THE EFFECTS OF ATRIAL REPOLARIZATION ON EXERCISE-INDUCED ST-SEGMENT DEPRESSION IN APPARENTLY HEALTHY FEMALES

by

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The Effects of Atrial Repolarization on Exercise-Induced ST-Segment Depression in Apparently Healthy Females

ABSTRACT

The relationship between the PQ-segment slope on ST-segment depression during vigorous exercise was examined in 26 apparently healthy females between 18 and 26 years of age. Each subject performed 2 submaximal cycle ergometer exercise tolerance tests (trial A and trial B) on nonconsecutive days wherein the following variables, as delta scores, were measured; P-wave amplitude (microvolts), PQ-segment slope (uV/sec), and J-point at 0 and 60 msec (uV). Each variable was measured by both visual and computer averaging. The degree of reproducibility within and between trials differed for the visual and computer averaged measures. Generally higher reproducibility was found with computer averaging particularly within trial B ($r = 0.63-0.89$, $p<0.01$). Trial b served as a basis for assessment of PQ-segment slope effect on ST segment response. Computer analysis of frequency distribution for responses revealed a greater frequency of downsloping PQ-segment with clinically significant ST-segment depression (>50 uV) at both 0 and 60 msec after the J-point in lead II. However, there was a greater percentage (91%) of flat PQ-segment slopes with clinically significant ST-segment depression at J-point O msec in lead V5. These findings suggest possible influence of lead selection on the

measurements of the PQ-segment slope and ST-segment. Implication of clinical application would be to use lead V5 for diagnosing CHD and by measuring ST-segment depression at J-point 60 msec. However when screening exercise ECG tests in apparently healthy women use J-point at 0 msec.

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key words: females, false-positive tests, atrial repolarization, ST-segment depression

The Big Dream

If there were ever a time to dare, to make a difference,
to embark on something worth doing, it is now.
Not for any grand cause, necessarily-
but for something that tugs at your heart,
something that's your aspiration, something that's your dream.
You owe it to yourself to make your days here count.
Have fun. Dig deep. Stretch. Dream big.
Know, though, that things worth doing seldom come easy.
There will be good days. And there will be bad days.
There will be times when you want to turn around,
pack it up, and call it quits. Those times tell you
that you are pushing yourself, that you are not afraid to learn by trying. Persist.
Because with an idea, determination, and the right tools,
you can do great things. Let your instincts, your intellect,
and your heart guide you. Trust.
Believe in the incredible power of the human mind. Of doing something that makes a difference. Of working hard. Of laughing and hoping. . . . . .
The start of something new brings the hope of something great.
Anything is possible.
There is only one you. And you will pass this way only once.
Do it right.

anonymous

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Chapter I

Introduction

Cardiovascular disease is a devastating cause of death which emanates throughout our society. Though there are various means to control this disease, cures remain elusive. Effective clinical approaches must first involve effective screening of diagnostic tests for patients with significant coronary artery disease risk. Such tests should be easily managed, low cost, reliable, and relatively free of risk. For coronary heart disease, the electrocardiography exercise test serves this purpose.

In recent years, the electrocardiographic exercise test (GXT), has gained widespread acceptance as a screening technique for diagnosis of coronary heart disease. This test has been used often because it is noninvasive, cost-effective, easily performed, and has a low risk of cardiovascular complications (Froelicher, 1987). By design, the GXT has relied on the physiological adequacy of the coronary vessels for myocardial perfusion under conditions of increasing myocardial demand afforded by incremental exercise. Many patients with single vessel coronary disease often show ST-segment depression and angina. The most reliable measure on an exercise electrocardiogram for detecting heart disease is the reversible depression of the ST-segment. This measure has correlated with the severity of myocardia ischemia based upon when it occurred in the GXT, how long it persisted in recovery, and its maximal magnitude during exercise. For

example, early onset of -2 mm (-0.2 mV) or more of downsloping ST-segment depression that continues for 5 minutes into the recovery stage is predictive of three-vessel or left main coronary artery stenosis (ACSM, 1991).

Statement of Problem:

Though exercise-induced ST-segment depression has been one of the most reliable measures of clinically significant myocardial ischemia, it may be observed when there is no underlying ischemia. In such cases, the GXT yields a false-positive result. Exercise-induced ST-segment depression has most often been observed in women (Cumming et al., 1973; Murayama et al., 1985; NcHenry, 1977; Deckers et al., 1990). Therefore, technical difficulties which have affected the interpretation of the ECG may be particularly problematic for diagnosis in women. Explanations for the gender differences in exercise test results have ranged from hemodynamic or hemoglobin concentration differences to ECG interference due to breast tissue. Though many causes have been hypothesized for the high rate of false positive findings in women, the area of gender and false-positive results have not been adequately addressed (Froelicher, 1987).

In one area of research, it was postulated that exaggerated atrial repolarization produced ST-segment depression that imitated myocardia ischemia. Accordingly, Sapin and associates (1991) examined exercise-induced changes

in atrial repolarization patterns in groups with true-positive and false-positive findings. Both groups were defined by coronary angiography. They found that the false-positive group was characterized by: 1) definite downsloping PQ-segment at maximal exercise, 2) longer duration of exercise and rapid succession of peak heart rate, and 3) absence of exercise-induce chest pain (Sapin, 1991).

Research Hypotheses:

The following hypotheses originated from the development of this study:

> Ho_1: The appearance of P-wave amplitude increase during dynamic vigorous exercise (70% cardiac reserve) on cycle ergometer did not differ between Mason-Likar leads II and V5.
>
> Ho_2: The responses of the P-wave amplitude and PQ-segment slope did not have any influence on ST-segment depression in apparently healthy females.

Significance of the Study:

Exercise electrocardiography (ECG) has gained widespread acceptance as a screening technique for the diagnosis of coronary heart disease (CHD) because it is noninvasive, cost-effective, easily performed, and has a low risk of cardiovascular complications (Froelicher, 1987). However,

one problematic issue concerning these tests or any diagnostic test is the prevalence of both false-positive and false-negative results, especially in women. False-positive responses in exercise are of concern because they suggest disease presence that cannot be confirmed by invasive criterion reference test, such as coronary angiography (defines atherosclerotic lesions in the coronary vessels of the heart). It has been especially important to identify the factors that increase false-positive findings so that more accurate diagnosis is possible. However, research in this area has not adequately addressed the high rate of false-positive findings in women. It has been postulated that gender differences in the exercise ECG are attributable to hormonal influences, electrical impedance, central blood flow or hemoglobin. It has even been suggested that technical factors, such as placement of electrodes on the torso may amplify these false-positive responses (Herbert & Froelicher, 1991a). Exaggerated atrial repolarization responses in exercise (Ta), primarily revealed in male patients, constitutes yet another potential factor that recently has been suggested to explain false-positive test results (Sapin et al., 1991).

Delimitations:

In this study, the following delimitations will be imposed by the researcher:

1. Subjects are limited to apparently healthy 18 to 26 year old female volunteers who are physically active and have no symptoms suggestive of CAD defined by a health-risk questionnaire.
2. Subjects qualify for the study if they exhibit exercise-induced ST-segment depression at J-point zero milliseconds in lead V5.
3. The exercise session involves the performance of a high intensity (70% cardiac reserve), exercise test on a cycle ergometer.
4. The potential exercise-induced slope change in the PQ-segment will be visually analyzed 40 msec before the Q wave in leads II and V5.
5. The dependent measures will be limited to exercise-induced J-point depression at 0 and 60 milliseconds and P-wave amplitude shifts during exercise.

Limitations:

The following limitations affect any generalizations evolving from this research:

1. The results of this study will only apply to this sample of apparently healthy college-age females selected on the basis of producing ST-segment depression at J+0

with vigorous exercise.

2. Application of the results will be limited to submaximal graded exercise test performed on a cycle ergometer.

3. No intra-observer reproducibility was practiced between same ECG's on two different occasions.

Basic Assumptions:

The following assumptions have been made by the researcher:

1. Leads II and V5 are clinically revelent for examining exercise-induced J-point depression.

2. The computer derived averages of ST-segment depression will be correct in lead V5. This process excludes all PVCs, aberrent beats, and excessive noise by choosing beats that are similar.

3. The protocol that will be used for testing is valid and reliable measure of vigorous (70% cardiac reserve) exercise in the female population.

4. None of the subjects would be taking drugs that would affect the J-point during the 24 hours prior to the exercise test based upon the health-risk questionnaire.

Definitions:

Predictive value: the ability or capacity of a test to distinguish between diseased versus nondiseased individuals (Froelicher, 1987).

Sensitivity: the percentage of total cases in which a test

produces abnormal results when diseased subjects were tested (Froelicher, 1987).

Specificity: the percentage of total cases in which a test produces normal results when nondiseased subjects were tested (Froelicher, 1987).

isoelectric line: the level of the horizontal inscription on the recorder between the ECG complexes, i.e. between the end of the P wave and the beginning of the Q wave; used as a reference for ST and PR segment slopes.

J-point (J+0): the junction between the end of the QRS complex and the beginning of the ST-segment (Goldberger & Goldberger, 1990).

ST-segment depression: a horizontal or downsloping negative shift of the ST-segment on the ECG with reference to the isoelectic line, usually within the finite time between 40 and 80 msec after the J-point.

ST level or J+60: the difference in amplitude in millimeters between the level of ST-segment at 60 milliseconds and the isoelectric line (Mortara ECG recorder manual, 1991).

Lead V5: precordial, unipolar lead positioned at the level of the fifth intercostal space in the left anterior axillary line.

PQ-segment: the inscription on the ECG complex between the end of the P wave and beginning of the Q wave.

PQ-segment slope: the angle (mV/sec) of the PQ-segment

(horizontal or downsloping) in relation to the isoelectric line over the interval of 20-30 msec before the beginning of the PQ-junction but without the encroachment on the P-wave (Sapin, 1991).

Lead II: torso-mounted limb lead where the positive electrode is below the left pectoral muscle and the negative below the right clavicle. (The lead comprises of right arm and left leg electrodes, having an inferior orientation with respect to the heart.)

P wave: the first positive ECG peak prior to the R wave that represents the depolarization of the atrium.

P-wave amplitude: the vertical distance in mV between the peak of the p wave and the isoelectric baseline (Sapin, 1991).

Rate of Perceived Exertion (RPE): a categorical 6-20 Borg scale that quantifies subjective intensity during exercise (Borg, 1950).

YMCA Cycle Ergometer Test: a branching test protocol in which the workload begins at 25 Watts or 150 kp/m/min and is increased to a load that is inversely related to heart rate response observed at 25 Watts. This protocol includes four (3 minute) stages (ACSM,1991).

Cardiac Reserve: a method of determining target heart rate for subject by taking the percentage of exercise intensity of the difference between the age-predicted maximal heart rate(220-age) and resting heart rate (ACSM, 1991).

Electrocardiographic(ECG) artifact: any electrical signal that is foreign to or that distorts the true ECG waveform. Artifact may be present due to any combination of muscle, respiration, and/or poor skin preparation disturbances (Froelicher, 1987).

SUMMARY

Cardiovascular disease has been a devastating yet silent killer in today's society. Though medical intervention and techniques have advanced in combating this disease, a cure has remained obsure. For this reason, early screening has been imparative for effective diagnoses. A widely accepted tool for screening has been the GXT which advocated noninvasive techniques, cost-efficiency, and relatively low risk procedure. There has been a general consensus that the most reliable measure for diagnosing heart disease on the ECG is the depression of the ST-segment. The criteria for ischemia has depended on the depth and slope of the segment, therefore the greater the depth and downsloping of the segment, the more severe the disease. Unfortunately, the value of the GXT has been criticized because ST-segment depression of no ischemic origin was frequently observed in women. Sapin and associates have postulated that exaggerated atrial repolarization causes a shift in the ST-segment depression, thus falsely diagnosing ischemia. One of the characteristics found in false-positive group by Sapin et al. was a definite downsloping PQ-segment.

Discovering if there has been a relationship between a definite downsloping PQ-segment and ST-segment depression could help to improve the exercise testing procedures for women.

CHAPTER II

REVIEW OF LITERATURE

INTRODUCTION:

Cardiovascular disease has remained to be a prominent health issue in today's world. For this reason, research has been multidimensional and well documented due to its complexity and intricacy within our society. There has been a consensus among the medical profession that the graded exercise test is a well established and reliable tool for diagnosing myocardia ischemia. Several issues concerning the utilization and significance of this tool has been addressed in research. The following areas are discussed in this chapter: 1) Sensitivity and Specificity in Graded Exercise Tests, 2) Utility of Different Lead Systems in Detecting Myocardia Ischemia, 3) ECG Measures Used to Diagnose Myocardia Ischemia, 4) False-positive GXTs and Gender, and 5) Atrial Repolarization.

Sensitivity and Specificity in Graded Exercise Tests:

The integrity and the use of the GXT has depended upon the ability of the test to diagnose myocardia ischemia. This has been controlled by conditional probabilities. Specifically, the predictive value of the test has relied upon how accurate the test result, either positively or negatively, diagnoses the presence of disease in the patients. The predicted ability of the exercise test has been determined by the sensitivity and specificity of the test procedures as well as the prevalence of disease in the population being tested

(ACSM, 1991). Sensitivity has reflected the ability of a test to identify abnormal responses on the ECG when disease was actually present. Likewise, specificity was the ability of the test to identify normal responses given that no disease was present (Froelicher, 1987). Therefore, sensitivity reflected how reliable a positive test identified disease, and specificity reflected how reliable a negative test identified the absence of disease (ACC/AHA, 1986). These values were inversely related; when specificity was high, sensitivity was low and visa versa
(Froelicher,1987).

Sensitivity and specificity have been affected by several factors which have involved testing procedures and the testing population. Sensitivity has been increased when GXTs use patients with higher incidents of coronary lesions, and multi-lead ECGs (Froelicher, 1987). Increasing the number of leads from 1 to 12, increased sensitivity from 56 to 76%, while the specificity decreased from 94 to 82% (ACC/AHA, 1986). Maximal exercise testing also increased sensitivity. Previous anterior myocardia infarctions have tended to complicate the diagnosis of disease, thereby decreasing the sensitivity of the test.

Specificity was increased when stringent definitions for positivity were used; for example, horizontal or downsloping ST depression of 0.01 mV or greater at J-point 80 (msec). On

the contrary, specificity was decreased by abnormal resting electrocardiograms, hypoxic and/or anemic patients as well as certain drugs (Froelicher, 1987).

Sensitivity and specificity were greatly affected by the population utilized for testing. Specificity was lowered when subjects, like women, who are more likely to produce false-positive results were chosen for a study. Likewise, the sensitivity of a test was raised when subjects with triple-vessel disease versus those with single-vessel coronary disease were utilized (Fletcher, 1991).

The GXT has significant limitations as a diagnostic tool for ischemia. On the contrary, when evaluating methods for diagnosing early signs and symptoms of myocardia ischemia in individuals with high risk for heart disease, the use of GXT to induce abnormal responses not present at rest has merit. The exercise electrocardiography has a sensitivity of approximately 50% and a specificity of 90% in apparently healthy subjects. This predictive value was based upon nine prospective studies with ST depression as the criterion for positivity in asymptomatic men and involving men and women with atypical chest pain (ACC/AHA, 1986).

UTILITY OF DIFFERENT LEAD SYSTEMS IN DETECTING MYOCARDIA ISCHEMIA:

Sensitivity and specificity of a test have been greatly affected by the type of electrocardiographic lead system used

for testing. Specifically, there has been alterations in the slope as well as the amount of depression in the J-point depending on which lead was evaluated. Therefore, considerable discussion concerning how many leads to use when testing as well as which ones produce the greatest accuracy has been waging among researchers. The type of population utilized for testing tends to be the key factor.

Electrodes have been placed in a variety of configurations according to the different lead systems. The situation has been complicated when a comparison was made between ST segment changes and exercise. Therefore, modified lead systems have been developed to reduce ECG artifact during exercise (Pina & Chahine, 1984). The major lead systems utilized in research have been the Mason-Likar 12-lead, bipolar leads; both of which use the Wilson's central terminal, and multiple leads which collectively utilize electrodes from both bipolar and Mason-Likar lead systems.

In the standard 12-lead system the limb leads were placed at the end of each limb. However, the Mason-Likar electrode placement used a modified standard 12-lead system in which limb leads were centrally located in order to reduce motion artifact. Therefore, the right arm electrode has been placed on the infraclavicular fossa medial to the border of the deltoid muscle and 2 cm below the clavicular edge. Likewise, the left arm electrode was placed symmetrically to the right

arm electrode. The optimal place for the left leg electrode has been at the anterior axillary line, midway between the costal margin and the left iliac crest. Respectively, the right leg electrode was symmetrically placed with the left leg electrode. The precordial electrodes were placed in the standard ECG position (Pina & Chahine, 1984).

The bipolar lead system has been utilized often because it required fewer leads and there also was a reduction of motion artifact due to exercise. Leads CC5 and CM5 were the most frequently used in testing. The positive placement for the ECG leads has been V5. The negative reference for V5 has been the Wilson central terminal which consists of the triangular connection of the limb electrodes; left arm, right arm, and left leg.

Research concerning the utility of the bipolar lead system in predicting disease has shown that the CM5, as a single bipolar lead, to be just as sensitive to ST segment changes as multi-lead systems in a population suspected of multi-vessel disease with a normal resting ECG (Ascoop et al., 1989 & Chaitman et al., 1979).

However, bipolar lead CC5, has been the most popular single lead monitored during testing (Pina & Chahine, 1984). CC5 excluded the vertical component which was included in CM5, thereby reduced the prevalence of false-positive responses (Fletcher et al., 1991).

Froelicher and associates (1976) evaluated the behavior of bipolar leads CC5 and CM5 in relation to lead V5 (standard 12 lead) using Wilson's central terminal as a modification of Mason-Likar. Both visual and computer analyses were compared with the different lead systems. They reported that both leads CC5 and V5 are almost identical in predicting ECG changes with the use of visual ECG analysis, but were significantly different when computer measurements were used (Froelicher, 1976). However with Ascoop and his associates (1989), lead CM5 was found to be no different from other leads like V5 and CC5 when interpreting the ECG based upon classic criteria of positivity using subjects subgrouped by disease.

Considering a 12-lead system, lead V5 was the best single lead for detecting ischemia by several researchers as an established and reliable fact (Miranda et al., 1992, Ascoop et al., 1989, ACSM, 1991, Fletcher et al., 1991, & Froelicher, 1987). Computer analyzed exercise-induced ST depression in lead V5 was an reliable measure of coronary artery disease with a specificity of 84% and a sensitivity of 65%. The human eye has tended to round off values. Consequently, the use of other leads like lead II decreased both specificity and sensitivity by making the evaluation of the ST segment more difficult. Lead II tended to have a high false-positive rate (Miranda et al., 1992).

The lead system controversy has not been the result of

the discrepancies among the lead systems but the result of the net differences in techniques used to analyze ECG's. Not only must researchers categorize populations with varying degrees of disease, but also their techniques used for research. Froelicher et al. (1976) discovered statistically significant differences between ECG leads when utilizing ECG computer analyses. Therefore, new specific criteria for defining positive responses on ECG's is necessary for comparable diagnostic significance.

Concerning the utility of the multi-lead system which includes both the Mason-Likar and bipolar lead systems, Chaitman and colleagues (1978) reported the usefulness of both multiple-lead ECG's and clinical subsets for interpreting GXTs. 200 men with normal resting ECG's underwent a maximal GXT using a 14 ECG leads (Mason-Likar and 3 bipolar leads) and then coronary angiography. The predictive value for ST depression in any of the leads was 45% in subjects with nonspecific chest pain, 70% in subjects with probable angina, and 55% in typical angina subjects. Thus, an increase of diagnostic accuracy occurs when a multi-lead system was used in a symptomatic population. For subjects with nonspecific chest pain, a recording of CM5 was adequate. A discrepancy in enhancing the diagnostic results on a GXT occurs with typical angina subjects. The authors recommend in addition to the 14 leads that other parameters be evaluated for example: 1) the

time of first ischemia, 2) pressure-rate product at time of first ischemia, and 3) maximum exercise capacity (Chaitman et al., 1978).

However most recently, the use of the multiple lead system has proven not to provide any further useful information than obtainable by standard 12 lead or bipolar systems. With 21 leads (18 unipolar and 2 bipolar leads), researchers have not been able to predict the site or extent of cornonary artery disease by measuring the ST-segment deviations in patients with obstructive cornonary artery disease. The use of multiple lead system has increased patient prepatory time, is more expensive to use,and was not recommended for research or in routine tests (Bowles, Khumi, Davies, and Raftey, 1985).

Accordingly, Ascoop and associates (1989) observed that multiple lead systems did not greatly improve the diagnosis of multivessel disease when compared to one bipolar lead such as CM5. Bipolar lead, CM5 was adequate even with typical or atypical chest pain with a normal resting ECG. They also suggested in assessing patients with documented coronary disease that other parameters should be evaluated. They include arterial pressure, heart rate, exercise duration, and cardiac volume. All of which are found to have great importance in diagnosis (Ascoop et al., 1989).

Guiteras and colleagues (1982) evaluated the diagnostic

accuracy of exercise lead systems in clinical subsets of 112 women. Their results coincide with Chaitman et al. (1978) and Ascoop et al. (1989). They recommended a 11-14 lead ECG for women with typical or variant angina or those with prior infarctions. With a 14 lead system, sensitivity was at 57% and specificity 80% in lead V5. Bipolar leads CC5 and CM5 were sufficient for subsets of probable angina or nonspecific chest pain and no prior infarction (Guiteras et al., 1982).

From these studies, classifying clinical subsets as well as techniques enhanced the diagnostic accuracy of ECG lead systems.

Considering the question of how many leads were needed for accuracy during a GXT has not been answered, it seems advisable to record as many electrodes as economically and practically possible. For patients with normal resting ECGs, a V5 or similar bipolar lead,CM5, was adequate. In patients with ECG evidence of damage or with a history of coronary spasms, additional leads were required. The minimal approach has been three leads: V5 lead type, anterior V2 type lead, and an inferior lead like AVF; can be used (Froelicher, 1987).

ECG MEASURES FOR DIAGNOSING MYOCARDIA ISCHEMIA:

Several variables have been reported as useful criteria for detecting myocardia ischemia on the ECG. They include ST segment depression, ST segment slope, and ST integral. However, the depression of the ST segment below the baseline

has received the most attention. Though most researchers agree to the use of ST depression as a criteria for positivity on the ECG, disagreements have occurred concerning the quantitation of the ST segment depression measurements (Gianrossi et al.,1989).

Mason, Likar, Bierm, & Ross (1967) evaluated what was the best criteria for a positive GXT using both normal and angina pectoris subjects. Multiple lead electrocardiography and coronary angiography were also used. They found that the use of 0.75 mm ST depression at 0.8 msec as the criterion for positivity would more clearly separate the angina patients, but this standard would also include 3 more false-positive responses. If the value of 0.5 mm ST depression for 0.8 msec was accepted, nine more false-positives would be included. Therefore, the criteria at 1.0 mm ST depression for 0.8 msec for a positive test was the best indicator of disease. Furthermore, displacements of less that 1.0 mm can not be measured accurately by the eye (Mason et al., 1967).

Herbert and Froelicher (1991b) have reported that only 1 out of 20 asymptomatic individuals has significant CAD. Furthermore, the likelihood of one having CAD, when just evaluating ST depression, has depended upon the amount of ST depression, the slope, the timing of onset and its relation to exercise capacity, the number of leads in which it is observed in, and its persistence during recovery. The severity of

disease was increased when the ST depression is greater than or equal to 1.0 mm and is horizontal or downsloping. If depression has occurred early and few stages were achieved in the exercise test then the disease is clinically significant. Usually ischemic ST depression has occurred in the lateral leads I, V4, V5, and V6. ST segment changes that have occurred in the anterior and inferior leads like V2, aVF, and II were usually indicative of false-positive responses. Also, ST depression that remained observable through recovery was considered clinically significant (Herbert & Froelicher, 1991b).

Besides defining ST segment depression, controversy has existed with the ST slope as the criteria for positivity on the ECG. The ST slope has been defined as the rate of change in the ST segment. The slope has been described as downsloping in which there is a negative rate of change; upsloping - a positive rate change; and horizontal, in which there is no rate of change. McHenry, Stowe, & Lancaster (1968) defined the ST slope within the parameters of 70 to 110 msec beyond the R wave.

Ascoop, Distelbrink, & De Lang (1977) evaluated the criterion for the ST slope in terms of sensitivity and specificity. They found that whether one used 0 to 80 msec or 10 to 50 msec from the R wave as a definition of ST slope, similar results were found in sensitivity and specificity. In

lead CC5, sensitivity and specificity were 60% and 93% respectively, while in lead CM5, 50% and 93% were the sensitivity and specificity respectively.

There has also been controversy on considering upsloping ST segment as an abnormal response on the ECG. When upsloping ST segment was considered abnormal, specificity was decreased by 4.4% (Gianrossi et al., 1989).

It is estimated that over fifty percent of the 100 million electrocardiograms (ECGs) recorded annually in the U.S. have been analyzed by a computer (Willems et al., 1991). The reduction of the amount of ECG data collected during testing and the movement artifact due to exercise have been two critical problems in exercise ECG testing. These problems have prompted researchers to devise better ways of collecting data. Micocomputers have been used to digitalize electrocardiography signals and immediately apply digital techniques while the data was still being collected during an exercise ECG test. Accordingly, computerized ECG measurement have been devised to measure the ST-segment.

The ST integral was the computed analysis of the surface between the baseline and negative part of the ST segment. In computer systems , it has been the area of ST depression from 60 to 140 msec after the R wave (Frolicher, 1987).

Sheffield, Holt, Lester, Conroy, & Reeves (1969) evaluated the accuracy of the ST integral when the area was

measured from the end of the QRS to either the beginning of the T-wave or to where the ST segment first crossed the isoelectric baseline. Two groups were compared; normal and CAD patients. A normal range for the ST integral was 0 to -7.5 mV/sec while an abnormal ST integral was considered greater or than -10 mV/sec. Using these definitions, Sheffield observed 81% sensitivity and 95% specificity with these measures (Sheffield et al., 1969).

Sketch, Mohiuddin, Lynch, Zencka, & Runco (1980) also tested the validity of this measure and observed that ST area was accurate and comparable to visual analysis. Accordingly, Forlini, Cohn, & Langston (1975) using a similar protocol as Sheffield found a 85% sensitivity and 90% specificity for this measure.

McHenry, Phillips, and Knoebel studied the usefulness of a computerized exercise electrocardiographic system to measure the ST-segment amplitude over a 10 msec interval, starting at 60 msec after the peak of the R-wave. The ST-segment slope was quantified from 70 msec to 110 msec pass the R-wave peak. The ST index measurement was defined abnormal when the ST-segment depression was one millimeter or greater and if the sum of the ST-segment depression in millimeters and the ST slope in millivolts per second equaled or was less than one during or immediately after exercise. Using a comparison of two groups of subjects, one diagnosed with angina and the

other age-matched clinically normal people, there was 83% specificity and 95% sensitivity (Froelicher, 1987).

On the contrary, Milliken, Abdollah, and Burggraf (1990) have observed through their research that there was an abrupt rise at the end of the ST-segment on computer analyses of the ECG. It was postulated this upswing of the ST-segment was produced by the computer averaging of the ST-segment depression on a twelve lead ECG. Thus, the series of averaged complexes are pushed together. They recommend that before citing any computerized exercise test positive, review the raw or true 12 lead tracing (Milliken et al., 1990).

Willems and colleagues (1991) underwent a comparison of the performance of nine electrocardiographic computer programs with that of eight cardiologists in evaluating ECGs in 1220 validated cardiac disorders such as left or right ventricualr hypertrophy, and anterior or inferior myocardial infarction. The researchers did not evaluate the agreement of ST-segment or T-wave deviations because these diagnoses could not be validated on the basis of nonelectrocardiographic evidence such as cardiac catherization and echocardiography. They found that the computer programs correctly classified 91.3 percent of the ECGs as opposed to 96 percent by experienced cardiologists. Though, based on this study, the computer programs evaluation were comparable to cardiologists' interpretations, there still remains a need to improve ECG

computer programs (Willems et al., 1991).

False-positve Responses and gender:

Exercise electrocardiography has been a well established technique for predicting myocardia ischemia in men but its diagnostic accuracy in women has remained questionable. Research has described exercise-induced ST depression in symptom free women with no angiographic evidence of disease to be similar in value to the GXT in both women and men. However, little research has evaluated exercise-induced ECG changes in women.

Deckers, Vinke, Vos, & Simoons (1990) attempted to study the possible sex differences in ECG changes by evaluating the P wave, QRS complex, ST segment and T wave during and after exercise in 117 female volunteers assumed to be disease free. They found that exercise-induced ECG changes were no different from that of men. The most significant finding was that ST depression increased with age in women. In 2-50% of symptom free middle-aged women, greater than or equal to 1 mm ST depression was observed. Furthermore, ST depression at greater than or equal to 1 mm was a poor predictor of ischemia in women. Guiteras et al. (1982) observed that specificity of the GXT in women with normal coronary arteries ranged from 63% to 92%. Deckers et al. (1990) reported that the specificity was higher in men than women, quoting a 74% specificity for men as opposed to women at 64%. However, when men and women

were paired by age and presence and extent of CAD, there was no statistically significant difference between gender (Deckers et al., 1990).

Cumming, Dufresne, & Samm (1973) sought to explain why 25-50% of women produce abnormal GXT responses that qualified under the classical criteria of positivity when only 10% of these women would develop CAD. 357 asymptomatic women were exercised near maximum level. The subjects' ages ranged from 20 to 83. The most significant finding was that as age increased, the incidents of false-positive responses on the GXT also increased. Therefore, women were three times likely to have a false-positive response than men at the same age (Cumming et al., 1973).

Research has lead to the evaluation of different mechanisms such as estrogen and hemoglobin concentration differences as well as medications like digitalis which might explain the prevalence of false-positive responses in women. However, gender has an effect on the exercise ECG that has not been explained by either hormones or hemodynamics (Cumming et al., 1973).

Atrial Repolarization:

The exercise ECG has been an important tool for diagnosing myocardia ischemia. Despite its reliability, this technique has its limitations, particularly specificity. False-positive responses were prevalent with this technique.

Known factors that attribute to a false-positive response have included electrolyte abnormalities, drug use, and repolarization abnormalities on the resting ECG. However, often none of these factors were present. The cause of exercise-induced ST segment depression in the absence of ischemia has remained unclear.

Depression of the ST segment due to ischemia has been the result of both local changes in cellular membrane potential at rest and the shape of the action potential. These ischemic changes result in current flow that have caused TQ segment elevation and ST segment depression (Sapin et al., 1991).

However, the P wave was created by the action potential originating in the SA node which activated both the right and left atria and traveled inferiorly and posteriorly. The P wave was rounded with a notch corresponding to the separation between right and left atrial activation. The P wave and the Ta segment, or atrial repolarization, define atrial electrical systole. The Ta wave has represented the recovery process of the electrical excitation in the atrium. The Ta wave has been usually difficult to observe because the amplitude of the wave is very small, and it is inscribed during the QRS complex and the early part of the ST segment (Abramson et al., 1938). Riff and Carleton through their research found that as much as 160 msec of the ST segment can be distorted by Ta wave. This equates to as much as 0.19 mv deviation at the J-point (Riff

& Carleton, 1971). It was best observed in the presence of AV block. The Ta wave was important because it can provide a diagnostic clue for atrial infarction and better yet cause false-positive depression of the ST segment (Hayashi et al., 1976).

Atrial repolarization may be affected by different factors which result in morphological changes in ECG's. Primary alterations to the P-ta wave are occur due to atrial infarction, postoperatively after heart surgery, pericarditis, and sympathetic stimulation. Dilation of the atria and inter-atrial block affect the depolarization state of the atria electrical activity. Displacement of the PR segment as a change in atrial repolarization has also been observed in patients during general anesthesia and due to electrolytic imbalance. A difference in the atrial gradient is also produced in normal young adults by the subcutaneous injection of isopropylarterenol (Sivertssen, 1972).

Hayashi, Okajima, & Yamada (1976) studied 25 AV block patients by dividing them into 2 groups; one without symptoms or significant cardiovascular disease and the other with significant symptoms and disease. In the group without significant symptoms or disease, the P wave was tall and sharp spiked, and was followed by a gently drawn dome-like Ta wave on a standard resting ECG (Hayashi et al., 1976). The Ta wave was proportional in size and had a negative polarity to the P

wave (Hayashi (1969), Tranchesi (1960), & Sivertssen (1972). In the other group with disease, the P wave was smaller and notched. The Ta wave was larger than the P wave and had the same polarity. Hayashi and his colleagues concluded that when the Ta wave was large and negatively polarized to the P wave, this situation might cause a false ST depression and lead to a false-positive response on the GXT (Hayashi et al., 1976).

Gross (1954) evaluated the correlation between the Ta wave and cardiac rate in 210 healthy males and females. He discovered that the downward displacement of the P -Ta segment is due to two factors: cardiac rate and surface area of the P wave. The deepening of the Ta wave is partly due to the increase size of the P wave. As the Ta wave shortens, it must deepen in order to maintain an area equal and opposite to that of the P wave. Gross identified that the deepening of the P-Ta segment with increasing cardiac rate was due to the maintanence of equal surface area betweem P and Ta waves by increasing the depth with shortened duration. He also observed that the P-Ta segment is invisible at cardiac rates below 70 beats per minute but becomes increasingly visible from 71 to 90, and over cardiac rate of 91 is constantly present (Gross, 1954).

However Wasserburger, Ward, Cullen, Rasmussen, and Juhl (1957) observed an increase of mean P wave amplitude independent of cardiac rate reached a value of 100 per minute

in patients with pulmonary emphysema. It is believed that clinically evident pulmonary emphysema may alter atrial repolarization pattern (Wasserburger et al., 1957). Though there is a direct correlation between displacement of P-Ta segment and cardiac rate, the height and surface area of P wave are directly related with frequency and degree of displacement of segment but independent of cardiac rate (Gross, 1954).

Tranchesi, Adelardi, and Martins de Oliveria (1960) evaluated atrial repolarization as a whole by observing changes in both the atrium and ventricle especially at downward shift of PR segment. They concluded that careful analysis of ST-segment depression was necessary in view of PR segment so that false positive result would not be concluded. There is no pathological significance when the PR and ST segments have similar deviations or "arcs of same circumference." Thereby the ECG tracing are morphologically compared to an anchor. Myocardial injury is diagnosed when PR and ST segments are discordant or of different radii (Tranchesi et al.,1960).

However, Hayashi (1969) concluded that when depression of PR segment or ST segment does not exceed the amplitude of the Ta wave expected from that of P wave, the depression is influenced by the Ta wave. Conversely, if the ST segment depression superceeds the amplitude of Ta wave expected, then

there is clinical ST depression (Hayashi, 1969).

Sapin and associates (1991) also observed atrial repolarization as a possible cause of false ST segment depression. They postulated that exaggerated atrial repolarization waves during exercise could produce ST depression imitating myocardia ischemia. True-positive and false-positive groups were formed based on angiography and GXT results. Their research indicated that the short, steeply downsloping PR segment, in the inferior leads, is an independent and reliable indicator of a false-positive GXT response, in the presence of significant horizontal ST depression. The downsloping PR segment has caused the Ta wave to shift further into the ST segment, thus give the ST segment a horizontal slope. They also noticed in the false-positive group the P wave amplitude increased from the start of test to peak in all six leads. The PR segment duration was also shorter than in the true-positive group. When identifying a false-positive test using the criteria for positivity such as an exercise time of greater than four minutes and a marked downsloping PR segment in two of three inferior leads, the GXT had a sensitivity of 84% and a specificity of 89%.

SUMMARY:

Research has indicated the evaluation of the ST segment as a reliable technique to diagnose myocardia ischemia. However, the most accurate method of measuring the ST segment

depression remains questionable. Lead V5 has been consistently chosen the most accurate in detecting ST segment changes while the inferior leads were considered most likely to produce false-positive responses on the ECG. As to what lead system was consistent in detecting changes has depended upon the population that was being tested. If the asymptomatic subjects has a normal resting ECG, a V5 or similar bipolar lead like CC5 was usually adequate, though a minimum of three leads was usually recommended. They included a V5 type lead, an anterior lead such as V2, and a inferior lead like aVF. When the ECG tracing revealed myocardia ischemia, more leads were necessary for testing. Consequently, women have been more difficult to accurately diagnose ischemia through ECGs than men. Some researchers have recommended the use other parameters like exercise duration and abnormalities in recovery in order to improve the sensitivity of the GXT. Nevertheless, new criteria for a positive test on the GXT has been greatly needed. Future research concerning atrial repolarization and the quantitation of the ST segment may provide answers as well as means for accurately diagnosing ischemia in GXTs.

Chapter III

Journal Manuscript

Title: The Effects of Atrial Repolarization on Exercise-Induced ST-Segment Depression in Apparently Healthy Females

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Abstract

The relationship between the PQ-segment slope on ST-segment depression during vigorous exercise was examined in 26 apparently healthy females between 18 and 26 years of age. Each subject performed 2 submaximal cycle ergometer exercise tolerance tests (trial A and trial B) on nonconsecutive days wherein the following variables, as delta scores, were measured; P-wave amplitude (microvolts), PQ-segment slope (uV/sec), and J-point at 0 and 60 msec (uV). Each variable was measured by both visual and computer averaging. The degree of reproducibility within and between trials differed for the visual and computer averaged measures. Generally higher reproducibility was found with computer averaging particularly within trial B ($r = 0.63 - 0.89$, $p < 0.01$). Trial b served as a basis for assessment of PQ-segment slope effect on ST segment response. Computer analysis of frequency distribution for responses revealed a greater frequency of downsloping PQ-segment with clinically significant ST-segment depression (>50 uV) at J-point 0 msec in lead II. However, there was a greater percentage (91%) of flat PQ-segment slopes with clinically significant ST-segment depression at J-point 0 msec in lead V5.

These findings suggest possible influence of lead selection on the measurements of the PQ-segment slope and ST-segment. Implication of clinical application would be to use lead V5 for diagnosing CHD and by measuring ST-segment depression at J-point 60 msec. However when screening exercise ECG tests in apparently healthy women use J-point at 0 msec.

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key words: females, false-positive tests, atrial repolarization, ST-segment depression

INTRODUCTION:

Exercise electrocardiography has proven to be an effective screening tool for the diagnosis of myocardial ischemia. However it is not absent of inherent factors that confound interpretation. Specifically, the exercise test has poor accuracy in diagnosing abnormal ECG responses produced by apparently normal individuals; thus false-positive responses. Gianrossi and associates have quoted a rather low specificity of 77% for the exercise tolerance test (Gianrossi et al., 1989). In addition, false-positive results are quite frequent in women without ischemic origin (Murayama et al., 1985; McHenry, 1977; Froelicher,1987; Deckers et al.,1990; Cumming et al., 1973). However, the cause of exercise-induced ST segment depression in the absence of myocardial ischemia has remained unclear and inadequately addressed.

Sapin and associates (1991) have postulated that the cause of exercise-induced ST segment depressions in healthy individuals was due to exaggerated atrial repolarization. In a false-positive group, they observed a markedly downsloping PR segment and ST depression with a horizontal slope. Sapin et al. (1991) concluded that the downsloping PR segment caused a downward shift in the ST segment, thus a false-positive response.

One purpose of this study was to determine if the appearance of P-wave amplitude increase at 70 % of cardiac

reserve on a cycle ergometer differed between Mason-Likar leads II and V5. The major objective was to determine if the P-wave amplitude and PQ-segment slope responses influenced the ST-segment depression in apparently healthy females.

METHODS:

Subject Selection and Screening: All exercise testing was performed in the Laboratory for Health & Exercise at Virginia Polytechnic Institute and State University in Blacksburg, VA.

Twenty-six volunteer female students were selected for this study through a screening process. A personal interview and a health history questionnaire were administered to qualify each candidate as "apparently healthy", according to the standards of the American College of Sports Medicine (ACSM, 1991). The following exclusion criteria were imposed: 1) evidence of abnormal resting ECG (i.e.LBBB, WPW, ST-segment depression); and 2) excessive ECG artifact and baseline wandering greater than +/- 0.2 mV vertical displacement between the onset of the P-wave and onset of the Q-wave of two ECG complexes) during the exercise test. Tables 1 & 2 illustrate the physical characteristics of the subjects utilized in this study.

Table 1 & 2 -physical characteristics of subjects

Exercise Test: The exercise test was performed using the YMCA cycle ergometer test protocol (Golding et al., 1982). The standard manner for the Mason-Likar lead system was used. Skin sites were carefully cleansed and prepared for ECG monitoring. Following 10 minutes of seated rest, a baseline ECG tracing, resting HR and BP were obtained. Heart rate, blood pressure, and rate of perceived exertion (RPE) were measured during the second minute of each exercise stage. The ECG tracings were obtained during the last 10 seconds of each exercise stage and immediately post-exercise. The test was terminated when the subject achieved 70% of their cardiac reserve.

ECG Recordings and Measurements: ECG tracings were recorded without the use of signal filters at a speed of 50 mm/sec and at a sensitivity of 20 mm/mV. The ECG tracings were analyzed visually and by computer-signal averaging using the X-Scribe Mortara Stress Testing System (Mortara Instruments, Milwaukee, WI). Visual analysis required the averaging of two morphologically similar ECG complexes, each from a single continuous record. Records were analyzed repeatedly at rest and peak exercise in both leads II and V5. The computer averaged ECG complexes included one averaged ECG complex taken from the same records and leads used for the corresponding visual analysis. The delta scores of the ECG

variables were examined because they represent the way exercise test results are interpreted in clinical settings for diagnosis (Figure 1). No significant differences were observed between the testing conditions among the ECG variables. Stability of the dependent measures was maintained by using lead V4 when lead V5 was unclear due to baseline wandering and muscle-induced artifact.

The following dependent measures are illustrated in Figure 1:

P-wave amplitude shift: The shift was defined as the vertical displacement of the P-wave between peak exercise and baseline in leads II and V5.

PQ-segment slope: The PQ-junction served as the isoelectric point for ECG complexes with each exercise level. The PQ-segment displacement was measured (+/- 0.25 uV) over the time interval of 20-30 msec before the PQ junction but without the encroachment on the P-wave. PQ-segment slope that was less than -2.5 uV/sec was quantified as flat; and a slope greater than or equal to 2.5 quantified as downsloping.

J-point depression: J-point depression was evaluated at 0 and 60 msec after the J-point. The delta scores for J-point depression were determined by subtracting baseline values from peak exercise values. If the measurements of the J-point depression at 0 and 60 msec were elevated above the isoelectric line at rest, the value was evaluated from the

isoelectric line at peak exercise.

Figure 1 - dependent variables illustration

Statistical Analysis: A correlation between the raw and computer-signal averaged ECG complexes were evaluated based upon the measurements of J-point depression and PQ segment slope using the Spearman rank order correlation analysis. Because the values of P-wave amplitude shift were continuous, the Pearson's Product Moment was used to evaluate their relationship. In order to determine the distribution of flat and downsloping PQ-segments among P-wave amplitude and J-point at 0 and 60 milliseconds, a frequency distribution graph was created. All statistical analyses were performed on Statgraphics Statistical System. Throughout the data analyses, the significance was set at an alpha level of 0.05.

Results

Hemodynamic responses: The hemodynamic responses are presented in Tables 1 and 2. Subjects were college-aged, non-obese, active females. The tables reflect normal ranges in age, body mass index (BMI), heart rate, blood pressure, and power for this population. There was no significant difference among physical characteristics, hemodynamics, and power between the flat PQ and downsloping PQ groups.

Atrial Repolarization and ST level:

P-WAVE AMPLITUDE: The average P-wave amplitude delta score was greater in the inferior lead II (142 uV) than in precordial lead V5 (103 uV). In lead V5, twelve percent of the twenty-six cases expressed P-wave amplitudes greater than or equal to 200 uV as opposed to the twenty-three percent of the twenty-six cases in lead II. The frequency of exercise-induced ST-segment shifts greater than 50 uV at J-point 0 and 60 msec in relation to P-wave amplitude shifts and lead selection (II vs V5) were expressed in Figure 4. Non-significant P-wave change was a delta score of less than 200 uV; and a significant P-wave amplitude change was a delta score of greater than or equal to 200 uV. The subjects that expressed nominal ST-segment shifts (< 50 uV) were not presented in this figure. J-point depression greater than 50 uV was used as a marker for clinically important ST-segment depression because it was observed to be sensitive to the differential effects of PQ-segment slope and ECG resolution in this healthy population. The purpose of this figure was to determine if the appearance of P-wave amplitude increase differs between leads II and V5 as well as influence ST-segment depression in apparently healthy females. In lead V5 there was a seven-fold greater tendency of clinically important ST-segment depression when the P-wave amplitude change was less than 200 uV at J-point 0 msec. In lead II,

there was two times greater tendency of non-significant P-wave amplitude change (<200 uV) at J-point 0 msec with clinically important ST-segment depression. However, there was an exact same frequency of non-signicant P-wave amplitude change (<200uV) between lead II and V5 with clinically significant ST-segment depression. The frequency of signicant P-wave amplitude change (>200uV) with clinically significant ST-segment depression was three times more likely in lead II. Whether there was significant(>200uV) or non-significant (<200uV) P-wave amplitude change, the frequencies of clinically important ST-segment depression were the exact same between leads II and V5 60 msec after the J-point.

PQ-SEGMENT SLOPE: There was a greater occurrence of downsloping PQ-segment shifts in lead II than in lead V5. Downsloping PQ-segment in lead II was statistically significant by Chi-square analysis (15.5, p=0.001). Eighty-eight percent of the 26 subjects showed flat PQ-segment slope shifts with exercise in lead V5. In contrast, only 46% of the 26 cases showed flat PQ-segment slope shifts in lead II. However, 15 % of the subjects in the downsloping PQ-segment group expressed 100 uV ST-segment depression 0 msec after J-point as opposed to the 4% in the flat PQ-segment group in lead II. Table 3 displays a frequency distribution of ST-segment level between the flat and downsloping PQ-segment groups. The purpose of this table was to look at the degree

of ST-segment depression and how it was distributed between the PQ-segment groups as well as leads. No ST-segment depression was noted at greater than 100 uV in either PQ-segment slope group or lead selection. In the flat PQ-segment slope group, there was twice as many of 50-100 uV ST-segment depression 0 msec after J-point in lead V5 than in lead II. However, 50-100 uV ST-segment depression 0 msec after J-point four times more likely in lead II of the downsloping PQ-segment group. There was a greater frequency of less than 50 uV ST-segment depression 60 msec after the J-point in both leads of the flat PQ-segment slope group. The ST-segment was upsloping.

Figure 5 shows the frequency of exercise-induced ST-segment shifts greater than 50 uV at J-point 0 and 60 msec in leads II and V5. The subjects that expressed nominal ST-segment shifts (< 50 uV) were not presented. The purpose of this figure was to determine if the appearance of downsloping PQ-segment influenced the ST-segment levels for important clinical analysis. It is evident in lead II that clinically important ST-segment depression was four times more likely to occur when PQ-segment shifts in exercise became downsloping as compared to V5. These lead differences in ST-segment response did not persist at 60 msec after the J-point (J-60). Lead V5 also showed twice as many cases of flat PQ-segment slopes with clinically significant ST-segment

depression in contrast to lead II. When differentiating between flat and downsloping PQ-segment groups within V5 responses, there was a seven-fold greater tendency of clinical important ST-segment depression when the PQ-segment slope was flat. In contrast, J-point depression was about equally distributed between the flat and downsloping PQ-segment groups in lead II.

Discussion

Methodological Concern: Analyses of stability for ECG responses to exercise suggested that the quality of the ECG tracings became an important factor in this study. Procedural factors like the preparation of the skin and placement of the electrodes along the breast tissue were readily controlled in order to prevent poor ECG signal quality from muscle tension and/or poor skin preparation. One person performed the skin preparation and electrode placement for consistancy. No underwire brassieres were allowed in this study.

Another methodological concern was the subject response stability during each trial as well as between two trials; regardless of computer-signal or visual analysis (Figures 2 & 3). The same test was performed on different days in order to prove reproducibility and/or stability of subject responses. However when Spearman rank order correlations were performed, trial B correlations were higher in every variable except for PQ slope in V5 than trial A. In addition, during the same

trial the computer-signal analysis correlations were moderately stable and more statistically significant ($p < 0.01$) among the ECG dependent variables as opposed to the visually analyzed. Therefore, the computer-signalled analyses during trial b were operationalized in further analyses (Figure 4) to safeguard for uncontrolled variables.

Responses in Lead II vs V5: Both precordial lead V5 and inferior lead II were utilized in order to determine if there was a relationship between ST level and atrial repolarization with false-positive responses. Precordial lead V5 is the most reproducible and extensively used lead in diagnosing myocardia ischemia (Herbert and Froelicher, 1991b; and Miranda et al. , 1992). Though lead II has been proven to be a false-positive lead (Miranda et al., 1992), it best represents atrial repolarization based upon its vector. Inferior lead II is a torso-mounted limb lead where the positive electrode is below the left pectoral muscle and the negative below the right clavicle. The Spearman Rank order correlations(Figures 2 & 3) of the P-wave amplitude and PQ-segment slope were moderately higher in lead II than lead V5 regardless of computer signal or visual analysis. In Figure 4 there was a greater frequency distribution of downsloping PQ-segments in lead II than in lead V5. These results demonstrate that inferior lead II best represents the P-wave and PQ-segment slope.

Downsloping PQ-segments and false-positive responses: Sapin

and associates (1991) suggested that exaggerated atrial repolarization waves during exercise could produce ST-segment depression that imitated myocardial ischemia. Their research indicated that the short, steeply downsloping PQ-segment, in the inferior leads, was an independent and reliable indicator of false-positive graded exercise test response in the presence of significant horizontal ST-segment depression.

In addition, Cumming et al, (1973) reported that women were three times more likely to have a false-positive response than men at the same age. When Deckers et al. (1990) attempted to evaluate possible gender differences, they found that ST-segment depression at greater than or equal to 1 mm was a poor predictor of ischemia in women. However when men and women were paired by age and presence and extent of CAD, there was no statistically significant difference between gender.

Sapin et al. (1991) found their false positive group expressed significantly greater increase in P wave amplitude between rest and peak exercise in leads II, III, aVF, V4, V5, and V6. However in this study, greater means of P-wave amplitude delta scores were found in lead II and not in lead V5. This was to be expected since inferior lead II best represents the P-wave based upon the placement of electrodes. The frequency of significant (>200uV) and non-significant (<200 uV) P-wave amplitude change among the ST level variables

was reported in Figure 4. There was three times greater frequency of significant P-wave amplitude increase with clinically significant at J-point 0 msec in lead II vs V5. However there was the exact same frequency of non-significant P-wave amplitude increase with clinically significant ST-segment depression at J-point 0 msec in both leads II and V5. The results had little influence as expected on J-point 60 msec in apparently healthy females during moderately vigorous exercise because the ST-segment was upsloping.

The frequency of either a downsloping PQ-segment or flat PQ-segment slope among the ST level variables was reported in Figure 5. In lead II, there was a greater frequency of downsloping PQ-segments with significant ST-segment depression (> 50 uV) in J-point at 0 msec. However, there was a greater percentage (91%) of flat PQ-segment slopes with clincally significant ST-segment depression in precordial lead V5. 15% of the total number of subjects expressed downsloping PQ-segment with 100 uV ST-segment depression 0 msec after the J-point. In healthy young women with moderately vigorous exercise, the results as expected have little influence at 60 msec from J-point because the ST-segment is upsloping. Our study does not support other papers that discuss the appearance of atrial repolarization (P-wave amplitude increase and downsloping PQ-segment) and the increase frequency of exercise-induced false-positive ST-segment responses.

Conclusions

The results of this study reveal the difficulty in clearly determining the influence of PQ-segment slope on the ST-segment during moderately vigorous exercise in females. However, these findings suggest the possible influence of lead selection on the measurements of the P-wave amplitude increase, PQ-segment slope, and ST-segment. The presented findings are from statistically insufficient data base. However, it appears that lead II is representative of apparently healthy subjects with fifteen percent speculation of likely false-positive results of which is not observed in lead V5. In contrast, there was a small tendency of downsloping PQ-segments in lead V5 with clinically significant J-point depression at 0 msec. J-point at 60 msec was not a applicable measure for this type of population. However, previously reported data suggest the effect of atrial repolarization will be maximal at the J-point and ST-segment will be upsloping.

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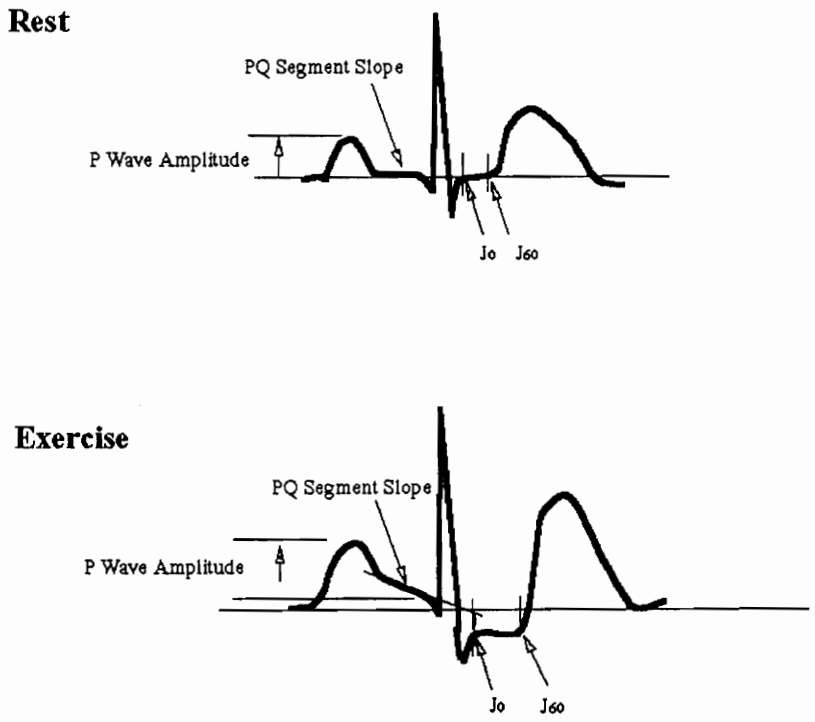
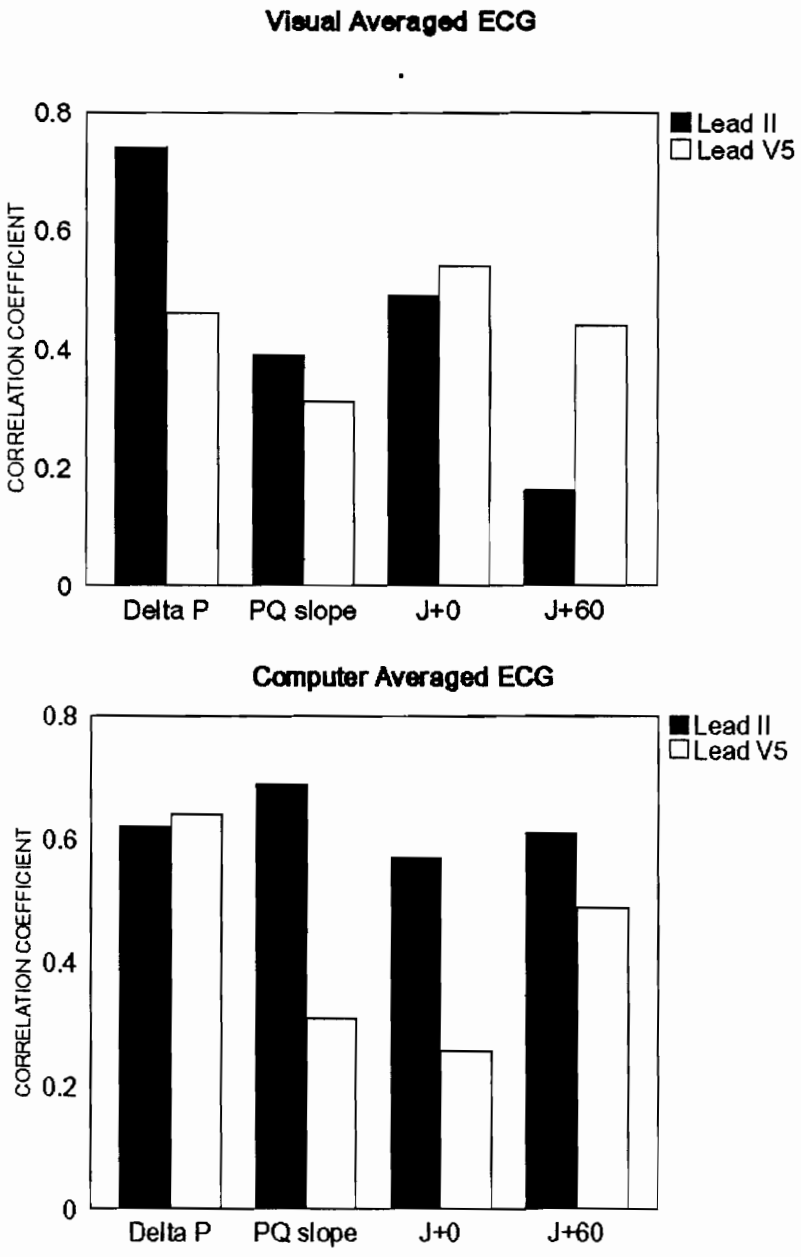


Figure 1:

Illustration of Exercise-Induced ECG Changes with Dependent Measures.

For each dependent measure, a delta score was calculated to represent the maximal shift that occurred in exercise, e.g., delta scores for P amplitude, PQ segment slope, J_0 and J_{60}.

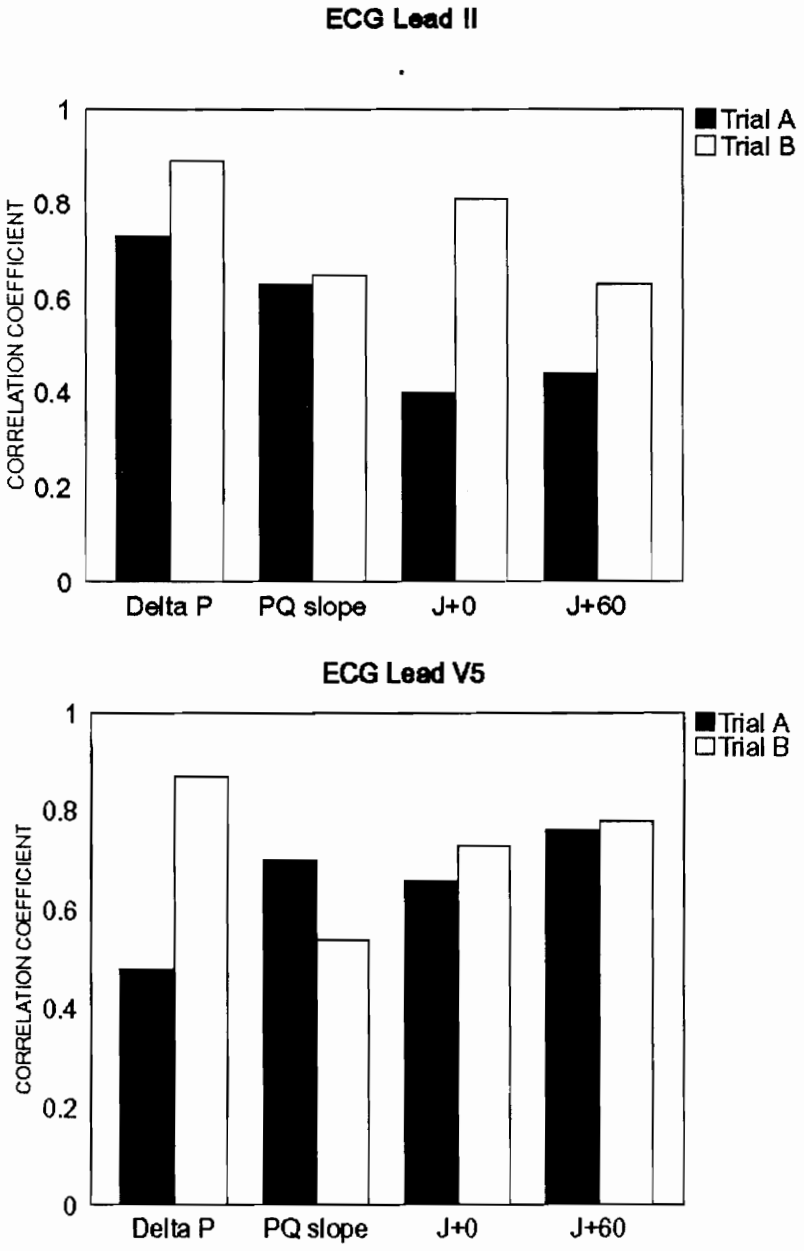


r @ $p < 0.05 = 0.42$; df 24

Figure 2

Stability of Selected Exercise-Induced ECG Responses

Inter-trial correlations



r @ $p < 0.05 = 0.42$; df 24

Figure 3

Stability of Selected Exercise-Induced ECG Responses

Within-trial correlations: visual vs computer signals

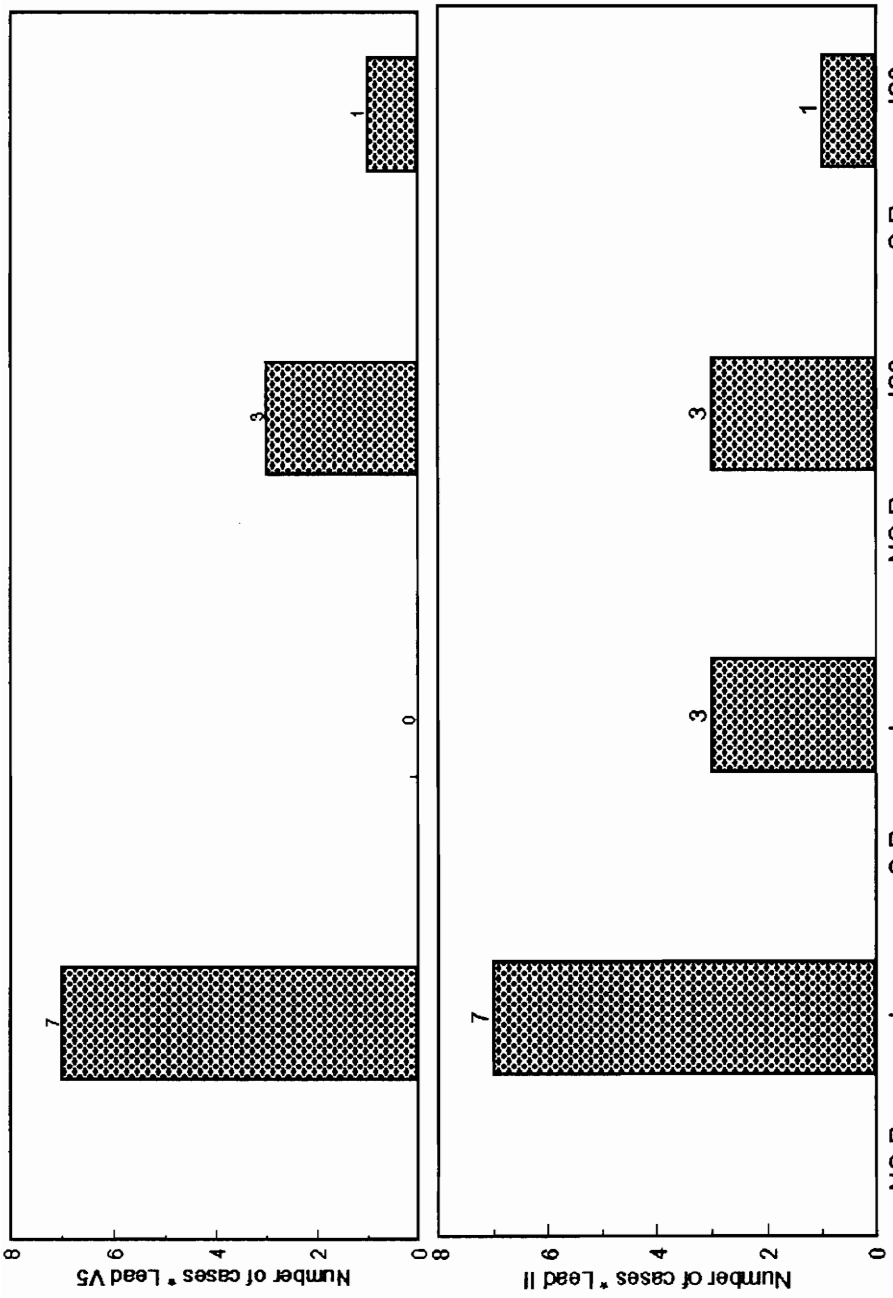


Figure 4 :

Frequency distribution of exercise ST responses > 50 uV in young healthy women according to non-significant (<200uV) vs significant (≥200uV) P-wave amplitude shifts in ECG Leads II vs V5.

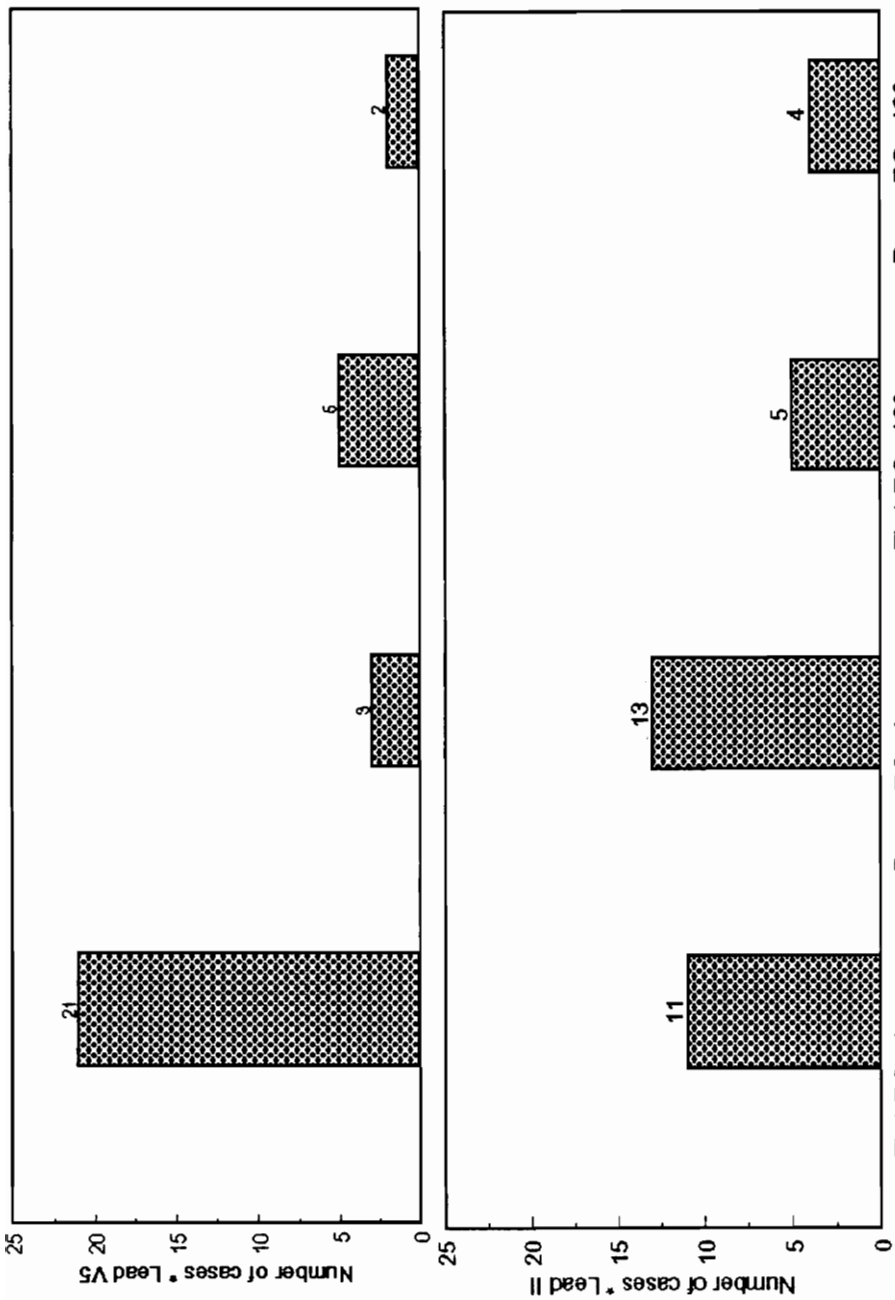


Figure 5 :
Frequency distribution of exercise ST responses > 50 uV in young healthy women according to flat vs downsloping PQ Segment shifts in ECG Leads II vs V5.

Table 1
Physical Characteristics and Hemodynamics of Subjects: Lead II, trial B

	Mean	Standard Deviation
Age(yr)		
Flat PQ (N=12)	21.3	0.9
Down PQ (N=14)	21.5	1.7
Total (N=26)	21.4	1.4
BMI (kg/m2)		
Flat PQ	22.0	1.9
Down PQ	24.0	1.7
Total	23.0	1.7
RHR * (b/min)		
Flat PQ	76	10
Down PQ	85	13
Total	81	13
RBP *(SBP/DBP)		
Flat PQ	100/68	7/5
Down PQ	98/65	9/4
Total	99/67	8/5

---

* Values were taken from seated resting positions.

Groups:

Flat PQ = subjects who expressed PQ-segment slope < 2.5 uv/sec

Down PQ = subjects who expressed PQ-segment slope > 2.5 uv/sec

Table 2
Cycle Ergometer Workload and Exercise Responses of Subjects: Lead II, trial B

	Mean	Standard Deviation
Power(watts)		
Flat PQ (N=12)	120	0.4
Down PQ (N=14)	126	0.4
Total (N=26)	124	0.4
Exercise HR*(b/min)		
Flat PQ	162	3.3
Down PQ	164	5.2
Total	163	4.5
Exercise BP* (SBP/DBP)		
Flat PQ	147/73	12/10
Down PQ	142/72	13/7
Total	144/73	12/9

---

* Values were taken from seated position.

Groups:

Flat PQ = subjects who expressed PQ-segment slope < 2.5 uv/sec

Down PQ = subjects who expressed PQ-segment slope > 2.5 uv/sec

Table 3
Frequency Distribution of ST-segment level between Flat and Downsloping PQ-segment

Flat PQ-Segment Slope

ST Level (uV)	Lead V5		Lead II	
	J+0	J+60	J+0	J+60
< 50	2	16	1	17
50-100	20	7	11	5
> 100	0	0	0	0
Total	22	23	12	22

Downsloping PQ-Segment

ST Level (uV)	Lead V5		Lead II	
	J+0	J+60	J+0	J+60
< 50	0	1	1	9
50-100	3	2	13	5
> 100	0	0	0	0
Total	3	3	14	14

Chapter IV

Summary and Recommendations for Future Research

Summary

Overview: Moderate to vigorous (> 60 % age-predicted maximum heart rate) exercise has been reported to induce false-positive ST segment shifts. As to date, the mechanism behind the high rate of false-positive findings in women remains unknown and inadequately addressed. The purpose of this study was to determine if the appearance of P-wave amplitude increase and PQ-segment slope influenced ST-segment depression in apparently-healthy, college-aged females during moderately vigorous exercise in leads II and V5.

Atrial Repolarization and false-positive responses: Sapin and associates (1991) suggested that exaggerated atrial repolarization waves during exercise could produce ST-segment depression that imitated myocardial ischemia. Their research indicated that the short, steeply downsloping PQ-segment, in the inferior leads, was an independent and reliable indicator of false-positive graded exercise test response in the presence of significant horizontal ST-segment depression. Sapin et al. (1991) also found that the false-positive group expressed significantly greater increase in P wave amplitude between rest and peak exercise in all six leads. The frequency of either a downsloping PQ-segment or flat PQ-segment slope among the ST level variables was reported on a figure. In lead II, there was a greater frequency of downsloping PQ-segments with significant ST-segment depression

(> 50 uV) in J-point at 0 msec. However, there was a greater percentage (91%) of flat PQ-segment slopes with clincally significant ST-segment depression in precordial lead V5.
In healthy young women with moderately vigorous exercise, the results as expected have little influence at 60 msec from J-point. Our study does not support other papers that discuss the appearance of downsloping PQ-segment, thus atrial repolarization, with the increase frequency of exercise-induced false-positive ST-segment responses.

The frequency of significant (> 200uV) and non-significant (<200 uV) P-wave amplitude change among the ST level variables was reported. There was three times greater frequency of significant P-wave amplitude increase with clinically significant at J-point 0 msec in lead II vs V5. However there was the exact same frequency of non-significant P-wave amplitude increase with clinically significant ST-segment depression at J-point 0 msec in both leads II and V5. The results had little influence as expected on J-point to msec in apparently healthy females during moderately vigorous exercise because the ST-segment was upsloping.

Responses in Lead II vs V5: Both precordial lead V5 and inferior lead II were utilized in order to determine if there was a relationship between ST level and atrial repolarization with false-positive responses. The Spearman Rank order correlations of the P-wave amplitude and PQ-segment slope were

moderately higher in lead II than lead V5 regardless of computer signal or visual analysis. There was a greater frequency distribution of downsloping PQ-segments in lead II than in lead V5. These results demonstrate that inferior lead II best represents the P-wave and PQ-segment slope.

Methodological Concern: Analyses of stability for ECG responses to exercise suggested that the quality of the ECG tracings became an important factor in this study. Procedural factors like the preparation of the skin and placement of the electrodes along the breast tissue were readily controlled in order to prevent poor ECG signal quality from muscle tension and/or poor skin preparation. Another methodological concern was the subject response stability during each trial as well as between two trials; regardless of computer-signal or visual analysis. The same test was performed on different days in order to prove reproducibility and/or stability of subject responses. However when Spearman rank order correlations were performed, trial B correlations were higher in every variable except for PQ slope in V5 than trial A. In addition, during the same trial the computer-signal analysis correlations were moderately stable and more statistically significant ($p< 0.01$) among the ECG dependent variables as opposed to the visually analyzed. Therefore, the computer-signalled analyses during trial b were operationalized in further analyses to safeguard for uncontrolled variables.

Conclusions: These findings suggest the possible influence of lead selection on the measurements of the P-wave amplitude increase, PQ-segment slope, and ST-segment. The presented findings are from statistically insufficient data base. However, it appears that lead II is representative of apparently healthy subjects with fifteen percent speculation of likely false-positive results of which is not observed in lead V5. In contrast, there was a small tendency of downsloping PQ-segments in lead VR with clinically significant J-point depression at 0 msec. J-point at 60 msec was not an applicable measure for this type of population. However, previously reported data suggest the effect of atrial repolarization will be maximal at the J-point and ST-segment will be upsloping.

Research Recommendations

The results of this study have indicated several areas of concern which should be addressed in future research. Further examination of the relationships between gender, atrial repolarization, and exercise false-positive responses is needed. The following is a discussion of some areas that may assist in the understanding of these relationships for future researchers.

1. The most important task of any research is to determine subject selection. This establishes the pool from which all

results will emanate. The small sample size of the study may be a source of the insignificant statistical findings. Unpaired T-tests and crosstabulations were impossible to use due to the small number in one of the groups. This is the reason why frequencies were used to determine possible effects of downsloping PQ-segment on ST-segment level. A larger sample size with more subject variability (i.e. older individuals from a clinical population and/or men) may be necessary to ensure greater statistical power. In addition, selection of subjects should rectify the situation by selecting equal numbers for each group.

2. The results of this type of research center around the analysis and interpretation of ECG records. Thus, the quality of the ECG is an important factor in the research process. The completion of this study revealed two aspects that affect the quality of the ECG. These aspects are the placement of electrodes and the type of brassiere worn by the subject. This study in addition to lead II, utilized lead V5 in the analysis of the results. The location of this lead allows the brassiere to affect the ECG tracings. Exercise brassieres were encountered in this study. If the mode of exercise is cycling as in this study, it is suggested that subjects be instructed not to wear a brasiere that provides excessive support below the breasts. Due to the non-jarring properties of cycling a maximum supporting bra is not needed. No matter

what type of bra is worn by the subjects, some difficulties are going to encounter in electrode placement. Future research should continue to experiment with the moving of electrodes and/or preclude the use of a brassiere in the study in order to maximize ECG tracings. It is also suggested during first trial to mark electrode placement with permanent marker to ensure same electrode placement between trials.

3. Great care was taken to minimize variability between the trials. Prior to testing, subjects were required to minimally exercise (35% of heart rate reserve) on the cycle ergometer. Testing days were scheduled during the same week and 1 day between tests (i.e. Monday & Wednesday or Tuesday & Thursday). Subjects were also instructed to follow same night routine prior to actual test day. However, variability was found between the trials. Lower reproducibility between trials could have existed due to the learning effect, difference in ECG tracings due to the use of two leads (II and V5), or the method of measuring the variables. In the future, research should experiment ECG computer systems that could reliably measure the PQ-segment slope.

4. Implication of clinical application should improve methods of stress testing as well as decrease poor interpretation of results in apparently healthy, non-obese but active college-aged females. This could be accomplished during stress testing by using the precordial lead V5 for diagnosing

coronary heart disease and by measuring ST-segment depression at J-point 60 msec instead of 0 msec.

5. The use of Beta-blockers on apparently healthy subjects would be another recommendation for future research. This drug increases the filling pressure of the atrium which in turn could induce exaggerated P wave responses.

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APPENDIX A

METHODOLOGY

Subject Selection and Screening:

All exercise testing was performed in the Laboratory for Health & Exercise Science, 230 WMH. Volunteer female students were selected for this study through a screening process. A personal interview and a health history questionnaire (Appendix G) were administered in order to select candidates who met the criteria of "apparently healthy" (Appendix C), according to the standards of the American College of Sports Medicine (ACSM, 1991). Exclusion from the screening exercise test included: any orthopedic or medical problems that impaired performance on a cycle ergometer; and any medications that affected resting and/or exercise ECG (Appendix E).

Upon qualifying as "apparently healthy", an informed consent (Appendix F) was also secured from each candidate. The candidate was then oriented to the testing procedures and equipment by performing mild exercise on the Monark cycle ergometer at an intensity equal to 35% of her cardiac reserve. Heart rate responses were measured every minute of exercise by a HeartWatch (Unisec Corp., NY), a heart rate monitoring watch. In addition, instructions were provided to each subject as follows: RPE scale; pedalling speed; proper sitting position; proper hand placement; and appropriate exercise attire.

On two nonconsecutive testing days, the candidate

returned to the lab and performed identical exercise tests. Thirty subjects then were selected from the candidate pool on the basis of an exercise screening test in which qualification required exhibiting exercise-induced J-point depression on the ECG (Lead V5 or V4) at 0 msec. For this exercise screening test, the YMCA cycle ergometer test protocol (Golding et al., 1982) was used. The intensity of this test was limited to 70% of the predicted cardiac reserve. The exercise ECG was evaluated visually and by computer averaging interpretation of the peak exercise ECG tracing.

Exclusion Criteria:

The following exclusion criteria were imposed:

1) subjects who did not produce exercise-induced J-point depression at 0 milliseconds in lead V5 at 70% of their cardiac reserve upon visual analysis;

2) abnormal resting electrocardiogram (Appendix C); and

3) excessive exercise-induced electrocardiographic artifact and baseline wandering during the test (greater than +/-0.2 mV vertical displacement between the onset of the P-wave and onset of the Q-wave of two morphologically similar ECG complexes)

Procedures:

ECG electrodes were positioned on the subject in the standard manner for Mason-Likar lead system: I,II, III, aVF, aVR, aVL, V1, V2, V3, V4, V5, and V6. The seat height on the

Monark cycle ergometer was adjusted to fit the subject. Following 10 minutes of seated rest, a baseline ECG tracing was obtained. Subject then exercised at the pedal speed of 50 RPM. Heart rate, blood pressure, and rate of perceived exertion (RPE) were measured during the second minute of each exercise stage. The ECG tracings were obtained during the last 10 seconds of each exercise stage and immediately post-exercise. In order to reduce ECG artifact, subjects were instructed to keep their torsos as still as possible and to keep their arms down by their sides during the test. They also were advised to temporarily refrain from breathing (3 seconds) during recording of the ECG tracings. Once the subject reached the 70% of their cardiac reserve, the subject immediately stopped pedalling and an ECG tracing was recorded. After the termination of the exercise test, the subject remained seated on the ergometer until heart rate and blood pressure responses returned to baseline (+/-10 b/min and mmHg).

ECG Recordings and Measurements:

ECG tracings were recorded without the use of signal filters at a speed of 50 mm/sec and at a sensitivity of 20 mm/mV. The ECG tracings were analyzed visually and by computer averaging using the X-Scribe Mortara stress testing system (Mortara Instruments, Milwaukee). Visual analysis required the averaging of two morphologically similar ECG

complexes that were recorded at baseline and at peak exercise in leads II and V5. The computer averaged ECG complexes included one mean ECG complex for the same leads used in visual analysis. During exercise, if the ECG complexes became distorted in lead V5, then lead V4 was used in both visual and computer analyses throughout the test.

The delta scores of the ECG variables were used because they represent the way exercise test results are interpreted in clinical settings for diagnosis. J-point depression was evaluated at 0 and 60 msec after the J-point. The delta scores for J-point depression were determined by subtracting baseline values from peak exercise values. If the measurements of the J-point depression at 0 and 60 msec were elevated above the isoelectric line at rest, the score for delta J-point depression was evaluated from the isoelectric line at peak exercise.

In order to determine the effects of atrial repolarization, P-wave amplitude shift and PQ-segment slope were also evaluated at both baseline and at peak exercise in leads II and V5. During exercise, if the PQ-segment slope was unclear in lead V5, then lead V4 was used for analysis. P-wave amplitude shift was the difference in vertical displacement of the P-wave between peak exercise and isoelectric baseline.

The PQ-junction served as the isoelectric point for

complexes with each exercise level. The PQ-segment displacement was measured (+/- 25 uV) over the interval of 20-30 msec before the PQ junction but without encroachment on the P-wave. The PQ-segment slope then was calculated as the displacement over time (uV/sec). PQ-segment slope shift was determined between baseline and peak exercise, as in the delta score for J-point depression. PQ-segment slope that was less than -2.5 uV/sec was considered flat while a slope greater than or equal to -2.5 uV/sec qualifies as downsloping. Based upon the PQ-segment slope definitions, the subjects' records were sorted into Group F= flat PQ-segment slope and Group D= downsloping PQ-segment.

Data Analysis:

A correlation between the raw and averaged ECG complexes was evaluated based upon the measurements of J-point depression, and PQ-segment slope using the Spearman Ranked correlation analysis. Because the P-wave values were continuous, Pearson's Product Moment was used for the correlation analysis. In order to determine the distribution of flat and downsloping PQ-segments among the dependent variables, a frequency distribution table was constructed. This table was used to determine the distribution of the two independent PQ-segment slope groups as determined in leads II and V5 to each dependent measure; delta J +0, delta J+60, and

delta P-wave amplitude. The delta scores of the J-point depression was ranked as follows: 1 is equivalent to less than or equal to 50 uV; and 2 is equal to greater than 50 uV.

Statistical analysis was performed on Statgraphics Statistical System. Throughout the data analyses, the significance was set at an alpha level of 0.05.

External Validity:

The characteristics of the subjects, asymptomatic, apparently healthy females between the age of 18 and 24, allow the experimental findings from this investigation to be generalized only to the population possessing comparable characteristics.

Internal Validity:

Variance of the measurements was minimized by: 1) familiarizing subjects with the testing protocols and procedures, 2) calibrating the equipment prior to testing, 3) conducting all testing at the same time of day, and 4) limiting participant's physical activity 24 hours before testing.

Appendix B

Statistical Procedures

In order to determine reliability of the data, a Spearman rank order correlation (Figures 2 & 3) was performed on the delta scores of PQ-segment slope and ST level which included J-point at 0 and J-point at 60 msec. A Pearson's Product Moment correlation (Table 4) was used to analyze the delta scores of P-wave amplitude due to their parametric nature.

Trial B r values in P-wave amplitude, PQ-segment slope, J-point at 0 milliseconds(msec) and J-point at 60 msec were greater in lead II (r=0.89, r=0.65, r=0.81, and r=0.63 respectively) than in trial A. However, the trial B r values of P wave amplitude, J-point at 0 msec, and J-point at 60 msec (r=0.87, r=0.73, and r=0.78 respectively) were greater except for the delta score of PQ segment slope (r=0.54) in precordial lead V5. These results demonstrate a higher reproducibility in trial B testing.

During the same trial the computer signal ECG measurements of P wave amplitude, PQ segment slope, J-point at 0 msec, and J-point at 60 msec (r=0.62, r=0.69, r=0.57, and r=0.61 respectively) were greater in lead II than the visually measured. In precordial lead V5, computer signals were more reproducible in P wave amplitude and J-point at 60 msec (r=0.64 and r=0.49 respectively) than with the variables of PQ segment slope and J-point at 0 msec as compared to the visually measured on the same trial.

The r value for the visually measured PQ segment slope in lead V5 was the same as the computer-signal measured during the same trial. These results suggested that the computer-signal averaged measurements were more predictive and reproducible than the variables visually-measured ECG tracings.

Based upon these results, the trial B computer-signal averaged variables were used in the frequency distribution (Figure 4) in order to determine the influence of P-wave amplitude shifts on exercise-induced ST-segment shifts greater than 50 uV at J-point 0 and 60 msec in leads II and V5. The subjects that expressed nominal ST-segment shifts (>50 uV) were not presented. J-point depression of greater than 50 uV was used as a marker for clinically important ST-segment depression. In lead V5 there was a seven-fold greater tendency of clinically important ST-segment depression when the P-wave amplitude shift was less than 200 uV at J-point 0 msec. In lead II, there was two times greater tendency of non-significant P-wave amplitude shift (<200 uV) at J-point 0 msec with clinically important ST-segment depression. However, there was an exact same frequency of non-significant P-wave amplitude shift (<200 uV) between lead II and V5 with clinically significant ST-segment depression. The frequency of significant P-wave amplitude change (>200uV) with clinically significant ST-segment depression was three times

more likely in lead II. Whether there was significant (>200uV) or non-significant (<200uV) P-wave amplitude shift, the frequencies of clinically important ST-segment depression were exactly the same between leads II and V5 60 msec after the J-point.

A similar frequency distribution (Figure 5) was also created to determine the influence of PQ segment slope on exercise-induced ST-segment shifts greater than 50 uV at J-point 0 and 60 msec in leads II and V5. It is evident in lead II that clinically important ST-segment depression was four times more likely to occur when PQ-segment shifts in exercise became downsloping as compared to V5. These lead differences in ST-segment response did not persist at 60 msec after the J-point (J-60). Lead V5 also showed twice as many cases of flat PQ-segment slopes with clinically significant ST-segment depression in contrast to lead II. When differentiating between flat and downsloping PQ-segment groups within V5 responses, there was a seven-fold greater tendency of clinical important ST-segment depression when the PQ-segment slope was flat. In contrast, J-point depression was about equally distributed between the flat and downsloping PQ-segment groups in lead II.

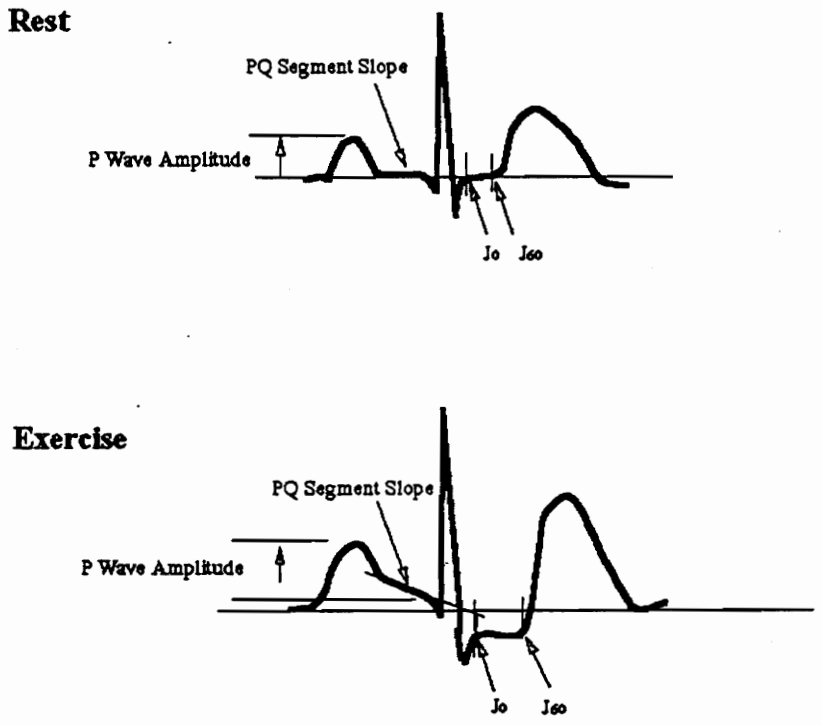


Figure 1:

Illustration of Exercise-Induced ECG Changes with Dependent Measures.

For each dependent measure, a delta score was calculated to represent the maximal shift that occurred in exercise, e.g., delta scores for P amplitude, PQ segment slope, J_0 and J_{60}.

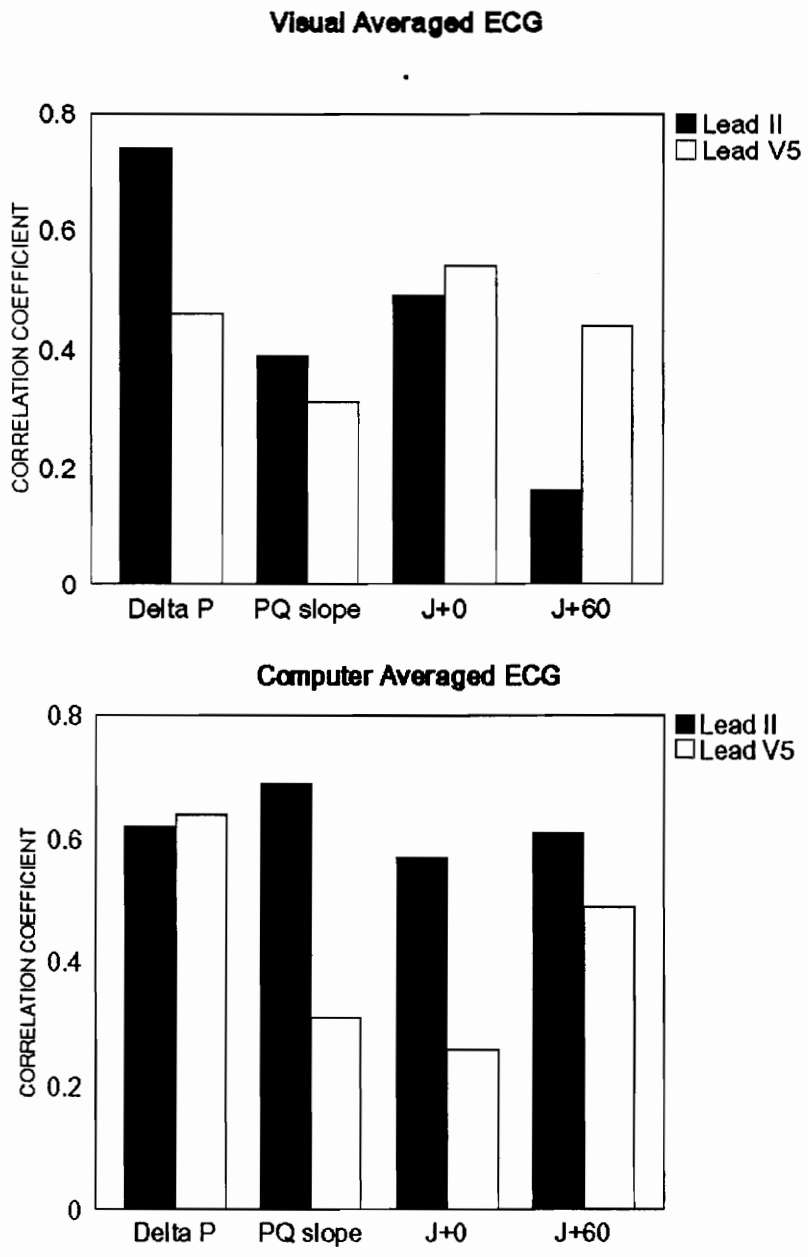
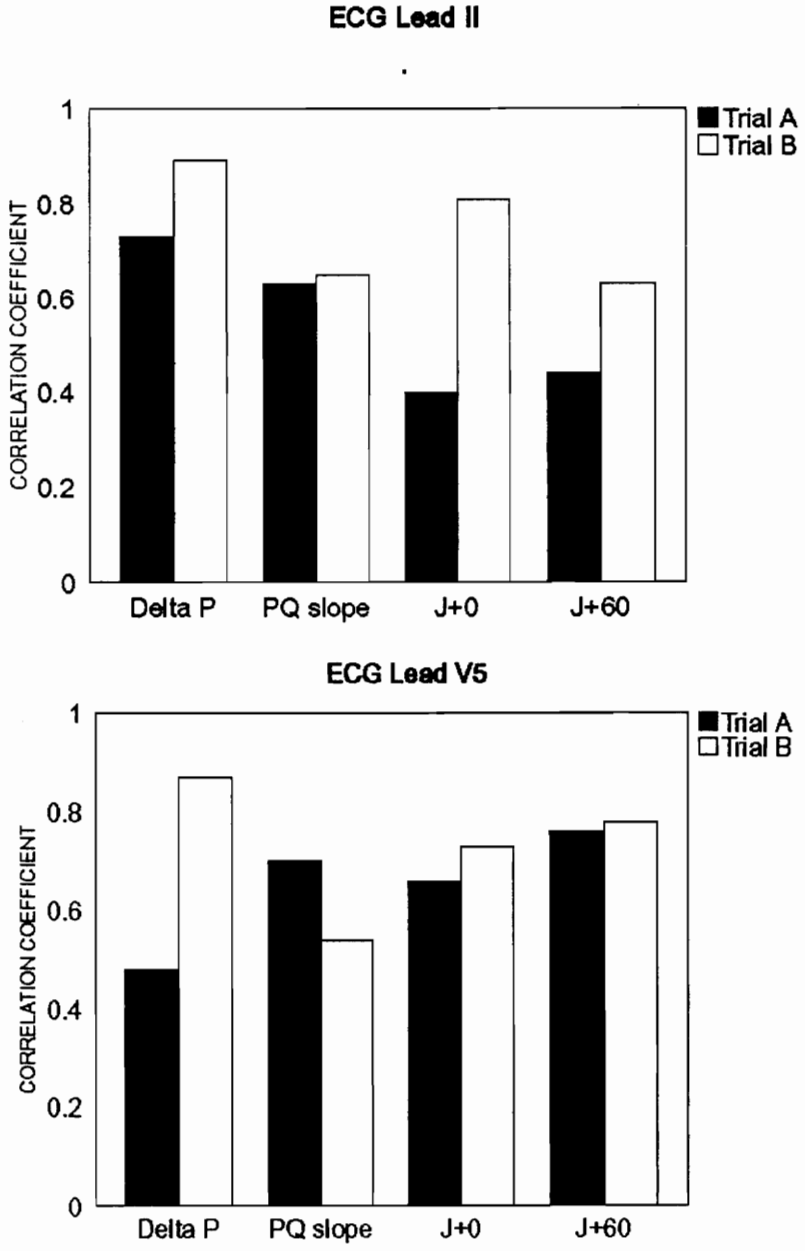


Figure 2

Stability of Selected Exercise-Induced ECG Responses

Inter-trial correlations



r @ $p < 0.05 = 0.42$; df 24

Figure 3

Stability of Selected Exercise-Induced ECG Responses

Within-trial correlations: visual vs computer signals

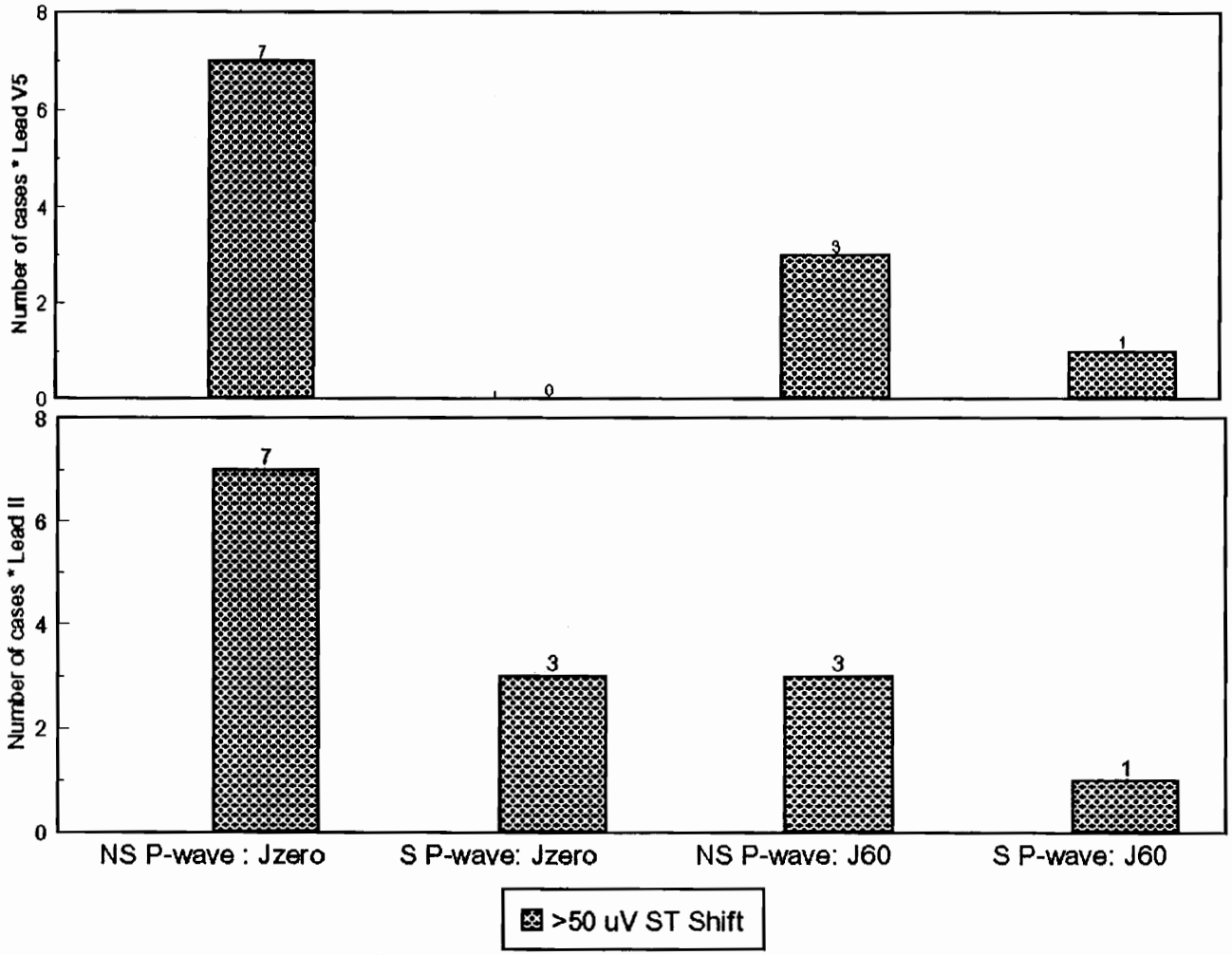


Figure 4 :

Frequency distribution of exercise ST responses > 50 uV in young healthy women according to non-significant (<200uV) vs significant (>200uV) P-wave amplitude shifts in ECG Leads II vs V5.

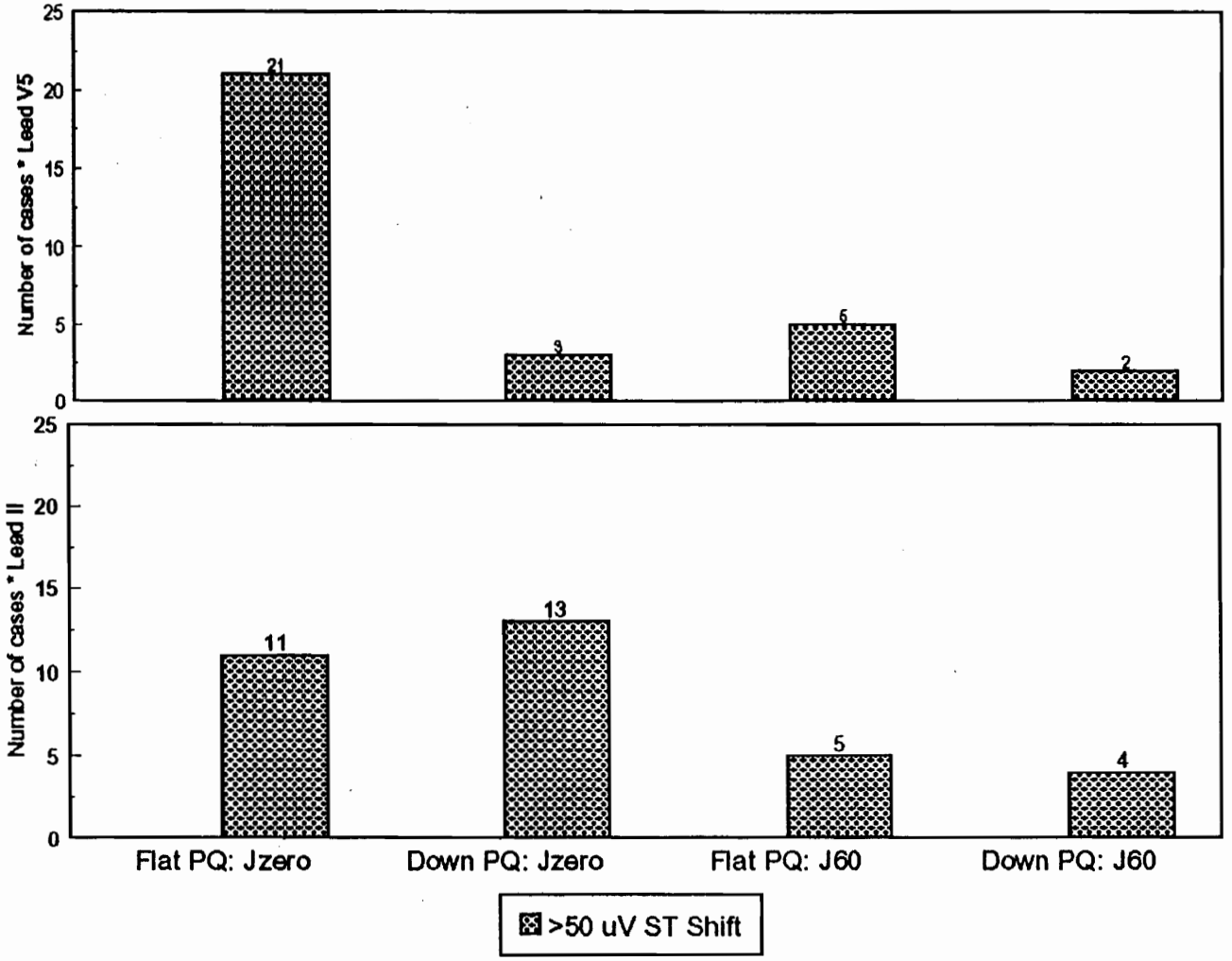


Figure 5 :

Frequency distribution of exercise ST responses > 50 uV in young healthy women according to flat vs downsloping PQ Segment shifts in ECG Leads II vs V5.

Table 4
Descriptive Statistics and Correlations of ECG computer averaged delta scores in trial B

Measure	Mean	Standard Deviation	DF	r value	Signif (p<0.01)
Delta P wave amp, lead II (uV)	123	63			
			24	0.43	0.16
Delta PQ slope, lead II (uV/sec)	2.16	1.19			
Delta P wave amp, lead V5 (uV)	103	52			
			24	0.9	0.02
Delta PQ slope, lead V5 (uV/sec)	1.22	0.60			
J-pt 0 msec, lead II (uV)	64.4	23			
			24	0.49	0.01
J-pt 0 msec, lead V5 (uV)	54.8	18			
J-pt 60 msec, lead II (uV)	30.8	29			
			24	0.56	0.005
J-pt 60 msec, lead V5 (uV)	24.0	24			

APPENDIX C

APPARENTLY HEALTHY CRITERIA

Criteria for Apparently Healthy

asymptomatic and apparently healthy with no more than one major coronary risk factor:

Major Coronary Risk Factors

1. Diagnosed hypertension or systolic blood pressure greater than or equal to 160 or diastolic blood pressure greater than or equal to 90 mmHg on at least 2 separate occasions, or on antihypertensive medication
2. Serum cholesterol greater than or equal to 6.20 mmol/L (greater than or equal to 240 mg/dl)
3. Cigarette smoking
4. Diabetes mellitus
5. Family history of coronary or other athersclerotic disease in parents or siblings prior to age 55

(ACSM.1991)

APPENDIX D

RESTING ECG ABNORMALITIES

Resting Electrocardiographic Abnormalities

atrial fibrillation

Q-wave abnormalities

ST-segment depression

T-wave changes

ventricular conduction defects

left axis deviation

left ventricular hypertrophy

(Froelicher,1987)

APPENDIX E

MEDICATIONS THAT AFFECT THE ECG

Medications that Affect the Electrocardiogram

digitalis

diuretics

antiarrhythmic agents

bronchodilators

hyperlipidemic agents

antidepressants

lithium

nicotine

thyroid medications

alcohol

APPENDIX F

INFORMED CONSENT

INFORMED CONSENT

Title of Study: **Effects of Atrial Repolarization on Signs of Myocardial Ischemia in the Exercise ECG Responses of Healthy Females**

Purpose of Study: False-positive electrocardiographic(ECG) exercise tests (stress tests) are common among the female population. It is the purpose of this study to determine if atrial repolarization is responsible for indicating myocardial ischemia (heart disease) during exercise in healthy females.

Requirements of Study:

1. Completion of a health history questionnaire that includes information concerning family history of heart disease and hypertension, past and present illnesses, injuries, or health related problems that require medical attention, and current exercise habits.
2. Participation in a screening process to determine if I qualify as a subject. Screening involves the application of electrodes onto the chest, performing submaximal exercise, and having ECGs (a tracing of the electrical activity produced by contractions of the heart) recorded.

UPON QUALIFYING AS A SUBJECT, THE FOLLOWING APPLY:

3. The measurements of blood pressure, heart rate, ECG tracing at both rest and during submaximal exercise on a cycle ergometer.

4. Abstinence of exercise and smoking 24 hours prior to testing.

5. Fasting state of at least 2 hours prior to testing.

6. Exercise testing will be performed in the Human Performance Laboratory. Upon arrival, electrodes will be applied to the chest. Subjects will not be allowed to wear any form of under-wire brassier during testing. They will then be seated on the cycle ergometer for a 10 minute rest. After this time, the subject will exercise until 70% of the age-predicted maximum heart rate is achieved. Once the target heart rate is achieved, the exercise test is terminated. The subject will remain seated on the cycle until heart rate and blood pressure values are equal to resting values.

Risks Associated With Participation:

Participation in this study may produce some discomfort and/or risks. They include:

1. temporary muscle soreness due to the exercise test;
2. possible skin irritation due to the skin preparation for the application of electrodes and to the adhesives on the electrodes.

Personal Benefits Associated With Participation:

The following personal benefits could a

pply due to your participation in this study:

1. knowledge of heart rate and blood pressure values during rest and exercise;

2. approximation of fitness level;

3. personalized exercise prescription (if desired).

Confidentiality:

I understand that any data of a personal nature will be held in confidence and will only be used for research purposes. I also understand that of the data used, my name will remain anonymous.

I understand that I have the right to withdrawal from this study at any time if I feel that the participation may be hazardous to my health. The researcher also has the right to terminate my participation should she feel that it may be hazardous to my health.

It is also the participant's responsibility to inform the researcher of any discomforts or injuries, as well as any medical problems (preexisting or not) that may occur during the course of this study and/or affect this study in any way. In the course of any medical emergency a telephone will be available to notify the emergency services. The researcher is also certified in both Basic Life Support(BLS) as well as Advanced Cardiac Life Support (ACLS).

I have read and understood the above statements and have had the opportunity to ask questions. I understand that the researcher will, at any time, answer my inquires concerning the procedures used in this study.

DATE:_____ TIME:_____AM/PM

P A R T I C I P A N T

SIGNATURE:_____

WITNESS:_____

If at any time the subject has questions, contact:

Project Chairperson: **Dr. William Herbert** (703-231-6565)

University Institutional Review/ Research Division:

Janet Johnson (703-231-6077)

APPENDIX G

Health History Questionnaire

HEALTH HISTORY QUESTIONNAIRE

Name:_____ Age:_____

Local Address:_____

_____

Local Phone #:_____

Are you currently taking any medications (prescription and non-

prescription)?_____ If Yes, please list.

Medication Name	Dosage per Day	Reason

Do you smoke?_____ If yes, please indicate below how many cigarettes do you smoke per day?_____

Do you have any medical or orthopedic conditions? If so, please
describe._____

_____

_____

_____

Average Weekly Exercise Routine

Type of Activity	Duration	Frequency
1.		
2.		
3.		
4.		

Appendix H

Data Collection Sheet

DATA COLLECTION SHEET

Date:_____ I.D._____

Weight(kg):_____ Height(cm):_____

Target Heart Rate:_____

Testing Protocol:

	Workload	HR	BP	RPE
Rest		____	____/____	
Exercise				
I	_____	____	____/____	____
II	_____	____	____/____	____
III	_____	____	____/____	____
IV	_____	____	____/____	____
V	_____	____	____/____	____
Recovery				
0 min	_____	____	____/____	____
1 min		____	____/____	
2 min		____	____/____	
4 min		____	____/____	
6 min		____	____/____	
8 min		____	____/____	

Appendix I

Raw Data

The following codes apply to the variables listed in the preceding pages of raw data tables:

a. a = trial one

b. b = trial two

c. HR = heart rate

d. SBP = systolic blood pressure

e. DBP = diastolic blood pressure

f. RPE = Rate of Perceived Exertion (Borg)

g. D = delta score

h. E = peak exercise value

i. P = P wave amplitude (microvolts)

j. PQ = PQ segment slope (microvolts/sec)

k. J0 = ST segment measurement of J-point at 0 msec (microvolts)

l. J60 = ST segment measurement of J-point at 60 msec (microvolts)

m. 2 = Lead II

n. 5 = precordial lead V5

o. r = raw or visual ECG analysis

p. v = computer averaged signal ECG analysis

Table 1
Raw Data of Subjects

Subject	Age	Height a	Height b	Weight a	Weight b
1	20	164	164.5	67.7	66.4
2	22	163.5	163.5	70	72
3	22	155	156.5	50.4	50.1
4	20	163.8	163	56.2	54.4
5	21	171	172.5	64	64.2
6	21	159.8	159.3	58.2	57.6
7	22	158	158	53.1	52.7
8	19	165	164	60.6	65
9	21	156.5	156.5	50.2	50.3
10	20	164.5	165	63.3	62.2
11	21	152.5	151	53.7	54.8
12	22	163	162	57	56.6
13	20	161.5	161	65.4	65.3
14	22	158	157.5	53	53.7
15	22	168.5	169.3	60.4	59.5
16	22	156.5	157	53	52.1
17	21	161.3	161.5	56	56.2
18	22	159.3	159.3	68.5	67.7
19	23	161	160.5	63.5	63
20	22	158.3	157.5	60	58.8
21	20	162	162	62.2	61.9
22	21	176	176.5	62.5	62.3
23	23	174	176	64.5	63.5
24	20	162	162	60.2	61.9
25	26	157.5	156.5	57.2	58.4
26	21	167.5	167	60	59.7

Table 2
Raw Data of Subjects

Subject	RestHRa	PHRa	DHRa	RestHRb	PHRb	DHRb
1	89	167	78	86	166	80
2	88	165	77	90	166	76
3	85	164	79	86	164	78
4	95	169	74	108	172	64
5	74	162	88	72	161	89
6	77	162	85	73	161	88
7	92	166	74	95	167	72
8	120	176	56	100	171	71
9	84	165	87	88	166	78
10	71	160	89	72	161	89
11	87	167	80	83	163	80
12	101	169	68	90	165	75
13	84	166	82	86	166	80
14	90	164	74	80	164	84
15	83	164	81	88	165	77
16	66	158	92	66	158	92
17	71	161	90	62	158	96
18	82	164	82	88	165	77
19	51	154	103	50	152	102
20	100	166	66	73	161	88
21	90	165	75	89	166	77
22	81	163	82	81	163	82
23	62	157	95	66	155	89
24	67	160	93	66	160	94
25	72	155	83	86	157	71
26	84	164	80	75	162	87

Table 3
Raw Data of Subjects

Subject	RestSBPa	PSBPa	DSBPa	RestSBPb	PSBPb	DSBPb
1	100	146	46	92	142	50
2	114	160	46	102	132	30
3	92	132	40	112	124	12
4	92	122	30	92	124	32
5	104	160	56	114	154	40
6	94	140	46	90	156	66
7	108	144	36	112	138	26
8	94	150	56	104	140	36
9	112	174	62	104	184	80
10	102	148	46	90	142	52
11	92	132	40	112	132	20
12	102	162	60	112	132	20
13	100	142	42	102	152	50
14	102	142	40	100	132	32
15	102	152	50	102	130	28
16	114	170	56	102	156	54
17	88	124	36	80	132	52
18	96	162	66	90	162	72
19	92	132	40	94	128	34
20	104	152	48	92	150	58
21	84	152	68	92	150	58
22	92	162	70	96	162	66
23	102	142	40	92	144	52
24	92	142	50	100	144	44
25	114	174	60	102	166	64
26	112	150	50	96	144	60

Table 4
Raw Data of Subjects

Subject	RestDBPa	PDBPa	DDBPa	RestDBPb	PDBPb	DDBPb
1	66	60	6	62	68	6
2	80	84	4	70	80	10
3	64	64	0	64	62	2
4	64	64	0	60	60	0
5	64	74	10	72	64	8
6	76	66	10	64	62	2
7	72	72	0	78	68	10
8	70	88	18	74	82	8
9	82	88	6	72	86	14
10	70	80	10	68	82	14
11	64	72	8	62	70	8
12	74	58	16	64	72	8
13	70	68	2	64	80	16
14	80	90	10	64	82	18
15	64	64	0	66	64	2
16	70	80	10	78	84	6
17	66	80	14	60	68	8
18	70	72	2	66	86	20
19	76	68	8	70	64	6
20	60	76	16	60	80	20
21	64	72	8	70	70	0
22	76	80	4	64	70	6
23	66	72	6	64	66	2
24	70	88	18	62	74	12
25	70	84	14	64	70	6
26	70	82	10	60	72	8

Table 5
Raw Data of Subjects

Subject	PRPEa	PRPEb	DrP2a	DrP2b	DvP2a	DvP2b
1	13	13	200	200	125	125
2	13	13	150	200	150	125
3	12	12	200	50	150	75
4	14	14	200	225	200	200
5	14	13	150	150	100	150
6	15	16	100	125	150	150
7	14	14	250	175	275	200
8	12	10	50	0	50	50
9	13	13	100	25	100	25
10	17	17	100	150	100	125
11	13	13	50	125	75	100
12	16	16	50	100	75	75
13	14	13	100	125	100	125
14	13	14	75	50	100	75
15	17	17	100	125	125	100
16	10	10	50	75	100	50
17	13	14	300	250	125	250
18	15	15	300	325	250	300
19	15	16	275	300	250	350
20	14	13	100	225	125	175
21	16	16	100	100	125	50
22	15	15	200	225	275	150
23	15	16	150	75	150	150
24	16	15	175	150	125	150
25	12	10	125	100	125	100
26	17	17	100	150	75	175

Table 6
Raw Data of Subjects

Subject	DrP5a	DrP5b	DvP5a	DvP5b	PrPQ2a	PrPQ2b
1	100	100	100	100	2.5	2.5
2	75	50	50	100	2.5	2.5
3	125	50	50	75	1.67	1.87
4	100	100	125	100	2.5	5.0
5	75	125	100	100	1.67	1.25
6	100	75	100	100	0.63	1.88
7	125	125	125	125	1.5	1.67
8	100	0	75	0	2.5	2.5
9	75	25	75	25	1.5	2.5
10	125	200	100	150	5.0	1.67
11	50	50	25	75	2.5	7.5
12	150	100	25	100	2.5	5.0
13	75	25	50	50	1.0	2.5
14	100	25	100	25	1.0	2.5
15	50	100	75	100	2.5	3.3
16	100	75	75	75	0.63	0
17	200	150	175	200	2.5	3.33
18	175	175	175	150	1.25	2.5
19	150	200	150	200	2.5	2.5
20	125	75	100	150	1.66	2.5
21	75	125	50	100	5.0	2.5
22	75	125	175	150	1.88	2.5
23	75	150	125	150	1.25	0
24	100	100	75	100	2.5	1.67
25	75	75	100	75	2.5	2.5
26	100	100	100	100	5.0	2.5

Table 7
Raw Data of Subjects

Subject	PrPQ5a	PrPQ5b	PvPQ2a	PvPQ2b	PvPQ5a	PvPQ5b
1	1.67	0.63	2.5	2.5	1.67	1.67
2	0	1.25	2.5	5.0	0.83	1.25
3	1.25	1.25	0	1.67	1.25	1.25
4	1.25	2.5	2.5	3.33	1.25	2.5
5	1.67	1.25	1.67	1.25	0.83	1.25
6	1.5	1.25	1.67	1.67	0.83	0.63
7	1.0	1.25	1.67	1.25	0.63	1.25
8	1.66	1.0	1.25	2.5	1.43	1.25
9	1.25	1.25	1.67	1.2	1.67	1.25
10	1.67	1.67	1.25	1.67	1.25	0.83
11	3.75	0.83	2.5	5.0	1.25	1.25
12	3.75	2.5	2.5	2.5	1.25	2.5
13	1.25	1.25	1.25	1.25	1.25	1.25
14	1.25	1.25	0.88	1.67	1.67	1.25
15	2.5	2.5	2.5	2.5	2.5	2.5
16	0.63	0	1.25	0	0.63	0
17	1.67	1.67	1.67	1.25	1.67	1.67
18	1.25	1.25	1.25	2.5	0.83	0.63
19	2.5	0.83	2.5	2.5	2.5	0.83
20	0.83	1.25	2.5	2.5	0.83	1.66
21	3.33	1.67	5.0	2.5	2.5	0.83
22	0.83	0.83	1.67	2.5	0.83	0.83
23	0.63	0.67	0.63	0	0.63	0.67
24	1.67	0.63	1.67	1.67	1.67	0.63
25	1.67	1.25	2.5	2.5	0.83	1.25
26	0.83	0.83	5.0	3.33	0.83	0.83

Table 8
Raw Data of Subjects

Subject	DrJ02a	DrJ02b	DrJ05a	DrJ05b	DvJ02a	DvJ02b
1	50	50	50	50	50	50
2	50	50	25	25	50	25
3	50	75	50	50	75	75
4	50	100	75	100	100	100
5	50	50	50	50	50	50
6	25	50	75	50	50	75
7	50	50	50	50	50	50
8	50	50	75	50	75	50
9	50	75	50	75	75	75
10	50	50	50	50	50	50
11	100	50	50	50	50	50
12	100	75	50	50	50	75
13	0	50	50	50	100	50
14	0	50	50	0	50	50
15	100	100	50	50	100	100
16	50	25	0	0	25	25
17	100	100	100	50	100	100
18	100	50	50	50	100	50
19	50	50	50	50	50	50
20	50	50	50	50	50	50
21	50	50	50	50	50	75
22	50	50	50	75	100	100
23	100	75	75	75	100	75
24	50	50	50	50	75	50
25	75	75	50	50	75	75
26	100	100	50	50	100	100

Table 9
Raw Data of Subjects

Subject	DvJ05a	DvJ05b	DrJ602a	DrJ602b	DvJ602a
1	50	50	0	25	50
2	50	50	100	100	100
3	50	75	0	0	0
4	100	75	25	50	50
5	50	50	25	25	25
6	75	50	25	50	25
7	50	50	0	0	0
8	75	75	50	0	50
9	50	75	50	0	0
10	50	50	50	0	0
11	100	50	50	50	50
12	100	50	0	0	50
13	50	50	50	0	0
14	50	25	50	25	50
15	50	50	0	25	50
16	0	0	0	50	0
17	100	50	50	100	100
18	50	75	25	0	25
19	50	50	0	0	0
20	50	50	0	0	0
21	50	50	100	0	75
22	50	75	50	0	0
23	75	75	25	25	25
24	75	50	0	0	0
25	75	50	0	0	0
26	75	75	0	25	0

Table 10
Raw Data of Subjects

Subject	DvJ602b	DrJ605a	DrJ605b	DvJ605a	DwJ605b
1	25	0	25	25	50
2	100	100	50	75	50
3	25	0	0	0	0
4	50	0	50	0	25
5	50	0	0	25	0
6	25	50	50	50	25
7	25	0	0	0	25
8	0	25	0	0	25
9	0	0	25	0	0
10	50	25	0	0	0
11	50	0	50	0	25
12	0	0	0	0	0
13	25	0	0	0	0
14	50	50	50	50	75
15	75	75	100	25	75
16	50	0	50	0	50
17	75	100	25	100	25
18	25	0	0	0	25
19	0	0	0	0	25
20	0	0	0	0	0
21	75	50	50	50	50
22	0	25	0	25	0
23	25	25	50	75	50
24	0	0	0	0	0
25	0	25	0	25	0
26	0	0	25	25	25

VITA

Rhonda Kay Brown was born on Feburary 20, 1969 in Lynchburg, Virginia. Rhonda was raised in Amherst and graduated from Amherst County High School in 1987.

Rhonda continued her education at Virginia Polytechnic Institute and State University. She received her B.S. in Biology with a minor in psychology. Rhonda was planning to apply to physical therapy school and was required to take a few classes in the department of Health and Physical Education. Rhonda enjoyed the classes so well that she applied for the M.S. program in Education with the concentration in Adult Fitness and Rehabilitative Exercise.

Rhonda is currently employed by Radford Community Hospital in Cardiac Rehabilitation. Her ultimate dream is to work for NASA.