

Effects of Submaximal Exercise and Hyperventilation on ECG
Components in Healthy, Young Adult Men with Recording
Leads Typically Used for Evaluation of Ischemic
Heart Disease

by

Libby A. Gallagher

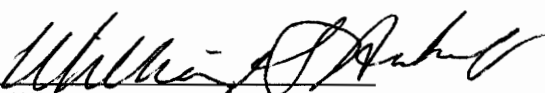
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APPROVED:



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Effects of Submaximal Exercise and Hyperventilation on ECG Components

In Healthy, Young Adult Men with Recording Leads Typically Used

For Evaluation of Ischemic Heart Disease

by

Libby A. Gallagher

Committee Chairman: William G. Herbert

Exercise Science

(ABSTRACT)

The present study was undertaken to determine if leads CM_5 , CC_5 , and V_5 are equally sensitive in detecting ST segment depression with exercise or hyperventilation in apparently normal males. Seven physically active men (29.4 ± 2.9 yrs, 180.9 ± 2.5 cm, 77.9 ± 3.4 kg, $x \pm SEM$), free of risk factors for heart disease, were initially found to have J point (J_0) depression with mild exercise in lead V_5 . Simultaneous ECG recordings from CM_5 , CC_5 , and V_5 during seated rest (REST), immediately post-moderate exercise (IPE), and after 30 s of hyperventilation (HVT). ECG signals were manually evaluated for ST segment depression at the J point and 60 ms and 80 ms past the J point (J_{60} , J_{80}). None of the three leads differed in their ability to detect ST segment changes. With exercise, J_0 was significantly ($P < .05$) reduced compared to REST; neither J_{60} nor J_{80} differed from REST. HVT reduced J_0 significantly but not J_{60} or J_{80} . Exercise provoked greater reductions than HVT. These data suggest that, in apparently healthy adult males, these three ECG leads are equally able to detect J point changes with exercise and hyperventilation, but exercise results in a relatively greater downward ST segment shift than does hyperventilation.

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TABLE OF CONTENTS

	<u>Page</u>
Acknowledgements	iii
I. Introduction	1
II. Review of Literature	8
ECG Lead Systems	8
Single Lead Systems	9
J Point and St Segment Alterations with Maximal Graded Exercise Testing ..	13
ECG Responses to Hyperventilation	17
III. Journal Manuscript	21
Introduction	24
Methods	26
Results	28
Discussion	29
References	32
Figures	35
IV. Summary and Conclusions	39
Recommendations for Future Research	41
References Cited	42
Appendices	
A. Detailed Methodology	47
B. The Informed Consent and Divisional Approval	51
C. Raw Data	59
D. Summary ANOVA Tables	67

Chapter I

INTRODUCTION

Coronary heart disease is the leading cause of death in the United States today (AHA, 1993). It has been reported that over 1.2 million people die due to this disease each year, while an additional 2 million are hospitalized because of it. In addition to this elevated mortality and morbidity, this disease is expensive both on an individual basis and to society as a whole. For example, coronary heart disease has been reported to cost Americans \$2.3 billion annually in health care costs (AHA, 1993). While the mortality rate can be reduced with an early diagnosis and aggressive interventions of the disease, the costs are extremely high and continue to rise with newer innovative approaches. Nevertheless, other than primary prevention, early detection and intervention of ischemic heart disease (IHD), constitutes the best contemporary approach.

In the domain of early detection, electrocardiographic (ECG) exercise testing is a procedure commonly used in the routine screening for IHD. Electrocardiography is a technique whereby the bioelectrical activity and the conductive pathways of the heart are assessed via visual record of this activity. This tracing, or electrocardiogram (ECG), is obtained from an array of unipolar and bipolar leads obtained by electrodes placed upon the subject's torso and limbs. Obtaining an ECG is a relatively simple procedure that, because of this apparent simplicity, is often done incorrectly. Both electrode placement and lead selection can play critical roles in the proper diagnosis of

ischemic heart disease.

In the exercise ECG test, changes in the ECG complex are measured during stepwise progressive exercise that raise both the heart rate and systolic blood pressure. In those with clinically significant IHD, the hearts demand for oxygen rises beyond the capacity of the coronary arteries to perfuse the cells and transitory ischemia results. In such cases, the ECG often shows evidence of myocardial ischemia. In that event, depression of the ECG ST-T segment becomes pronounced. Chest pain that peaks and ebbs in relation to the ST-T changes may occur also. These ST segment changes have been historically diagnosed as a physiological result of ischemia of the heart. As early as 1918, ECGs were recorded with changes that are now read as ischemic ST changes (Bousfield, 1918). Thus, the goal of the exercise ECG test is to provoke myocardial ischemia under controlled conditions such that the underlying IHD can be identified.

Because of its relative simplicity, graded exercise testing has become a cornerstone of the early detection and intervention of IHD. Nevertheless, there are processes other than ischemia that can result in ST segment changes. Conditions such as digitalis toxicity, technically poor tracings, hyperventilation, incorrect electrode placement and lead selection can all contribute to this phenomenon. False positive test results may occur, i.e., appearance of exercise-induced ischemic ST changes, without the presence of underlying angiographically documented coronary disease.

Some of the conditions leading to a false positive test can be alleviated prior to the graded exercise test (GXT). For example, because the subject is usually walking

during a GXT, skin site preparation and electrode placement may be optimized to minimize signal artifact when preparing an exercise test. Historically, electrodes have been placed on the extremities as well as the subject's chest when recording ECGs. In 1966, a system was developed by which the extremity leads are placed on the torso, thereby alleviating motion artifact (Mason and Likar, 1966). This technique has become the modern standard method used by most clinical exercise testing laboratories.

Voluntary elevations in breathing pattern in the absence of exercise-induced elevations in heart rate can lead to the presence of false-positive ECG changes. Since respiratory alkalosis, hyperventilation, changes the coronary blood flow relative to myocardial oxygen needs, it is capable of causing myocardial ischemia. (Pribble, Kusumi & Bruce, 1987). This false-positive phenomenon is more common in certain populations and is thought to be caused by alterations in parasympathetic tone of the central nervous system (Fardy, 1988). Often these changes manifest themselves as ischemia. As a result, exercise testing laboratories often use hyperventilation tests before beginning a GXT in order to rule out any hyperventilatory ECG changes. Monitoring via a standard 12-lead is the method most used.

Another factor contributing to a false positive test is that of J point depression. This shift may occur as a normal variant in the exercise response of healthy individuals. Frequently, J point depression may precede the onset of ST changes during exercise. As this may occur in an otherwise healthy individual, the implica

tions of this finding are controversial. Robbs and Marks (1967), who studied 2,224 males between the ages of 40 and 65, found that patients with IHD who exhibit J-point depression appear to have a higher mortality rate than those with normal ST segments. Ellestadt (1986) found J-point depression to be a normal finding, but was a sign of developing ischemic heart disease.

Lead selection is another important factor in the determination of IHD via a graded exercise test. These are often quicker to prepare and less expensive than the standard Mason-Likar system. However, some lead configurations have become associated with an increased incidence of false-positive ECG changes (Herbert & Froelicher, 1991). Nevertheless, some of these lead configurations have been shown to be sensitive to ST segment changes. Froelicher and colleagues (1976) demonstrated V_5 and CC_5 to be superior to the use of a standard chest lead in the determination of ischemic changes in an apparently healthy population.

Statement of the Problem

As described, electrocardiography in conjunction with graded exercise testing is a useful tool in determining the likelihood of IHD. However, problems with lead placement, hyperventilation and the correct interpretation of J point depression during these tests increase the incidence of false-positive GXTs. The aftermath of a false-positive test can include an increased anxiousness on the part of the patient, further and unnecessary diagnostic tests to rule out IHD and, of course, increased medical expenses. Because of these problems, the purpose of this study was to determine

whether those components of the ECG complex which are widely used in clinical practice to screen individuals for ischemic heart disease are affected by the interactive factors of electrode placement and hyperventilation during moderate intensity stationary cycling exercise in young healthy adult males.

Research Hypotheses

The hypotheses tested with this study are:

Ho₁: There is no difference in the degree of J-point depression seen in the ECG leads CC₅, CM₅, and V₅ with exercise.

Ho₂: There is no difference in the degree of J-point depression seen in the ECG leads CC₅, CM₅, and V₅ with a 30-s hyperventilation maneuver.

Delimitations

The following delimitations are present in this study:

1. Young, healthy, physically-active male subjects who volunteered were selected in this study.

Limitations

1. The findings may be limited to apparently healthy male subjects.
2. The findings are not generalizable to the entire population since non- random selection was employed and specific ECG inclusion criteria was applied .

Basic Assumptions

1. The screening procedure was adequate to identify false-positive responders.

2. Subjects did not have ischemic heart disease.
3. The equipment and techniques used were adequate to delineate ECG differences in the leads examined.

Definitions and Symbols

Electrocardiography (ECG) - Pictorial display of the mean electrical activity of the heart during the cardiac cycle. Based upon the differential measurement of the electrical potential between two points on the body.

Electrode - an adhesive patch, placed upon the subject, that allows for the monitoring of the heart's electrical activity from that particular area.

Lead - a very specific "view" of the heart's electrical activity. Can be either unipolar or bipolar. If unipolar, this view represents the difference in electrical potential between a given electrode and an electrical constant or zero. If bipolar, this view represents the difference in electrical potential between the positive and negative poles (or electrode sites) of the given lead.

CC_s - a bipolar lead configuration with the negative electrode in the right V_s position and the positive electrode in the left V_s position.

CM_s - a bipolar lead configuration with the negative electrode placed on the manubrium and the positive electrode in the left V_s position.

J-point (J_o)- the point representing the termination of the S wave and the onset of the ST segment. Characterized by the initial sharp lateral deflection following the terminus of the S wave.

J_{60} - the point on the ST segment occurring 60 ms after the J-point.

J_{80} - the point on the ST segment occurring 80 ms after the J-point.

ST Segment - the portion of the ECG baseline extending from the J-point to the onset of the T wave; it is typically depressed below the isoelectric line ($> 0.1\text{mV}$) by subendocardial ischemia; it is elevated with transmural ischemia.

V_5 - A unipolar lead with the positive electrode situated along the anterior axillary area of the left chest wall on the level of the (anterior) fifth intercostal space.

Chapter II

REVIEW OF LITERATURE

ECG Lead Systems

Electrocardiography (ECG) is based on the differential measurement of the electrical potential between two points on the body. This fundamental concept forms the basis of the numerous lead selections currently available for ECG monitoring. Since Einthoven first developed this idea with leads I, II, and III (Goldberger & Goldberger, 1994), the lead configuration consisting of six extremity leads and six precordial leads has become the most widely used. This system has also become the standard by which other ECG lead systems are compared. This 12-lead system allows for a three-dimensional view of the heart.

With the advent of graded exercise testing, the conventional 12-lead configuration was modified to allow for monitoring of the ECG response to exercise. This modification, i.e., moving of the limb electrodes to the torso, has gained acceptance but does alter the ECG configuration compared to the more traditional 12-lead (Gamble, McManus, Jensen & Froelicher, 1984; Papouchado, Walker, James & Clarke, 1987; Sevilla, Dohrmann, Somelofski, Wawrzynski, Wagner & Wagner, 1989). As some researchers have suggested that the 12-lead system is redundant and may exhibit some decrease in the sensitivity of ST segment depression (Ellestadt, 1986), numerous single-lead systems have been studied with regard to their ability to detect ST segment depression. Those relevant to this study are the leads V_5 , CM_5 and CC_5 .

In the context of graded exercise testing, ST segment depression is considered the hallmark of ischemic heart disease (Simoons, 1989; Surawicz, 1989). However, the nature, location and leads exhibiting this ST segment depression make the diagnostic importance of this measure uncertain. As part of this chapter, studies on performance of the aforementioned three leads, as well as those that address ST segment alterations in exercise associated with IHD and the influence of hyperventilatory maneuvers are reviewed.

Single Lead Systems

Single lead systems can be either unipolar or bipolar. A bipolar lead is one which measures the difference in electrical potential between two points. These points are usually separate electrodes placed upon the subject's skin. A unipolar lead assesses the potential difference at a single point referenced to a constant potential. In humans, this constant potential is the sum of the electrical activity seen at the three electrodes placed on the arms (RA and LA) and the left leg (LL) (MacFarlane, 1989).

A component of the traditional 12-lead configuration, lead V_5 is a unipolar lead. The positive pole of this lead is situated in the anterior axillary area of the left chest wall on a level of the fifth intercostal space used to place V_4 . The RA, LA and LL electrodes jointly serve as the negative pole of the lead. The CM_5 lead is a bipolar lead consisting of a negative electrode placed on the manubrium of the sternum and a positive electrode placed in the conventional left V_5 position. The CC_5 lead is another bipolar lead often used in special monitoring situation, such as the coronary care unit.

This lead, with its negative electrode in the right V_5 position also uses the left V_5 position as its positive electrode. While these three leads share a similar positive pole, they do not share a one-to-one correspondence of ECG changes associated with IHD (MacFarlane, 1989). In other words, for a given amount of myocardial ischemia, each of these three leads would show different degrees of ST- segment depression.

Froelicher and colleagues (1976) compared the use of CM_5 and CC_5 against the standard precordial V_5 lead for the purposes of elucidating differences in ST segment changes. They included CC_5 in order to incorporate a vertically oriented lead for comparison. Froelicher and colleagues (1976) found that CC_5 and V_5 yielded similar results, but that CM_5 appeared normal when other leads had abnormal changes. The CM_5 lead was also found to be relatively less sensitive than lead V_5 or CC_5 when classic criteria for slope measurement were used. Thus, some authors have questioned the use of CM_5 to monitor changes in the ST segment.

Others have studied the exercise responses of 100 men with normal resting ECG's and no clinical history of MI (Chaitman, Bourassa, Wagniard, Corbara & Ferguson, 1978). These male subjects between the ages of 31 and 62 were chosen based on no previous history of a myocardial infarction and a resting electrocardiogram. They monitored the standard 12-lead as well as leads CM_5 and CC_5 during maximal treadmill tests. Using lead V_5 alone allowed for the identification of 37 of the 66 subjects with IHD compared to 43 with CC_5 and 45 with CM_5 . The standard 12-lead configuration (minus aV_R) identified 50 men, the

combined use of CM₅, CC₅ and a bipolar inferior lead (CL) found 52 while the 14-lead system (12 lead + CM₅, CC₅, CL) identified 58 of the 66 subjects with IHD. While the multi-lead systems were more sensitive, the specificity of each lead system was similar. Those investigators concluded that, because 14-lead recordings are time-consuming, a combination with some fewer number of leads would be an acceptable alternative.

In related work, it was concluded that the use of a 14-lead system was indicated for a population of men with typical or probable angina (Chaitman, Waters, Bourassa, Tubau, Wagniart & Ferguson, 1979). Here, 65% of those subjects with typical angina and angiographically documented IHD were identified by ECG changes in V₅, 85% by the combined use of CM₅, CC₅ and CL₅, and 87% by the 14 leads. This trend held true for subjects with multivessel IHD. Conversely, in men with non-specific chest pain and less severe IHD, false-positive tests occurred frequently; the use of multiple leads may thus increase the rate of false-positive test results. For those subjects with less severe IHD, the authors suggested that the use of CM₅ would be adequate.

The findings of the above described study were extended by the evaluation of lead sensitivity in survivors of transmural infarctions undergoing graded exercise testing (Tubau, Chaitman, Bourassa & Waters, 1980). The sensitivity of the test for detecting multivessel disease was similar when using either 14 ECG leads (72%) or both CM₅ and CC₅ (64%). Both were superior to the isolated use of V₅ (50%). As

before, these investigators felt that the judicious use of a few ECG leads would be adequate in detecting multivessel IHD. In using the ST/HR slope as the index of exercise-induced ST segment depression, Okin and Kligfield (1989) drew similar conclusions.

Bowles and colleagues (1985) evaluated the efficacy of 18 unipolar precordial leads versus the use of the bipolar leads, CM_5 and CC_5 . The precordial leads consisted of the conventional V_1 to V_6 as well as parallel rows of electrodes one rib above and below. Mean maximum ST segment change at peak exercise was 0.24mV for the bipolar lead system versus 0.18 mV for the unipolar system ($p<.001$). Because of these results, the investigators concluded that use of the standard lead system with precordials considered was not superior to the multiple bipolar lead system. Others have reached similar conclusions (Rijneke et al., 1980).

In comparing the post-GXT ECG results to coronary arteriograms in 203 men, it appeared that only the isolated leads V_5 (61%), and CM_5 (60%) had sensitivities comparable to that seen with a conventional 12-lead system (65%) (Sketch, Nair, Esterbrooks & Mohiuddin, 1978). These investigators chose to study 203 males who were referred to their facility for evaluation of chest pain. The mean age of the subjects was 50 years \pm 9. Any subject with previous cardiac conditions such as valvular disease, myocarditis, pericarditis, and cardiomyopathy were excluded. Moreover, the predictive value of V_5 compared to multiple leads did not differ significantly. For this study, ST segment depression that appeared only during

the use of one or two leads as being adequate to detect ischemia, evaluations of the CM₅ lead in Holter monitoring do not confirm this (Eggeling, Günther, Treis-Mueeler, Osterspey, Höher & Hombach, 1988).

J Point and ST Segment Alterations with Maximal Graded Exercise Testing

The J point (J_0) has been defined as the junction of the QRS complex and the ST segment (Becker, 1988). This particular component of an ECG complex represents the reciprocal change associated with the end of the atrial repolarization process (Sapin, 1991). When evaluating J point changes, the atrial T wave thus becomes important. The atrial T (T_a) wave represents normal atrial repolarization and can influence the ST response during an exercise test. Sapin (1991) states that this is a common variant with no "apparent" clinical consequences. In making this statement, however, Sapin fails to cite supporting evidence. Moreover, others suggest that J point depression is not modified by T_a , but rather affected to competition between normal repolarization "obscured in the early ST segment by (what is) possibly delayed terminal depolarization forces" (Mirvis, Keller, Cox, Zettergren, Dowdie & Ideker, 1977).

The most commonly studied change seen with maximal graded exercise testing is that of J point depression with an upsloping ST segment. While many studies have evaluated this variable, there is still controversy over its significance. Robb and Marks (1967), who studied 2,224 males referred for life insurance physicals, reported that J point depression after exercise was a normal clinical finding. Subjects with

that J point depression after exercise was a normal clinical finding. Subjects with diagnosed IHD exhibiting this finding also had a better survival rate than those who had normal ST segments.

Using a CM₅ lead configuration, Kurita and colleagues (1977) evaluated junctional depression during exercise and correlated it with angiographic findings in 230 patients. Importantly, they purposely excluded subjects with the classic flat ST segment depression of 1 mm, that lasts 0.08 sec after the J point. Multivessel disease was rare when exercise-induced junctional depression of less than 1.5 mm was present. Furthermore, junctional depression of 2 mm or more appeared to be associated with the same incidence of disease when the ST segments were either slowly upsloping or horizontal. One potential weakness of this study is that the investigators arbitrarily accepted junctional depression of less than 0.14 mV to be a normal response during exercise. Ten of the 75 subjects in this category subsequently were shown to have at least one 50% (or larger) stenosis of a coronary artery. This finding re-affirms the larger problem in the literature of no known "acceptable" amount of J point depression in a normal population.

Apart from studies evaluating J point shifts with exercise, ST segment alterations also have received considerable attention. During a six-year follow-up of 438 patients who underwent maximal GXTs, it was noted that the annual incidence of coronary events were 13% for subjects with 0.2mV downsloping ST segment depression and 9% for those with either 0.2 mV horizontal or upsloping ST depression

(Stuart & Ellestad, 1976). In a separate group of 248 subjects, 60% of those subjects exhibiting any of the aforementioned ST segment changes (192 subjects) were angiographically shown to have significant multivessel disease. However, 41 of these 192 subjects had no coronary obstructions.

An earlier study indicated similar results. Of 100 consecutive patients undergoing GXTs, 26 of the 46 with normal resting ECGs manifested J point depression ≥ 1 mm for ≥ 0.08 sec (Roitman, Jones & Sheffield, 1970). Of those 26, 24 had abnormal coronary angiograms. Of the remaining 20, only 6 had abnormal angiograms and four of these six were predictable based on the clinical evidence of previous myocardial infarction.

These classic ECG criteria of ST segment shift in exercise were later compared to the criteria of junctional depression with upsloping ST segments of either 1 or 2 mm ≥ 0.08 sec past the J point. New definitions of junctional depression slowly upsloping included 0.1 mV ≥ 80 msec after the end of the QRS. Including these criteria to the more conventional ones significantly increased the sensitivity of maximal GXT administration by 7-8% relative to the detection of coronary obstructions $\geq 50\%$ (Rijneke, Ascoop & Talmon, 1980). Specificity was unaffected. Note that the ECG leads used were CM_5 and CC_5 . Due to its relative simplicity, the authors suggested including slowly upsloping ST segments in the routine analysis of exercise ECGs.

Others have correlated the angiographic findings of asymptomatic subjects with abnormal exercise ECGs, defined here as ≥ 1 mm of horizontal or downsloping ST

segment depression in orthogonal leads (Froelicher, Yanowitz, Thompson & Lancaster, 1973). This study was unique in that, other than the findings of abnormal ECGs at rest or with exercise, the subjects were entirely free of symptoms. Of those subjects with a normal resting ECG coupled with abnormal exercise ECGs, 38.9% (7/18) were found to have at least one coronary lesion. All subjects with this response under age 34 (n=5) did not have CHD while those over 45 years (n=5) did. In contrast, 55% (32/26) of those subjects with abnormal resting ECGs and abnormal exercise ECGs had angiographic evidence of coronary blockages. The authors concluded that, while maximal exercise ECGs are a sensitive tool for detecting significant IHD, they lack adequate specificity.

Frequently, the use of exercise ST segment changes as indicators of myocardial ischemia have been criticized. In a meta-analysis of 147 papers evaluating the diagnostic accuracy of exercise ECGs, it was noted that the reported sensitivity varied from 23-100% (mean=68%) while the specificity ranged from 17-100% (mean=77%) (Gianrossi, et al., 1989). Factors affecting sensitivity were the treatment of equivocal test results, comparison with a "better" test (e.g. thallium scintigraphy), and exclusion of patients on digitalis. For specificity, these included the treatment of upsloping ST depression, excluding subjects with previous myocardial infarctions or left bundle branch block and the use of hyperventilatory responses prior to testing.

Consequently, it appears that exercise ECGs are a useful tool for specific subpopulations of patients. In other words, their use may not be overly helpful in

subjects with an intermediate pretest likelihood of IHD of 20 to 80% (Simoons, 1989). More extensive follow-up testing is suggested for subjects with similar post-test likelihoods of IHD.

ECG Responses to Hyperventilation

Hyperventilation is not commonly viewed as being a factor in increasing the incidence of false-positive graded exercise tests. However, numerous studies have shown this opinion to be incorrect. Lewis (1953) characterized the cardiac responses to hyperventilation in the "hyperventilation syndrome" to be that associated with arrhythmias. Namely, he noted episodes of palpitations, tachycardia, "skipped beats" and either brief, sharp or persistent dull chest pains. Lewis (1953) further suggested that the lowered arterial CO₂ content results in splanchnic vasodilatation via inhibition of vasomotor centers. The net result is a possible drop in venous return and \dot{Q} . Earlier electrocardiographic studies also noted arrhythmias and altered ST segments (Thompson, 1943).

Others have evaluated the systemic and coronary hemodynamics of hyperventilation in humans (Rowe, Castillo & Crumpton, 1962). The subjects hyperventilated for 5 to 10 minutes which calls into question how vigorous was the hyperventilation. Nevertheless, these researchers noted that blood pressure fell, while cardiac index increased a nonsignificant 9.4%. Total peripheral resistance also did not change significantly. Coronary blood flow fell a mean 30.3% ($p < .05$) but varied considerably across subjects. Concomitantly, the arterial-coronary sinus O₂

considerably across subjects. Concomitantly, the arterial-coronary sinus O₂ difference increased 18.6% (p<.01) while the arterial-coronary sinus CO₂ difference increased 17% (p<.01). Thus, in some individuals, it appears that ST-segment alterations with hyperventilation *may* be associated with concomitant reductions in coronary blood flow.

Later work lent insight into the mechanisms behind these electrocardiographic alterations. In evaluating 350 patients with no evidence of CHD, 37 were noted to have precordial T-wave inversions after 10 to 15 seconds of hyperventilation (Wasserburger, Siebecker & Lewis, 1956). While both vagal blockade and oral administration of potassium salts abolished this response, breathing gases of various concentrations of O₂ and CO₂ did not significantly affect the ECG response. They concluded that these T-wave inversions are most likely due to a vagal reflex. This work was later extended by studying 65 patients with similar characteristics (Wasserburger & Lorenz, 1956). The ST-segment depression and T-wave inversions seen either at rest and/or with hyperventilation were completely abolished with vagal blockade. It is interesting to note that very early reports of the cardiac response to hyperventilation indicated that a sinus tachycardia occurred with this activity (Engel, Ferris & Logan, 1947).

Few early studies have evaluated the influence of hyperventilation in relation to the ECG response to maximal exercise. McHenry and co-workers (1968) mention this occurrence in noting that a 28 year old patient with a false-positive GXT also

exhibited ST-segment changes with hyperventilation. This group later suggested that these false-positive ST-segment changes typically occur early in the exercise test in the absence of any symptoms (McHenry, Cogan, Elliott, & Knoebel, 1970). Moreover, these alterations did not progress in magnitude as the GXT continued and frequently became less prominent as the exercise intensity approached maximum. Note that the ST-segment depression noted by these researchers was about 0.1 mV and that a CC₅ lead configuration was used.

This work was later extended by Lary and Goldschlager (1974). They evaluated 7 (out of a pool of 46 patients with false-positive GXTs) subjects with ST-segment changes after hyperventilation, but who had normal angiograms. As only 3% of 192 patients with true-positive GXTs demonstrated similar ischemic changes with hyperventilation, they concluded that the presence of these alterations "very probably" reflect an absence of CHD. They suggested that hyperventilation be performed as part of the pre-GXT protocol.

More recent work has evaluated the ST-segment responses to hyperventilation in patients with angiographically-documented CHD (Ardissino, et al., 1989). Of 329 patients studied, 160 had a positive response to hyperventilation; 75 manifested ST-segment elevation while 85 had ST-segment depression. These researchers used 79 male subjects who had exhibited a ST depression of at least 0.1mV 80 msec after the J point as criteria for inclusion in the study. All of the subjects participated in a hyperventilation protocol that included breathing at least 30 respirations·min⁻¹ for 5

minutes. This protocol is longer in duration than most, possibly accounting for their reporting of a large number of early responders to this task. Not surprisingly, the patients exhibiting ST segment depression early during hyperventilation had similar changes occur 71% earlier in the GXT than those subjects with ST segment changes that were not induced until completion of the hyperventilation. The researchers suggested that the early responders, those thought to have poor coronary reserve, experienced ST-segment changes due to an increased $\dot{M}V\text{O}_2$ while, in the latter group, it is more likely due to a vagally mediated reduction in coronary blood flow. Thus, in these patients, ischemic changes in the ECG with hyperventilation were interpreted to reflect true ischemia.

As has been demonstrated, hyperventilation can elicit alterations in the ECG associated with ischemia. Pribble et al (1987) found that during hyperventilation (respiratory alkalosis), coronary blood flow is altered relative to the myocardial oxygen supply, thus capable of causing myocardial ischemia. It appears that these ST-segment alterations are usually moderate in size (0.1 mV) and predictable in that they appear both with hyperventilation and early in the GXT. While its rate of occurrence appears to be < 2% (Ardissino et al., 1989), misinterpretation of electrocardiograms taken in conjunction with a GXT can lead to significant problems on the part of the patient. Thus, efforts need to be made in order to identify correctly ST-segment alterations associated with CHD and those associated with hyperventilation.

Chapter III

Journal Manuscript

to

Journal of Cardiopulmonary Rehabilitation

Effects of Submaximal Exercise and Hyperventilation on ECG
Components in Healthy, Young Adult Men with Recording
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Heart Disease

Running Head: ECG Components in Healthy Men

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ABSTRACT

The present study was undertaken to determine if leads CM_5 , CC_5 , and V_5 are equally capable of detecting ST segment changes with exercise or hyperventilation in apparently normal males. Seven physically active men (29.4 ± 2.9 yrs, 180.9 ± 2.5 cm, 77.9 ± 3.4 kg, $x \pm SEM$), free of risk factors for heart disease, were initially found to have J point (J_0) depression with mild exercise in lead V_5 . Simultaneous ECG recordings from CM_5 , CC_5 , and V_5 during seated rest (REST), immediately post-moderate exercise (IPE), and after 30 s of hyperventilation (HVT). ECG signals were manually evaluated for ST segment depression at the J point and 60 ms and 80 ms past the J point (J_{60} , J_{80}). None of the three leads differed in their ability to detect ST segment changes. With exercise, J_0 was significantly ($P < .001$) reduced compared to REST; neither J_{60} nor J_{80} differed from REST. HVT reduced J_0 significantly but not J_{60} or J_{80} . Exercise provoked greater reductions than HVT. These data suggest that, in apparently healthy adult males, these three ECG leads are equally able to detect J point changes with exercise and hyperventilation.

Key words: ST segment depression, J-point, electrocardiography, CC_5 , CM_5 , V_5

Coronary heart disease is the leading cause of death in the United States today¹. It has been reported that over 1,200,000 people die due to this disease each year, while an additional 2 million are hospitalized because of it. In addition to this elevated mortality and morbidity, this disease is expensive both on an individual basis and to society as a whole. For example, coronary heart disease has been purported to cost Americans over \$56 billion annually in health care costs and lost productivity¹. While the mortality rate can be attenuated with early diagnosis and aggressive interventions of the disease, these diagnostic and related treatment procedures can be extremely high and continue to rise. Nevertheless, other than preventing the development of the disease, early detection and intervention of ischemic heart disease (IHD) constitute the best contemporary medical treatment.

Electrocardiographic assessment of the heart is a procedure commonly used to detect early IHD. A well-recognized indicator of myocardial ischemia is depression of the electrocardiographic ST-T wave. These ST segment changes have been historically diagnosed as a physiological result of ischemia of the heart. As early as 1918, electrocardiograms (ECGs) were recorded with ST-T wave changes that are now read as ischemic². While otherwise important in the detection of IHD, a resting electrocardiogram is useful only in determining the presence of acute myocardial ischemia or old infarctions. Consequently, subjects with suspected IHD are frequently required to undergo a graded exercise test (GXT). Provoking myocardial ischemia under controlled conditions with a GXT can allow for the identification and

subsequent treatment of underlying IHD. Because of its relative simplicity, graded exercise testing has become a cornerstone of the early detection and intervention of IHD.

Processes other than ischemia can result in ST segment changes and result in a false-positive GXT. Voluntary elevations in breathing pattern in the absence of exercise-induced elevations in HR can lead to the presence of false-positive ECG changes³. This is more common in certain populations and is thought to be caused by alterations in sympathetic tone⁴. Another factor contributing to a false positive test is that of J-point depression. While J-point depression may precede the onset of ST changes during exercise, it is often a normal finding⁵. Lead selection is another important factor in the determination of IHD via a graded exercise test. While the standard is a 12-lead ECG, bipolar lead configurations are gaining in popularity. However, some lead configurations have become associated with an increased incidence of false-positive ECG changes⁶.

As described, electrocardiography in conjunction with graded exercise is a useful tool in determining the presence of IHD. However, problems with lead placement, hyperventilation and the correct interpretation of J-point depression during these tests increase the incidence of false-positive GXTs. The aftermath of a false-positive test can include an increased anxiousness on the part of the patient, further medical tests to rule out IHD and, of course, increased medical expenses. Because of these problems, the purpose of this study was to determine whether these components

of the ECG complex which are widely used in clinical practice to screen individuals for ischemic heart disease are affected by the interactive factors of electrode placement and hyperventilation during moderate intensity stationary cycling exercise in young healthy adult males.

Methods and Procedures

Twelve male volunteers from the student and staff population of a large university served as subjects. These subjects regularly performed vigorous physical activity and met the criteria of "apparently healthy" exercise candidates according to the standards of the American College of Sports Medicine⁷. For each volunteer, standard 12-lead ECG recordings were obtained at rest and at a workload of 25 W on a cycle ergometer. Heart rate (HR) and blood pressure (BP) were monitored throughout the exercise. Subjects exhibiting a 0.1 mV exercise-induced J junction shift in the CM₅ ECG lead were considered to be J junction responders and, therefore, eligible for this study.

These seven J junction responders returned to the lab for an experimental exercise trial. Utilizing a 12-lead ECG machine (Q2000, Quinton Instruments, Seattle, WA), as well as a single lead system (Cambridge), the subjects were instrumented such that simultaneous ECG tracings could be acquired from the CC₅, CM₅, and V₅ lead positions. For CC₅, the negative electrode for the conventional limb lead II was positioned in the right V₅ position. For CM₅, the negative electrode for the limb lead III was placed on the manubrium of the sternum. Both these limb leads shared, as

their positive pole, an electrode placed in the conventional left V_5 position. Thus, simultaneous CC_5 and CM_5 tracings could be obtained with one ECG machine. The other ECG machine (Cambridge) was used to acquire the V_5 lead. The V_5 electrode was positioned such that it overlapped the electrode used as the positive pole of the CC_5 and CM_5 leads. Care was taken to ensure that the electrode sites were thoroughly cleaned and that the positioning of the electrodes was consistent between subjects. Both ECG machines were calibrated by evaluating the ECG signal seen following a 1 mV input to the machines. They did not differ.

Following instrumentation, the subjects sat quietly in a chair for 10 minutes. Arm position and posture were consistent between subjects. Subjects refrained from talking during this period so that breathing was normal for each subject. Thereafter, each subject exercised for three consecutive three-minute stages. The first workload was 50 W with subsequent workloads based upon the subject's heart rate response to the 50 W workload⁸. Following 10-minutes of seated rest, the subject hyperventilated for 30 seconds. Standardized instructions were used in describing this hyperventilation.

Multi-lead ECG recordings were acquired during pre-exercise rest (REST1), immediately post-exercise (IPE), during the 10-min post-exercise rest (REST2), and during hyperventilation (HVT). Copies of the ECG tracings were made at 200% original size. From these copies, ST segment depression was quantified by assessing the depth of three specific components of the ST segment relative to the isoelectric

line. These components were the J point (J_0) as well as the ST segment 60 ms (J_{60}) and 80 ms (J_{80}) after the J point. The isoelectric line was defined as a line drawn from the onset of the two consecutive P waves encompassing the ST segment being analyzed. For each lead (CC_5 , CM_5 , V_5), three consecutive ECG complexes from REST1, IPE, REST2 and HVT were evaluated. As REST1 and REST2 were found not to differ significantly, the mean of these two values have been expressed as REST.

Mean J_0 , J_{60} and J_{80} depression for each of the three leads for each of the three measurement periods (REST, IPE, HVT) were compared using two-way (leads x time) repeated measures analysis of variance. Significant differences were located using Student-Newman-Keuls test. Differences were considered statistically significant if $P < 0.05$. All data have been expressed as mean + SEM.

Results

Seven males met the criteria as a J junction responder. Subjects were 29.4 ± 2.9 yr old, 180.9 ± 2.5 cm tall and weighed 77.9 ± 3.4 kg. Peak workloads for the cycle ergometry test were 168 ± 26 W.

As illustrated in Figure 1, significant ($P < 0.001$) depression was seen for J_0 immediately post-exercise and during the 30 s HVT in all three leads compared to the two resting periods. The magnitude of this downward shift in J_0 did not differ between leads but was greater IPE than HVT. In evaluating the effects of exercise and hyperventilation on J_{60} , the degree of elevation in J_{60} did not differ significantly from the baseline conditions in either IPE or HVT (Figure 2). This trend was also seen for

J_{80} (Figure 3). Neither exercise nor hyperventilation significantly altered J_{80} compared to baseline for any of the leads.

INSERT FIGURES 1 TO 3 HERE.

Discussion

The purpose of this investigation was to determine if exercise and hyperventilation affect components of the ECG complex normally used to determine the presence of ischemic heart disease. Graded exercise testing is a widely used tool to assess the presence of coronary heart disease. Identification of coronary heart disease is often based upon interpretation of the ECG response to the exercise. Consequently, errors in interpreting these tests can have serious repercussions. Therefore, the present study was deemed to be worthwhile since both exercise and hyperventilation are usually part of graded exercise testing and previous research suggests that both factors may affect interpretation of ECG changes seen with these tests.

The major finding of this study is that apparently healthy subjects may exhibit J point depression with both moderate exercise and hyperventilation. None of the three leads tested was superior in identifying these changes. Contrary to our findings, Froelicher and colleagues⁹ found leads V_5 and CC_5 to exhibit similar ST segment depression and slope in groups of men with normal and abnormal ECG responses to exercise. These researchers found lead CM_5 to have greater ST segment depression

and a more upward slope than the other two leads; we found each lead to exhibit nonsignificant differences in the magnitude of their J point depression. Our results disagree with Froelicher et al.⁹ who concluded that interpreting CM₅ changes must be done using criteria differing from those classically employed. However, their conclusion is supported by the relatively high incidence (37% in men 61 to 65 yrs old) of ischemic changes seen in exercising asymptomatic men when lead CM₅ was used as the diagnostic lead with conventional ECG interpretation criteria¹⁰. Collectively, these studies suggest that ischemic changes seen with CM₅ must be interpreted with care.

Others disagree, concluding that CM₅ suffices for most situations where "screening" for IHD is desired¹¹. Related research suggests that CM₅ may be adequate for detecting ischemia of the anterior wall¹². However, CM₅ does not appear to be sensitive to inferior ischemia¹³ or occlusions of the right coronary artery¹². In detecting inferior ischemia, recent research suggests that V₅ is superior to inferior leads such as lead II¹⁴.

In comparing the three bipolar leads studied here to multiple lead systems in detecting ischemia, others found CM₅ to be slightly though nonsignificantly more responsive than CC₅ and V₅¹⁵. Our findings reinforce these; the J point depression and ST segment depression 60 ms past the J point seen in our subjects was similar across the three leads studied. While multiple lead systems remained more sensitive than the three single-lead systems used¹⁵, the combined use of these three leads may be as good as a 14-lead system¹⁶. Interestingly, because of the increased sensitivity of

multiple lead systems and resultant reduced specificity, some researchers advocate using a single-lead system in patients with nonspecific chest pain¹⁷. In this group of patients, the pre-test likelihood of having IHD is low and both CC_5 and V_5 have better predictive value when positive than a multiple lead system¹⁷.

This study evaluated the degree of J point depression in leads CM_5 , CC_5 , and V_5 during both exercise and hyperventilation. While we found no significant differences in the magnitude of J point between the leads, this does not rule out the further study of the optimal use of electrocardiographic lead configurations. While most clinical and research facilities use a 12-lead system during exercise testing, the role of single lead monitoring is not an important consideration. These leads would be useful in a rehabilitative setting where monitoring for dysrhythmias is often of greater importance than identifying ischemic changes. As entry into a cardiac rehabilitation program usually entails a symptom-limited GXT, overt ischemia is usually identified at that time. A single lead system may be sensitive enough to detect ischemia with exercise; however, the present study suggests that the specificity of the lead may be attenuated by the exercise provoking the ischemia. The hyperventilatory response to exercise may affect the J point change seen with exercise, but the present study suggests that its influence is minor. Consequently, the present study reinforces the notion that single-lead monitoring may be useful in detecting ischemia but its utility in an exercise setting for this purpose may be limited.

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Figure Captions

- Figure 1. Effects of mild exercise and hyperventilation on J point deflection in three leads. * $p < .05$ vs rest; + vs hyperventilation.
- Figure 2. Effects of mild exercise and hyperventilation on ST segment depression 60 ms past the J point in three leads. Symbols are as in Fig. 1. * $p < .01$ vs other leads
- Figure 3. Effects of mild exercise and hyperventilation on ST segment depression 80 ms past the J point in three leads. Symbols are as in Fig. 1. * $p < .05$ vs other leads.

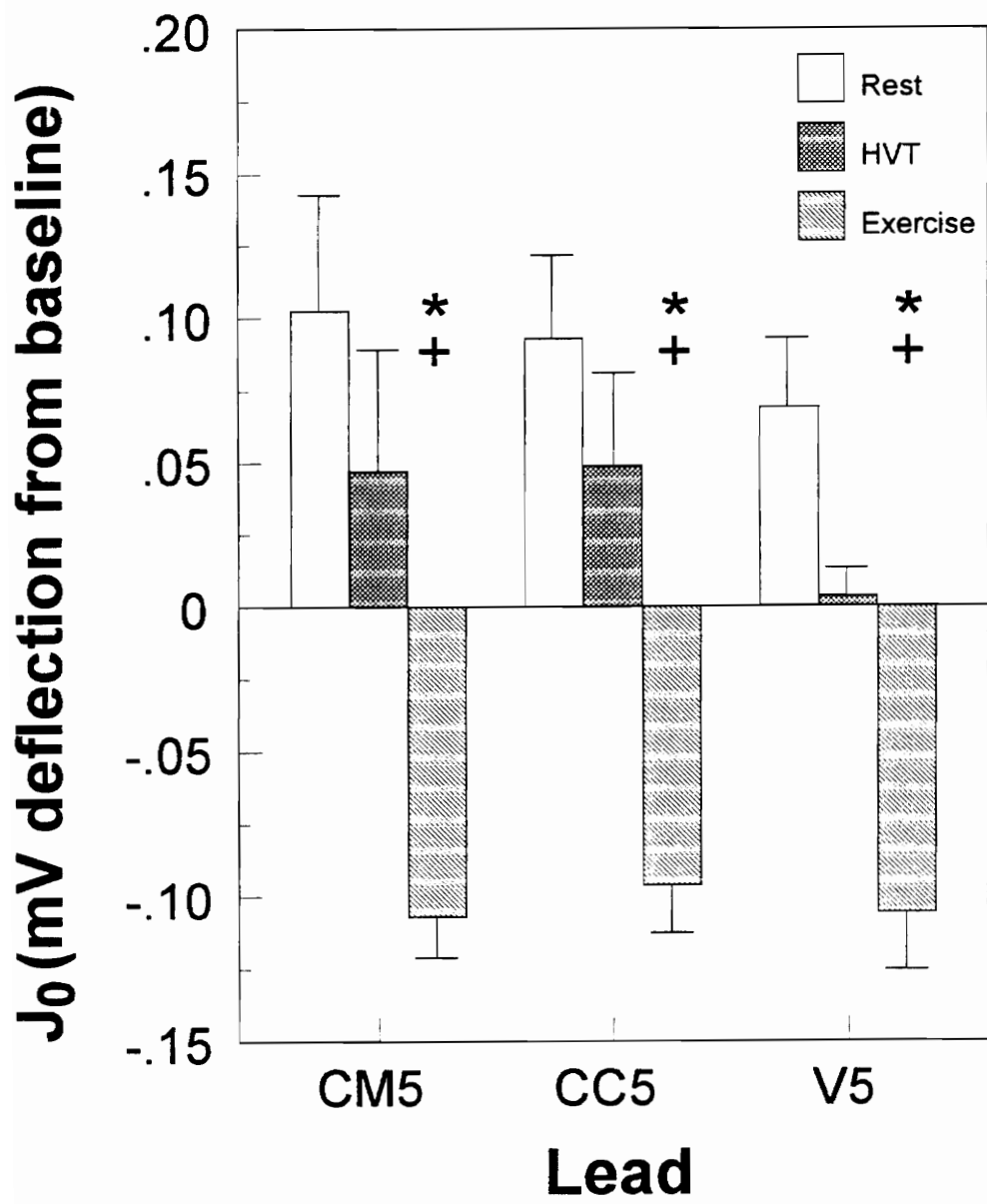


Figure 1.

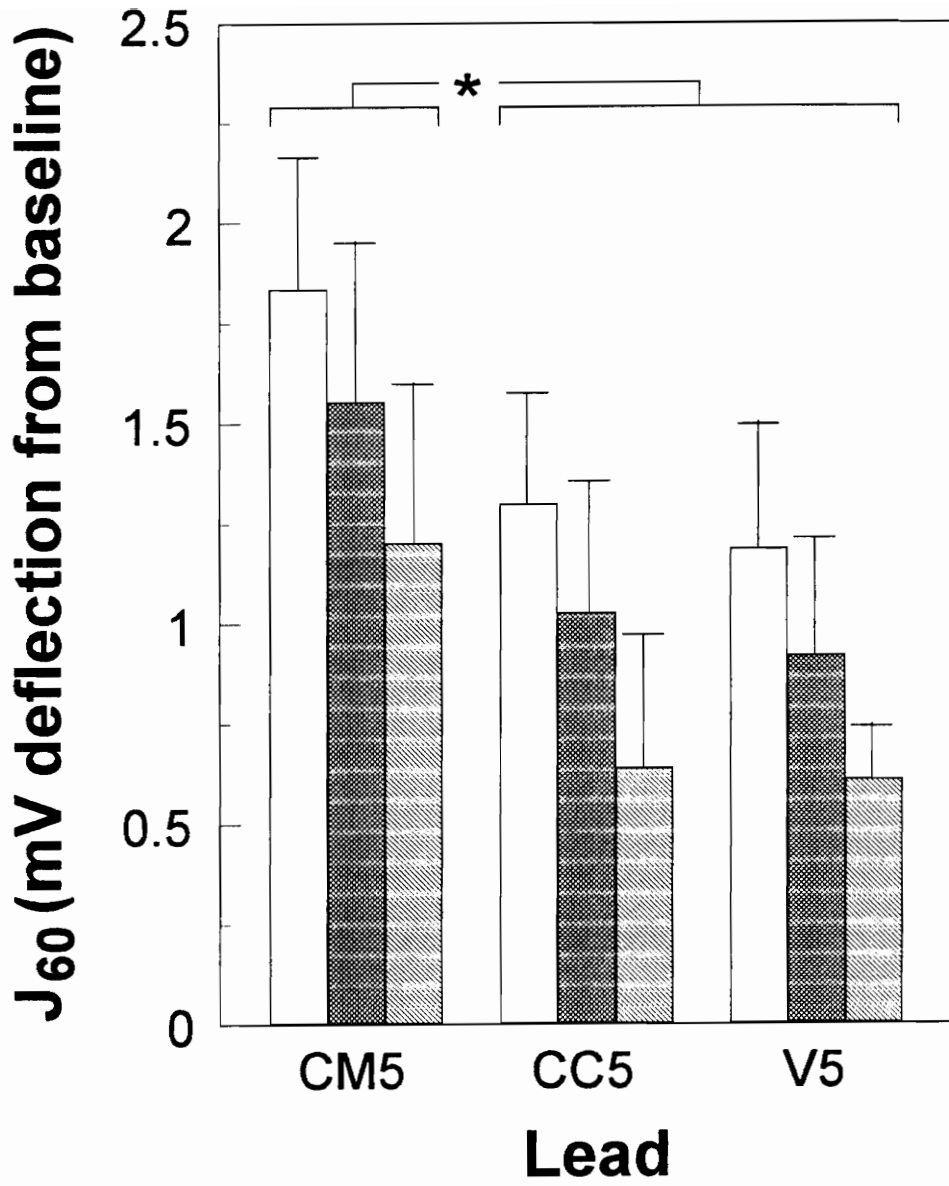


Figure 2.

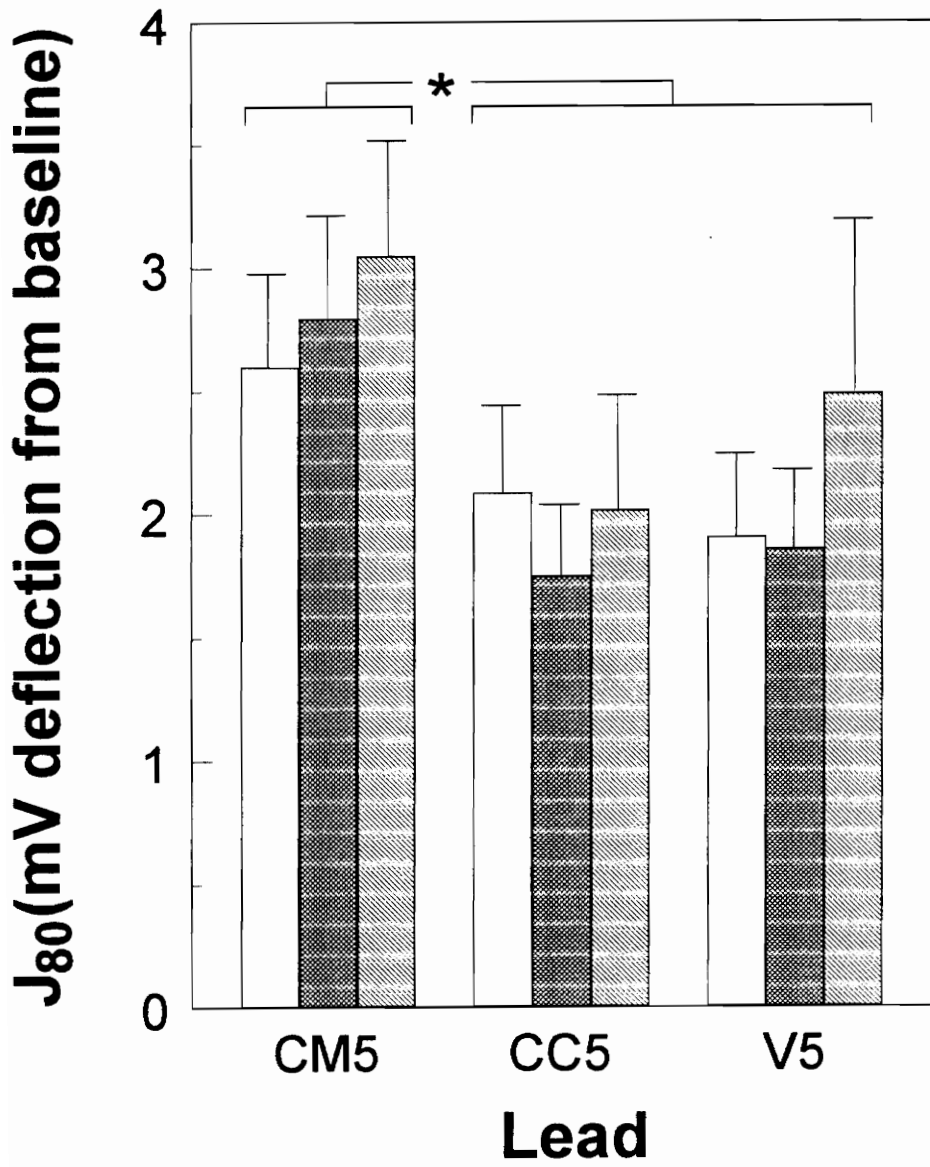


Figure 3.

Chapter IV

SUMMARY AND CONCLUSIONS

The primary clinical purpose of a graded exercise test is to determine the presence of ischemic heart disease and the most common method of doing so is to have the patient exercise until his myocardial oxygen demand exceeds coronary blood flow. The resultant ischemia is seen on the patient's electrocardiogram as ST Segment depression. Unfortunately, this test is not "perfect," having a sensitivity of 50 to 90% and a specificity of 60 to 98% (ACSM, 1991).

Components of the ST segment such as the J point and the ST segment 60 ms after the J point are often depressed with exercise in patients with ischemic heart disease. Unfortunately, these phenomena can occur in subjects with (Stuart and Ellestad, 1976; Kurita et al., 1977) or without (Robb and Marks, 1967; Roitman, Jones & Sheffield, 1970) disease which complicates interpreting the ECG results of a GXT for the presence of heart disease. Another factor contributing to a reduction in the specificity of a GXT is the effects of hyperventilation on an otherwise normal ECG. Hyperventilation may lead to ECG manifestations of heart disease, such as ST segment depression or T-wave inversions, due to respiratory alkalosis (Pribble, Kusumi & Bruce, 1987), reductions in coronary blood flow (Rowe, Castillo & Crumpton, 1962) or a vagal reflex (Wasserburger, Siebecker & Lewis, 1956). As this effect can occur in both normal (Lary & Goldschlager, 1974) and abnormal (Ardissino et al., 1989) populations, it can complicate the interpretation of a GXT.

Because of these problems, this study was designed to determine if there were any differences in the degree of J-point depression seen in three common ECG leads (CC_5 , CM_5 , V_5) with either exercise or hyperventilation in apparently healthy young men. In the present study, several apparently healthy males were initially found to have J point depression with mild exercise in lead V_5 . We then assessed whether this J point depression differed between the three aforementioned leads, whether this depression extended into the ST segment and whether hyperventilation also affected the ST segment. The results of this study suggest that CC_5 , CM_5 , and V_5 are equally effective in detecting J point depression. Exercise did not affect the ST Segment 60 or 80 ms after the J point as J_{60} or J_{80} did not differ from baseline. Hyperventilation did not result in ST segments differing from those seen at rest except for the J point. Consequently, this study suggests that any of the three leads investigated would be acceptable in assessing J point depression with exercise but more severe ST segment depression is evoked with exercise rather than hyperventilation. This disagrees with Froelicher and colleagues (1976) who noted that CM_5 differed in its appearance compared to CC_5 and V_5 . They noted that CM_5 appeared normal when CC_5 and V_5 appeared abnormal and vice versa.

Our study also suggests that hyperventilation does not affect the ECG in otherwise normal men. This differs from Wasserburger and colleagues (1956) who found that ECG changes could be induced with hyperventilation. As they could block this response with vagal blockade, the different responses between the two groups of

subjects could be due to differences in the amount of vagal input experienced by the subjects. Other researchers (Rowe et al., 1962) could induce ST segment depression with prolonged (5 - 10 minutes) hyperventilation. Our subjects hyperventilated for a much shorter period (30 seconds); perhaps the mechanism of the ECG changes seen by Rowe and colleagues (1962) takes longer than 30 seconds to manifest itself.

In summary, the three lead systems utilized here are equally sensitive to detecting ST segment changes seen with mild exercise in apparently healthy males. All three leads exhibited significant ECG changes with hyperventilation, but only at the J point.

Recommendations for future research

The following are general observations based upon the present study and the associated review of literature.

1. Repeat the present study but use subjects with angiographically documented heart disease.
2. Repeat the present study but increase both the intensity and duration of the exercise and hyperventilation bouts.
3. Repeat the present study with the addition of vagal blockade to determine if this affects the ST Segment responses seen with exercise.

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APPENDIX A
DETAILED METHODOLOGY

Subject Selection

Volunteer male students from Virginia Polytechnic Institute and State University were recruited into this study. Initial screening was done so as to select subjects who regularly performed vigorous physical activity and otherwise met the criteria of "apparently healthy" exercise candidates according to the standards of the American College of Sports Medicine (1991). These individuals are those who are asymptomatic and apparently healthy with no more than one major coronary risk factor. No medical examination was required of the subjects, but a standard 12 lead electrocardiogram (ECG) was recorded in a resting supine position (Quinton 2000, Quinton, Seattle, WA). This ECG was reviewed by an ACSM certified Exercise Specialist for evidence of waveform or rhythm irregularities. A physician on the staff of the lab's Cardiac and Intervention Center also evaluated these ECGs before a candidate was allowed to serve as a subject. If no ECG irregularities were found, the subject then underwent testing to determine if they were a J junction responder.

J Junction Responder Identification

To determine if a subject experienced J_0 depression with exercise, each subject underwent a bout of mild cycling activity. For this exercise, the subject exercised on a cycle ergometer (Bodyguard 990, Oglænd, Norway), following the branching protocol of the YMCA (Golding, Myers & Sinning, 1982). Here, the subject exercised for three minutes at 50 W. The subject exercised a second three-minute stage at either 100, 125 or 150 W followed by a third stage that varied from 150 to 225 W. The

individual workloads used were based upon the heart rate response to the previous workload.

Throughout this exercise bout, the subject's ECG, heart rate and blood pressure response was monitored. Using a CM_5 lead, the ECG was monitored for J junction (J_0) shifts with exercise. For this lead, the electrodes used for bipolar lead II were moved to correspond to CM_5 : the right arm electrode was moved to the manubrium, the left leg electrode was placed in the left V_5 position while the right leg remained the ground. Paper copies of this ECG were obtained every minute of the exercise bout as well as prior to the bout. Heart rate was determined from these tracings. Blood pressure was assessed using the auscultatory method every third minute of each stage.

Experimental Procedure

Upon qualifying as a J junction responder, the subject was asked to return to the laboratory at a later date. At that time, they were instrumented for the experimental trial. Here, the subject was instrumented such that the ECG leads CM_5 , CC_5 , and V_5 could be viewed simultaneously. V_5 was determined with a single-channel ECG monitoring system (Cambridge) and CM_5 and CC_5 using a multi-channel system (Quinton 2000). For the CM_5 lead configuration, the negative electrode for limb lead III was placed on manubrium. CC_5 was determined using a modified lead III with the left arm electrode placed in the right V_5 position and the left and right leg electrodes being common to the CM_5 lead. The V_5 lead was determined using a five-

determined using a five-electrode system: the four limb electrodes and an electrode placed in the left V_5 position. Prior to hard copies of the ECGs being obtained, the two separate ECG systems were synchronized by simultaneously depressing the "standardization" button on each system.

After instrumentation, the subject rested quietly, seated upright in a chair, for 10 minutes. During this period, resting ECGs were obtained. The subject was then assisted onto the cycle ergometer. He then cycled for three minutes against a light pedal resistance. They then exercised at a heavier workload for five minutes. This workload corresponded to a rating of perceived exertion of 15-17 on the Borg scale, *i.e.*, "hard" to "very hard" but not maximal exercise. Adjustments in workload were made to maintain this rating. Multi-lead ECG recordings were made in two 10-second periods during the last minute of cycling and, similarly, during a one-minute recovery period of low-intensity cycling. The subject then stopped pedalling and sat quietly on the cycle ergometer for 10 minutes. A multi-lead ECG recording was made at that time. The subject then hyperventilated for 30 seconds, following standardized instructions. Multi-lead ECG recordings were then made immediately after the cessation of hyperventilation. Following this hyperventilation trial, the subject was monitored closely for 10-15 minutes before being released by the investigator.

APPENDIX B
THE INFORMED CONSENT
AND
DIVISIONAL APPROVAL

The Informed Consent

Title of Study:

Effects of Submaximal Exercise and Hyperventilation on ECG Components in Healthy, Young Adult Men with Recording Leads Typically Used for Evaluation of Ischemic Heart Disease

The purpose of the study is:

To determine whether use of certain electrode positions on the chest during moderate exercise or with rapid breathing for 30 seconds cause certain changes in the electrocardiogram which may be of value for physicians to consider when they do medical exercise test for their patients

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

1) The initial determination of a number of physiological measures:

- a. heart rate, ECG and blood pressure at rest and in exercise;
- b. submaximal work performance in stationary cycling - this is an estimation of my aerobic fitness level.
- c. height and weight

2) During the data collection part of this study, I will be asked to come to the lab for two exercise sessions. For each portion of the data collection, heart rate (HR) will be measured electrocardiographically using several electrodes that are placed on my upper torso. My electrocardiographic (ECG) measurements will be monitored by the same method. The ECG provides a way of assessing the electrical

activity of the heart. Blood pressure (BP) will be measured by an inflatable cuff placed around the upper arm and a stethoscope.

Upon entering the lab, resting measures of BP,HR and EKG will be recorded while I am seated in an upright position for 10 minutes. I will then exercise at a light workload on a cycle ergometer for a few minutes as a cardiovascular warm-up. At the end of warm up, I will exercise for 6-10 minutes at a workload that corresponds to a rating of perceived exertion of 15-17, that is , what I feel to be no more than hard exercise .After exercising, I will then rest in a seated position for 10 minutes, allowing my heart rate to decrease. I will then be asked to hyperventilate for 30 seconds while the technician obtains my heart rate and ECG pattern. After this last measurement, I will be monitored for 10-15 minutes to make sure I am feeling well.

All the above mentioned measures will be taken by a trained exercise physiology graduate student with 100 hours of experience in assisting medical personnel in patient exercise testing.

I understand that participation in this experiment may produce certain discomforts and risks including:

- 1) temporary muscle soreness as a result of the exercise session d
- 2) some degree of lightheadedness due to hyperventilation.

Certain personal benefits may be expected from participation in this experiment. These include:

- 1) estimation of my aerobic fitness level and

2) determination of my heart rate and blood pressure at rest and in exercise.

I have had the opportunity to ask questions about these procedures and receive answers to satisfy me about safety and benefits afforded by my participation. I understand that in the event of any harm or injury arising from my participation in this study, that no compensation will be available from Virginia Tech and its agents.

Questions/Answers:

I understand that although a physician or nurse is not available to supervise this exercise test, that the investigator is a exercise technician who has been trained to recognize the appearance of major problems that should lead non-physicians to stop such tests. The investigator is also currently certified in cardiopulmonary resuscitation. Emergency medical support is almost never needed as a contingency in exercise test for healthy subjects, but such support is readily available through the local rescue squad.

I have received a copy of this form and understand that, if I have any questions or concerns about my treatment as a subject in this study that I should try to resolve these with the P.I., Libby Gallagher (231-5006 or 552-5169). The individuals below are available to answer questions which cannot be resolved with the P. I.

Signature of Subject

Witness (Investigator)

Faculty Member Supervising this Study: Dr. William G. Herbert; 703/231-6565

HPER Human Subjects Committee Representative: Dr. Charles Baffi; 703/231-8284

University Institutional Review Board Representative: Dr. Ernest Stout; 703/231-9359

CERTIFICATE OF APPROVAL FOR
RESEARCH PROPOSAL

Title of Study:

Submaximal Exercise and Hyperventilatory Effects on ECG Components in Healthy Young Adult Men with Recording Leads Typically Used for Evaluation of Ischemic Heart Disease

Background/Scientific Justification:

Exercise treadmill testing utilizing ECG measurements is the most common method for early, economical and safe detection of ischemic heart disease. By no means is this method without error. Exercise ECG testing is characterized by the same technical limitations known to exist with other clinical laboratory procedures. An ongoing issue of importance in research with this type of testing is to delineate patient specific and instrumentation specific factors that may minimize the rates of both false-negative and false-positive outcomes. The false-positive outcomes are particularly important because they incorrectly significant disease suggest an increased likelihood of disease when those which raise the likelihood of resulting in an interpretation of Examining alternative measurement techniques which may reduce the rates of occurrence in people who otherwise have no cardiac pathology. Therefore, many clinicians have begun to use non-standard EKG lead configurations in order to prevent the presence of these false-positive tests in their patients. During stress

testing, a person will undergo a natural state of hyperventilation, due to the body's inability to keep up with the stress put upon them. Many times this condition may bring about EKG changes that simulate those changes seen in a person with cardiac disease.

Purpose:

The purpose of this study is to determine whether hyperventilation and/or exercise will induce differential EKG changes.

Experimental Methods/Procedures

For inclusion into this study, subjects will be screened for J point depression during exercise. Potential subjects will exercise on a cycle ergometer for 5 minutes (at a workload of 100 W) in order for the experimenter to determine if J point depression occurs. Heart rate and EKG will be monitored throughout the exercise session. Further screening measures include a medical questionnaire to rule out potential cardiac risk factors.

Upon entering the lab for the exercise session, subjects will undergo skin preparation for the outfitting of ECG electrodes. Heart rate (HR) and ECG changes will be monitored throughout the data collection session via these electrodes. Blood pressure (BP) will also be monitored every 3 minutes. The subject will rest quietly, seated upright in a chair, for 10 minutes. Subjects will then exercise 3 minutes at a workload of 50 W, on a cycle ergometer, as a means of cardiovascular warm-up. Immediately following the warm-up, the subject will continue to ride for an additional

5 minutes at a workload that corresponds to a rating of perceived exertion of 15 on the Borg scale. After completion of this exercise the subject will resume a seated posture for 10 minutes, allowing their heart rate to decrease to a level comparable to resting measures. At this point, the subject will be instructed to hyperventilate for 45 seconds, while the experimenter obtains HR and EKG data. After the last measurement, the subject will be monitored for 10-15 minutes.

Statement describing level of risk to subjects:

Risks associated with this study include:

- 1) temporary muscle soreness due to the exercise session,
- 2) some degree of lightheadedness due to hyperventilation.

Risk/benefit ratio:

The subject will have an estimation of his aerobic fitness level, as well as a determination of EKG changes during exercise and hyperventilation. The risks of this study are very minimal. Other measurements used in this study, (HR, BP) pose no risk for the subject.

APPENDIX C

RAW DATA

Subject Characteristics

<u>Subj</u>	<u>Age(y)</u>	<u>Ht(cm)</u>	<u>Wt(kg)</u>	<u>Peak Work(W)</u>
1	27	184	81	150
2	23	188	73	225
3	25	169	74	175
4	25	186	97	175
5	42	181	79	200
6	28	183	72	225
7	38	177	70	225

Dependent Variable: J Point (mV change from baseline)

<u>Subj</u>	<u>Lead</u>	<u>REST1</u>	<u>IPE</u>	<u>REST2</u>	<u>HVT</u>
1	CM ₅	-.07	-.09	-.05	-.07
	CC ₅	-.05	-.06	-.03	-.05
	V ₅	-.02	-.08	-.02	-.08
2	CM ₅	.18	-.08	.12	.05
	CC ₅	.10	-.09	.10	-.03
	V ₅	.10	-.09	.10	-.03
3	CM ₅	.10	-.14	.10	.10
	CC ₅	.10	-.10	.10	.09
	V ₅	.05	-.13	.05	.03
4	CM ₅	-.02	-.08	.02	.03
	CC ₅	.03	-.06	.03	.00
	V ₅	.05	.08	-.02	-.02
5	CM ₅	.13	-.18	.12	-.11
	CC ₅	.10	-.14	.07	.08
	V ₅	.07	-.10	.05	-.03
6	CM ₅	.25	-.07	.20	.16
	CC ₅	.30	-.06	.27	.20
	V ₅	.20	-.13	.17	.15

7	CM ₅	.20	-.12	.15	.16
	CC ₅	.12	-.17	.07	.05
	V ₅	.05	-.13	.03	.01

Dependent Variable: J_{60} (mV change from baseline)

<u>Subj</u>	<u>Lead</u>	<u>REST1</u>	<u>IPE</u>	<u>REST2</u>	<u>HVT</u>
1	CM ₅	.07	.05	.08	.07
	CC ₅	.02	.03	.02	.01
	V ₅	.00	.05	.04	.03
2	CM ₅	.33	.28	.33	.28
	CC ₅	.20	.21	.27	.10
	V ₅	.22	.13	.08	.09
3	CM ₅	.18	.10	.22	.20
	CC ₅	.10	.05	.12	.12
	V ₅	.10	.02	.10	.08
4	CM ₅	.10	.21	.13	.09
	CC ₅	.10	.15	.12	.06
	V ₅	.10	.10	.08	.09
5	CM ₅	.13	-.03	.12	-.02
	CC ₅	.12	.00	.10	.00
	V ₅	.10	-.02	.08	.01
6	CM ₅	.25	.15	.20	.24
	CC ₅	.20	.05	.20	.24
	V ₅	.30	.09	.23	.25

7	CM ₅	.23	.08	.20	.23
	CC ₅	.12	-.03	.15	.25
	V ₅	.10	.05	.12	.09

Dependent Variable: J_{80} (mV change from baseline)

<u>Subj</u>	<u>Lead</u>	<u>REST1</u>	<u>IPE</u>	<u>REST2</u>	<u>HVT</u>
1	CM ₅	.17	.18	.12	.18
	CC ₅	.07	.11	.03	.01
	V ₅	.07	.13	.10	.13
2	CM ₅	.40	.55	.47	.43
	CC ₅	.30	.44	.40	.30
	V ₅	.30	.60	.27	.26
3	CM ₅	.23	.34	.32	.33
	CC ₅	.18	.23	.20	.18
	V ₅	.17	.10	.17	.15
4	CM ₅	.17	.38	.30	.20
	CC ₅	.20	.27	.18	.13
	V ₅	.13	.30	.15	.18
5	CM ₅	.23	.12	.20	.13
	CC ₅	.16	.07	.20	.09
	V ₅	.15	.10	.13	.10
6	CM ₅	.30	.37	.30	.33
	CC ₅	.27	.19	.27	.24
	V ₅	.38	.33	.33	.33

7	CM ₅	.28	.20	.25	.31
	CC ₅	.23	.11	.22	.20
	V ₅	.15	.18	.17	.16

APPENDIX D

SUMMARY ANALYSIS OF VARIANCE TABLES

Dependent Variable: J point

<u>Source</u>	<u>DF</u>	<u>SS</u>	<u>MS</u>	<u>F</u>	<u>P</u>
Subject	6	14.0485	2.2414		
Lead	2	0.9235	0.4618	1.866	.197
Lead x Subject	12	2.9701	0.2475		
Time	2	40.7377	20.3689	23.014	<0.001
Time x Subject	12	10.6207	0.8851		
Lead x Time	4	0.4585	0.1146	0.954	0.451
Residual	24	2.8849	0.1202		
Total	62	72.6440	1.1717		

Dependent Variable: J_{60}

<u>Source</u>	<u>DF</u>	<u>SS</u>	<u>MS</u>	<u>F</u>	<u>P</u>
Subject	6	23.0471	3.8412		
Lead	2	4.8486	2.4243	7.066	0.009
Lead x Subject	12	4.1173	0.3431		
Time	2	4.0908	2.0454	2.659	0.111
Time x Subject	12	9.2302	0.7692		
Lead x Time	4	0.0153	0.0038	0.033	0.998
Residual	24	2.7399	0.7756		
Total	62	48.0892	0.7756		

Dependent Variable: J_{80}

<u>Source</u>	<u>DF</u>	<u>SS</u>	<u>MS</u>	<u>F</u>	<u>P</u>
Subject	6	54.8524	9.1421		
Lead	2	9.9392	4.9696	16.655	<0.001
Lead x Subject	12	3.5977	0.2998		
Time	2	1.5860	0.7930	0.887	0.437
Time x Subject	12	10.8217	0.9018		
Lead x Time	4	0.8531	0.2133	1.256	0.316
Residual	24	1.1028	0.2757		
Total	62	86.6355	1.3812		

VITA

Libby Anne Gallagher was born October 26, 1966 in Jamestown, New York. She is the daughter of James and Cynthia Gallagher. Raised in Jamestown, she attended Jamestown Community College and graduated in 1988 from the State University of New York at Buffalo with a B.S. in Sport and Exercise Studies.

She began her graduate studies at Virginia Tech in 1989. She moved to Iowa in 1991 with her husband, Warren Franke. Since then Libby has been employed in the medical field as a cardiovascular technician. She is glad to be finally finishing her studies.

Libby Anne Gallagher