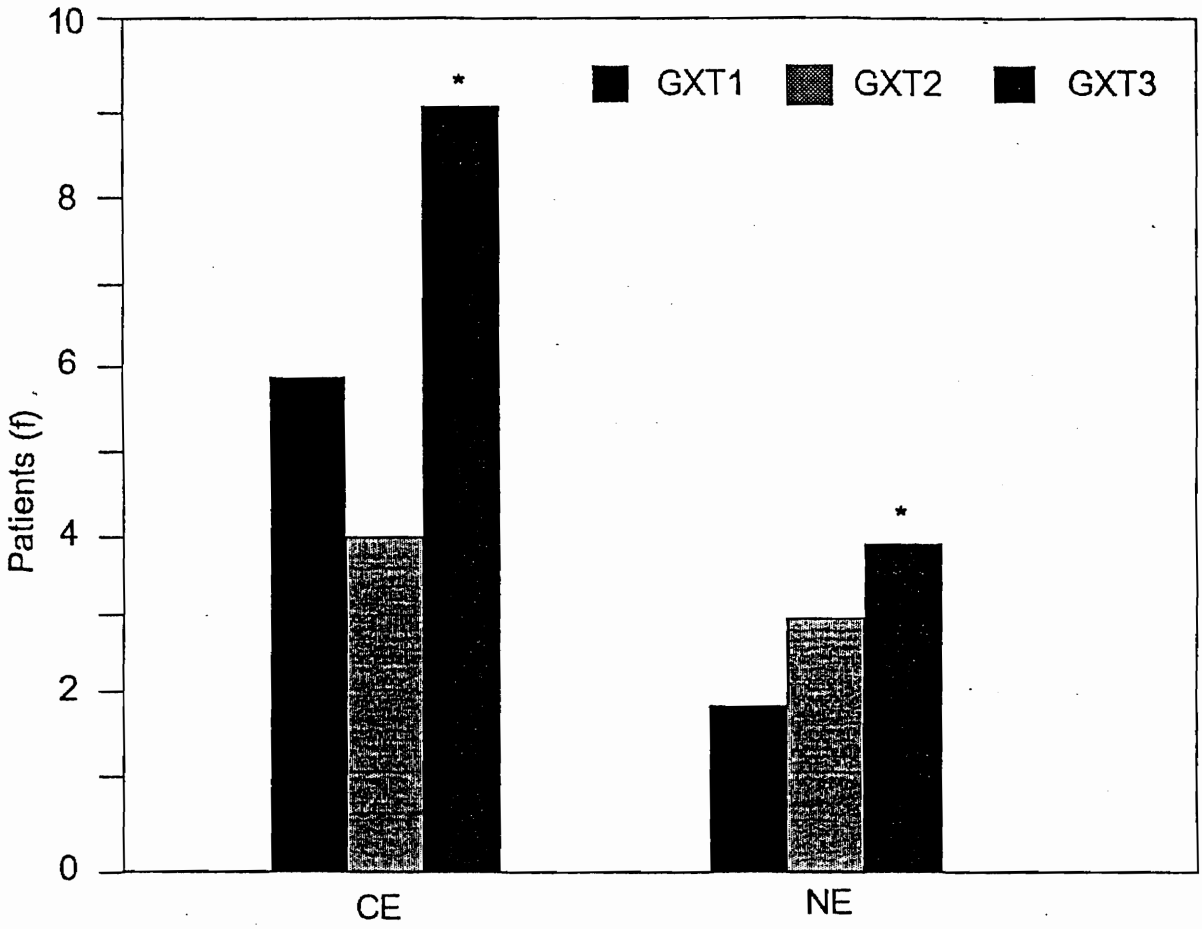


Figure 4: Exercise-Induced Chest Discomfort Across Serial GXTs.
* p <0.01

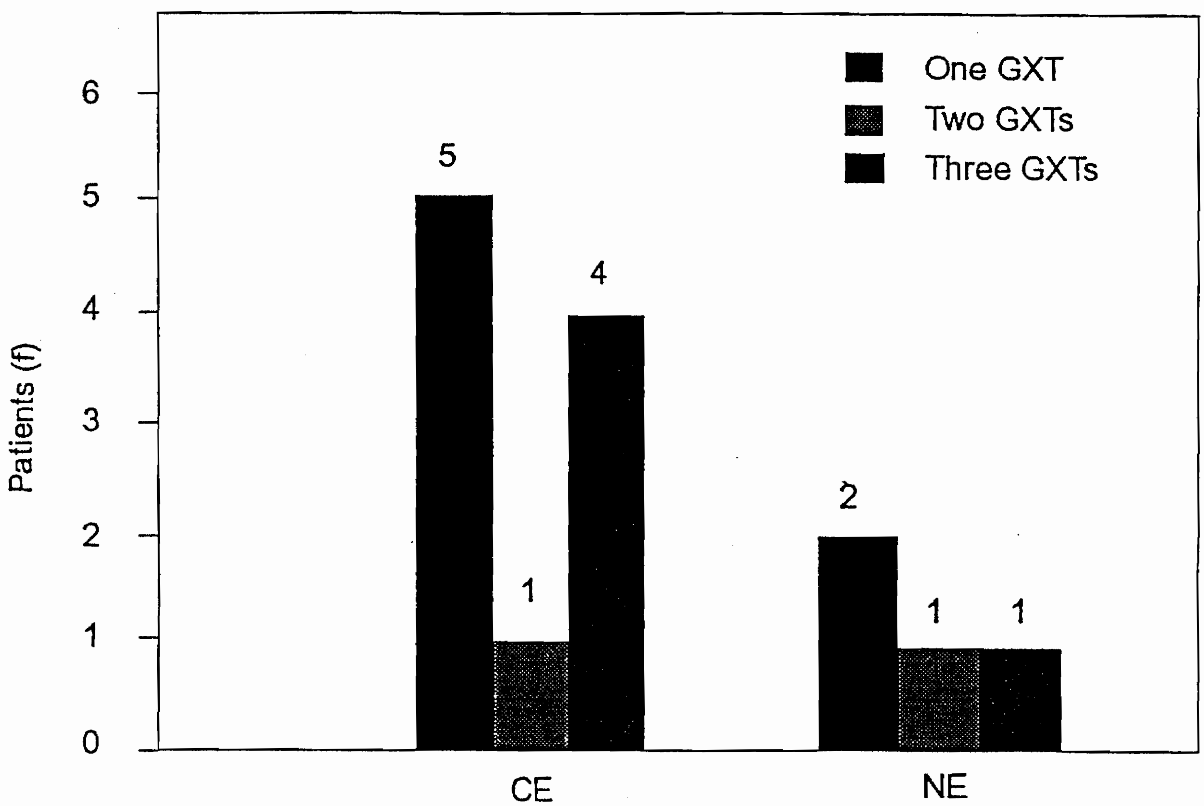


Figure 5: Frequency of Occurence in GXTs for Exercise-Induced Chest Discomfort

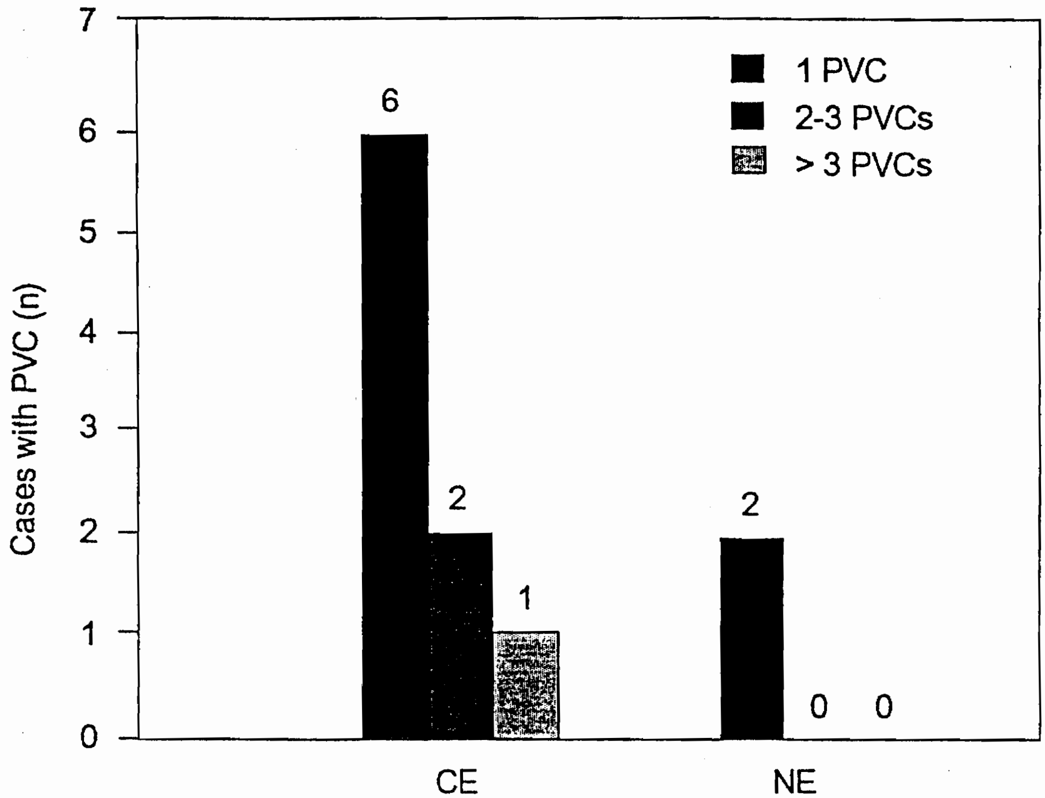


Figure 6: PVC Patterns in GXT3 During Exercise

CHAPTER 4

SUMMARY AND CONCLUSION

There are several clinical and exercise variables obtained from GXTs which yield important prognostic information in populations with moderate to severe CAD or early post-MI groups (Markiewicz et al. 1977). However, little research has been done to identify prognostic indicators obtained from GXTs within a population of stable physically active CAD patients.

The purpose of this study was to determine whether selected GXT variables that are known to have prognostic value in severe CAD and early post-MI patients also can determine risk of future cardiac events among stable CAD patients undergoing serial exercise testing and who are following exercise maintenance programs.

This study was retrospective in design, involving a sample of 46 male diagnosed CAD and post-MI patients from three collaborating cardiac rehabilitation centers. Data were obtained from patient files using serial results from three consecutive GXTs in those participants who had been active (>50% attendance) in a supervised exercise maintenance program. Records from a cardiac event (CE) participant, as defined by having either a MI, CABG, PTCA, or cardiac death, as endpoints were matched with records for a non-event (NE) participant so that matched pairs were established within each center. It is of concern that 13(59%) revascularization surgical patients were included in the event group which may have biased the results. The CE and NE subjects were matched according to selection criteria at the earliest of the three consecutive GXTs prior to the cardiac event. The CE and NE responses of ST depression, exercise-induced chest pain, the ST/HR index and ventricular ectopy, were collected from serial GXTs and evaluated statistically.

There was no statistical evidence that these GXT variables differed between these retrospectively matched groups. However, ST depression and angina were twice as prevalent in the event compared to non-event patients. Thus, ischemic signs and symptoms induced in exercise appear to be helpful in perodically screening clinical status in patients who participate in exercise maintenance programs. Perhaps, such testing may also help affirm decisions about the timing of coronary surgical intervention.

Recommendations for Future Research

The results of this investigation suggest certain priorities for future research projects. The following recommendations are offered:

1. Expand the sample size to include several more cardiac rehabilitation centers with large patient populations to increase the power of the statistical analyses;

2. evaluate other measures with global potential to assess critical status of the ischemic heart disease e.g. the Rate Pressure Product (RPP=HRxSBPx10) related change in ST-segment depression during exercise;

3. restrict clinical endpoint criteria to more objective endpoints such as angiographic confirmed CAD progression, MI or death;

4. further match observation periods between CE and NE groups to assure similar exercise prescription and training programs and GXT evaluation procedures;

5. evaluate the value improving discriminating power of the GXT responses by adding coronary risk factors such as cholesterol and smoking, as predictor variables.

Recommendations for Clinical Practice

Results from this study were consistent with physician's continuing to utilize serial GXTs in supporting clinical management decisions regarding the ischemic patient. Consistent exercise-induced ST-segment depression and angina manifestation may help identify subsets that increase surveillance and suggest more thorough assessments. Further investigation needs to be done with a larger population while attempting to devise new measures and more sensitive changes in cardiovascular status among physically active CAD patients.

REFERENCES

1. Ameisen, O., Okin, P.M., Devereux, R.B., Hochreiter, C. Miller, D.H., Zullo, M.A., Borer, J.S., and Kligfield, P. (1985) Predictive Value and Limitations of the ST/HR Slope. British Heart Journal, 53, 547-551.

2. American Association for Cardiovascular and Pulmonary Rehabilitation. Guidelines for Cardiac Rehabilitation Programs. 1991.

3. American College of Sports Medicine. Guidelines for Graded Exercise Testing and Prescription. 1991. 4th ed., Philadelphia, Lea and Febiger.

4. American Heart Association. (1992). Heart Facts. Dallas, Texas

5. American Heart Association (1990). Special Report on Exercise Standards. Circulation. 82:2286-2322.

6. Balady, G.J. & Weiner, D.A. (1991) Risk Stratification in Cardiac Rehabilitation. Journal of Cardiopulmonary Rehabilitation. 11:39-45.

7. Balcon, R., Brooks, N. and Layton, C. (1984) Correlation of Heart Rate/ST Slope and Coronary Angiographic Findings. British Heart Journal, 52:304-7.

8. Bigger, J.T. Jr., and Weld, F.M. (1981) Analysis of Prognostic significance of ventricular arrhythmias after myocardial infarction: Shortcomings of Lown grading system. British Heart Journal, 45: 717-24.

9. Boyle, R. M., Adiakha, H. L., and Mary, D.A.S.G. (1987) Diagnostic Value of the Maximal ST Segment/Heart Rate Slope in Asymptomatic Factory Populations. Journal of Electrocardiology. Suppl. Oct. 128-134.

10. Deckers, J.W., Rensing, B.J., Tijssen, J.G.P., Vinke, R.V.H., Azar, A.J., and Simmoons, M.L. (1989) A Comparison of Methods of Analysing Exercise Tests for Diagnosis of Coronary Artery Disease. British Heart Journal. 62:438-444.

11. Detry, J.M.R., & De Jonghe, D. (1987) Exercise Testing in the Evaluation of Ventricular Arrhythmias in Coronary Artery Disease. European Heart Journal. 8(Supplement D):55-59.

12. Froelicher, E.S. & Perdue, S.T. (1991) Clinical, Epidemiologic, and Statistical Methods Used in Prognostic Studies of Survivial After Myocardial Infarction. Journal of Cardiopulmonary Rehabilitation. 11:16-22.

13. Froelicher, V.F. Exercise and the Heart: Clinical Concepts, 2nd ed. Chicago Year Book Medical Publishers, Inc. 1987.

14. Gianrossi, R., Detrona, R., Mulvihill, D., Lehmann, K., Dubach, P., Colombo, A., McArthur, D., and Froelicher, V. (1989) Exercise-Induced ST Depression in the Diagnosis of Coronary Artery Disease: A Meta Analysis. Circulation. 80:87-98.

15. Gohlke, H., Gohlke-Barwolf, C., Samek, L., Sturzenofecker, P. Schmuziger, M., and Roskamm, H. 1983) Serial Exercise Testing Up to 6 Years After Coronary Bypass Surgery: Behavior of Exercise Parameters in Groups With Different Degrees of Revascularization Determined by Postoperative Angiography. The American Heart Journal, 51:1301-1306.

16. Gore, J. (1988) Dramatic Increase in Diagnositc Testing for MI Patients Reported. The Exercise Standards and Malpractice Reporter. Volume 2: 28.

17. Herbert, W.G., Dubach, P. Lehmann, K.G., and Forelicher, V.F. (1991) Effect of B-blockade on the Interpretation of the Exercise ECG: ST Level Versus Delta ST/HR Index. American Heart Journal. 122:993.

18. Kligfield, P., Ameisen, O., and Okin, P.M. (1987) Relation of the Exercise ST/HR Slope to Simple Heart Rate Adjustment of ST Segment Depression. Journal of Electrocardiology, Supplemental: 135-140.

19. Lachterman, B., Lehmann, K.G., Detrano, R. Neutel, J., and Froelicher, V.F. (1990) Comparison of ST Segment/Heart Rate Index to Standard ST Criteria for Analysis of Exercise Electrocardiogram. Circulation. 82:44-50.

20. Markiewicz, W., Houston, N., DeBusk, R.F., (1977) Exercise Testing Soon After Myocardial Infarction. Circulation, 56:26-31.

21. McHenry, P.L. (1985) Role of Exercise Testing in Predicting Sudden Death. Journal of American College of Cardiology, 5:9B-12B.

22. McNeer, J.F., Margolis, J.R., Lee, K.L., Kisslo, J.A., Peter, R.H., Kong, Y., Behar, V.S., Wallace, A.G., McCants, C.B., & Rosati, R.A. (1977) The Role of the Exercise Test in the Evaluation of Patients for Ischemic Heart Disease. Circulation,57:64-70.

23. Miranda, C. P., Herbert, W. G., Dubach, P. Lehmann, K.G., and Froelicher, V.F. (1991) Post-Myocardial Infarction Exercise Testing: Non-Q Wave Versus Q Wave Correlation With Coroanry Angiography and Long-term Prognosis. Circulation, 84:2357-2365.

24. Murray, D.P., Salih, M., Tan, L.B., Derry, S., Murray, R.G. and Littler, W.A. (1988) International Journal of Cardiology, 20:353-363.

25. Nair, C.K., Thomson, W., Aronow, W.S., Pagano, T., Ryschon, K., and Sketch, M.H. (1984) Prognostic Significance of Exercise-Induced Complex Ventricular Arrhythmias in Coronary Artery Disease with Normal and Abnormal Left Ventricular Ejection Fraction. The American Journal of Cardiology, 54. 1136-1138.

26. Okin, P.M., Kligfield, P., Ameisen, O., Goldberg, H.L. and Borer, J.S. (1985) Improved Accuracy of the Exercise Electrocardiogram: Identification of Three-Vessel Coronary Disease in Stable Angina Pectoris by Analysis of Peak Rate-Related Changes in ST Segments. The American Journal of Cardiology, 55: 271-276.

27. Okin, P.M., Kligfield, P., Ameisen, O., Goldberg, H.L., and Borer, J.S. (1988) Identification of Anatomically Extensive Coronary Artery Disease by the Exercise ECG ST Segment/Heart Rate Slope. American Heart Journal, 115. 1002-1012.

28. Okin, P.M., Kligfield, P., Milner, M.R., Goldstein, S.A., and Lindsay,Jr., J. (1988) Heart Rate Adjustment of ST-Segment Dpression for Reduction of False Positive Electrocardographic Responses to Exercise in Asymptomatic Men Screened for Coronary Artery Disease. The American Journal of Cardiology, 62:1043-1047.

29. Okin, P.M., Chen, J. and Kligfield, P. (1990) Effect of Baseline ST Segment Elevation on Test Performance of Standard and Heart Rate-Adjusted ST Segment Depression Criteria. American Heart Journal, 119:1280-1286.

30. Okin, P.M., Bergman, G. & Kligfield,P. (1991) Effect of ST Segment Measurement Point on Performance of Standard and Heart Rate-Adjusted ST Segment Criteria for the Identification of Coronary Artery Disease. Circulation, 84:57-66.

31. Sami. M.. Kraemer, H. & DeBusk. R.F. (1979) The Prognostic Significance of Serial Exercise Testing After Myocardial Infarction. Circulation. 60:1238-1246.

32. Sami, M., Chaitman. B., Fisher, L.. Holmes, D.. Fray, D.. and Alderman, E. (1984) Significance of Exercise-Induced Ventricular Arrhythmia in Stable Coronary Artery Disease: A Coronary Artery Surgery Study Project. American Journal of Cardiology. 54. 1182-1188.

33. Schechtman. K.B.. Capone. R.J.. Kleiger, R.E.. Gibson. R.S., Schwartz, D.J., Roberts. R., Young, P.M.. Boden, W.E.. and the Diltiazem Reinfarction Study Research Group. (1989) Circulation. 80:1148-1158.

34. Theroux. P.. Waters. D.D.. Halpien, C., Debaisieux. J.C., & Mizgala. H.F. (1979) Prognostic Value of Exercise Testing Soon After Myocardial Infarction. New England Journal of Medicine. 301:341-345.

35. Yang. J.C.. Wesley. R.C.. and Froelicher. V.F. (1991) Ventricular Tachycardia During Routine Treadmill Testing: Risks and Prognosis. Archives of Internal Medicine. 151:349-353.

36. Weiner, D.A.. Levine. S.R.. Klein, M.D. & Ryan. T.J. (1984) Ventricular Arrhythmias During Exercise Testing: Mechanism. Response to Coronary Bypass Surgery and Prognostic Significance. American Journal of Cardiology.53:1553-1557.

37. Zoler, Mithcell L. (1990) Exercise Tests: Detecting Asymptomatic CAD. Medical World News. 24-30.

38. ACC/AHA Task Force on Assessment of Cardiovacular Procedures.(1986) Report on Guidelines for Exercise Testing. Journal of American College of Cardiology, 8: 725-738.

APPENDIX A

DETAILED METHODOLOGY

This study was designed to assess graded exercise test (GXT) measures known to have prognostic importance for coronary artery disease (CAD) and post-myocardial infarction (MI) patients. The objective of this study was to differentiate risk levels for male patients with diagnosed CAD or post-MI, participating a supervised exercise maintenance program with three serial GXT evaluations, for rehospitalization due to a coronary event (MI, CABG, PCTA, CATH, or death). Screening information and selection criteria for entering subjects are presented in the following sections. Assignment of subjects to experimental groups, choice of dependant measures, and the statistical analyses of the dependant measures are also included.

Subjects

The data for the study was obtained from only three cardiac rehabilitation centers. These centers were selected due to their standardized GXT procedures and patient participation. The centers are:

Virginia Polytechnic Institute & State University
Blacksburg, Virginia 24060

Wake Forest Unviersity
Winston-Salem, North Carolina 27109

Glen Frye Regional Hospital
Hickory, North Carolina 28601

Selection of Subjects

There were 46 cardiac event (CE) and non-event (NE) subjects chosen based upon the selection criteria (appendix B). The cardiac event subjects were categorized as having been hospitalized for a coronary event within 12 months following three serial GXTs while participating in a supervised exercise maintenance program. The NE subjects were categorized as not having been hospitalized following the three serial GXTs while participating in the supervised exercise maintenance program. Appropriate subjects were also selected on the quality of the GXT results and continuous attendance (>50%) in the exercise maintnance program.

The CE subject and matched counterpart, the NE subject, were chosen from the same cardiac center and corresponding time period. The CE and NE subjects on cardiac medications were closely matched to further normalize the data to control for medication affects during exercise. CE and NE smokers were also taken into consideration to enhance normalization.

The following selection criteria was applied to the design of the study to screen patients files before data entry: male gender; age >71 yrs; absence of digitalis therapy; were not obese (body mass index ≤40), a mild to moderate risk of increased mortality; and attainment of the near-maximal endpoints in the three serial GXTs (R=1.00 and/or RPE=17).

Exclusion of subjects due to age gender, and digitalis therapy were based on the recommendations by Froelicher (1979). The BMI index was based on a relationship with overall mortality (Grundy, Greenland, Herd, Huesbach, Jones, Mithcell, and Schlant, 1987). The numerical range was based on life insurance statistics, which does not define causes of death. However, the American Heart Association speculates the marked increase in risk of death is probably due to cardiovascular disease. For subjects on medications such as beta blockers or calcium channel blockers, the attainment of a near maximal end point was validated by utilizing ratings of perceived exertion (RPE) and the respiratory exchange ratio (R). Data collection was through the investigators and on-site assistants.

<u>Graded Exercise Test Procedures at the Cardiac Centers</u>

The cardiac centers selected for this study have met the following requirements:

a. upon entry into the supervised exercise maintenance program, each subject was evaluated through an initial GXT;

b. serial GXT testing occurred at $\leq$12 month interval;

c. patients were assessed for height and weight at the time of the GXT;

d. the GXTs were performed on a motor driven treadmill using a modified Balke or similar protocol, intensity increased by approximately 1-3 METS every 2-3 minutes;

e. resting measures were recorded in a supine position, such as heart rate and blood pressure;

f. a multiple lead ECG, heart rate and blood pressure were obtained and recorded during each stage;

g. signs and symptoms of exertion were recorded during each stage;

h. recovery heart rate and blood pressure were taken in a supine position immediate post exercise (IPE);

i. GXT termination criteria were based on onset of signs and symptoms, appearance of abnormal ECG recordings established by the American College of Sports Medicine Guidelines (1986), or the attainment of the near maximal end point.

j. a physician was present for all GXTs;

k. final interpretation of the results were by the physician.

Cardiac Rehabilitation Center Exercise Protocol

The exercise rehabilitation sites follow this or a similar exercise protocol:

1. A 10 minute stretch warm-up;

2. a 20-30 minute cardiovascular (aerobic) session at assigned individualized target heart rate zone;

3. a single or combination of an aerobic mode of exercise ie., walking, jogging, cycling, or swimming;

4. a 10 minute active cool-down relaxation period.

Exercise sessions were conducted at least three times per week. Resting heart rate and blood pressure were recorded prior to each exercise bout. Periodic and continuous ECG monitoring was conducted throughout the aerobic session.

Data Collection

The following independent and dependent measures were collected and assessed in this study.

Independent Measures

Subject I.D.- each subject was identified by a number and code from the specific rehabilitation center.

Type of Subject - recorded as either cardiac event (CE) and non-event (NE).

Type of Cardiac Event - defined as myocardial infarction (MI), anatomic location of, whether death or survival; angiography finding, number of vessels involved, ejection fraction; coronary artery by-pass surgery (CABG), number of vessels involved; and percutaneous transluminal angioplasty (PCTA).

Patient Medical History - included initial entry diagnosis and summary of physician's hospital discharge diagnosis if warranted.

Graded Exercise Test Intervals - recorded time in exercise program before GXT(1); time between GXT(1) and GXT(2); time between GXT(2) and GXT(3); and time between GXT(3) and the cardiac event.

Initial GXT and Date - the exercise test performed at the time of entry into the supervised exercise maintenance program. Date recorded as month/day/year.

GXT(1) and Date - the earliest of three consecutive GXTs prior to the date of rehospitalization and the coronary event for the CE subject; for the NE subject, this is the first of three consecutive GXTs corresponding to the CE subjects GXT(1). Date recorded as month/day/year.

GXT(2) and Date - the second of the three consecutive GXTs prior to the date of rehospitalization and the coronary event performed 6-12 months +/-1 months following GXT(1); for the NE subject, this is the second GXT also performed 6-12 months +/- 1 month following GXT(1). Date recorded as month/day/year.

GXT(3) and Date - the final GXT of the three consecutive GXTs prior to rehospitalization and the coronary event performed 6-12 months +/-1 month following GXT(2); for the NE subject, this is also the final GXT performed 6-12 months +/-1 month following GXT(3). Date recorded as month/day/year.

Coronary Heart Disease Risk Factors - information on the

following risk factors were collected:

a. serum cholesterol and sub-fractions HDL and LDL were recorded.

b. smoking history, type of tobacco, # of cigarettes packs per year, and # of years of use.

c. hypertension history, how long have been diagnosed, and blodd pressure reading at time of hospitalization.

d. body mass index (BMI), at the time of GXT(1).

e. family history of premature CAD, # of family members, relationship to, and age of diagnosis or cardiac death.

Age - age was recorded at the time of each GXT.

Measured Peak Oxygen Consumption (VO2) - defined as the highest measured oxygen uptake in the GXT, taken from the last stage in which at least 1 minute of exercise was completed. (+/- 1 ml/kg/min)

R Exchange - defined as the ratio of carbon dioxide expired to oxygen consumption in the minute at which peak VO2 was measured.

Treadmill Protocol - recorded as the name of the protocol utilized for each test. Protocols were copied and are included in the appendix.

Rating of Perceived Exertion (RPE) - based on the Borg Scale, a numerical grading system in which the corresponding number to the perception of exertion is chosen by the patient.

Signs and Symptoms - exercise-induced symptoms suggestive of acute cardiovascular dysfunction during exercise in the GXT, chest discomfort, claudication, dyspnea on a scale of +1-4.

Medications - current medications, dosages and frequencies were recorded.

Dependent Measures

Heart Rate Maximum (HRpk) - highest measured heart rate during the last minute of exercise or immediately post-exercise, recorded from the ECG (+/-1 b min-1).

ST Segment Deviation Maximum (STdevmax) - maximum ST-segment deviation (+/-0.01mV) averaged for three succesive ECG complexes at a reference point of 0.08 sec after the J-point, using the horizontal level of the PQ junction for threee consecutive complexes as the reference isoelectric baseline.

ST/HR Slope - the maximum ST-segment deviation from the same lead and maximum heart rate for the last three stages of exercise are utilized to compute a slope using linear regression analysis. Intermediate data points are entered into the linear regression analysis to determine a significant slope (<0.05). The highest slope value with a significant correlation coefficient will be used as the slope value for that test.

Delta St/HR Slope - calculated by dividing the maximal ST Segment depression at end exercise (as above) by the exercise-induced change in heart rate.

Dysrhythmias - documented from the ECG as ventricular ectopic beats (PVCs), and graded by the Lown's classification: No PVC = 0; occassional, isolated PVCs = 1; frequent (more than 30/hr) = 2; mulitform PVCs = 3; repetitive (couplets) = 4; and early (abutting or interrupting the T wave) = 5.

Statistical Analysis

Descriptive statistics were computed for key characteristics of the two patient subgroups and dependent t-tests were used to examine relevant variables. For analysis of exercise responses, either analysis of variance or Chi-square were used to evaluate responses between groups or serially across the three GXTs; selection of method depended upon the scaling properties of the measure.

DATA COLLECTION INSTRUCTIONS

The following instructions need to be followed in order to provide proper data collection. The patient selection criteria will be listed in Stage One to ensure only viable patients are considered. Stage Two will consist of the independent and dependent measures needed for the study.

Before beginning the data recording, please put the name of the recorder, site, and date the data was collected.

If problems or questions arise, please call Vernon Baker (703)552-4419 or Sharon Bruce (816)455-4195. Both can be left a message at (703)231-5006.

STAGE ONE

Stage one contains the selection criteria for all possible subjects. Completion of stage one will ensure proper subject selection for this study. Several key directions must be followed in order to minimize the time requirement and compare subjects as specified. These are:

1. Subjects must meet all the selection criteria. If any of the criteria are not met, stop the selection process, subject cannot be used for the study.

2. Record data for all of the cardiac event subjects first, then record data for all of the non-event subjects. This will allow for subjects (CE & NE) to be easily compared.

3. CE event subjects must be compared with NE subjects having the same entry Dx and tests from the same GXT testing period.

Example: Both CE and NE were Dx CAD upon entry. The cardiac event subject was rehospitalized with a coronary event or intervention (MI, CABG, PCTA, or Death). GXT(1) for the CE subject must be 3 GXTs prior to the rehospitalization. GXT(1) for the NE subject must be within ± 1 month of the CE's GXT(1).

4. Data such as BMI, age, periods between GXTs, and absence of digitalis therapy must be taken from NE subjects GXT(1), which is determined by the CE subjects GXT(1).

SELECTION CRITERIA

Sex - All subjects must be male.

Subject I.D. - The subject's identification code must be recorded on every form. This code provides for identification of program site, grouping (CE or NE), and subject number.

Entry Diagnosis and Date - defined as myocardial infarction (MI), or coronary artery disease (CAD) from the patient's referring physician form. Date recorded as month/year.

Category - Cardiac event (CE) or non-event (NE) based on whether the subject has been rehospitalized for a coronary intervention or event (CABG, PCTA, MI, or cardiac death). Cardiac death subjects must have died due to coronary disease or complications thereof.

Type of Cardiac Event and Date - Recorded as the physician's primary diagnosis after rehospitalization: (CABG), noting the severity i.e., 1+ or 2+ vessel and reasons for the surgical intervention, (PCTA), (MI), or death (D) and date (month/day/year) at which the event occurred.

Absence of Digitalis Therapy - The 3 GXTs prior to the cardiac event for the CE subject must be without digitalis as well as the corresponding GXTs for the NE subject.

Age - Subjects must be between the ages of 35-70 years of age during the GXTs that are to be used for study. At each program site, select all CE subjects first, then compute mean age for CE group before selecting comparably aged NE group.

Body Mass Index (BMI) - Weight/height index, weight will be classified in kilograms ($\pm$ 0.1 kg), and height in meters ($\pm$ 0.1 m). BMI is calculated by dividing height (meters squared) into weight (wt/ht^2). Range $\leq$ 40, high moderate CAD risk.

Period Before GXT(1) - Subject must have been in the rehabilitative exercise program for at least 3 months.

Period Between GXTs - Months between GXT(1)-GXT(2), GXT(2)-GXT(3) and the period between GXT(3) and the cardiac event must be $\leq$ 13 months.

End of Selection Criteria

Beginning of Stage Two

1. The three GXT data collection forms follow the same format. The forms will be labeled GXT(1), GXT(2), and GXT(3).

2. After you have read the instructions for each GXT measure, find the necessary data from the patient's file, and record in the space provided on the data collection form.

DATA CATEGORIES

Subject I.D. - The subject's identification code.

Category - Cardiac event (CE) or non-event (NE) based on whether the subject has been rehospitalized for a coronary intervention or event (CABG, PCTA, MI, or Cardiac Death).

Type of Event - Record the type of event in the space provided.

Initial GXT - Date of the initial GXT upon entry into the rehabilitative exercise program or hospital based test. Date will need to be recorded month-day-year.

Ejection Fraction - The percentage of total ventricular volume that is ejected during each contraction, that is, stroke volume divided by end-diastolic volume.

GXT(1) and Date - The earliest of three consecutive GXTs prior to the date of the CE; for NE subjects this is the first of three GXTs which corresponds to approximately the same calendar month-year (± 1 month). Date recorded as month-day-year.

NOTE: Spaces for the dates of GXT(2) and GXT(3) will be on the GXT(2) and GXT(3) forms, respectively.

GXT(2) and Date - The second of the three consecutive GXTs, given prior to the date of the CE, and also given $\leq$ 13 months after GXT(1); for NE subjects this is the second of the three GXTs which corresponds to approximately the same calendar month-year (± 1 month) as the CE subject. Date recorded as month-day-year.

GXT(3) and Date - The last of three consecutive GXTs prior to the date of the CE, and also given ≤ 13 months after GXT(2). For NE subjects record the last of the three GXTs which corresponds to approximately the same calendar month-year (± 1 month). Date recorded as month-day-year.

Age - Record subject's age in years at time of GXT.

Weight - Record the subject's weight (± 0.1 kg) at time of GXT.

Height - Record the subject's height (± 0.1 m) at time of GXT.

Stage 2 VO_2 - Oxygen consumption at stage 2 of GXT.

VO_{2pk} - Record the peak volume of oxygen consumption during the last stage of exercise in which at least one minute of exercise was completed (± 0.1 ml/kg/min). Record whether the measurement was measured or estimated.

R Exchange - Record the ratio of carbon dioxide expired to oxygen consumption at the minute that VO_{2pk} was measured (± 0.1 units).

Exercise Test Protocol - Record the specific name of the treadmill protocol used for each of the three GXTs.

Blood Pressure Rest - Record the systolic and diastolic measures (± 2 mmHg) taken in a supine position before the given GXT.

Blood Pressure Peak - Record the systolic and diastolic measures (± 2 mmHg) taken during the last minute of exercise or immediately following (IPE) exercise.

Heart Rate Rest - HR taken in the pre-GXT baseline posture, record from the resting ECG (± 1 $b \cdot min^{-1}$).

Heart Rate Peak - Highest measured HR during the last minute of exercise or immediately following (IPE) exercise, record from the ECG (± 1 $b \cdot min^{-1}$).

Dysrhythmias - Dysrhythmias documented from ECG as ventricular ectopic beats (PVCs), and graded by Lown's classification: No PVC = 0; occasional, isolated PVCs = 1; frequent (more than 30/hr) = 2; multiform PVCs = 3; repetitive (couplets) = 4; and early (abutting or interrupting) = 5. Record the physician's statement as well as the corresponding numeral.

Medications - List the dosages of medications and frequencies used at the time of the respective GXT.

Stage - Record each stage or workload the subject attained during the GXT. Record as workload I, II, etc.

Treadmill Speed and Grade Percentage - Record the peak speed (mph) and grade (%) the subject achieved during each stage of the GXT. The completion of one minute at the speed and grade will determine the peak level achieved.

Exercise Heart Rate - Record the maximum heart rate for each stage, measured the last 30 secs of each stage ($\pm$ 1 $b \cdot min^{-1}$).

Exercise Blood Pressure - Record the BP measured during the last minute of each stage ($\pm$ 2 mmHg).

Rating of Perceived Exertion - Record the RPE utilizing the Borg scale of perceived exertion in the final stage of exercise.

ST Segment Deviation (STdevmax) - Maximum ST-segment deviation ($\pm$ 0.01 mV), averaged for three successive ECG complexes at a reference point 0.08 sec after the J-point, using the horizontal level of the PQ junction for three consecutive complexes as the reference isoelectric baseline.

Record STdevmax as follows:

*The max ST segment deviation will be recorded for each workload, utilizing all leads as possible references. The lead in which the max ST segment deviation is found will need to be the reference lead for the entire test. Example: ST Depression 0.2 mV in V_5.

**Please photocopy the ECG strip from the resting and peak stage with the maximum ST deviation.

Signs and Symptoms - Record all exercise-induced symptoms suggestive of acute cardiovascular dysfunction at peak exercise in the GXT, i.e., chest discomfort, claudication, dyspnea (scale +1 - +4). Please record the symptom along with the scale number.

GXT - CARDIAC EVENT STUDY

DATA RECORDING FORM

Subject I.D. ________________________________

(Site) (CE/NE) (S#)

<u>Disqualifying Criteria</u>

____ female

____ age > 71 years

____ digitalis therapy

____ formal exercise < 3 months before GXT_1

____ < 3 GXTs completed after therapeutic program, with test intervals > 13 months

____ BMI ≥ 40

1. Type of Subject: ____CE ____NE

2. Type of Cardiac Event (if CE)

   a. Diagnosis/Autopsy Result

      ____ MI ______________________ Anatomic Location

      ____ Death ____ Survival

   b. Angiography Finding & Date: ____

      (Describe vessels involved and severity of disease): ______________________

      ____

      ____

      ____ %EF, if available

   c. Other Types of Events:

   ____ CABG, Date: __________

   ____ PCTA, Date: __________

Subject I.D. ______________________

(Site) (CE/NE) (S#)

3. Summary of Patient Medical History (Overview of important factors, secondary diagnosis, etc.)

   Initial Cardiac Diagnosis: ______________________ Date: __________

   Summary: ______________________

   ____

   ____

   ____

   ____

4. GXT Intervals

   a. Time in exercise before GXT_1: ____ months

   b. Time between GXT_1 and GXT_2: ____ months

   c. Time between GXT_2 and GXT_3: ____ months

   d. Time between GXT_3 and CE: ____ months

5. CHD Risk Factors

   a. Serum Cholesterol: _____ mg/dl

   b. HDL Cholesterol: _____ mg/dl

   c. LDL Cholesterol: _____ mg/dl

   d. Smoking History: Smoker: Y/N

      Form of Tobacco: ______________________

      # cigarettes/day, if applicable: _____

      # years of use: _____

   e. History of High Blood Pressure: Y/N

      How Long: ____ months

      BP @ Diagnosis: ____/____ mmHg

   f. Overweight: Body Mass Index @ GXT_1: _____

   g. Family History of Premature CAD:

Family Members	Age @ Diagnosis/Cardiac Death
______________	_____
______________	_____
______________	_____
______________	_____

SITE – ____________________

DATE – __________

RECORD ADMINISTER – ____________________

SUBJECT I.D.: ____________________ INITIAL GXT DATE: __________

(SITE) (CE/NE) (S #)

GXT(1) DATE: ________ AGE(yr): ____ WT.(kg): ____ HT.(m): ____ STAGE 2 VO2: ________

VO2pk(est./meas.): ________ R EXCHANGE: ____ PROTOCOL: __________

BP REST: ____ BP PEAK: ____ HR REST: ____ HR PEAK: ____ DYSRHYTHMIAS: ______________

CURRENT MEDICATIONS(type & dose): ______________________________

EXERCISE

STAGE	METS	MPH/GRADE%	MIN	HR	BP	RPE	LEAD: ____ ST DEV MAX	SIGNS/SYMPTOMS
		/			/			
		/			/			
		/			/			
		/			/			
		/			/			
		/			/			
		/			/			
		/			/			
		/			/			
		/			/			
		/			/			
		/			/			

SITE – ____________

DATE – ____________

RECORD ADMINISTER – ____________

SUBJECT I.D.: ____________
(SITE) (CE/NE) (S #)

GXT(2) DATE: ______ AGE(yr): ____ WT.(kg): ____ HT.(m): ____ STAGE 2 VO2: ______

VO2pk(est./meas.): ______ R EXCHANGE: ____ PROTOCOL: ______

BP REST: ____ BP PEAK: ____ HR REST: ____ HR PEAK: ____ DYSRHYTHMIAS: ______

CURRENT MEDICATIONS(type & dose): ____________

EXERCISE

STAGE	METS	MPH/GRADE%	MIN	HR	BP	RPE	LEAD: ____ ST DEV MAX	SIGNS/SYMPTOMS
		/			/			
		/			/			
		/			/			
		/			/			
		/			/			
		/			/			
		/			/			
		/			/			
		/			/			
		/			/			
		/			/			
		/			/			

SITE – ______________________

DATE – __________

RECORD ADMINISTER – ______________________

SUBJECT I.D.: ______________________

(SITE) (CE/NE) (S #)

GXT(3) DATE: ________ AGE(yr): ____ WT.(kg): ____ HT.(m): ____ STAGE 2 VO2: ________

VO2pk(est./meas.): ________ R EXCHANGE: ____ PROTOCOL: __________

BP REST: ____ BP PEAK: ____ HR REST: ____ HR PEAK: ____ DYSRHYTHMIAS: ______________

CURRENT MEDICATIONS(type & dose): ______________________________

EXERCISE

STAGE	METS	MPH/GRADE%	MIN	HR	BP	RPE	LEAD: ____ ST DEV MAX	SIGNS/SYMPTOMS
		/			/			
		/			/			
		/			/			
		/			/			
		/			/			
		/			/			
		/			/			
		/			/			
		/			/			
		/			/			
		/			/			
		/			/			

3		EVENT	GXT	HRDIFF	SBPDIFF	VO2PEAK	
3Row 1	1		1	35	22	18.8	
3Row 2		0	1	55	52	19.9	
3Row 3		1	1	81	36	29.6	
3Row 4		0	1	55	40	33.3	
3Row 5		1	1	83	32	38.6	
3Row 6		0	1	95	30	40.4	
3Row 7		1	1	76	40	25.7	
3Row 8		0	1	89	48	29.9	
3Row 9		1	1	50	20	17.6	
3Row 10		0	1	55	42	19.4	
3Row 11		1	1	98	46	24	
3Row 12		0	1	58	50	25	
3Row 13		1	1	55	34	22.5	
3Row 14	0		1	73	54	29.4	
3Row 15		1	1	36	34	22.4	
3Row 16		0	1	69	42	25.2	
3Row 17		1	1	52	30	33.3	
3Row 18		0	1	37	10	18.9	
3Row 19		1	1	74	54	22.7	
3Row 20		0	1	49	32	20.8	
3Row 21		1	1	54	22	33.3	
3Row 22		0	1	100	51	23.1	
3Row 23		1	1	112	64	32.8	
3Row 24		0	1	109	50	30.4	
3Row 25		1	1	62	34	35.4	
3Row 26		0	1	82	84	30.8	
3Row 27	1		1	34	-26	22.4	3
3Row 28		0	1	77	14	25.9	3
3Row 29		1	1	85	104	33.3	3
3Row 30		0	1	106	75	35.7	3
3Row 31		1	1	75	64	25.5	3
3Row 32		0	1	82	24	36.4	3
3Row 33		1	1	100	38	23.5	3
3Row 34		0	1	50	48	33.6	3
3Row 35		1	1	98	58	44.3	3
3Row 36		0	1	107	42	38.9	3
3Row 37		1	1	65	84	15.7	3
3Row 38		0	1	78	20	18.7	3
3Row 39		1	1	45	-6	18.9	3
3Row 40	0		1	46	0	39	3
3Row 41		1	1	92	24	18.4	3
3Row 42		0	1	91	30	22.3	3
3Row 43		1	1	62	30	23.6	3
3Row 44		0	1	61	20	12.5	3
3Row 45		1	1	87	40	28	3
3Row 46		0	1	78	44	39.6	3
3Row 47		1	2	49	56	25.2	3
3Row 48		0	2	65	70	33.3	3
3Row 49		1	2	107	64	27.7	3
3Row 50		0	2	62	46	29.6	3
3Row 51		1	2	82	38	37	3
3Row 52		0	2	93	44	40.3	3
3Row 53	1		2	71	40	28.8	3
3Row 54		0	2	100	60	27	3
3Row 55		1	2	50	42	21.2	3
3Row 56		0	2	46	30	17.3	3
3Row 57		1	2	78	36	24.7	3
3Row 58		0	2	63	46	32.9	3
3Row 59		1	2	40	7	29.8	3
3Row 60		0	2	85	88	30.3	3
3Row 61		1	2	70	-22	22.4	3
3Row 62		0	2	57	36	29.8	3
3Row 63		1	2	49	38	20	3
3Row 64		0	2	46	10	21	3
3Row 65		1	2	69	22	25.2	3

		EVENT	GXT	HRDIFF	SBPDIFF	VO2PEAK
JRow 66	0		2	55	32	20.9
JRow 67		1	2	70	30	33.5
JRow 68		0	2	97	46	29
JRow 69		1	2	95	70	28.3
JRow 70		0	2	110	84	28.3
JRow 71		1	2	53	30	21
JRow 72		0	2	82	52	45.5
JRow 73		1	2	47	-16	25.1
JRow 74		0	2	91	32	26.6
JRow 75		1	2	85	98	31.2
JRow 76		0	2	114	92	35
JRow 77		1	2	88	110	35
JRow 78		0	2	85	40	60.2
JRow 79	1		2	90	62	20
JRow 80		0	2	62	80	25.9
JRow 81		1	2	58	32	36.1
JRow 82		0	2	119	70	22.1
JRow 83		1	2	57	70	25.9
JRow 84		0	2	85	14	11.6
JRow 85		1	2	48	2	19.9
JRow 86		0	2	43	6	22.4
JRow 87		1	2	86	30	20.1
JRow 88		0	2	89	20	25.4
JRow 89		1	2	61	30	24.3
JRow 90		0	2	61	20	15
JRow 91		1	2	88	56	31.8
JRow 92	0		2	78	44	39.6
JRow 93		1	3	45	44	19
JRow 94		0	3	53	20	18.8
JRow 95		1	3	75	28	31.9
JRow 96		0	3	54	36	33.3
JRow 97		1	3	90	50	32.8
JRow 98		0	3	96	68	47.6
JRow 99		1	3	72	40	24.5
JRow 100		0	3	92	44	23.7
JRow 101		1	3	39	18	16.6
JRow 102		0	3	50	34	20.2
JRow 131	1		3	45	14	7.1
JRow 132		0	3	44	38	18.6
JRow 133		1	3	63	36	17.8
JRow 134		0	3	94	80	24.7
JRow 135		1	3	61	30	23.7
JRow 136		0	3	28	8	13.6
JRow 137		1	3	76	30	23.1
JRow 138		0	3	85	36	39.6

3	ST/HR	STDEP	PVC	ANGINA	HRREST	3
3Row 1	6.6	.2	0	1	66	3
3Row 2	5.5	.1	0	1	58	3
3Row 3	0	0	0	0	69	3
3Row 4	6.4	.15	0	0	69	3
3Row 5	6.8	.3	0	0	45	3
3Row 6	0	0	0	0	65	3
3Row 7	5.3	.15	0	0	54	3
3Row 8	0	0	1	0	84	3
3Row 9	15.1	.4	0	1	78	3
3Row 10	0	0	0	0	46	3
3Row 11	2.9	.2	0	0	57	3
3Row 12	4	.15	1	1	58	3
3Row 13	11.7	.2	0	1	57	3
3Row 14	9	0	0	0	77	3
3Row 15	0	0	0	0	60	3
3Row 16	3.9	.15	0	0	49	3
3Row 17	6.3	.15	0	1	67	3
3Row 18	13.7	.25	0	0	55	3
3Row 19	4.2	.15	0	0	58	3
3Row 20	0	0	0	0	74	3
3Row 21	1.6	.1	3	0	54	3
3Row 22	1.4	.1	0	0	60	3
3Row 23	2.2	.2	1	0	63	3
3Row 24	1.3	.1	0	0	58	3
3Row 25	8.4	.4	0	0	48	3
3Row 26	2.9	.15	0	0	54	3
3Row 27	2.5	.15	0	0	65	3
3Row 28	5	.35	0	0	75	3
3Row 29	2.4	.2	0	0	75	3
3Row 30	3.4	.2	0	0	60	3
3Row 31	3.7	.1	0	0	50	3
3Row 32	0	0	0	0	68	3
3Row 33	1.8	.15	1	0	65	3
3Row 34	3.7	.2	4	0	75	3
3Row 35	0	0	0	0	68	3
3Row 36	0	0	0	0	64	3
3Row 37	3.8	.15	0	0	60	3
3Row 38	2.9	.1	0	0	74	3
3Row 39	4.5	.1	0	1	57	3
3Row 40	4.3	.15	0	0	43	3
3Row 41	10	.4	1	0	68	3
3Row 42	.85	.05	0	0	72	3
3Row 43	0	0	1	0	55	3
3Row 44	0	0	0	0	62	3
3Row 45	3.5	.1	1	1	68	3
3Row 46	0	0	0	0	67	3
3Row 47	13.8	.3	0	1	58	3
3Row 48	1.5	.05	0	1	63	3
3Row 49	0	0	0	0	44	3
3Row 50	4.8	.15	0	0	58	3
3Row 51	7.8	.3	0	0	47	3
3Row 52	0	0	0	0	72	3
3Row 53	4.1	.15	1	0	64	3
3Row 55	17.5	.45	0	0	72	3
3Row 56	0	0	0	0	46	3
3Row 57	2.8	.15	0	0	74	3
3Row 58	4.4	.1	0	0	54	3
3Row 59	5.9	.175	0	0	60	3
3Row 60	0	0	0	0	66	3
3Row 61	0	0	1	0	58	3
3Row 62	0	0	0	0	55	3
3Row 63	0	0	0	1	66	3
3Row 64	10.8	.3	0	0	48	3
3Row 65	1.4	.05	0	0	61	3

3	ST/HR	STDEP	PVC	ANGINA	HRREST	3
3Row 66	0	0	0	0	71	3
3Row 67	0	0	0	0	50	3
3Row 68	1.4	.05	0	1	68	3
3Row 69	6.4	.2	1	0	65	3
3Row 70	0	0	0	0	55	3
3Row 71	9.3	.35	0	0	62	3
3Row 72	4.1	.2	1	0	54	3
3Row 73	3.7	.2	0	0	47	3
3Row 74	3.3	.3	1	0	69	3
3Row 75	2.4	.2	0	0	75	3
3Row 76	2.1	.2	0	0	52	3
3Row 77	1.6	.1	0	0	57	3
3Row 78	0	0	0	0	74	3
3Row 79	2.6	.15	0	0	70	3
3Row 80	3.3	.15	0	0	48	3
3Row 81	0	0	0	0	108	3
3Row 82	0	0	1	0	48	3
3Row 83	5.5	.15	0	0	55	3
3Row 84	1.5	.1	0	0	75	3
3Row 85	7.1	.15	0	1	56	3
3Row 86	12.4	.2	0	0	40	3
3Row 87	2.7	.2	1	0	74	3
3Row 88	0	0	1	0	82	3
3Row 89	0	0	0	0	66	3
3Row 90	0	0	1	0	69	3
3Row 91	3.?	.2	1	1	79	3
3Row 92	0	0	0	1	57	3
3Row 93	7	.2	0	1	56	3
3Row 94	0	0	0	1	53	3
3Row 95	1.8	.1	0	0	61	3
3Row 96	4	.1	0	0	62	3
3Row 97	6.5	.35	1	0	50	3
3Row 98	0	0	0	0	74	3
3Row 99	12.2	.15	1	0	50	3
3Row 100	1.2	.05	0	0	74	3
3Row 101	10.1	.3	0	0	80	3
3Row 102	0	0	0	1	46	3
3Row 103	4.4	.2	0	1	54	3
3Row 104	4	.2	0	0	63	3
3Row 105	8.4	.2	0	1	62	3
3Row 106	0	0	0	0	70	3
3Row 107	0	0	4	0	58	3
3Row 108	1.4	.05	0	0	50	3
3Row 109	0	0	0	1	60	3
3Row 110	14.8	.25	0	1	52	3
3Row 111	3.4	.25	3	0	80	3
3Row 112	0	0	0	0	65	3
3Row 113	2.9	.1	3	1	51	3
3Row 114	0	0	0	0	60	3
3Row 115	12.9	.4	1	0	69	3
3Row 116	0	0	0	0	53	3
3Row 117	2.7	.2	0	0	58	3
3Row 122	2.4	.2	0	0	54	3
3Row 123	2.6	.15	0	0	59	3
3Row 124	1	.075	0	0	75	3
3Row 125	5	.1	1	0	71	3
3Row 126	2.3	.2	0	0	42	3
3Row 127	0	0	0	0	70	3
3Row 128	0	0	0	0	64	3
3Row 129	5.3	.15	0	1	50	3
3Row 130	17.9	.15	0	0	71	3
3Row 131	2	.05	0	1	57	3
3Row 132	6.5	.2	0	0	42	3
3Row 133	2.5	.15	1	0	84	3
3Row 134	1.6	.1	0	0	81	3
3Row 135	0	0	1	0	66	3
3Row 136	0	0	1	0	58	3
3Row 137	2.8	.1	0	1	79	3
3Row 138	0	0	0	1	65	3

3	HRPEAK	SBPREST	DBPREST	SBPPEAK	DBPPEAK	3
3Row 1	101	134	92	156 90		3
3Row 2	113	130	84	182	96	3
3Row 3	150	120	74	156	78	3
3Row 4	124	112	70	152	70	3
3Row 5	128	130	90	162	90	3
3Row 6	160	120	70	150	86	3
3Row 7	130	130	74	170	88	3
3Row 8	173	108	72	156	80	3
3Row 9	128	132	92	152	104	3
3Row 10	101	124	88	166	94	3
3Row 11	155	112	68	158	70	3
3Row 12	116	118	70	168	78	3
3Row 13	112	130	80	164	88	3
3Row 14 150		118	78	172	88	3
3Row 15	96	148	80	182	76	3
3Row 16	118	130	90	172	94	3
3Row 17	119	144	82	174	86	3
3Row 18	92	118	82	128	86	3
3Row 19	132	122	80	176	94	3
3Row 20	123	140	92	172	94	3
3Row 21	108	104	64	126	64	3
3Row 22	160	119	76	170	84	3
3Row 23	175	116	82	180	86	3
3Row 24	167	130	82	180	80	3
3Row 25	110	124	72	158	92	3
3Row 26	136	112	64	196	80	3
3Row 27 99		126	94	100	70	3
3Row 28	152	116	78	130	80	3
3Row 29	160	138	88	242	70	3
3Row 30	166	123	72	198	80	3
3Row 31	125	106	74	170	90	3
3Row 32	150	174	110	198	96	3
3Row 33	165	128	84	166	84	3
3Row 34	125	116	72	164	76	3
3Row 35	166	124	72	182	90	3
3Row 36	171	112	72	154	66	3
3Row 37	125	98	72	182	72	3
3Row 38	152	130	94	150	84	3
3Row 39	102	124	84	118	74	3
3Row 40 89		140	78	140	74	3
3Row 41	160	120	80	144	88	3
3Row 42	163	110	80	140	80	3
3Row 43	117	110	68	140	88	3
3Row 44	123	140	90	160	100	3
3Row 46	145	114	74	158	86	3
3Row 47	107	112	78	168	88	3
3Row 48	128	118	76	188	100	3
3Row 49	151	122	78	186	90	3
3Row 50	120	110	72	156	72	3
3Row 51	129	144	84	182	92	3
3Row 52	165	120	78	164	82	3
3Row 53 135		120	68	160	72	3
3Row 54	170	112	76	172	88	3
3Row 55	122	112	80	154	96	3
3Row 56	92	124	80	154	94	3
3Row 57	152	112	70	148	78	3
3Row 58	117	118	76	164	86	3
3Row 59	100	129	78	136	68	3
3Row 60	151	122	68	210	76	3
3Row 61	128	160	90	144	82	3
3Row 62	112	112	82	148	92	3
3Row 63	115	150	78	188	82	3
3Row 64	94	110	72	120	72	3
3Row 65	130	134	92	156	98	3

	HRPEAK	SBPREST	DBPREST	SBPPEAK	DBPPEAK	3
3Row 66	126	130	78	162	82	3
3Row 67	120	110	90	140	88	3
3Row 68	165	102	68	148	86	3
3Row 69	160	128	78	198	82	3
3Row 70	165	150	90	234	108	3
3Row 71	115	130	80	160	90	3
3Row 72	136	112	68	164	72	3
3Row 73	94	136	94	120	60	3
3Row 74	160	126	80	158	76	3
3Row 75	160	140	82	238	75	3
3Row 76	166	118	80	210	98	3
3Row 77	145	108	70	218	88	3
3Row 78	159	128	88	168	82	3
3Row 79	160	122	84	184	80	3
3Row 80	110	104	68	184	60	3
3Row 81	166	130	80	162	80	3
3Row 82	167	104	62	174	78	3
3Row 83	112	90	60	160	80	3
3Row 84	160	126	80	140	80	3
3Row 85	104	126	88	128	74	3
3Row 86	83	130	80	136	78	3
3Row 87	160	120	74	150	80	3
3Row 88	171	150	90	170	94	3
3Row 89	127	120	68	150	78	3
3Row 90	130	158	90	178	104	3
3Row 91	167	124	82	180	72	3
3Row 92	135	128	78	172	84	3
3Row 93	101	134	82	178	70	3
3Row 94	106	120	82	140	82	3
3Row 95	136	122	82	150	80	3
3Row 96	116	102	72	138	64	3
3Row 97	140	128	78	178	94	3
3Row 98	170	122	84	190	90	3
3Row 99	122	118	74	158	92	3
3Row 101	119	126	82	144	100	3
3Row 102	96	128	78	162	70	3
3Row 103	159	128	82	188	90	3
3Row 104	140	126	86	172	90	3
3Row 105	100	128	68	166	70	3
3Row 106	144	116	60	192	78	3
3Row 107	122	158	108	182	108	3
3Row 108	111	126	86	174	90	3
3Row 109	110	140	80	170	70	3
3Row 110	99	114	82	142	90	3
3Row 111	160	138	90	118	86	3
3Row 112	118	142	96	180	100	3
3Row 113	114	126	82	144	84	3
3Row 114	169	124	82	182	90	3
3Row 115	150	116	78	186	86	3
3Row 116	170	132	84	200	96	3
3Row 117	107	112	60	166	76	3
3Row 118	136	98	60	122	74	3
3Row 119	115	166	88	110	56	3
3Row 120	150	126	88	166	70	3
3Row 121	115	138	92	174	84	3
3Row 122	165	125	80	210	60	3
3Row 123	162	128	80	210	88	3
3Row 124	155	134	80	162	96	3
3Row 125	150	130	90	164	92	3
3Row 126	133	100	68	168	66	3
3Row 127	160	130	80	170	90	3
3Row 128	166	106	68	150	70	3
3Row 129	107	110	64	164	70	3
3Row 130	150	128	80	144	90	3
3Row 131	102	138	96	152	90	3
3Row 132	86	122	78	160	80	3
3Row 133	147	124	84	160	80	3
3Row 134	175	140	80	220	100	3
3Row 135	127	120	68	150	78	3
3Row 136	86	130	80	138	80	3
3Row 137	155	140	86	170	84	3
3Row 138	150	122	76	158	72	3

3

		AGE	BMI	SMOKER	HIST.HBP	EVENTTYP	
3Row 1		59	30.3	1	0 2		3
3Row 2		49	29.7	1	0		3
3Row 3		53	21.2	1	0	0	3
3Row 4		55	25.2	1	0	1	3
3Row 5		55	22.8	0	0	0	3
3Row 6		47	23.6	1	0	2	3
3Row 7		62	25.6	0	0	0	3
3Row 8		64	24.3	0	0	2	3
3Row 9		49	23.8	1	1	0	3
3Row 10		52	22	1	1	2	3
3Row 11		46	27.8	1	0	0	3
3Row 12		57	22.4	0	0	1	3
3Row 13		63	27.7	0	1	0	3
3Row 14	56		22.7	0	0	4	3
3Row 15		54	25.5	1	1	0	3
3Row 16		54	26.4	0	0	4	3
3Row 17		59	29.6	1	0	0	3
3Row 18		62	21.9	1	0	2	3
3Row 19		62	25.6	1	0	0	3
3Row 20		55	25	1	1	4	3
3Row 21		61	21.4	1	1	0	3
3Row 22		56	22.9	0	1	2	3
3Row 23:		53	21.1	1	0	0	3
						2	3
3Row 25		50	25.1	1	1	4	3
3Row 26		52	26	0	0	0	3
3Row 27	65		25	1	1	2	3
3Row 28		63	26.3	1	1	0	3
3Row 29		54	22.2	1	0	2	3
3Row 30		52	26	1	0	0	3
3Row 31		39	27.7	1	0	3	3
3Row 32		49	24.2	1	0	0	3
3Row 33		60	26.1	0	0	4	3
3Row 34		64	23.4	1	1	0	3
3Row 35		47	25.5	0	0	2	3
3Row 36		58	23.8	0	0	0	3
3Row 37		46	24.7	1	0	2	3
3Row 38		64	28.6	1	0	0	3
3Row 39		58	34.6	0	1	3	3
3Row 40	64		26.7	1	1	0	3
3Row 41		62	25.1	1	0	2	3
3Row 42		59	27.7	1	1	0	3
3Row 43		61	28.1	0	0	3	3
3Row 44		56	29.2	1	0	0	3
3Row 45		54	30.1	1	1	2	3
3Row 46		69	21.6	0	0	0	3

Table 1

Repeated Measures ANOVA Table for ST Dep (80) and Delta ST/HR Index Across Group, Time and Time x Group

Variable	Df	SS	Mean Square	F Value	Prob>F
ST Dep(80)	1	0.17	0.17	13.87	0.0001
GXTS	2	4.25	2.12	0.18	0.8384
Time x Gp	2	2.72	1.36	0.00	0.9989
ST/HR Index	1	102.88	102.88	6.49	0.0120
GXTs	2	6.40	3.20	0.20	0.8175
Time x Gp	2	1.73	0.87	0.05	0.9468

Table 2

Results of Chi - Square Analysis for Exercise Premature Ventricular Contractions

CE vs. NE Gp comparisons for:	Chi-Square Value	p-level
GXT1	3.53	0.32
GXT2	1.03	0.60
GXT3	6.40	0.09

Table 3

Results of Dependent t-tests for CE and NE Subject Descriptive Characteristics and Hemodynamic Values

Variable	Mean	Variance	Df	t-ratio	p-value
Age (yr)					
CE	55.3	6.74	44	1.29	0.28
NE	56.8	5.94			
BMI					
CE	25.9	3.30	44	1.79	0.09
NE	25.1	2.46			
CHOL					
CE	233.2	41.6	44	1.65	0.12
NE	211.6	32.4			
Smok HX					
CE	0.7	0.47	44	1.13	0.39
NE	0.6	0.50			
HR REST					
CE	63.8	10.5	44	1.59	0.14
NE	61.2	8.3			
SBP REST					
CE	124.1	14.5	44	1.40	0.22
NE	125.0	12.3			
DBP REST					
CE	80.0	10.4	44	1.57	0.15
NE	79.4	8.3			
METS					
CE	7.5	2.1	44	1.18	0.35
NE	8.1	2.3			

VITAE

Sharon D. Bruce was born in Corpus Christi, Texas on September 28, 1964. Received a Physical Education with Fitness Specialist Concentration BS degree from Longwood College in Farmville, Virginia in 1986. Took one year to work in the fitness field at the Health Club of Reston in Reston, Virginia. Attended Virginia Polytechnic and State University from 1987 to 1989. Finished the required course work, but left one thing unfinished, the thesis, and moved on to Kansas City, Missouri to work at St. Luke's Hospital in cardiac rehabilitation. After a year and a half, in 1991 Sharon moved west to Los Angeles, California to continue cardiac rehabilitation education and employment at The Hospital of the Good Samaritan. Two years later in 1993, Sharon changed rehabilitation programs and is presently employed at Brotman Medical Center in Culver City, California.

Sharon D. Bruce