HYPERVENTILATION AND ECG COMPONENTS USED IN EXERCISE FOR DIAGNOSIS OF ISCHEMIC HEART DISEASE IN HEALTHY FEMALES

BY

TIMOTHY M. ROSE

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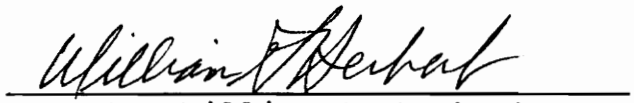

Dr. William G. Herbert
(Chairperson)

Dr. Don Sebolt

Dr. John C. Lee

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Blacksburg, Virginia

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Abstract

Hyperventilation has been reported to cause false-positive ischemic shifts in the ST-segment of the electrocardiogram during exercise. These responses have been observed to occur at a higher incidence in females than males. Therefore, the purpose of this study was to determine the effects of the performance of pretest hyperventilation on ECG components that are suggestive of myocardial ischemia in females. A standard 12-lead Mason-Likar recording set was used including leads I, II, II, aVR, aVL, aVF, V_2, and V_5. Fifteen females comprised the subject pool for this study, which was screened on the basis of J-point depression in a preliminary exercise procedure. The fifteen subjects each performed two exercise sessions, one with no hyperventilation and the other with a preliminary hyperventilation. Statistically significant differences were found between the baseline and post-hyperventilation ECG ($P<.05$). Analysis of the results revealed no significant differences in J-junction depression, ST slope, and the ST integral between the two testing conditions. Hyperventilation did affect the ST responses of the ECG in these young adult females at baseline and its continued use in conjunction with graded exercise testing may help uncover ST-segment changes associated with false-positive exercise responses. Hyperventilation may be performed in

young adult females in conjunction with GXTs without the liklihood of augmenting ST-segment shifts during the exercise.

key words: females, hyperventilation, false-positive tests, J-junction depression, ST slope, ST integral

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Chapter I

Introduction

Cardiovascular disease is a devastating killer that affects today's society. Various means exist which aid in controlling this disease. The prognosis of the disease must first be established in order to choose a route of action to follow. This task is accomplished through the use of clinical graded exercise tests (GXTs). The prognostic use of GXTs falls under two categories: (1) to provide accurate answers to questions concerning the probable outcome of the disease; and (2) to identify individuals in whom interventions might improve the outcomes (Fletcher et al., 1990). During GXT performance, the probability of latent coronary artery disease (CAD) or disease severity is evaluated in terms of heart rate responses, blood pressure changes, electrocardiographic (ECG) changes, and symptoms. The ECG is used extensively in diagnosing heart disease, primarily through the evaluation of ST-segment changes.

The importance of the ECG is evident because the probability and severity of CAD are directly related to the amount of J-junction depression and are inversely related to the slope of the ST-segment, i.e., the greater the depression and the downslope, the more likely and more severe CAD (Fletcher et al., 1990). The most common manifestation of exercise-induced myocardial ischemia is ST-segment depression. Most authorities consider ST depression of 1.0 mm (0.10 mV) below the resting post-hyperventilation baseline for a

duration of 80 msec or longer from the J-point as significant evidence of myocardial ischemia (ACSM, 1991; Fletcher et al., 1990).

Statement of the Problem

Although the GXT serves as a standard first line technique utilized in diagnosing heart disease, it is not free from technical problems that confound interpretation. One such problem occurs in the diagnostic accuracy of abnormal exercise ECG findings for women versus men. False-positive test results occur at a greater frequency in women than men (Lepeschkin & Surawicz, 1958; Profant et al., 1972; Murayama et al., 1985).

The use of hyperventilation as a procedure preliminary to the clinical GXT is yet another area of controversy (Bruce, 1988). There is controversy as to whether hyperventilation should be performed routinely and, if so, whether to utilize it as a pre-GXT or post-GXT challenge. Some studies indicate that hyperventilation performed pretest is utilized to unveil ST-segment changes that might be associated with false-positive exercise ECG responses (Gianrossi et al., 1989; Fletcher et al., 1990). Other studies indicate that performance of pretest hyperventilation can induce ST depression during exercise that is indicative of hyperventilation-induced myocardial ischemia (Ardissino et

al., 1989; Bruce, 1988)). Resolution of problems in these areas would provide a means for enhancing the clinical efficiency of diagnostic exercise electrocardiographic testing.

Purpose

The purpose of this study was to determine whether J-point depression and ST-segment changes during exercise are affected by the performance of pretest hyperventilation in a young, healthy adult female population performing moderate intensity stationary cycling.

Significance of the Study

Since the GXT has become the foremost tool in diagnosing heart disease, optimizing results from these tests has evolved with utmost importance. One important area of ongoing research seeks to delineate technical factors which affect the rates of false-positive and false-negative responses. False-positive responses to exercise are extremely problematic as they suggest the presence of disease. However, these results are not confirmed by invasive studies of coronary artery anatomy. Therefore, false-positive responses present problems to the physician in determining which individuals require further diagnostic procedures. Evidence exists that false-positive changes in the ECG complex during exercise are

amplified with certain electrode placement sites on the chest wall (Herbert & Froelicher, 1991a) and by voluntary hyperventilation (Pribble, Kusumi, & Bruce, 1987; Herbert & Froelicher, 1991b). Furthermore, it is known that hyperventilation-induced false-positive responses occur more frequently in women (Cumming, Dufresne, & Samm, 1973).

This study provided answers concerning the increased incidence of false-positive responses to the GXT in conjunction with the performance of pretest hyperventilation. Specific attention was be focused on females and if the performance of pretest hyperventilation elicits false-positive ECG changes. The scope of this study offered valuable information concerning testing procedures which will aid in decreasing the occurrence of false-positive responses.

Research Hypotheses

The following hypothesis evolved from the development of this study:

H_o^1: Performance of pretest hyperventilation will have no effect on J-point depression, ST integral, and ST slope in lead V_5 in females performing submaximal exercise, representing 60% age-predicted maximal heart rate, via a cycle ergometer.

Delimitations

The following are delimitations imposed by the researcher in this study:

1. Subjects utilized were limited to apparently healthy college aged female volunteers.
2. Subjects were selected only if they elicited J-point depression with moderate intensity exercise.
3. Each exercise session consisted of the performance of exercise on a stationary cycle ergometer representing 60% heart rate reserve predicted maximal.
4. Hyperventilation was performed pretest at one exercise session and was not performed at the other exercise session.
5. The dependent measures were limited to J-point depression, ST slope, and ST integral.

Limitations

The following limitations affect the generalizability of the findings:

1. The results of this study are applicable only to populations of similar age and sex.
2. Subject selection was performed in a non-random fashion.
3. The results of this study are not applicable to

exercise testing involving the performance of posttest hyperventilation.

Basic Assumptions

The following assumptions were made by the investigator:

1. Lead V_5 is an adequate lead for analyzing J-point depression, ST integral, and ST slope in exercising individuals.
2. All subjects were not taking drugs that would affect the J-point and ST-segment during exercise 24 hours prior to the exercise test.
3. The protocol utilized for testing is a valid and reliable measure of submaximal exercise in a female population.
4. The computer derived averages of J-point depression, ST integral, and ST slope are accurate in all tests.

Definitions and Symbols

The following definitions and symbols are utilized throughout this study:

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

2. ST Depression: horizontal or downsloping ST-segment depression, below the isoelectric line, of 0.10 mV or more for 80 msec beyond the J-point.
3. ST Integral: area measured from the end of the QRS complex to the beginning of the T wave or where the ST-segment crosses the isoelectric line.
4. ST Slope: the slope of the ST-segment, in relation to the isoelectric line, as measured 60 or 80 msec beyond the J-junction.
5. V_5: precordial, unipolar lead positioned at the level of the fifth intercostal space in the left anterior axillary line.
6. YMCA submaximal bicycle protocol: protocol established by the YMCA consisting of 3 to 5 workloads which last for 3 minutes each.

Summary

Cardiovascular disease is a prolific killer in today's society. However, medical interventions and procedures have provided a means of combating cardiovascular disease's devastating effects. The GXT has developed as a tool to determine the extent of cardiovascular disease. This is accomplished by analyzing ECG recordings, primarily J-point and ST-segment changes occurring with exercise. As part of

the GXT procedure, hyperventilation has been performed either pretest or posttest. If performed pretest, it provides insight as to possible changes to be expected during exercise. However, hyperventilation has been suggested to be a cause of false-positive responses to the GXT. Therefore, a question looms over the ordering of hyperventilation and its effect on J-point and ST-segment changes. Additionally, females have been associated with a higher incidence false-positive responses to the GXT, further clouding the issue.

Answering a hypothesis that addresses the above components of the GXT procedure would increase the efficacy of medical interventions aimed at preventing or controlling the disease. Therefore, reducing the mortality and morbidity rates associated with one of today's most prolific killers - cardiovascular disease.

Chapter II

Review of the Literature

Cardiovascular disease is a well documented health problem. The literature deals with all facets of the disease, as well as methods of controlling the disease. The graded exercise test is a well established and accepted tool for diagnosing the existence or extent of cardiovascular disease. Numerous areas related to the graded exercise test have an impact on the utilization and value of the test results. These areas are covered in this chapter, and include 1) Sensitivity and Specificity of Graded Exercise Tests, 2) ECG Measures of Exercise Induced Myocardial Ischemia, 3) Lead Systems Utilized in Graded Exercise Testing, 4) Hyperventilation, and 5) False Positive Exercise Tests and Gender.

Sensitivity and Specificity of Graded Exercise Tests

Sensitivity and specificity are the terms used to define how effectively a test separates people with significant coronary artery disease from healthy people, how well a test diagnosis disease (Fletcher et al., 1990). Tests can be classified as true-positive, true-negative, false-positive, and false-negative. A true-positive test is one that exhibits abnormal ECG changes and the individual has disease. A true-negative test is one with normal ECG findings and the individual has no disease. A false-positive test is one with apparently abnormal ECG findings in an individual with no disease. A false-negative test is one with a normal ECG

finding; however, the individual has disease. The sensitivity of exercise testing is based on the percentage of the population with coronary artery disease who have a positive test. The specificity of exercise testing is based on the percentage of the population without coronary artery disease who have a negative test. Often, in various study groups, sensitivity and specificity have shown an inverse relation. If sensitivity is at its highest, then specificity is at its lowest and vice-versa (Fletcher et al., 1990).

Sensitivity is affected by various factors that are intertwined with exercise stress testing. Sensitivity is decreased by tests involving submaximal exercise, insufficient ECG leads, drugs that alter cardiac function, and increasing criteria for a positive test (ACSM, 1991). The use of submaximal exercise, as compared to maximal exercise, decreases sensitivity by 8 to 10 percent (Chaitman and Hanson, 1981). Sensitivity is increased by utilizing multiple leads, computer analysis of the ECG data, and by reducing the criteria for a positive test (ACSM, 1991). However, by utilizing the latter technique one increases the rate of false-positive responses.

Specificity, like sensitivity, is affected by numerous factors associated with exercise testing. Specificity is decreased by false-positive responses in individuals without coronary artery disease (ACSM, 1991). It is also decreased

when testing is done on women (Fletcher et al., 1990; Froelicher, 1987) and on patients with ST depression at rest (Froelicher, 1987).

The most important determinant of sensitivity or specificity is the criterion or discriminant value used to define an abnormal test (ACC/AHA Guidelines, 1986). As the criteria increases, sensitivity decreases and specificity increases. Another important determinant is the number of leads used to monitor the test (ACC/AHA Guidelines, 1986). As the number of leads increases from 1-12, sensitivity increases from 56-76% and specificity decreases from 94-82%.

ECG Measures of Exercise-Induced Myocardial Ischemia

ST-segment Depression. Numerous variables have been identified as useful in analyzing electrocardiographic results, but ST-segment depression has received the most attention. Gianrossi et al. (1989) conducted a meta-analysis of 147 consecutively published reports on exercise-induced ST depression. They found that the most common measurement technique of ST depression is to measure 80 msec after the J-point. Chaitman et al. (1979) examined the diagnostic impact of maximal treadmill testing using 14 ECG leads in 200 men with normal ECGs at rest. They found that measuring ST depression 80 msec after the J-point provided the highest predictive value; thus, supporting Gianrossi et al. (1989).

Ardissino et al. (1989) examined the significance of hyperventilation-induced ST depression in 329 patients with angina and documented coronary artery disease (CAD). They used ST depression of at least 1.0 mm 80 msec after the J-point as criteria for positivity, which is considered to be the standard criteria for significant ST depression suggesting myocardial ischemia. However, Froelicher et al. (1976) measured it 60 msec after the J-point, if the ST-segment was horizontal, flat, or downsloping, or 80 msec after the J-point if the ST-segment was upsloping. Thus, various techniques of measuring ST-segment depression exist.

The ST depression utilized for diagnostic purposes usually has a horizontal or downsloping ST-segment. A controversy exists whether upsloping ST depressions should be considered as abnormal tests (Gianrossi et. al, 1989). The importance of this controversy lies in the fact that a patient's probability of coronary disease depends on clinical characteristics and the sensitivity and specificity of test results. Therefore, accurate estimates of sensitivity and specificity are necessary to accurately predict disease possibilities. Gianrossi et. al (1989) report from their meta-analysis on ST depression that including upsloping ST depressions as abnormal tests decreases specificity approximately 4.4%. However, Chaitman and Hanson (1981), in their review of published reports dealing with sensitivity and

specificity, indicate that if single leads are recorded, slow upsloping ST depression may be the only ST-segment response in patients. Since the literature supports the usage of bipolar leads, such as CM_5 or CC_5, the categorization of upsloping ST depressions may warrant re-evaluation. The controversy of upsloping ST depression must presently be dealt with on the basis of the situation presenting itself.

ST Integral. ST integral, also called ST area, is utilized to express the magnitude of ST-segment deviation from the baseline. In a study that tested 72 patients with CAD, Sheffield, Holt, Lester, Conroy, & Reeves (1969) measured the area from the end of the QRS to either the beginning of the T wave or where the ST-segment crossed the baseline. They found an ST integral greater than $-10uV \cdot sec^{-1}$ to be an abnormal response, the normal range was from 0 to $-7.5uV \cdot sec^{-1}$. The authors obtained a sensitivity of 81% and a specificity of 95% using the ST integral.

In their study of 107 patients with chest pain, Sketch, Mohiuddin, Nair, Mooss, and Runco (1980) measured the ST integral over an interval from 60 to 140 msec after the peak of the R-wave. The range they utilized as normal was 0 to $-6uV \cdot sec^{-1}$.

Forlini, Cohn, and Langston (1975) tested 133 patients in an attempt to test the diagnostic value of the ST integral.

The authors obtained a sensitivity of 85% and a specificity of 90%. Sheffield et al. (1969) and Forlini et al. (1975) provide support for using the ST integral to analyze ECG tracings for diagnostic purposes. However, Ascoop, Distelbrink, and DeLang (1977) studied 147 men suspected of having ischemic heart disease with leads CC_5 and CM_5. They computed the ST integral as the area between the baseline and the negative part of the ST-segment from the junction to the point where the ST-segment crossed the baseline. Using the ST integral, they found a sensitivity of 60% and a specificity of 93% in CC_5 and a sensitivity of 38% and a specificity of 93% in CM_5. The findings of these authors provide some doubt about the use of the ST integral for diagnostic purposes.

ST Slope. ST slope is a variable utilized in analyzing ECG results. ST slope represents the rate of change in the directional movement of the ST-segment. Therefore, slope is referred to as downsloping (negative change), upsloping (positive change), or horizontal/flat (no change). McHenry, Stowe, and Lancaster (1968) measured ST slope from 70 to 110 msec beyond the peak of the R-wave. Ascoop et al. (1977) measured ST slope from 0 to 80 msec, from 10 to 50 msec, and from 50 to 70 msec after the end of the QRS in leads CC_5 and CM_5. They observed that measuring from 0 to 80 msec and from 10 to 50 msec provided similar results in terms of sensitivity

and specificity (60% and 93% respectively in CC_5; 50% and 93% respectively in CM_5).

Computer Signal Processing and Analysis of the ECG. Diagnostic sensitivity of exercise testing is inadequately low, with some 25 to 50 percent of patients with coronary disease remaining undetected by exercise stress testing (Forlini et al., 1975). Therefore, computer analysis has been utilized in an attempt to increase sensitivity and specificity of testing. For computer analysis to be a valid technique, it must approach a near-equal sensitivity and specificity that can be obtained through visual analysis. Sketch et al. (1980) have presented data that provides some validation for the use of computer analysis. They found that automated analysis versus visual analysis of V_5 yielded statistically similar findings in terms of sensitivity (63% vs. 59%), specificity (85% vs. 92%), and predictive value (85% vs. 90%). Although automated analysis of the ECG data is an accepted technique, it should not be presumed that the need for visual review of exercise tests and physician evaluation of other factors, such as heart rate response, blood pressure response, and chest pain, should be deleted.

When analyzing ECG data from an exercise test, two critical problems surface. These problems are a decrease in

the amount of ECG data recorded during the test and the presence of electrical noise and movement artifact associated with exercise (Froelicher, 1987). Forlini et al. (1975) observed that computer signal averaging minimizes motion and muscle noise artifact and baseline drift, which improves the quality of the ECG tracing. Thus, the functions of computerized exercise systems are designed to aid in overcoming these two problems. Froelicher (1987) outlined the functions common to all computerized exercise systems. These functions include the recognition of ECG complexes, locating a fiducial point or landmark, choosing beats to average, signal averaging, and waveform recognition.

Lead Systems Utilized in Graded Exercise Testing

The diagnostic value of ST-segment shifts can be affected by the population studied and the lead system monitored. Chaitman and Hanson (1981) report from their comparison of various studies that ST-segment depression increases with age and is more common in young and middle-aged women than in men. Deckers, Vinke, Vos, and Simoons (1990) studied 116 women without chest pain or history of cardiovascular disease. Like Chaitman and Hanson (1981), they found that ST depression increased with age and heart rate.

In terms of lead systems, the literature analyzes multiple leads and bipolar leads. The early recommendations

for the use of single- and multiple-lead systems were based on the ability of a lead or leads to identify an ischemic response. The use of multiple (3-12) leads increases sensitivity of exercise ECGs for detecting abnormal ST-segment depression by 8-20% compared to a single lateral precordial lead (Fischer et al., 1986). The most popular lead combination used today is aVF, II, and V_5.

In their study of 107 normal subjects and 67 patients with angina, Mason, Likar, Biern, and Ross (1967) showed that a modified 12-lead ECG recorded during exercise was more sensitive than individual leads, but they did not evaluate bipolar leads such as CM_5 and CC_5. Bowles, Khurmi, Davies, & Raftery (1985) conducted a study on a system of 21-lead electrocardiography to assess 21 patients with severe angina during and after exercise. A comparison was made between results obtained from 18 unipolar precordial leads and those from bipolar leads CM_5 and CC_5. It may seem reasonable to expect improvement in sensitivity when recording from a large surface area versus a single or bipolar lead system, but no more useful information is obtainable (Bowles et al., 1985).

Miranda et al. (1992) performed a retrospective analysis of 173 men in order to ascertain the diagnostic accuracy of inferior limb lead II compared with precordial lead V_5. The authors found a better combination of sensitivity and

specificity (65% and 84%, respectively) in V_5 than in lead II (sensitivity 71%, specificity 44%). They determined that V_5 is a better marker for CAD than lead II in patients with normal ECGs. The authors concluded that V_5 outperformed lead II because lead II had a high rate of false-positive responses.

Since the early days of electrocardiography, numerous body-surface sites have been recommended for measurement of the heart's electrical activity. Electrodes have been placed all over the body and in all natural orifices, searching for significant and useful leads. Standard 12-lead ECG monitoring is impractical owing to excess artifact introduced by motion of the limb leads placed on the extremities. Bipolar leads have been found to be advantageous because only two electrodes in addition to a ground electrode are required; thus, noise is easily controlled and its cause is easily identified (Froelicher et al., 1976). In their symposium on lead systems, Pina and Chahine (1984) support Froelicher by reporting that bipolar leads diminish motion artifact. However, the major advantage may be the preparation time of two minutes for bipolar leads versus a minimum of ten minutes for multiple-lead systems (Bowles et al., 1985).

The use of many different lead systems have complicated the comparative interpretation of the ST-segment response to

exercise, since the representation of the ST-segment vector varies in different lead systems (Rautaharju & Wolff, 1971). Some investigators believe bipolar leads are the most sensitive for ST-segment changes. Bowles et al. (1985) found that the magnitude of ST depression was greater in bipolar leads. Thus, validation of the use of bipolar lead systems would enhance the interpretive value of results of ST-segment responses.

Froelicher et al. (1976) examined CM_5 and CC_5 compared to V_5 based on ST depression and ST slope in 47 men. They reported that CC_5 and V_5 presented numerically similar values. Lead CM_5 elicited greater ST depression, but was shown to be less sensitive than CC_5 and V_5. Thus, concluding that CC_5 is comparable to V_5 while CM_5 is not. McHenry, Phillips, and Knoebel (1972) support Froelicher's findings in their study, which reports a greater sensitivity in CC_5 than was observed in other studies. Contradicting these two studies is the study by Chaitman et al. (1979). The authors of this study found CM_5 to have a greater sensitivity than CC_5 and V_5. Sketch, Nair, Esterbrooks, and Mohiuddin (1978) observed similar values for sensitivity, specificity, and predictive value for CM_5 and V_5 (60% vs. 61%, 81% vs. 86%, and 83% vs. 84%, respectively) in their study of 203 men with chest pain. These contradictory findings may cause some doubt to be cast

over the value of bipolar leads. However, when weighing all the findings, bipolar lead systems may provide adequate sensitivity and specificity of stress tests for clinical purposes (Pina & Chahine, 1984).

Guiteras et al. (1982) performed 14-lead electrocardiography on 112 women without a history of myocardial infarction. Using the standard criteria for diagnosing coronary disease, the authors obtained a sensitivity of 57% and a specificity of 80% in lead V_5. The authors found the specificity of exercise-induced ST-segment depression in women was dependent on the lead system chosen. They observed the lowest specificity in leads II, III, aVF, V_5, and CM_5.

There exists a concern that using multiple-lead systems can increase the number of false-positive tests. Chaitman et al. (1979) reported that using single-leads such as CM_5 would suffice when using horizontal or downsloping ST depression $\geq$ 1 mm or ST elevation $\geq$ 1 mm as criteria for positivity. Ascoop, Deckers, Laarman, and Hemel (1989) reviewed literature to assess the utility of multiple lead systems in predicting CAD during exercise. They indicated that a simple bipolar lead such as CM_5 would suffice in most situations, even in patient's with typical or atypical chest pain in the presence of a normal resting ECG. Therefore, it would appear unnecessary to record several ECG lead systems. Using

multiple-lead systems compared to CM_5 will not improve the detection of coronary vessel disease in patients with a normal ECG at rest (Ascoop et al., 1989).

Hyperventilation

Hyperventilation is performed as an adjunct to exercise stress testing. Its purpose is to identify any abnormal ECG responses that may occur from the hyperventilation associated with exercise rather than exercise itself. Hyperventilation is known to be associated with ECG changes in individuals without apparent heart disease (Lary & Goldschlager, 1974; Gardin, Isner, Ronan, & Fox, 1980; Lisker & Leff, 1983; Ardissino et al., 1989). Hyperventilation can cause ECG changes resembling myocardial ischemia in as much as 15% of patients with normal coronary arteries (McHenry et al., 1970; Lary & Goldschlager, 1974). These abnormal ECG responses are often viewed as false-positive responses.

Gianrossi et al. (1989) reported that hyperventilation performed pretest is utilized to unveil ST-segment changes that might be associated with false-positive results. In his editorial on false-positive ST-segment responses, McHenry (1977) indicates that he has previously utilized hyperventilation to reveal subjects with labile ST depression (0.5 mm or greater) or T wave inversion who were considered to have

false-positive ST-segment responses during exercise. However, utilization of hyperventilation prior to exercise testing may yield unpredictable information that is not necessarily false-positive. Bruce (1988) adamantly challenges the performance of pretest hyperventilation. He states that hyperventilation should never be performed immediately before exercise testing. It can be performed separately, preferably more than 5-10 minutes after completion of the exercise test.

Ardissino et al. (1989) examined 329 patients with angina and documented CAD to investigate the significance of hyperventilation-induced ST-segment depression. They observed that hyperventilation can induce ST depression, and concluded that this ST change is indicative of hyperventilation-induced myocardial ischemia. The authors also observed that hyperventilation was associated with the appearance or accentuation of nondiagnostic T wave inversion. Thus, ECG recordings are affected by hyperventilation. Hence, whether to use hyperventilation prior to testing is a point that is argued throughout the literature.

Protocol. The performance of hyperventilation is standardized in terms of how to conduct the test. The individual is instructed to breathe as deeply and rapidly as possible (at least 30 respirations per minute). However, the time period of performance varies throughout the literature. Time periods range from 30 to 90 seconds (Lary & Goldschlager,

1974; Jacobs, Battle, & Ronan, 1974; Gardin et al., 1980; Lisker & Leff, 1983).

Mechanisms. Various mechanisms have been proposed as causes for hyperventilation-induced ECG changes. These mechanisms include 1) electrolyte concentration changes, 2) respiratory alkalosis, 3) coronary vasospasm, 4) changes in heart position, 5) sympathetic autonomic stimulation, 6) hyperventilation-induced tachycardia, and 7) combinations of these mechanisms.

Electrolyte concentration changes have focused on potassium, but also include sodium, calcium, and magnesium. Some studies have reported an increase in serum potassium with hyperventilation (Jacobs et al., 1974; Yu, Yim, & Stansfield, 1959). While others have reported no changes in electrolyte concentrations (Gardin et al., 1980). Because of the inability of the literature to repeatedly confirm significant electrolyte changes, Lary and Goldschlager (1974) suggested that extracellular potassium be excluded as a cause of the ECG changes.

Respiratory alkalosis is a metabolic abnormality that occurs when arterial pH increases above 7.4. When this occurs, coronary blood flow is changed, up to a 30% decrease, relative to myocardial oxygen needs as well as to oxyhemoglobin dissociation (Jacobs et al., 1974; Pribble, Kusumi, & Bruce, 1987; Ardissino et al., 1989; Yu et al., 1959). This

reduction in coronary blood flow causes ischemia, which can result in ST-segment depression. However, not all the literature is in agreement concerning respiratory alkalosis. Lary and Goldschlager (1974) and Gardin et al. (1980) have excluded respiratory alkalosis as a mechanism. They showed that hyperventilation into a closed system produced ECG changes in the absence of concomitant alterations in arterial pH or partial pressure of carbon dioxide (P_{CO2}).

Coronary vasospasm is caused by a decrease in hydrogen ion concentration or P_{CO2} or both (Gardin et al., 1980). Therefore, coronary spasms are triggered by a change in pH, which can cause ST-segment depression (Jacobs et al., 1974; Ardissino et al., 1989).

Changes in heart position have been suggested as a mechanism causing hyperventilation-induced ECG changes. Lary and Goldschlager (1974) reported that movement of the diaphragm alters the heart's position and causes ECG changes. However, Gardin et al. (1980) has excluded heart position as a mechanism. They found that ECG changes resulting from position changes revert to normal; whereas, hyperventilation-induced changes persist throughout the hyperventilation period.

Sympathetic autonomic stimulation has been postulated in various ways as being a mechanism causing ECG changes during

hyperventilation. Yu et al. (1959) reported that an increase in sympathetic tone occurs when the secretion of epinephrine is augmented. The secretion of epinephrine causes a shift in intracellular potassium, which alters myocardial membrane potentials. Lary and Goldschlager (1974) postulated that adrenergic stimulation by endogenous catecholamine release occurring during hyperventilation may cause asynchrous myocardial repolarization. Jacobs et al. (1974) postulated a sympathetic autonomic mechanism based on the findings that propranolol and probanthine administration has been shown to block the effects of hyperventilation.

Hyperventilation-induced tachycardia is caused by increasing myocardial oxygen consumption (Gardin et al., 1980). However, it is unlikely that the hyperventilation-induced ECG changes are solely related to heart rate. If this was the case, the ECG changes would occur during exercise due to the high heart rates achieved. Therefore, hyperventilation-induced tachycardia is not considered an important mechanism of the ECG changes (Yu et al., 1959).

It has been proposed that hyperventilation-induced ECG changes are due to the combined effects of respiratory alkalosis and augmented sympathetic tone (Yu et al., 1959). When respiratory alkalosis occurs, an exchange of ions across cell membranes takes place. This causes blood pH to rise; thus, allowing potassium to exit the cells. Sympathetic tone

is increased through the secretion of epinephrine, which causes a migration of intracellular potassium and alteration of membrane potentials across myocardial cell membranes. The end result may be ST-segment depression.

False-Positive Exercise Tests and Gender

The exercise ECG is a valuable tool in diagnosing heart disease, but certain factors can cause false-positive exercise test results. Factors known to be associated with false-positive exercise tests include electrolyte abnormalities, drug use, and repolarization abnormalities on the rest ECG (Sapin et al., 1991). Therefore, ST-segment depression in the absence of myocardial ischemia may be due to alterations in the action potential produced by electrolyte abnormalities, cardioselective drugs, pericarditis, and nonischemic myocardial disease (Sapin et al., 1991).

Atrial repolarization waves (Ta wave) has been suggested as a cause of false-positive exercise tests. The Ta waves exhibit a negative deflection and often extend into the ST-segment and T wave. Sapin et al. (1991) studied 69 patients whose exercise ECG suggested ischemia to identify ECG criteria that could be used in predicting false-positive exercise tests. The authors found three characteristics that applied to false-positive tests resulting from atrial repolarization. First, finding a mean value for J-point depression to be

slightly greater than that for ST depression at 80 msec after the J-point indicates atrial repolarization caused false-positive results. Second, the false-positive changes would occur at higher heart rates when the P wave and Ta wave amplitudes are augmented. Third, the false-positive test might exhibit a shortened PR segment duration, which shifts the deepest part of the Ta wave further into the ST-segment, causing horizontal ST depression.

Furthermore, Sapin et al. (1991) observed a very strong association between PR segment slope and false-positive results. They found that in any given lead, the more downsloping the classification of PR segment slope, the more likely a false-positive test. The authors concluded that the finding of short, steeply downsloping PR segments is an independent marker of a false-positive exercise test even in the presence of significant horizontal ST-segment depression.

Ellestad (1991) wrote an editorial comment in response to the study by Sapin et al. (1991). He pointed out that the Ta wave should produce its maximal effect on the J-point, resulting in an upsloping ST-segment reaching baseline before the usual J+80 msec point considered standard for the measurement of ST depression. Furthermore, he reported that if the P plus Ta interval becomes extended past 400 msec, it extends into the ST-segment and can cause ST depression of clinical significance.

Hyperventilation has been suggested as a cause of false-positive test results (Jacobs et al., 1974; Lary & Goldschlager, 1974; Pribble et al., 1987). These results are manifested in RST segmental depression resulting from the performance of hyperventilation. In the ACC/AHA guidelines for exercise testing (1986), the task force points out that hyperventilation may unmask false-positive changes. They state that if hyperventilation produces ST-segment depression ≥ 0.5 mm or a reversal of T wave polarity, abnormal ST-segment depression during exercise must be interpreted with caution. Lary and Goldschlager (1974) reported that hyperventilation-induced ECG changes are the most common cause of false-positive results.

Within exercise testing, differences exist between genders. The most disturbing of these differences is the high rate of false-positive tests associated with the female gender. Several mechanisms have been proposed as causes of the false-positive results in women. These mechanisms include medications (digitalis), resting ST-T abnormalities, and estrogens (Fletcher et al., 1990). In his book, Fried (1987) suggests that female reproductive hormones, not just estrogens, can directly enhance hyperventilation; thus, possibly leading to the development of hyperventilation-induced false-positive results. This lends support to the findings of Cumming et al. (1973), who observed that

hyperventilation-induced false-positive responses occur more frequently in women than in men.

Sketch, Mohiuddin, Lynch, Zencka, and Runco (1975) studied 56 women that presented with chest pain by near-maximal exercise tests and coronary cineangiography. They found that the incidence of abnormal ST-segment responses to exercise was 27%. Cumming et al. (1973) conducted near-maximal exercise tests on 357 asymptomatic women between the ages of 20 and 83. They found age adjusted incidence rates of abnormal ST-segment responses to exercise in women were almost three times greater than those reported for males of comparable age. The results of these two studies suggest the incidence of false-positive ST-segment responses to exercise are considerably higher in females compared to males.

Summary

The literature illustrates various techniques in measuring ST depression. Although a common practice is identified, no set rules apply. This allows utilization of the technique best suited for the situation at hand. The literature also does not reach a conclusion concerning lead systems for monitoring GXT performance. Multiple- and bipolar leads are suggested, with the most influential evidence provided for bipolar lead systems. However, no one bipolar lead is pinpointed as the optimal lead to be utilized.

Only a small amount of previously published research was available on hyperventilation. The literature presented differing views dealing with when hyperventilation should be performed and the advantages associated with its performance with no clear cut choice available. These areas appear to be as clouded as in the beginning, providing considerable room for future studies. Perhaps, in the near future, some concrete findings will prevail concerning these areas associated with graded exercise testing.

Chapter III

TITLE: Hyperventilation and ECG components used in exercise for diagnosis of ischemic heart disease in healthy females

AUTHORS: Timothy M. Rose, William G. Herbert, Don R. Sebolt, and John C. Lee

INSTITUTION: Laboratory for Health & Exercise Sciences
Virginia Polytechnic Institute and State University,
Blacksburg, VA 24061

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Abstract

Hyperventilation has been reported to cause false-positive ischemic shifts in the ST-segment of the electrocardiogram during exercise. These responses have been observed to occur at a higher incidence in females than males. Therefore, the purpose of this study was to determine the effects of the performance of pretest hyperventilation on ECG components that are suggestive of myocardial ischemia in females. A standard 12-lead Mason-Likar recording set was used including leads I, II, II, aVR, aVL, aVF, V_2, and V_5. Fifteen females comprised the subject pool for this study, which was screened on the basis of J-point depression in a preliminary exercise procedure. The fifteen subjects each performed two exercise sessions, one with no hyperventilation and the other with a preliminary hyperventilation. Statistically significant differences were found between the baseline and post-hyperventilation ECG ($P<.05$). Analysis of the results revealed no significant differences in J-junction depression, ST slope, and the ST integral between the two testing conditions. Hyperventilation did affect the ST responses of the ECG in these young adult females at baseline and its continued use in conjunction with graded exercise testing may help uncover ST-segment changes associated with false-positive

exercise responses. Hyperventilation may be performed in young adult females in conjunction with GXTs without the liklihood of augmenting ST-segment shifts during the exercise.

key words: females, hyperventilation, false-positive tests, J-junction depression, ST slope, ST integral

Although the graded exercise test (GXT) serves as a standard first line technique for diagnosing heart disease, it is not free from technical factors that confound interpretation. One such problem occurs in the diagnostic accuracy of abnormal exercise ECG findings for women versus men. Few studies are available that focus on this problem. Several studies have indicated that false-positive exercise ECG test results occur more frequently in women than in men[11,12,14]. Thus, suggesting gender as a problematic issue for disease diagnosis.

The use of hyperventilation as a procedure preliminary to the clinical GXT is yet another area of controversy[2]. The uncertainty relates to whether hyperventilation should be routinely performed, and if so, whether it should be done prior to or following the GXT. Some studies indicate that hyperventilation performed pretest is useful to unveil ST-segment depression that might be associated with false-positive ECG changes during exercise[4,5]. Other studies indicate that pretest hyperventilation may induce ST depression in some individuals that is indicative of myocar-dial ischemia, and that this may exacerbate myocardial ischemia in the GXT that immediately follows[1].

Resolution of these questions would provide a means for enhancing the clinical efficiency of diagnostic GXTs. The

purpose of this study was to determine if J-point depression and selected computer generated ST-segment scores during exercise are affected by the performance of pretest hyperventilation in young, apparently healthy women.

Methods

Screening of Subjects

A preliminary screening procedure was utilized in the selection of subjects. To qualify for the study, an individual had to evidence J-point depression of .05 mV (.5 mm) or more following five minutes of exercise at an intensity equal to 60% of predicted heart rate reserve. Twenty-two individuals participated in the screening procedure. From this group, fourteen individuals satisfied the criteria for inclusion in the study. Table 1 illustrates the physical characteristics of the subjects utilized in this study.

Place Table 1 Here

ECG Measurements

Electrocardiographic recordings were obtained immediately after exercise via a micro-computer supported ECG recorder (Q5000; Quinton Instruments, Seattle). The ECG lead utilized in analyzing the amount of depression each individual exhibited was V_5. In recording the ECG lead, the ECG filter

was not on and computer signal averaged complexes were utilized.

Figure 1 illustrates the ECG measures utilized in this study, i.e., ST-segment depression, ST slope, and ST integral. The amount of ST-segment depression was measured using the J-point (J+0) for time zero. Analyses were then conducted to measure the amount of ST-segment depression at J+60 msec and J+80 msec. The slope of the ST-segment was measured from the J-point to 60 msec after the J-point. The ST integral was measured from the J-point to 80 msec after the J-point or where the ST-segment crossed the isoelectric baseline, depending on which occurred first (see Figure 1A and 1B). Only delta ST scores were examined in this study, i.e., the measured differences between the ST value at baseline and that for the highest exercise level of each subject.

Place Figure 1 Here

Experimental Procedures

Prior to exercise testing, subjects were measured for height, weight, and breast size. Breast size was measured via two circumference measurements with a cloth measuring tape. All breast measurements were obtained with the subject standing in an erect position. The first measurement, the traditional chest circumference, was taken just below the

breasts, and the second measurement was taken so that the measuring tape covered the nipple of each breast. In order to obtain a measure of breast size, the first measurement was subtracted from the second measurement. Height and weight of each individual was obtained via laboratory scales, without the subject wearing shoes.

All subjects then had electrodes attached in configurations representing leads I, II, III, aVF, aVR, aVL, V_2, and V_5. At the beginning of each test, subjects were seated on a Bodyguard cycle ergometer for ten minutes. After this rest period, baseline ECG recordings were obtained. Exercise was performed on the bicycle ergometer following the YMCA submaximal bicycle protocol for females[6]. Exercise was performed until each subject achieved a heart rate representing 60% of their heart rate reserve [(predicted HR max - HR rest) * 60%], or until they were unable to maintain the required cadence of 50 revolutions per minute. The ECG recordings were obtained at the end of each stage and immediately after exercise. A ten minute recovery period followed exercise, consisting of two minutes of low intensity cycling and eight minutes of sitting recovery. Hyperventilation was either performed preexercise (HYP) or not at all (No HYP). The hyperventilation procedures were performed for 60 seconds at a rate of at least 30 respirations per minute. An

ECG recording was obtained immediately following the cessation of hyperventilation. Each subject performed HYP and No HYP trials with stationary cycle ergometry exercise testing. The order of trials was randomly assigned.

Statistical Analysis

All ECG recordings were analyzed by computer signal averaging via the Quinton Q5000. Differences in the dependent variables between trials were assessed by a repeated measures ANOVA with two within subject factors (trial and time). Significance level was set at $p < .05$. Values are expressed as means ± SEM. Subsequently, Student's dependent t tests were performed to determine the presence of any significant differences on the **delta scores** of J-point depression, ST integral, and ST slope (dependent variables) between the HYP and No HYP trials. Test/retest reliability for the dependent measures was determined via a Spearman rank order correlation procedure.

Results

Hemodynamic responses. Table 2 shows the response patterns for hemodynamic measures that were important to equate so that exercise ECG responses might be appropriately compared. There was no significant differences in the maximum rating of perceived exertion, heart rate, systolic blood pressure, or diastolic blood pressure. This finding held

constant through the different measurement points and test conditions.

Baseline and exercise ECG variables. Changes occurring with exercise are shown in Table 3. Analyses were performed via the Quinton Q5000 to analyze J+60 and J+80 in addition to J+0. These three common measurement points are referred to as the ST level in Table 3. No significant differences were observed across the testing conditions for ST level, ST slope, and ST integral.

Delta scores of ECG variables. The delta scores of the ECG variables were examined because these represent the way exercise test results are commonly interpreted. No significant differences were observed across the testing conditions in ST level, ST slope, and ST integral (Table 4).

Place Tables 2, 3, 4 Here

Relationships of key measures. A correlation matrix was generated to examine the relationship among delta scores for all variables in the hyperventilation and no hyperventilation trials. High correlations included those between the following delta scores: J+0 NoH vs. J+0 Hyp ($r=0.86$) and J+0 NoH vs. ST integral NoH ($r=0.89$). The first of these correlations demonstrates that the ST depression shifts of individual subjects in exercise were closely related, whether

or not preliminary hyperventilation was performed. The second shows that measured shifts in ST integral during exercise were highly dependent upon shifts in the J-point. In contrast, the J+60, J+80, and ST slope were much less dependent on the exercise shifts in the J-junction. These findings suggest the vlue of focusing attention in this study on changes in the J-point and ST integral.

To estimate the reliability of the data, a Spearman rank order correlation was performed on baseline measurements of the dependent measures. The baseline of each dependent measure was compared against its counterpart in the different testing condition (ie. baseline ST slope no hyperventilation versus baseline ST slope with pretest hyperventilation). The correlation between ST slope baselines without hyperventilation and with pretest hyperventilation was r=0.72. The correlation between ST integral baselines without hyperventilation and with pretest hyperventilation was r=0.99.

Discussion

Physiological variables. All results were analyzed in the context of control (exercise without hyperventilation) versus exercise with pretest hyperventilation. Table 2 reports the descriptive statistics of hemodynamic measures applied to each subject. No significant differences were found in any measure between the two testing conditions. Thus, providing support for the equivalence of each testing

procedure.

Hyperventilation and its uses. Studies by Fletcher et al.[4] and Gianrossi et al.[5] have suggested that hyperventilation performed pretest can be utilized to unveil ST-segment changes that might be associated with false-positive ECG changes. In contrast, a study by Ardissino et al.[1] indicates that the performance of pretest hyperventilation can induce ST depression that is indicative of hyperventilation-induced myocardial ischemia. Figure 2 shows the effects of hyperventilation and exercise on the ECG. The significant differences in ST level and ST slope baselines that occurred as a result of hyperventilation observed in our study (P=0.015 and P=0.038, respectively) lead one to place confidence in the interpretation of Gianrossi et al.[5] and Fletcher et al.[4]. This conclusion was reached because all subjects were young, healthy females with no documented history of CAD.

Place Figure 2 Here

Relationships of key ECG responses. The three most extensively utilized ECG measures of exercise-induced myocardial ischemia are ST level, ST slope, and ST integral. The results associated with these measures are reported in Tables 3 and 4. No significant differences were found between

any of the dependent measures at baseline, exercise, or delta (the difference between exercise and baseline). These results do not agree with Ardissino et al.[1]. The performance of pretest hyperventilation did not serve to cause any alterations in the ECG that were not caused by exercise alone.

The most common indice used to evaluate disease is ST depression. The results of the Spearman's rank order correlation showed low correlations between all measurement points of the ST-segment and high correlations between ST slope and ST integral within the two trials. Thus, our findings suggest a greater reliability for the use of the ECG measures of ST slope and ST integral as a basis of test interpretation.

False-positive responses. False-positive exercise tests result when ECG changes are present that suggest disease in an individual without disease. Pribble et al.[13] and Herbert and Froelicher[8] summarized the current literature on testing, indicating that voluntary hyperventilation amplifies false-positive changes in the ECG during exercise. Cumming et al.[3] reported that hyperventilation-induced false-positive responses occur more frequently in women. All ECG changes exhibited by subjects of this study were classified as false-positive responses due to age, absence of symptoms, and health characteristics of the subjects studied. Changes in the ECG

were exhibited by 80% (12 of 15) of the subjects; thus, supporting Cumming et al.[3]. However, no support was found for Pribble et al.[13] and Herbert and Froelicher[8]. Alterations in ST depression, ST slope, and ST integral were equally distributed between the two testing conditions. Thus, supporting that the performance of pretest hyperventilation did not cause any ECG changes that were not caused by exercise alone.

Fletcher et al.[4] stated the importance of the ECG was evident because the probability and severity of CAD are directly related to the amount of J-junction depression and inversely related to the slope of the ST-segment. In the present study, both J-junction depression and ST slope were less during exercise with hyperventilation than during exercise alone (M ± SEM= -0.89 ± 0.09 vs. -0.95 ± 0.08 and 14.20 ± 1.84 vs. 14.40 ± 1.78, respectively). These results point out two findings related to the literature. First, hyperventilation had an insignificant role in causing any alterations in the ECG during exercise. Second, using Fletcher et al.[4] as a basis for interpretation, subjects in this study exhibited false-positive ECG changes. While J-junction was at significant levels, ST slope was upsloping. This finding is opposite the criteria used to interpret the probability and severity of disease.

Lead selection. Lead V_5 was utilized as the primary lead to analyze ECG changes because it is the most extensively used lead in exercise stress testing[7]. This lead is located on the anterior axillary line in the fifth intercostal space on the left side of the body. The location of this lead prompted examination of breast size as a possible cause of any ECG changes. Being questioned was what affect would increases in body mass in this body region have on the ECG. A correlation matrix was conducted which yeilded low correlations, with r values ranging from -0.10 to 0.68. Thus, the results revealed no relationship between breast size and ECG changes found in lead V_5.

Methodological concerns. Certain methodological concerns arose from the completion of this study. The most important appears to be the selection of subjects. Subjects in this study were selected on the basis of a screening procedure in which they had to manifest at least 0.5 mm of J-junction depression in exercise to qualify. In order to maximize results, a more stringent criterion may need to be implemented for qualification in the study. In addition, a larger sample size may provide more stability in the obtainable results.

The quality of the ECG tracings became an important factor in some of the subjects' results. Two aspects that affected the quality of the ECG were the placement of

electrodes and the type of brassiere worn by the subjects. The lead utilized for analysis of results was V_5. Due to the location of this lead (just below the left breast), the type of brassiere worn by the subjects affected the tracings. Two types of brassieres were encountered during the study, underwired and motion control. Both types employ tight fitting straps just below the breasts for support. These straps interfered with the placement and recording ability of electrodes.

Another methodological concern was the variability found in the baseline ECGs of each testing condition. A Spearman's rank correlation of J+0, J+60, and J+80 between the two testing conditions yielded low correlations (r=0.33, r=0.43, and r=0.53, respectively). A Spearman's rank correlation of ST slope and ST integral yielded acceptable correlations (r=0.72 and r=0.99, respectively). However, the most widely utilized indice is ST depression; thus, the low correlations are reasons for concern.

Conclusions. The results of this study reveal that hyperventilation did not cause any ECG changes during exercise that were not caused by exercise alone. Thus, hyperventilation appears not to be an influence on the ECG of young, non-obese females. These findings may be population specific. Utilizing a group of individuals that is not classified as

healthy, such as individuals with silent ischemia or one vessel disease, could possibly yield different results.

The results showed no relationship between breast size and ECG changes. This is another finding that could be population specific. Thus, indicating that breast size is probably not a factor in causing ECG changes in young, non-obese females.

Although this study shows that hyperventilation does affect the ECG, all changes resolved themselves during exercise. It was beyond the scope of this study to pinpoint the mechanism(s) which caused the changes. For additional information concerning mechanisms of change induced by hyperventilation, refer to outside literature[1,9,10,13,15].

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Table 1
Physical Characteristics of Female Subjects*

Characteristic	(N=14)
Age (yr)	
M	22.0
SD	1.5
Height (cm)	
M	164.6
SD	10.1
Weight (kg)	
M	61.3
SD	11.1
Breast Size (cm)	
M	11.5
SD	3.5

*M=mean; SD=standard deviation

Table 2
Hemodynamic Responses to Submaximal Cycle Ergometry**

Variable Measured	Females (N=14)	
	No HYP*	Pretest HYP*
Maximum RPE During Exercise		
M	13.9	14.6
SEM	0.4	0.6
Exercise Heart Rate (b/min)		
M	148.9	148.7
SEM	1.6	2.4
Exercise Systolic Blood Pressure (mmHg)		
M	146.7	145.9
SEM	3.1	3.9
Exercise Diastolic Blood Pressure (mmHg)		
M	74.1	74.6
SEM	1.8	2.0

*HYP=hyperventilation
**M=mean; SEM=standard error of mean

Table 3
Baseline and Exercise ST-Segment Changes*

Measures	Exercise ECG Responses Control	Post-HYP.	(N=14) F value	Signif.
ST Level				
J+0 (mV)				
Baseline	0.02 ± 0.01	0.02 ± 0.01	0.03	NS
Exercise	-0.09 ± 0.01	-0.09 ± 0.01		
J+60 (mV)				
Baseline	0.03 ± 0.01	0.03 ± 0.01	0.00	NS
Exercise	-0.002 ± 0.02	0.005 ± 0.01		
J+80 (mV)				
Baseline	0.04 ± 0.01	0.05 ± 0.01	0.72	NS
Exercise	0.06 ± 0.02	0.07 ± 0.02		
ST Slope† (mm/sec)				
Baseline	2.0 ± 1.1	2.4 ± 1.3	0.00	NS
Exercise	15.1 ± 1.7	14.6 ± 1.9		
ST Integral† (uV-sec)				
Baseline	-0.3 ± 0.2	0.0 ± 0.0	0.86	NS
Exercise	-3.4 ± 0.7	-3.1 ± 0.7		

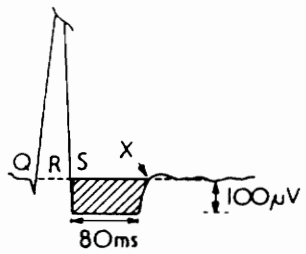
*Values are means ± SEM
†ST Slope and Integral remain the same throughout each condition (J+0, J+60, and J+80)

Table 4
Delta Scores of ST Segment Changes*

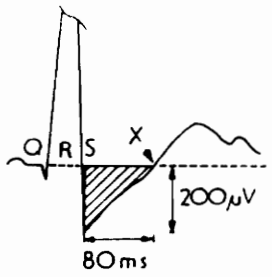
Measures	Exercise ECG Responses Control	Post-HYP	(N=14) t-ratio	Signif.
ST Level				
J+0 (mV)				
Delta**	-0.09 ± 0.01	-0.09 ± 0.01	0.07	NS
J+60 (mV)				
Delta**	-0.02 ± 0.01	-0.02 ± 0.01	0.00	NS
J+80 (mV)				
Delta**	0.01 ± 0.02	0.02 ± 0.02	0.59	NS
ST Slope (mm/sec)				
Delta**	12.5 ± 1.19	11.9 ± 1.15	0.48	NS
ST Integral (uV-sec)				
Delta**	-2.9 ± 0.62	-2.9 ± 0.71	0.13	NS

*Values are means ± SEM
**Delta values are derived from exercise values minus baseline values

A.



B.



C.

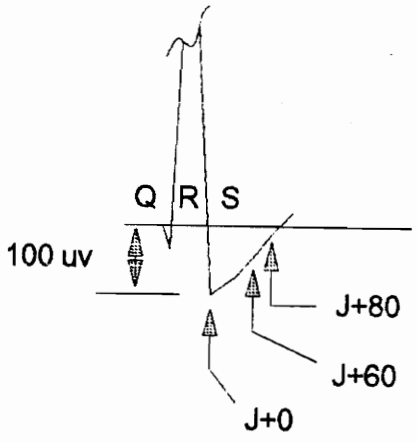


Figure 1. ECG measures utilized in evaluating stress test responses. Different measurement points for calculating the ST integral (A and B), ST depression at J+80, J+60, and J+0 (C). Note: 1mm = 0.1mV = 100uV

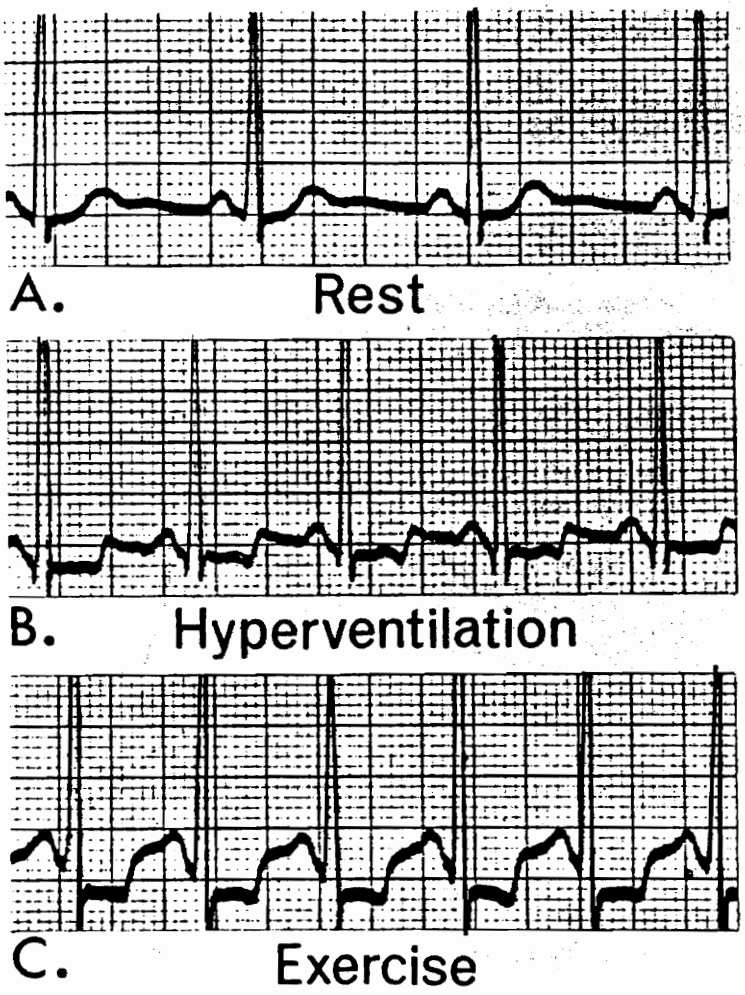


Figure 2. Changes in the ECG caused by hyperventilation and exercise. *A*, represents a resting electrocardiogram with no abnormalities. *B*, illustrates ST-segment depression caused by 60 seconds of hyperventilation. *C*, illustrates J-point and ST-segment depression during exercise testing.

Chapter IV

Summary and Recommendations for Future Research

Summary

Overview. Hyperventilation has been reported to cause false-positive ischemic shifts in the ST-segment of the electrocar-diogram during exercise. These responses have been observed to occur at a higher incidence in females than males. Therefore, the purpose of this study was to determine the effects of the performance of pretest hyperventilation on ECG components that are suggestive of myocardial ischemia in females.

Physiological variables. All results were analyzed in the context of control (exercise without hyperventilation) versus exercise with pretest hyperventilation. Table 4 (Appendix B) reports the descriptive statistics of methodological control measures applied to each subject. No significant differences were found in any measure between the two testing conditions. Thus, providing support for the equivalence of each testing procedure.

Hyperventilation and its uses. Studies by Gianrossi et al. (1989) and Fletcher et al. (1990) have suggested that hyperventilation performed pretest can be utilized to unveil ST-segment changes that might be associated with false-positive ECG changes. In contrast, a study by Ardissino et al. (1989) indicates that the performance of pretest hyperventilation can induce ST depression that is indicative of hyperventilation-induced myocardial ischemia. Table 7

(Appendix B) reports baseline changes that occurred as a result of hyperventilation. The significant differences in ST level and ST slope (P=0.015 and P=0.038, respectively) lead one to place confidence in the statement by Gianrossi et al. (1989) and Fletcher et al. (1990). This conclusion is reached because all subjects were young, healthy females with no documented history of CAD.

Relationships of key ECG responses. The three most extensively utilized ECG measures of exercise-induced myocardial ischemia are ST level, ST slope, and ST integral. The results associated with these measures are reported in Tables 5 and 6 (Appendix B). No significant differences were found in any of the dependent measures at baseline, exercise, or delta (the difference between exercise and baseline). These results do not agree with Ardissino et al. (1989). The performance of pretest hyperventilation did not serve to cause any alterations in the ECG that were not caused by exercise alone.

As an adjunct to the study, a visual analysis of the PR segment slope was conducted for each subject at each testing condition. Sapin et al. (1991) found that in any given lead, the more downsloping the classification of PR segment slope, the more likely a false-positive test as a result of atrial repolarization. Ellestad (1991) pointed out that the atrial repolarization wave should produce its maximal effect on the

J-junction. This would result in an upsloping ST-segment that reaches the isoelectric baseline before the usual J+80 msec point that is considered standard for the measurement of ST depression. Downsloping PR segments were observed in 73% of the subjects (11 of 15). Using the guidelines established by Sapin et al. (1991), we evaluated our subjects' responses, sorting all downsloping PR segments and classifying these as slightly downsloping. Horizontal or flat PR segments were observed in 13% of the subjects (2 of 15). The PR segments of two subjects were classified as borderline because visual analysis was inconclusive (13%, 2 of 15). When these results were combined with the results of our subjects (Tables 5 and 6, Appendix B), support was provided for the statements of Ellestad (1991) concerning the influence of atrial repolarization on ECG changes.

False-positive responses. False-positive exercise tests result when ECG changes are present that suggest disease in an individual without disease. Pribble et al. (1987) and Herbert and Froelicher (1991b) summarized the current literature on testing, indicating that voluntary hyperventilation amplifies false-positive changes in the ECG during exercise. Cumming et al. (1973) reported that hyperventilation-induced false-positive responses occur more frequently in women. All ECG changes exhibited by subjects of this study were classified as false-positive responses due to age, absence of symptoms, and

health characteristics of the subjects studied. Changes in the ECG were exhibited by 80% (12 of 15) of the subjects; thus, supporting Cumming et al. (1973). However, no support was found for Pribble et al. (1987) and Herbert and Froelicher (1991b). Alterations in ST depression, ST slope, and ST integral were equally distributed between the two testing conditions. Thus, supporting that the performance of pretest hyperventilation did not cause any ECG changes that were not caused by exercise alone.

Fletcher et al. (1990) stated the importance of the ECG was evident because the probability and severity of CAD are directly related to the amount of J-junction depression and inversely related to the slope of the ST-segment. In this study, both J-junction depression and ST slope were less during exercise with hyperventilation than during exercise alone (M ± SEM = -0.89 ± 0.09 vs. -0.95 ± 0.08 and 14.20 ± 1.84 vs. 14.40 ± 1.78, respectively). These results point out two findings related to the literature. First, hyperventilation had an insignificant role in causing any alterations in the ECG during exercise. Second, using Fletcher et al. (1990) as a basis for interpretation, subjects in this study exhibited false-positive ECG changes. While J-junction was at significant levels, ST slope was upsloping. This finding is opposite the criteria used to interpret the probability and severity of disease.

Lead selection. Lead V_5 was utilized as the primary lead to analyze ECG changes because it is the most extensively used lead in exercise stress testing (Herbert & Froelicher, 1991a). This lead is located on the anterior axillary line in the fifth intercostal space on the left side of the body. The location of this lead prompted examination of breast size as a possible cause of any ECG changes. Being questioned was what affect would increases in body mass in this body region have on the ECG. The results revealed no relationship between breast size and ECG changes found in lead V_5.

Methodological concerns. Certain methodological concerns arose from the completion of this study. The most important appears to be the selection of subjects. Subjects in this study were selected on the basis of a screening procedure in which they had to manifest at least 0.5 mm of J-junction depression during exercise to qualify. In order to maximize results, a more stringent criterion may need to be implemented for qualification in the study. In addition, a larger sample size may provide more stability in the obtainable results.

The quality of the ECG tracings became an important factor in some of the subjects' results. Two aspects that affected the quality of the ECG were the placement of electrodes and the type of brassiere worn by the subjects. The lead utilized for analysis of results was V_5. Due to the location of this lead (just below the left breast), the type

of brassiere worn by the subjects affected the tracings. Two types of brassieres were encountered during the study, underwired and motion control. Both types employ tight fitting straps just below the breasts for support. These straps interfered with the placement and recording ability of electrodes.

Another methodological concern was the variability found in the baseline ECGs of each testing condition. A Spearman's rank correlation of J+0, J+60, and J+80 between the two testing conditions yielded low correlations (r=0.33, r=0.43, and r=0.53, respectively). A Spearman's rank correlation of ST slope and ST integral yielded acceptable correlations (r=0.72 and r=0.99, respectively). However, the most widely utilized indice is ST depression; thus, the low correlations are reasons for concern.

Conclusions. The results of this study reveal that hyperventilation did not cause any ECG changes during exercise that were not caused by exercise alone. Thus, hyperventilation appears not to be an influence on the ECG of young, non-obese females. These findings may be population specific. Utilizing a group of individuals that is not classified as healthy, such as individuals with silent ischemia or one vessel disease, could possibly yield different results.

An examination of breast size as a possible contributing factor to any ECG changes that might have occurred in lead V^5

showed no relationship between breast size and ECG changes. This conclusion was reached based on the low correlations from a correlation matrix conducted to examine the relationship of breast size with any ECG changes (r values range from -0.10 to 0.68). This is another finding that could be population specific. Thus, indicating that breast size is probably not a factor in causing ECG changes in young, non-obese females.

Although this study shows that hyperventilation does affect the ECG, it was beyond the scope of this study to pinpoint the mechanism(s) which caused the changes. For additional information concerning mechanisms of change induced by hyperventilation, refer to Yu et al. (1959), Jacobs et al. (1974), Lary and Goldschlager (1974), Pribble et al. (1987), and Ardissino et al. (1989).

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, hyperventilation, and false-positive exercise tests is needed. Following is a discussion of some areas that may assist in the understanding of these relationships for future researchers.

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 this study may

be a source of the insignificant findings. A power analysis was conducted which called for ten subjects, but a final number of fifteen was chosen. In establishing the subject pool for this study, individuals had to exhibit J-junction depression of 0.5 mm or more during a screening procedure. This criterion may have been too lenient. In order to maximize results, a more stringent criterion may need to be utilized for participation in the study. The larger sample size and more stringent criterion may be necessary to ensure greater statistical power.

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 utilized lead V_5 in the analysis of the results. The location of this lead allows the brassiere to affect the ECG tracings. Under-wired and motion control 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 brassiere that provides excessive support below the breasts. Due to the nonjarring properties of cycling a maximum supporting brassiere such as the Jogbra is not needed. No matter what type of brassiere is worn by the subjects, some

difficulties are going to be encountered in electrode placement. One suggestion to accomodate the recording of the ECG is to relocate the electrode, but not to the degree that the integrity of the ECG tracings is compromised. Future research should continue to experiment with the moving of electrodes and/or with detailing what type of support should be worn by subjects to maximize ECG tracings.

Measures were taken to ensure equality in the baselines prior to each testing procedure of this study. Subjects were scheduled for participation in the exercise sessions on days in which their schedules were the same. Sessions were arranged so that the subjects would report to the laboratory on a Monday and Wednesday, Tuesday and Thursday, or Wednesday and Friday at the same time of day. Subjects were also instructed to follow the same routine each night before their scheduled participation. However, variability was found between the baseline ECGs of each testing condition. Future research should go to the extreme to ensure the equality of the baseline measurements.

Outside the scope of this study exists other areas that future research can direct its efforts towards. This study reports that pretest hyperventilation does not affect the ECG during exercise any differently than exercise alone. A question that still exists is how does post-test hyperventilation affect the ECG. Additional research should be directed

at different age groups and the use of different leads. Stress testing is moving towards the use of bipolar leads such as CC_5 and CM_5. Perhaps this is the next step for future research. One of the most controversial areas related to this study is the causes of the hyperventilation-induced ECG changes. The literature that is available indicates considerable room for futher research. All of these recommended areas need to be futher explored to increase the understanding of the relationships between gender, hyperventilation, and false-positive exercise tests.

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Appendix A

Methodology

Methodology

Subject Selection

Subjects were selected on the basis of a screening procedure that was utilized to determine if an individual elicited J-point depression with exercise. The screening consisted of each individual exercising at a heart rate representing 60% of heart rate reserve predicted maximal heart rate. Immediately post exercise, a ten second ECG tracing was obtained from a Quinton Q5000 ECG recorder (Quinton Instruments, Seattle). Upon visual and computer averaged interpretation of the tracing, if J-point depression of .05 mV or more was present, the individual was allowed into the study. All interpretations were performed on lead V_5. Other criteria which had to be met for participation in the study included:

1. no documented cardiovascular disease;
2. no significant orthopedic problems that would prohibit the individual from performing a submaximal bicycle exercise test;
3. presently not taking any medication(s) that would effect the exercise ECG.

Procedures

All subjects completed an informed consent form (Appendix C) and a health history form (Appendix D). This was accomplished at the initial exercise session of all subjects who elicited J-point depression during the screening procedure. At this time, all subjects were oriented as what to expect during participation in the two required sessions for the study. The health history was utilized to verify that subjects met the criteria for participation in the study.

When a subject reported to the Human Performance Laboratory for a session, the following measurements were taken prior to exercise - height, weight, and breast size. Breast size was measured via two circumference measurements with a cloth measuring tape. All breast measurements were obtained with the subject standing in an erect position. The first measurement, the traditional chest circumference, was taken just below the breasts, and the second measurement was taken so that the measuring tape covered the nipple of each breast. In order to obtain a measure of breast size, the first measurement was subtracted from the second measurement. Height and weight of each individual was obtained via laboratory scales, without the subject wearing shoes.

All subjects then had electrodes attached in configurations representing leads I, II, III, aVF, aVR, aVL, V_2, and V_5. The subject was then connected to the Quinton Q5000 for

recording of ECGs during the exercise sessions. Next, the seat height of the bike was adjusted to accommodate the subject. At the beginning of each test, subjects were seated on a Bodyguard cycle ergometer for ten minutes. After this rest period, baseline ECG recordings were obtained. Exercise was performed on the bicycle ergometer following the YMCA submaximal bicycle protocol for females (Golding, Myers, and Sinning, 1982). Exercise was performed until each subject achieved a heart rate representing 60% of their heart rate reserve [(predicted HR max - HR rest) * 60%], or until they were unable to maintain the required cadence of 50 revolutions per minute. The ECG recordings were obtained at the end of each stage and immediately after exercise. A ten minute recovery period followed exercise, consisting of two minutes of low intensity cycling and eight minutes of sitting recovery. Hyperventilation was either performed preexercise (HYP) or not at all (No HYP). The hyperventilation procedures were performed for 60 seconds at a rate of at least 30 respirations per minute. An ECG recording was obtained immediately following the cessation of hyperventilation. Each subject performed HYP and No HYP trials with stationary cycle ergometry exercise testing. The order of trials was randomly assigned. Each subject returned to the lab two days after their first session to perform another test utilizing the procedure opposite to their first session (HYP versus No HYP).

ECG recordings were analyzed on the basis of computer signal averaging performed by the Quinton Q5000. The variables analyzed included ST-segment depression, ST slope, and ST integral. Interpretation of the findings was focused on those observed in lead V_5.

Statistical Analysis

All ECG recordings were analyzed by computer signal averaging via the Quinton Q5000. Student's dependent t tests were performed to determine the presence of any significant differences on the delta scores of J-point depression, ST integral, and ST slope (dependent variables) between the HYP and No HYP trials. Differences in the dependent variables between trials were assessed by a repeated measures ANOVA with two within subject factors (trial and time). Significance level was set at $p < .05$. Values are expressed as means ± SEM. Test/retest reliability for the dependent measures was determined via a Spearman rank order correlation procedure. All t tests and Spearman rank order correlations were performed utilizing True Epistat 4.0 (Epistat Σ Services - Richardson, Texas). All repeated measures ANOVAs were performed with Statistical Analysis System (SAS - Cary, North Carolina).

Research Design

A randomized-group design was utilized. Subjects were randomly assigned to which test they would perform first, either pretest hyperventilation or no performance of hyperventilation.

External Validity

Subjects of this study were selected from a pool of individuals generated by a screening process. The ordering of tests was randomized, allowing some subjects to perform pretest hyperventilation while others performed no hyperventilation at their first visit to the laboratory. The results can be generalized to a female population ranging from 20-25 years of age.

Internal Validity

A within-subjects design was followed, as all subjects performed both tests. The ordering of the tests was randomized. Additional parameters taken to maximize internal validity included calibration of all equipment prior to each test and having all subjects perform each session at the same time on different days (Monday-Wednesday, Tuesday-Thursday, or Wednesday-Friday). Except for the performance of hyperventilation, both tests were administered following identical procedures.

Appendix B

Statistical Procedures

A correlation matrix was constructed to examine the relationship of the delta scores of all variables. All variables were compared against delta J+0 no hyperventilation and delta J+0 with pretest hyperventilation. Using $r \leq 0.65$ as a low correlation, all correlations with delta J+0 no hyperventilation were low except correlations with delta J+0 with pretest hyperventilation and integral difference no hyperventilation ($r=0.86$ and $r=0.89$, respectively). All correlations with delta J+0 with pretest hyperventilation were low except the correlations with delta J+0 no hyperventilation, integral difference no hyperventilation, and integral difference with hyperventilation ($r=0.86$, $r=0.75$, and $r=0.70$, respectively).

These results show the relationship between the J-junction and ST integral. These results suggest that the ST integral and J-junction provide similar views of myocardial ischemia. Meanwhile, J+60, J+80, and ST slope are independent of the J-junction; thus, suggesting greater importance in examining these variables compared to the J-junction and ST integral.

To estimate the reliability of the data, a Spearman rank order correlation was performed on baseline measurements of the dependent measures. The baseline of each dependent measure was compared against its counterpart in the different testing condition (ie. baseline J+0 no hyperventilation versus

baseline J+0 with pretest hyperventilation). The ST level was divided into the three measurement points - J+0, J+60, and J+80 (r=0.33, r=0.43, and r=0.53, respectively). The correlation between ST slope baselines without hyperventilation and with pretest hyperventilation was r=0.72. The correlation between ST integral baselines without hyperventilation and with pretest hyperventilation was r=0.99.

A power analysis was performed to estimate effect size and ultimately sample size. Using an alpha level of .05 and a beta level of .20, the power of this study was calculated to be 80%. Using data from a conducted pilot study, an effect size of .8 was obtained. Thus, resulting in a sample size of 10 subjects.

Table 1
Correlation Matrix of Delta Scores*

Measure	Delta J+0 NoH	Delta J+0 Hyp
Delta J+0 NoH	---	0.860
Delta J+0 Hyp	0.860	---
Delta J+60 NoH	0.510	0.330
Delta J+60 Hyp	0.480	0.360
Delta J+80 NoH	0.570	0.480
Delta J+80 Hyp	0.610	0.570
Delta Slope NoH	0.100	0.120
Delta Slope Hyp	0.014	0.040
Delta Integral NoH	0.890	0.750
Delta Integral Hyp	0.560	0.700

*$r \leq 0.65$ = low correlation

Table 2
Spearman Rank Order Correlation of Baselines

Measure	Correlation
ST Level	
J+0 no hyperventilation	$r_s = 0.325$
J+0 pretest hyperventilation	
J+60 no hyperventilation	$r_s = 0.434$
J+60 pretest hyperventilation	
J+80 no hyperventilation	$r_s = 0.526$
J+80 pretest hyperventilation	
ST Slope	
no hyperventilation	$r_s = 0.721$
pretest hyperventilation	
ST Integral	
no hyperventilation	$r_s = 0.987$
pretest hyperventilation	

Table 3
Physical Characteristics of Female Subjects*

Characteristic	(N=14)
Age (yr)	
M	22.0
SD	1.5
Height (cm)	
M	164.6
SD	10.1
Weight (kg)	
M	61.3
SD	11.1
Breast Size (cm)	
M	11.5
SD	3.5

*M=mean; SD=standard deviation

Table 4
Hemodynamic Responses to Submaximal Cycle Ergometry**

Variable Measured	Females (N=14)	
	No HYP*	Pretest HYP*
Maximum RPE During Exercise		
M	13.9	14.6
SEM	0.4	0.6
Exercise Heart Rate (b/min)		
M	148.9	148.7
SEM	1.6	2.4
Exercise Systolic Blood Pressure (mmHg)		
M	146.7	145.9
SEM	3.1	3.9
Exercise Diastolic Blood Pressure (mmHg)		
M	74.1	74.6
SEM	1.8	2.0

*HYP=hyperventilation
**M=mean; SEM=standard error of mean

Table 5
Baseline and Exercise ST-Segment Changes*

Measures	Exercise ECG Responses Control	Post-HYP.	(N=14) F value	Signif.
ST Level				
J+0 (mV)				
Baseline	0.02 ± 0.01	0.02 ± 0.01	0.03	NS
Exercise	-0.09 ± 0.01	-0.09 ± 0.01		
J+60 (mV)				
Baseline	0.03 ± 0.01	0.03 ± 0.01	0.00	NS
Exercise	-0.002 ± 0.02	0.005 ± 0.01		
J+80 (mV)				
Baseline	0.04 ± 0.01	0.05 ± 0.01	0.72	NS
Exercise	0.06 ± 0.02	0.07 ± 0.02		
ST Slope† (mm/sec)				
Baseline	2.0 ± 1.1	2.4 ± 1.3	0.00	NS
Exercise	15.1 ± 1.7	14.6 ± 1.9		
ST Integral† (uV-sec)				
Baseline	-0.3 ± 0.2	0.0 ± 0.0	0.86	NS
Exercise	-3.4 ± 0.7	-3.1 ± 0.7		

*Values are means ± SEM
†ST Slope and Integral remain the same throughout each condition (J+0, J+60, and J+80)

Table 6
Delta Scores of ST Segment Changes*

Measures	Exercise ECG Responses Control	Post-HYP	(N=14) t-ratio	Signif.
ST Level				
J+0 (mV)				
Delta**	-0.09 ± 0.01	-0.09 ± 0.01	0.73	NS
J+60 (mV)				
Delta**	-0.02 ± 0.01	-0.02 ± 0.01	0.00	NS
J+80 (mV)				
Delta**	0.01 ± 0.02	0.02 ± 0.02	0.59	NS
ST Slope (mm/sec)				
Delta**	12.5 ± 1.19	11.9 ± 1.15	0.48	NS
ST Integral (uV-sec)				
Delta**	-2.9 ± 0.62	-2.9 ± 0.71	0.13	NS

*Values are means ± SEM
**Delta values are derived from exercise values minus baseline values

Table 7
ST Segment Changes with Hyperventilation*

Measures	Females (N=14)			
	Baseline	Post-HYP	t-ratio	p
ST Level (mV)				
M	0.02	-0.002	2.4	0.02
SEM	0.07	0.12		
ST Slope (mm/sec)				
M	2.4	3.1	1.9	0.04
SEM	1.23	1.27		
ST Integral (uV-sec)				
M	0.0	-0.9	1.3	0.11
SEM	0.0	0.73		

*Changes are derived from post-hyperventilation value minus baseline value
**M=mean; SEM=standard error of mean

Table 8
Repeated Measures ANOVA for Baseline and Exercise Values of ST Level (J+0)

Source	DF	Type III SS	Mean Square	F value	PR > F
Trial	1	0.00001607	0.00001607	0.03	0.8616
Error (Trial)	13	0.00660893	0.00050838		
Time	1	0.15751607	0.15751607	141.13	0.0001
Error (Time)	13	0.01450893	0.00111607		
Trial* Time	1	0.00004464	0.00004464	0.13	0.7276
Error (Trial* Time)	13	0.00458036	0.00035234		

Table 9
Repeated Measures ANOVA for Baseline and Exercise Values of ST Level (J+60)

Source	DF	Type III SS	Mean Square	F value	PR > F
Trial	1	0.00000179	0.00000179	0.00	0.9742
Error (Trial)	13	0.02132321	0.00164025		
Time	1	0.01230179	0.01230179	8.03	0.0141
Error (Time)	13	0.01992321	0.00153255		
Trial* Time	1	0.00078750	0.00078750	1.92	0.1894
Error (Trial* Time)	13	0.00533750	0.00041058		

Table 10
Repeated Measures ANOVA for Baseline and Exercise Values of ST Level (J+80)

Source	DF	Type III SS	Mean Square	F value	PR > F
Trial	1	0.00244464	0.00244464	0.72	0.4117
Error (Trial)	13	0.04418036	0.00339849		
Time	1	0.00428750	0.00428750	1.40	0.2586
Error (Time)	13	0.03993750	0.00307212		
Trial* Time	1	0.00014464	0.00014464	0.34	0.5681
Error (Trial* Time)	13	0.00548036	0.00042157		

Table 11
Repeated Measures ANOVA for Baseline and Exercise Values of ST Slope

Source	DF	Type III SS	Mean Square	F value	PR > F
Trial	1	0.01785714	0.01785714	0.00	0.9733
Error (Trial)	13	198.732143	15.2870879		
Time	1	2250.44643	2250.44643	171.79	0.0001
Error (Time)	13	170.303571	13.1002747		
Trial* Time	1	3.01785714	3.01785714	0.50	0.4900
Error (Trial* Time)	13	77.7321429	5.97939560		

Table 12
Repeated Measures ANOVA for Baseline and Exercise Values of ST Integral

Source	DF	Type III SS	Mean Square	F value	PR > F
Trial	1	1.14285714	1.14285714	0.86	0.3717
Error (Trial)	13	17.3571429	1.33516484		
Time	1	132.071429	132.071429	25.85	0.0002
Error (Time)	13	66.4285714	5.10989011		
Trial* Time	1	0.00000000	0.00000000	0.00	1.0000
Error (Trial* Time)	13	14.5000000	1.11538462		

Table 13
Paired t Tests on Delta Values of ST Level (J+0, J+60, and J+80)

Source	Mean	Variance	DF	t ratio	p value
Delta J+0 No HYP	-0.9071	0.0776	13	0.7329	0.2383
Delta J+0 HYP	-0.8714	0.1253			
Delta J+60 No HYP	-0.200	0.1492	13	0.0000	0.5000
Delta J+60 HYP	-0.200	0.1415			
Delta J+80 No HYP	0.1429	0.3519	13	0.5858	0.2840
Delta J+80 HYP	0.2071	0.3469			

Table 14
Paired t Test on Delta Values of ST Slope

Source	Mean	Variance	DF	t ratio	p value
Delta Slope No HYP	12.5333	23.8381	13	0.4760	0.3207
Delta Slope HYP	11.9333	18.3524			

Table 15
Paired t Test on Delta Values of ST Integral

Source	Mean	Variance	DF	t ratio	p value
Delta Integral No HYP	-2.9333	5.2095			
			13	0.1258	0.4508
Delta Integral HYP	-2.8667	7.2667			

Table 16
Paired t Test on Baseline (HYP) and Post-HYP Values of ST Level (J+0)

Source	Mean	Variance	DF	t ratio	p value
Baseline J+0 HYP	0.2067	0.0735	13	2.4152	0.0150
Post-HYP J+0	0.0067	0.1950			

Table 17
Paired t Test on Baseline (HYP) and Post-HYP Values of ST Slope

Source	Mean	Variance	DF	t ratio	p value
Baseline ST Slope	2.2667	21.9238	13	1.9194	0.0378
Post-HYP ST Slope	2.9333	21.6381			

Table 18
Paired t Test on Baseline (HYP) and Post-HYP Values of ST Integral

Source	Mean	Variance	DF	t ratio	p value
Baseline ST Integral	0.0000	0.0000			
			13	1.2704	0.1123
Post-HYP ST Integral	-0.8667	6.9810			

APPENDIX C

INFORMED CONSENT

INFORMED CONSENT

I, _____, do hereby voluntarily agree and consent to participate in the study conducted by Timothy M. Rose of the Division of Health and Physical Education of Virginia Polytechnic Institute and State University.

Title of Study:

The Effects of the Performance of Pretest Hyperventilation on ECG Components Suggesting Ischemic Heart Disease in a Female Population Performing Submaximal Exercise

Purpose of the Study:

To determine if the performance of pretest hyperventilation causes any changes in the electrocardiogram which may be of importance to physicians when they perform exercise tests of their female patients.

I voluntarily agree to participate in this research study. It is my understanding that my participation will include:

1. Participation in a screening process to determine if I qualify as a subject. The process consists of having electrodes applied to the body, performing submaximal exercise, and having ECGs recorded.

IF I QUALIFY AS A SUBJECT, THE FOLLOWING APPLY TO ME:

2. Determination of:
    a. blood pressure, heart rate, and ECG measurements at rest and during exercise;

b. submaximal work performance via stationary cycling (an estimation of aerobic fitness);

c. height and weight;

d. breast size via girth measurements performed by a female technician.

3. Participation in two exercise sessions performed in the Human Performance Laboratory. Two exercise sessions are necessary because hyperventilation must be performed pretest at one visit and not at all at another visit. When the individual arrives at the lab, electrodes will be applied to the upper torso and they will be seated on the stationary bicycle for a ten minute rest period. Following the rest period, the individual will exercise for 6-12 minutes working up to a workload that corresponds to 60% heart rate reserve and a rating of perceived exertion of 12-15. After exercising, the individual will perform some cool-down cycling at a light load. Then the individual will rest for ten minutes or until heart rate and blood pressure return to preexercise values. Pretest hyperventilation will be performed seated on the bicycle following the initial rest period.

I understand that participation in this study may produce certain discomforts and risks. These discomforts and risks include:

1. temporary muscle soreness as a result of the exercise session;
2. some degree of light-headedness as a result of hyperventilation performance;
3. the possibility of fainting resulting from hyperventilation performance.

I understand that certain personal benefits may also be expected form participation in this study. These include:

1. estimation of aerobic fitness level;
2. determination of heart rate and blood pressure at rest and during exercise;
3. a personalized exercise prescription, if so desired and indicated.

I understand that any data of a personal nature will be held confidential and will be used for research purposes only. I also understand that these data may only be used when not identifiable with me.

I understand that I may abstain from participation in any part of the study or withdraw from the study should I feel the activities might be injurious to my health. The researcher may also terminate my participation should he feel that the activities might be injurious to my health.

I understand that it is my personal responsibility to advise the researcher of any preexisting medical problem(s) that may affect my participation or of any medical problem(s) that

might arise in the course of the study and that no medical treatment or compensation is available if injury is suffered as a result of this study. A telephone is available which would be used to notify the emergency service if any medical problem(s) should arise.

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

Date:_____ Time:_____a.m./p.m.

Participant signature:_____

Witness:_____

Project Director: Dr. William G. Herbert

Telephone: (703)231-6565

HPER Human Subjects Chairman: Dr. Charles Baffi

Telephone: (703)231-8284

University Institutional Review

Board Representative: Dr. Ernest Stout

Telephone: (703)231-9359

APPENDIX D

SUBJECT BACKGROUND INFORMATION

SUBJECT BACKGROUND INFORMATION

Name:_____ Date:_____

Age:_____ Phone #:_____

Address (local):_____

_____

Exercise/Activity History

Activity	Duration per session	Sessions per week
1.		
2.		
3.		
4.		
5.		

Do you smoke tobacco products?_____ If yes, indicate how much you smoke in a typical week:_____

Are you presently taking any medications?_____ If yes, please list all medications you are taking (both prescription and non-prescription drugs)

Name of Medication	Dosage	Doses per day
_____	_____	_____
_____	_____	_____
_____	_____	_____

Do you have any medical or orthopedic problems? If so, please explain. _____

_____

_____

APPENDIX E

DATA COLLECTION FORM

ID # _____

Height _____ Weight _____

GIRTH MEASUREMENTS

C _____

Difference _____

B _____

PROTOCOL Target HR:_____

	BP	RPE	LOAD
Rest			
-10			
0			
Exer			
I			
II			
III			
IV			
V			
Rec			
0			
2			
6			
10			

APPENDIX F

RAW DATA

The following abbreviations apply to the variables listed in the raw data tables on the following pages:

a. 1 = no hyperventilation trial

b. 2 = hyperventilation trial

c. BRSize = breast size

d. HR = heart rate

e. RPE = rating of perceived exertion

f. SBP = systolic blood pressure

g. DBP = diastolic blood pressure

h. J+0 = ST-segment measurement point defined as the J-point

i. J+60 = ST-segment measurement point defined as the J-point plus 60 msec

j. J+80 = ST-segment measurement point defined as the J-point plus 80 msec

k. SL = ST-segment slope

l. Int = ST integral

Table 1
Raw Data of Subjects

Subject	Age	Height1	Height2	Weight1	Weight2
1	22	172.5	174.5	64.0	64.0
2	23	166.9	164.8	62.5	62.5
3	22	172.9	173.0	62.8	62.4
4	22	166.4	165.9	51.8	51.8
5	20	175.5	176.8	78.8	79.4
6	22	181.1	179.1	85.7	84.6
7	21	150.1	151.9	56.9	57.0
8	20	155.4	154.9	45.1	46.6
9	23	161.0	160.0	51.2	52.5
10	24	169.9	167.9	55.1	56.1
11	25	171.9	170.7	69.1	68.2
12	23	146.6	145.5	48.5	49.0
13	20	162.1	161.0	60.3	60.4
14	21	155.4	154.9	64.8	64.0

Table 2
Raw Data of Subjects

Subject	BRSize1	BRSize2	RestHR1	ExerHR1	DeltaHR1
1	12.0	10.0	80	153	73
2	14.0	13.5	108	156	48
3	12.0	13.5	88	151	63
4	10.0	10.0	74	152	78
5	21.5	20.0	94	146	52
6	16.0	15.0	78	149	71
7	10.5	12.5	73	142	69
8	8.0	8.0	88	140	52
9	9.0	7.5	57	141	84
10	10.0	12.5	76	151	75
11	9.0	10.5	56	142	86
12	8.0	7.0	85	152	67
13	10.5	9.0	96	160	64
14	12.0	10.0	73	149	76

Table 3
Raw Data of Subjects

Subject	RestHR2	ExerHR2	DeltaHR2	MaxRPE1	MaxRPE2
1	100	156	56	16	15
2	106	169	63	13	15
3	74	144	70	12	13
4	75	142	67	15	15
5	83	146	63	14	20
6	86	156	70	15	15
7	72	150	78	13	12
8	80	135	55	13	14
9	55	139	84	14	15
10	64	149	85	15	15
11	71	145	74	13	13
12	103	154	51	13	13
13	93	157	64	12	12
14	81	140	59	16	17

Table 4
Raw Data of Subjects

Subject	RestSBP1	ExerSBP1	DeltaSBP1	RestSBP2	ExerSBP2
1	112	164	52	104	156
2	112	152	40	98	148
3	102	146	44	108	134
4	120	156	36	118	146
5	108	162	54	108	184
6	102	144	42	112	144
7	98	134	36	106	132
8	102	136	34	92	132
9	98	138	40	90	140
10	118	150	32	100	154
11	112	152	40	116	162
12	98	136	38	104	136
13	112	158	46	104	140
14	92	126	34	94	134

Table 5
Raw Data of Subjects

Subject	DeltaSBP2	RestDBP1	ExerDBP1	DeltaDBP1	RestDBP2
1	52	78	84	6	72
2	50	68	72	4	72
3	26	70	82	12	74
4	28	66	68	2	78
5	76	76	78	2	78
6	32	72	72	0	78
7	26	68	68	0	74
8	40	72	70	-2	72
9	50	60	70	10	65
10	54	80	84	4	72
11	46	76	74	-2	74
12	32	66	68	2	68
13	36	84	82	-2	68
14	40	62	66	4	60

Table 6
Raw Data of Subjects

Subject	ExerDBP2	DeltaDBP2	BaseJ+01	ExerJ+01	DeltaJ+01
1	82	10	0.02	-0.07	-0.07
2	72	0	-0.03	-0.11	-0.08
3	86	12	0.00	-0.11	-0.11
4	76	-2	0.02	-0.06	-0.06
5	84	6	-0.01	-0.07	-0.06
6	72	-6	0.02	-0.11	-0.11
7	70	-4	0.06	-0.09	-0.09
8	74	2	0.04	-0.13	-0.13
9	70	5	0.00	-0.10	-0.10
10	84	12	-0.01	-0.06	-0.05
11	74	0	0.05	-0.05	-0.05
12	64	-4	0.00	-0.09	-0.09
13	76	8	-0.01	-0.10	-0.09
14	60	0	0.08	-0.08	-0.08

Table 7
Raw Data of Subjects

Subject	BaseJ+02	ExerJ+02	DeltaJ+02	BaseJ+601	ExerJ+601
1	0.00	-0.07	-0.07	0.08	0.11
2	-0.01	-0.12	-0.11	0.04	-0.08
3	0.00	-0.12	-0.12	0.01	-0.01
4	0.00	-0.06	-0.06	0.05	0.07
5	-0.01	-0.06	-0.05	0.02	0.08
6	0.00	-0.10	-0.10	0.05	-0.02
7	0.04	-0.09	-0.09	0.00	-0.04
8	0.06	-0.15	-0.15	0.07	-0.01
9	0.04	-0.08	-0.08	0.02	-0.02
10	0.00	-0.15	-0.15	-0.01	-0.10
11	0.03	-0.05	-0.05	0.08	0.05
12	0.00	-0.09	-0.09	0.01	-0.02
13	0.06	-0.05	-0.05	0.01	-0.05
14	0.06	-0.05	-0.05	0.07	0.00

Table 8
Raw Data of Subjects

Subject	DeltaJ+601	BaseJ+602	ExerJ+602	DeltaJ+602	BaseJ+801
1	0.03	0.09	0.11	0.02	0.10
2	-0.08	-0.01	-0.02	-0.01	-0.03
3	-0.01	0.00	-0.02	-0.02	0.03
4	0.02	0.06	0.00	-0.06	0.07
5	0.06	0.00	0.08	0.08	0.04
6	-0.02	0.02	0.00	-0.02	0.04
7	-0.04	-0.01	-0.06	-0.05	0.00
8	-0.01	0.08	-0.02	-0.02	0.09
9	-0.02	0.04	0.02	-0.02	0.04
10	-0.09	0.00	-0.08	-0.08	-0.01
11	-0.03	0.04	0.03	-0.01	0.10
12	-0.02	0.02	0.00	-0.02	0.02
13	-0.04	0.10	0.07	-0.03	0.00
14	0.07	0.04	0.00	-0.04	0.09

Table 9
Raw Data of Subjects

Subject	ExerJ+801	DeltaJ+801	BaseJ+802	ExerJ+802	DeltaJ+802
1	0.25	0.15	0.16	0.28	0.12
2	-0.06	-0.03	-0.01	0.04	0.05
3	0.04	0.01	0.01	0.00	-0.01
4	0.17	0.10	0.03	0.08	0.05
5	0.13	0.09	0.01	0.13	0.12
6	0.01	-0.03	0.04	0.03	-0.01
7	-0.01	-0.01	-0.01	-0.05	-0.04
8	0.04	-0.05	0.12	0.04	-0.08
9	0.01	-0.03	0.07	0.10	0.03
10	-0.01	0.00	0.00	-0.02	-0.02
11	-0.13	0.03	0.06	0.08	0.02
12	0.00	-0.02	0.03	0.06	0.03
13	0.02	0.02	0.14	0.21	0.07
14	0.06	-0.03	0.07	0.03	-0.04

Table 10
Raw Data of Subjects

Subject	BaseSL1	ExerSL1	DeltaSL1	BaseSL2	ExerSL2	DeltaSL2
1	8	31	23	10	29	19
2	0	5	5	2	14	12
3	4	18	14	2	14	12
4	4	19	15	3	8	5
5	6	20	14	5	24	19
6	4	12	8	4	13	9
7	-9	7	16	-10	3	13
8	3	20	17	4	20	16
9	1	10	9	0	16	16
10	0	13	13	0	10	10
11	5	17	12	3	13	10
12	2	12	10	4	10	6
13	1	13	12	9	23	14
14	-1	15	16	-2	8	10

Table 11
Raw Data of Subjects

Subject	BaseInt1	ExerInt1	DeltaInt1	BaseInt2	ExerInt2
1	0	0	0	0	0
2	-3	-7	-4	0	-6
3	0	-3	-3	0	-3
4	0	0	0	0	-6
5	0	-1	-1	0	0
6	0	-4	-4	0	-3
7	0	-5	-5	0	-6
8	0	-5	-5	0	-5
9	0	-4	-4	0	-2
10	-1	-9	-8	0	-8
11	0	0	0	0	0
12	0	-3	-3	0	-2
13	0	-4	-4	0	-1
14	0	-2	-2	0	-1

Table 12
Raw Data of Subjects

Subject	DeltaInt2	PostHypECG	PostHypSL	PostHypInt
1	0	-0.02	13	0
2	-6	-0.12	0	-10
3	-3	0.00	2	0
4	-6	-0.01	3	0
5	0	-0.01	5	0
6	-3	0.00	5	0
7	-6	0.04	-7	0
8	-5	0.02	4	0
9	-2	0.04	2	0
10	-8	-0.05	1	-3
11	0	0.03	3	0
12	-2	-0.01	6	0
13	-1	0.00	9	0
14	-1	0.06	-2	0

VITA

Timothy Mark Rose was born on April 27, 1968 in Laurinburg, North Carolina. His family moved around the state of North Carolina before settling back in Wagram, North Carolina. He attended Scotland High School in Laurinburg, North Carolina, where he graduated in 1986.

Tim continued his education at Western Carolina University in Cullowhee, North Carolina. He began in computer science, but after a year and a half decided to change his major to Sport Management. He placed his concentration in exercise science and fitness mangement; afterwhich, he began working in the cardiac rehabilitation program. He graduated from Western in 1990.

Tim chose to continue his education at Virginia Polytechnic Institute and State University. He entered the M.S. program in Education concentrating in Adult Fitness and Rehabilitative Exercise. After two years, Tim graduated with his degree in August, 1992.

Tim hopes to obtain a position within a clinical setting working in cardiac rehabilitation. Eventually he hopes to move into a setting that involves working with all types of individuals, healthy and diseased.

Timothy M. Rose