NORMAL AND ABNORMAL FINDINGS FROM EXERCISE STRESS ECG, POST-EXERCISE ECHOCARDIOGRAPHY AND ANGIOGRAPHY STUDIES IN A SERIES OF HYPERTENSIVE AND NORMOTENSIVE INDIVIDUALS

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(ABSTRACT)

The purpose of this investigation was to compare the frequencies of normal and abnormal findings from exercise electrocardiography (ECG), post-exercise echocardiography (ECHO) and angiography studies in a series of hypertensive and normotensive individuals who underwent diagnostic testing. Data for the ECG and ECHO were obtained simultaneously and the angiography was performed either before or following the exercise stress test. Thirty-seven cases were included in this retrospective study. Records were excluded if patients had: history of myocardial infarction; valvular heart disease; ECG evidence of abnormal Q waves, left ventricular hypertrophy (LVH) with abnormal ST/T wave pattern, or left bundle branch block (LBBB); medications that would alter blood pressure responses or ECG interpretation, technically uninterpretable records; or failure to attain 85% of age-adjusted maximal heart rates during the exercise tests. Subjects were defined as hypertensive (HYP) if at least two of the following criteria were met: 1) SBP $\geq$ 140 mmHg or DBP $\geq$ 90 mmHg; 2) current use of antihypertensive medications; or 3) history of hypertension. Normotensive subjects (NORM) were defined as absence of the

above criteria. Data for the ECG and ECHO variables were obtained simultaneously in association with treadmill exercise studies. In each test, ECG measures were taken at peak exercise while the ECHO data were taken within 90 seconds immediately post exercise to obtain images. ECG response was considered abnormal if the ST shifted $\geq .1$ mV from baseline at J_{60}, while the ECHO response was considered abnormal when new or worsening of pre-existing wall motion abnormalities was observed. The 2-D ECHO's were recorded with the subject in the left lateral decubitus position, and parasternal long- and short-axis apical two and four chamber views were recorded for qualitative determination of wall motion abnormalities. Eleven of the 37 subjects also underwent angiography. Chi-square analysis demonstrated that high blood pressure status did not increase the frequency of abnormal test results for the ECHO (X^2= 0.00009, DF = 1, p>.05), the exercise ECG (X^2= 0.07, DF = 1, p>.05) nor for the angiography (X^2= 0.69, DF = 1, p>.05). These results indicate that resting blood pressure does not influence the occurrence of abnormal vs normal ECG and ECHO findings nor angiography findings between h ypertensive and normotensive subjects. There was also no significant differences between the ECG and ECHO in the occurrence of abnormal findings for NORM subjects (X^2=2.43E-015, DF = 1, p>.05) nor HYP subjects (X^2=0.13, DF = 1, p>.05). The ECHO showed 80% true-positive findings and the ECG showed 60% compared to the angiography. Both the ECG and ECHO had the same percentage of true-negatives (33%) compared to the angiography results. Since there was a higher percentage of ECHO true-positive results compared to the angiography then the ECG, this may indicate that the ECHO is comparable to the angiography findings and may be a better predictor in determining disease than the ECG. However, these data warrant further evaluation studies.

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CHAPTER I

INTRODUCTION

Cardiovascular disease is the leading cause of death in the United States and most of the developing world (Pate et al. 1991). Many techniques have been developed to detect coronary artery disease (CAD) in order to decrease the number of deaths linked with the disease. The most common invasive technique is angiography and many noninvasive assessments have been developed including electrocardiography, echocardiography, and thallium scintigraphy all used in conjunction with exercise testing.

The exercise stress testing procedure using electrocardiography has been used for years and is a very common screening test for CAD. It is a relatively inexpensive and simple procedure and can be fairly accurate in most patients (Armstrong et al, 1986). It is used to determine ischemic changes and to diagnose CAD by observing the changes on the ECG and the symptoms the patient exhibits during exercise (McNeer et al, 1977; Chaitman et al, 1977; Goldschlager et al, 1976). Unfortunately, the ECG has been known to give false-positive and false negative tests results therefore decreasing its sensitivity and specificity when compared to other noninvasive techniques including echocardiography (Borer et al, 1975; Chaitman et al. 1977).

Exercise echocardiography is the most common imaging procedure used for the diagnosis of CAD (Popp et al, 1990). It has been considered superior in detecting CAD to the exercise electrocardiography (Ryan et al, 1988). It is a safe, relatively inexpensive procedure, it gives cardiologists the ability to view the hearts chambers and blood flow for a more accurate diagnosis of CAD, and it has a high sensitivity in detecting wall motion abnormalities during exercise (Berberich et al, 1984; Galanti et al, 1991;. Ginzton, L.E., 1989). One of the disadvantages to echocardiography is difficulty in recording accurate measurements during exercise (Berberich et al., 1984).

Exercise echocardiography has also been used for the study of hypertension, a major risk factor for CAD. Hypertension has a number of effects on the heart including increased afterload on the left ventricle causing left ventricular hypertrophy (LVH) and an increase in the development of CAD (Pringle et al, 1991). This hypertensive population at rest has been known through research to experience silent ischemia without symptoms (Yurenev et al, 1990). These effects can be seen on echocardiography through measurements of regional wall motion abnormalities, systolic thickening and closely examining the left ventricle (Crouse et al, 1991; Feigenbaum, H., 1994).

STATEMENT OF THE PROBLEM

In diagnostic testing for CAD, the exercise ECG has limitations for certain populations. The false-positive exercise responses are more common in asymptomatic patients, hypertensives and those with LVH (Otterstad, 1993; Pringle et al. 1991; Froelicher et al, 1973). Therefore, further testing must be done to determine the presence of CAD.

Since hypertension has been shown to be associated with more severe CAD, both LVH and hypertension have been studied to determine their relationship with ischemia during exercise testing. Unfortunately, the presence of LVH increased the incidence of ST depression, thus reducing the specificity of the exercise test (Froelicher & Umann, 1995). Patients with systemic hypertension are also more likely to be asymptomatic due to silent ischemia (Pringle et al, 1991 Yurenew et al 1990). Thus, hypertensive patients may also be more likely than patients with normal blood pressure to show signs of ischemia during maximal exercise, and they may also be more likely to have an inaccurate results.

Therefore, the purpose of this investigation was to compare the frequencies of normal and abnormal findings from exercise ECG and post-exercise ECHO studies and compare the results to the invasive procedure, angiography in a series of hypertensive and normotensive individuals who underwent diagnostic testing.

SIGNIFICANCE OF THE STUDY

If hypertensive subjects are more likely than normotensive subjects to have inaccurate test results for exercise ECG studies, stress echocardiography may be a better initial testing method for detecting CAD. The results of these two diagnostic assessments will be compared to the invasive angiography results to determine if one is more accurate that the other. If one noninvasive testing procedure is indeed more accurate than the other, this may decrease the rate of repetitive testing as well as the overall cost to the patient. Also, if the hypertensive population is more likely to show signs of silent ischemia, it would be beneficial to perform diagnostic testing early to determine possible CAD before it progresses to more severe disease.

RESEARCH HYPOTHESIS

The purpose of this investigation was to determine whether hypertensive subjects are more likely to show signs of ischemia during exercise when measured by both electrocardiography and echocardiography and comparing these measures to angiography.

To delineate the purpose of this study, the following null hypothesis were established by the investigator:

1. There was no difference in the occurrence of abnormal findings for normotensive or hypertensive subjects during clinical exercise testing observed echocardiographically.
2. There was no difference in the occurrence of abnormal findings for normotensive or hypertensive subjects during clinical exercise testing observed electrocardiographically.
3. There was no difference in the occurrence of abnormal findings for normotensive or hypertensive subjects observed angiographically.
4. There was no difference between exercise electrocardiography and exercise echocardiography in the occurrence of abnormal findings for normotensive subjects.
5. There was no difference between exercise electrocardiography and exercise echocardiography in the occurrence of abnormal findings for hypertensive subjects.

ADDITIONAL RESEARCH QUESTION

In a clinical sample of subjects with a portion diagnosed with hypertension referred for angiography, is there the tendency for the exercise EKG or exercise ECHO to be more precise?

DELIMITATIONS

The following delimitations were incorporated into the design of this study:

1. Patients who were referred to Montgomery Regional Hospital for stress electrocardiography . stress echocardiography and angiography from 1993-1995.
2. Hypertensive subjects met at least two of the following criteria: 1. Systolic blood pressure $\geq$140 mmHg or diastolic blood pressure $\geq$90 mmHg, 2. Currently taking blood pressure medication, or 3. Having a past history of hypertension, denoted as a current risk factor on hospital exercise testing forms.
3. Normotensive subjects were defined as not meeting the above criteria.

LIMITATIONS

The following limitations were recognized by the investigator:

1. The results of the electrocardiographic measures during exercise testing were not known to the cardiologists performing the echocardiographic measures.
2. Angiography was in some instances performed before the stress echocardiogram. So the results of echocardiography measures may have been influenced by the angiography diagnosis.
3. Optimal data for the two methods were recorded at different time intervals. ECG data was recorded at peak exercise while ECHO data was recorded within 90 seconds of the post exercise period as performed by previous researchers (Berberich et al. 1984; Marwick et al, 1992; Presti et al, 1987). However, since the ECHO was not measured at peak heart rate, it was assumed the heart rate was lower at the time of measuring

the ECHO images which could effect the amount of ischemia present immediate post-exercise compared to peak exercise.

4. Placement of ECG lead V_2 and leads V_4-V_6 were not located in the standard position as not to overlie the acoustic echocardiographic window.
5. The investigator did not interpret the ECG nor ECHO results but based a positive or negative test result on the physician's interpretation only.
6. Of the 11 subjects which angiography was performed, four were HYP and were all female. These four subjects were the only ones who underwent all diagnostic procedures (CATH, ECG and ECHO) and were hypertensive.

BASIC ASSUMPTIONS

1. Echocardiography techniques were the same among the cardiologists performing the testing during the study following those standards set by the American Society of Echocardiography.
2. All subjects performed the exercise test with maximal effort.
3. Interpretations for ECG ,ECHO and angiography were done using the same techniques for all cardiologists as quantified by the American College of Cardiology and the American Society of Echocardiography.

DEFINTIONS AND SYMBOLS

- Angiography: cardiac catherization, an invasive technique to determine coronary artery disease.
- Cardiac catherization (CATH): also referred as angiography
- Coronary artery disease (CAD): disease of the coronary arteries

- Echocardiography (ECHO): analysis of the heart wall motion and blood flow through the use of ultrasound techniques.
- Electrocardiography (ECG): analysis of the electrical waveforms and rhythms of the heart using ten electrodes placed on the chest.
- Hypertensive (HYP): subjects, those with diagnosed high blood pressure
- Left ventricular hypertrophy (LVH): enlargement of the muscle fibers of the left ventricle of the heart, usually associated with valvular heart disease, systemic hypertension, or cardiomyopathy.
- MET: a unit of measurement for the metabolic cost of exercise.
- Normotensive (NORM): subjects who do not have high blood pressure.

SUMMARY

Many noninvasive techniques have been developed to detect coronary artery disease. The invasive technique, angiography, is many times the standard diagnosis used during research and the noninvasive techniques are sometimes compared to angiography results for a more accurate diagnosis. The most common noninvasive method is electrocardiography. However, stress echocardiography is gaining acceptance as a screening tool and is growing in popularity. It detects CAD by measuring wall motion abnormalities prior to and immediately after exercise. It has been researched that stress echocardiography gives a higher sensitivity than the ECG which leads to more true diagnosis of patients. Hypertensive subjects are at a higher risk for CAD and previous studies have shown that silent ischemia is common in patients with hypertension. The purpose of this study is to determine the association between resting blood pressure levels and signs of myocardial ischemia during clinical exercise testing observed both electrocardiographically and echocardiographically and compared to angiography testing results in hypertensive (HYP) and normotensive (NORM) subjects. Also to determine if the ECG or the ECHO shows a higher occurrence of abnormal findings in the NORM and HYP groups.

CHAPTER II

REVIEW OF LITERATURE

This review of literature provides research information regarding the use, technique and diagnostic precision of noninvasive cardiac procedures, exercise electrocardiography and exercise echocardiography. It provides an understanding of the difference between the ECG and ECHO and the advantages and disadvantages of each procedure in determining CAD. It also gives an understanding of the invasive procedure, angiography. This review provides information concerning the role of hypertension in ischemia, exercise blood pressure as a predictor of future hypertension, and hypertension as an indicator of myocardial ischemia in exercise testing. With this understanding of ECG, ECHO and angiography as well as the effect of hypertension as a predictor of CAD, it will provide an overview of the conflict of the noninvasive procedure of choice when compared to the invasive technique, angiography, on the hypertensive population.

EXERCISE ECHOCARDIOGRAPHY

Exercise echocardiography has proven to be a clinical tool and is the most common imaging procedure used for the diagnoses of heart disease (Popp et al., 1990). Exercise echocardiography is a procedure that examines regional wall motion abnormalities and systolic thickening as well as evaluating the status of the left ventricle (Crouse et al., 1991; Fiegenbaum, 1994). The advantages of echocardiography are that it is a safe and noninvasive technique, it is relatively inexpensive, and it gives cardiologists the ability to view the hearts chambers and blood flow for a more accurate diagnosis of coronary artery disease (CAD). Echocardiography also has been shown by some researchers to have a higher sensitivity in detecting wall motion abnormalities during exercise (Berberich et al., 1984; Galanti et al., 1991; Ginzton et al, 1989). One of the disadvantages of this procedure is the difficulty in obtaining echocardiograms during peak exercise. Therefore, echocardiograms are more easily recorded in the immediate post-exercise period than during exercise. This delay in recording data could result in inaccurate measurements (Berberich et al., 1984). It is easier to get quality echocardiograms immediately post-exercise but the problem with this is that the left ventricular function resolves quickly after exercise and may not detect these changes of the heart on the echo images (Berberich et al, 1984).

Berberich et.al. (1984) wanted to challenge this post-exercise echo to evaluate the sensitivity and specificity of immediate post-exercise echocardiogram in the detection of coronary artery disease in a group of patients undergoing cardiac catherization. The echo measures were obtained 1-5 minutes post exercise and were compared to those taken before exercise. The study found that if the echo was obtained immediately post-exercise that it was a reliable means to detect coronary artery disease. The physiologic effects of exercise in normal subjects persisted for several minutes into recovery. The overall sensitivity and specificity of the 2-dimensional M-mode echocardiogram in the post exercise appeared to be excellent for the detection of coronary artery disease (Berberich et al. 1984; Limacher et al, 1983).

Technique of Two-Dimensional Imaging

The two-dimensional echocardiography is probably the most universal technique used. It allows real time recordings of changes in cardiac shape and movement and provides information concerning cardiac structure. Armstrong et al. (1986) used two-dimensional echocardiograms taken at rest and after exercise in 95 patients. The resting and immediate post-exercise echocardiograms were done while the patient was lying in a left lateral decubitus position. The echocardiogram images were analyzed side by side and compared at rest and exercise. They found that the sensitivity and specificity (79.5% and 86.7%, respectively) of the echocardiogram was high in detecting coronary artery disease when using the 2-D technique. Limacher et.al (1983) reported an imaging success rate of 100% while patients were lying in the left lateral decubitus position. Other studies have confirmed the use of these techniques as well (Ryan et al., 1988;, Berberich et al. 1984).

Oberman et al. (1989) studied the reproducibility of two dimensional echocardiography. Nineteen subjects performed an exercise test with echocardiography images taken before and immediate post exercise with the patient in the left lateral decubitus position. These tests were repeated after 14 days with different observers and interpreters. The ejection fractions and wall motion abnormalities were highly correlated between the two tests.   The correlation coefficients between tests 1 and 2 were .92 for both pre- and post- exercise ejection fractions and .98 for both pre- and post- wall motion scores. The researchers concluded that two dimensional echocardiography is highly reproducible in its measures even when compared between different observers.

Robertson et al (1983) used the exercise two-dimensional echocardiography to detect coronary artery disease. Images were taken during rest and immediate post-exercise with the patient sitting in a chair on the treadmill. The images were taken for 12-30 minutes after exercise and the 30 minute post-exercise echocardiogram the patient was supine in the left lateral position. With the patient sitting in a chair at the treadmill, they found a higher percentage of studies were obtained that were adequate for interpretation (92%). The overall use of echocardiography with the treadmill exercise test significantly increased the diagnostic value of the test.

Regional Wall Motion Analysis

Schemes have been developed for evaluating wall motion abnormalities. Each scheme represents the segments the coronary arteries supply to the left ventricle. Presti et al (1988) developed a schematic representation of the left ventricular wall divided into sixteen segments in order to generate a wall motion score. Fiegenbaum (1986) has also developed a diagram representing the coronary arteries and the wall segments in the four chamber views in two-dimensional echocardiography: parasternal short- and long- axis and apical two- and four-chamber views.

The continuous loop technique is commonly used. This technique allows images to be placed side by side and analyzed for wall motion abnormalities. The scoring system consists of the qualitative analysis of each wall segment as either normal, hypokinetic, dyskinetic or akinetic. If abnormalities are present in the anterior, anteroseptal and mid and apical segments the patient is diagnosed with left anterior descending stenosis. Abnormalities in the lateral and posterior walls is considered disease of the circumflex and abnormalities of the inferior and basal septal segments is right coronary artery disease. The presence of akinesia or dyskinesia at rest determines a myocardial infarction (Ryan et al., 1988).

Exercise Echocardiography (ECHO) Clinical Performance

Studies have been done to determine the usefulness and quality of echocardiography. A study by Ryan et al. (1988) wanted to determine the diagnostic use of exercise echocardiograms in patients with normal wall motion at rest. Sixty-four patients were studied and had underwent a stress echocardiography, stress treadmill test and angiography. They found that the patients without coronary artery disease had a specificity of 50% on the treadmill and 100% on the echo. The treadmill test sensitivity was 60% while echocardiography sensitivity was 78%. The patients with multi-vessel disease had a 100% sensitivity in both the echo and ECG. The sensitivity was higher for the echo in patients with single vessel disease. The echocardiogram proved to have a higher sensitivity especially in patients with single-vessel disease.

A study by Crouse et al (1991) was done to determine if exercise echocardiography could be used as a screening test for coronary artery disease. Two hundred and twenty-eight patients with no known history of heart disease underwent exercise echocardiography and cardiac angiography. The researchers found that of the 175 patients with disease, the echo found 170 as positive giving a sensitivity of 97%. Of the 53 patients who were normal on the angiography, the echo found 34 normal echocardiograms giving a 64% specificity. The positive predictive value was 90% and the negative predictive value was 87%. Crouse et al. found that the exercise echocardiography compares well with the cardiac angiogram and it is a useful tool for detecting coronary artery disease, the number of vessels involved (1,2, or 3) and determining which vessels are involved (Crouse et al. 1991).

Marwick et al. (1992) also performed a study to evaluate the accuracy of the exercise echocardiogram while also examining the angiogram and electrocardiogram. The results showed that of the 150 total patients, echocardiography had a higher sensitivity than the electrocardiography (87% versus 63%, $p>0.01$), respectively. Also, the sensitivity for exercise echocardiography was higher in patients with multi-vessel CAD (96%) than in those with single vessel disease (68%).

Exercise echocardiography has also been compared to other screening tests to determine its accuracy. Galanti et al (1991) compared exercise echocardiography to the thallium scintigraphy. They found that the sensitivity for exercise echocardiography was 92.6% compared to the thallium test of 100%. The specificity of echocardiography and the thallium scintigraphy was 96.2% and 92.3%, respectively. When testing the involvement of individual coronary arteries, the scintigraphy and echocardiography sensitivities were 84.8% and 63% respectively with specificities of 98% and 98.2%, respectively. The exercise echocardiogram compared very close to the thallium scintigraphy. It was found to have a lower sensitivity on identifying multi-vessel disease. The echo has been considered to be equivalent to thallium imaging (Armstrong et al., 1986).

EXERCISE ELECTROCARDIOGRAPHY

The exercise stress testing procedure has been used for years to determine possible CAD. It is a relatively inexpensive and simple procedure and can be fairly accurate in most patients.(Armstrong et al., 1986). The electrocardiogram is used to determine ischemic changes and to diagnose CAD by observing the changes on the ECG and the symptoms the patient exhibits during exercise.

Technique of Electrocardiography

The clinical graded exercise test is usually performed using a multiple-lead ECG system. The use of the ECG is to monitor for abnormalities that might indicate exercise-induced myocardial ischemia and to determine coronary artery disease. The Mason Likar 12-lead ECG system has been widely used and accepted as a method for monitoring during a graded exercise test (Pollock. & Wilmore, 1990). This system utilizes a modified electrode placement of the limb leads at the shoulders and base of the torso. This helps eliminate artifact from movement when exercising. Chaitman et al (1977) found that the use of a multi-lead ECG system also increases the sensitivity and efficiency of the maximum treadmill exercise test. The ECG measurements are made at rest, continuously during exercise and post-exercise.

ST Segment Value

The ST segment response to exercise is an important tool in diagnosing CAD and the most widely used noninvasive method for detecting coronary artery disease. Even though there is no agreement on the best method for ST analysis, the standard definition for significant ST response is $\geq$1 mm of horizontal or downsloping ST depression or elevation for at least .08secs after the end of the QRS complex. An additional 1-2 mm of ST depression or elevation is needed when the ST segments at rest are abnormal. (Schlant et al., 1986). ST responses are labeled as J depression with downsloping, horizontal and slowly upsloping ST segments in determining CAD (Goldschlager et al., 1973). The timing of the J point is another factor in determining ST segment deviation. Okin et al

(1992) studied the exercise electrocardiogram to determine a point to measure ST depression , at the J-point or 60 msecs after the J-point (J+60). They used standard exercise electrocardiography criteria, the ST segment/heart rate index and the ST segment /heart rate slope for the detection of coronary artery disease. They found that the J+60 measures may provide a higher specificity than J-point measures for both ST/HR index and ST/HR slope. There was no significant difference in the sensitivity of standard criteria for either the J-point or J+60.

Exercise Electrocardiography (ECG) Clinical Performance

For many years, researchers have been studying the eletrocardiogram during stress tests in diagnosing coronary artery disease. A study by Goldschlager et al (1976) wanted to determine which type of ST segment response (J depression with downsloping, horizontal and upsloping ST segments) had the highest sensitivity and specificity. His subject selection included 410 patients. Three hundred and ten of these patients had been referred for diagnositc evaluation of proved coronary artery disease or chest pain. They all had treadmill testing and selective angiography performed. In 61 of these patients, they had normal coronary arteries and the remaining 80 were normal volunteers referred for treadmill testing only. The results showed that the downsloping ST had the highest specificity and suggested multi-vessel or main left involvement. The horizontal ST showed moderate specificity but of little help in finding those with more severe coronary artery disease. The upsloping ST gave a low specificity and minimized its diagnostic value. The timing of ischemic changes whether during the initial stage of exercise or during recovery or both may be indicators of the severity of coronary artery disease. Goldschlager et al (1976) suggests to look at the false positive and the false negative for reliability. He says that the reliability of the treadmill test can be improved by the configuration and the timing of ST changes rather than judging the ECG as normal or abnormal.

A study by Borer et al (1975) wanted to determine the limitations of the electrocardiographic response to exercise in predicting coronary artery disease. He wanted to compare the ECG to the angiography in 2 groups of patients; those subjects studied because of symptoms compatible with CAD, and those who were asymptomatic studied only because of a positive ECG response to exercise. The patients were divided into 3 groups; those who had suffered a MI at lease 6 months before the study or had typical angina or both; those patients with atypical angina; and those patients with a positive ECG response to exercise in the absence of symptoms or prior CAD history. The exercise test was performed on a bike ergometer. The results raised doubts on the ECG reliability. False negative tests occurred in 67% of patients with atypical angina or prior MI's. The false positive responses were more frequent in the asymptomatic patients. This study found the ECG as limited in determining coronary artery disease in various subject groups.

The exercise test has been criticized for its high incidence of false positive and false negative responses. McNeer et al (1978) argues that the exercise test parameters correlate with the extent of coronary artery disease. They argue that the sensitivity of the exercise test varies depending on the variables and parameters used to assess ST and to interpret the test as a positive or a negative. They wanted to determine if adding a parameter, test duration, with ST segment changes would improve the diagnostic value of the exercise test. One could assume that if a patient has a positive test with a shorter duration or a lower maximum heart rate they are the patients with more extensive coronary disease. One thousand four hundred and seventy two patients were studied. All had a treadmill test performed within 6 weeks of the time the angiogram was performed. Each patient exercised on the treadmill and the tests were titled as either positive, negative or indeterminant (neither positive nor negative) . A significant angiogram was defined as narrowing of the left main coronary artery of ≥50% occlusion.

The results of McNeer et al (1978) study showed that almost all the patients (>97%) with positive exercise tests had coronary artery disease and were only able to complete Stage I and II of the test, 60% of these had three vessel disease and >25% had >50% occlusion of the left main coronary artery. The patients who achieved Stage III of the treadmill test or longer had a lower result in having three vessel disease and less than 1% in the left main coronary artery. They also found that the nonsurgical patients who had a negative test or who achieved a maximum heart rate of ≥ 160 and who achieved an exercise duration of ≥ Stage IV on the treadmill test had a higher survival rate. Survival was 99% at 12 months and 93% at 48 months. The nonsurgical patients who had a positive test in Stage I or II of the treadmill test had a lower survival rate of 85% in 12 months and 63% in 48 months). This study argues that with the exercise test there should be more parameters used in those patients with suspected coronary artery disease to help increase the reliability and sensitivity of the exercise test

As has been stated previously, the electrocardiogram has been criticized for the high number of false positive tests it gives especially in asymptomatic patients. This high number of false positive GXT can lead to an increase in the number of unnecessary arteriograms being performed. A study by Chaitman et al (1977) looked at the combination of lead systems to determine if one is more likely to give more accurate results when compared to the angiography findings. Other predictors that were considered were time, heart rate, systolic blood pressure and duration of the exercise test to produce ST depression.

The subjects included 100 men who had no history of myocardial infarction and had a normal resting GXT. They all underwent a treadmill test one day prior to an arteriogram. A 14 lead ECG system was used and lead V_5 was compared to different lead combinations (11 lead system, inferior lead system and 14 lead system)and to the arteriogram findings. The results showed that the predictive value of a positive test (89-95%) did not change significantly with the addition of more leads. The sensitivity improved with the multiple leads than the single lead system especially in determining multi-vessel disease. Other studies have also confirmed these results (Schlant et al, 1986)

CORONARY ANGIOGRAPHY

The cardiac catherization procedure is an invasive technique in diagnosing coronary artery disease. One of the disadvantages of this procedure is that it is invasive and somewhat expensive when compared to the cost of electrocardiography and echocardiography. It is an excellent predictor in diagnosing CAD and the echocardiogram and electrocardiogram findings are often compared to the angiogram (cardiac catherization). Schlant et al (1990) states that 90% of men with a history of typical angina pectoris have coronary artery disease when studied by coronary angiography. Unfortunately , the percentage of detecting CAD in women is lower (60%). Most researchers consider a positive angiography test as a stenosis of $\geq$50% in at least one of the coronary arteries (Crouse et al., 1991, Okin et al., 1991, Limacher et al., 1983, Sawada et al, 1990). Schlant et.al (1986) found that defining disease as 70% narrowing of a coronary artery rather than 50%, decreases the sensitivity of the exercise test while it increases the specificity. Depending on how many vessels are diseased determines if the diagnosis is single vessel or multi-vessel disease. This procedure has a high sensitivity due to its invasive nature.

HYPERTENSION

Hypertension has a number of effects on the heart including increased afterload on the left ventricle causing left ventricular hypertrophy (LVH) and an increased development of coronary artery disease (CAD) (Pringle et al., 1991). Left ventricular hypertrophy is one of the most important risk factors for complications of hypertension (Yurenev et. al., 1990). This hypertensive population at rest has been known through research to experience silent ischemia which makes it difficult to determine CAD without proper testing procedures (Yurenev et al, 1990). Hypertension is the most common cardiovascular disease in humans and one of the most powerful predictors of CAD (Pollock & Wilmore, 1990). It is the most common cause of concentric left ventricular hypertrophy and congestive heart failure (Ewy et al., 1990).

Exercise Blood Pressure as a Predictor of Future Hypertension

It has been suggested that an elevated exercise blood pressure may detect patients early who may develop resting hypertension in the future (Jackson et al, 1983). The purpose of Jackson et al (1983) study was to determine the prevalence of exercise hypertension in a clinical population and to determine if exercise high blood pressure is factor to having a future resting high blood pressure. The retrospective study contained 4,856 patients. The patients were classified into 2 groups: those with resting high blood pressure (defined as systolic $\geq$140 mmHg and/or diastolic $\geq$90 mmHg), those who were normotensive at rest. The ones who were normotensive at rest but had high blood pressure readings during exercise were screened for 2 years to see if they had become hypertensive at rest. All of these patients were compared to an apparently healthy group of individuals.

The results showed that the patients who were normotensive at rest but hypertensive during exercise were at risk three times higher than the apparently healthy subjects for becoming hypertensive in the next 2-4 years. They determined that high risk normotensive men at rest may have an exaggerated blood pressure response to maximal exercise and may be at higher risk for future high blood pressure.

Wilson et al (1990) studied the exercise pressure responses of normotensive men who were high risk for hypertension. Those persons at high risk had a parental history of hypertension and a high normal resting BP (systolic BP between 135-154 mmHg and diastolic BP between 85-90 mmHg). They found that those at high risk were more likely to have high blood pressure responses to exercise than those subjects who were at low risk for hypertension. Those subjects who had an exaggerated response may be at greater risk for the development of future hypertension and could be at higher risk for the development of left ventricular hypertrophy and organ damage.

Hypertension and Indicators of Myocardial Ischemia in Exercise Testing

Hypertension combined with left ventricular hypertrophy increases the risk of coronary artery disease (CAD) including a myocardial infarction, stable and unstable angina. A study by Pringle et al. (1991) wanted to assess the prevalence of myocardial ischemia in hypertensive patients with left ventricular hypertrophy to determine which noninvasive method (electrocardiogram or echocardiogram) was best in determining CAD. A group of 90 subjects underwent a 12 lead exercise test and echocardiogram. Some of the patients also had a thallium scintigraphy and angiography performed. The results showed that it is difficult to rely on the ECG on patients with left ventricular hypertrophy and strain due to the difficulty in interpreting results because of baseline ECG abnormalities and the high possibility of false positive results. Overall, not all patients with LVH and strain are going to have CAD. The symptoms of chest pain during exercise or not are poor indicators of ischemia since so much of it can be silent.

Yurenev et al (1990) suggests that hypertension may contribute directly to the development of coronary atherosclerosis. Studies have proven that left ventricular hypertrophy (LVH) is an important risk and may be more important than blood pressure in determining death in patients with hypertension. Silent ischemia is common in patients with hypertension but Yurenuv et al wanted to determine its relationship to LVH and CAD. The echocardiogram was used to determine the measures. They found that asymptomatic ST depression occurs commonly in patients with hypertension but is not consistently related to the presence of CAD or LVH.

The method for detecting left ventricular hypertrophy (LVH) is a topic being researched. Traditionally, the ECG is the most popular method because of its availability and inexpensive cost. But, studies now are suggesting that the echocardiogram is a more sensitive method for detecting LVH in the hypertensive population. Devereux et al (1993) found that the ECG method is a strong predictor of increased cardiac and stroke morbidity in the hypertensive and general population but had a low sensitivity in detecting LVH. The echocardiogram scored a higher sensitivity in detecting LVH among the hypertensive population. Ewy et al. (1990) agrees that the echocardiogram is considered the noinvasive method preferred in evaluating cardiac effects of the hypertensive population due to its high sensitivity in diagnosing LVH.

SUMMARY

The objective of this review was to provide information regarding the role of the ECG and echocardiography during exercise testing and the changes induced in patients with hypertension. The accuracy of both methods were reviewed as well as the limitations of each. Research has shown that echocardiography may be the noninvasive method of choice due to its ability to view the hearts chambers and blood flow for a more accurate diagnosis of CAD. It has been shown that the ECHO has a higher sensitivity compared to the ECG. The disadvantage of the ECHO is the ability to obtain views during maximal exercise stress testing. But studies have shown that it is a useful tool in evaluating CAD despite its disadvantages.

The ECG is a technique that has been used for years to determine possible CAD. It is usually performed using a multiple lead ECG system to monitor for abnormalities that might indicate myocardial ischemia and to determine CAD. The ECG ST segment response to exercise is the most widely used noninvasive method for detecting CAD., but it has been criticized for its high number of false positive and false negative responses causing an increase of unnecessary angiograms being performed. It has been shown, however, that the sensivitivity of the ECG improves with multiple leads then with the single lead system.

The angiogram is the most accurate of all the methods because it is an invasive technique. The disadvantages of the angiogram is that it is invasive and can be somewhat expensive. But, it also has a high sensitivity and the results from an angiogram are often used to compare the ECG and echocardiography results

Hypertension may be an indicator for CAD. The hypertensive population has been shown through research to experience silent ischemia which makes it difficult to determine CAD without proper testing procedures. The research shows that hypertensive patients are more likely to have signs of ischemia during exercise testing. Therefore, it may be beneficial to test hypertensives using the echocardiogram over the ECG due to its high sensitivity and due to the fact that hypertensives are more likely to show signs of left ventricular hypertrophy and/or ischemia. The purpose of the current study was to determine whether hypertensive patients are more likely to develop ischemia during exercise when compared to normotensive patients. Both the exercise ECG and exercise echocardiography methods were used to determine the differences, if any, in detecting ischemia. These results were then compared to the angiography results in some of the patients studied.

CHAPTER III

JOURNAL MANUSCRIPT

NORMAL AND ABNORMAL FINDINGS FROM EXERCISE STRESS ECG, POST-EXERCISE ECHOCARDIOGRAPHY AND ANGIOGRAPHY IN A SERIES OF HYPERTENSIVE AND NORMOTENSIVE INDIVIDUALS

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ABSTRACT

NORMAL AND ABNORMAL FINDINGS FROM EXERCISE STRESS ECG, POST-EXERCISE ECHOCARDIOGRAPHY AND ANGIOGRAPHY STUDIES IN A SERIES OF HYPERTENSIVE AND NORMOTENSIVE INDIVIUALS

Angie G. Gerni

Purpose: This investigation was designed to compare the frequencies of normal vs abnormal findings from exercise electrocardiography and post-exercise echocardiography studies and compare the results to the invasive procedure, angiography in a series of hypertensive and normotensive individuals who underwent diagnostic testing.

Methods: Thirty-seven were included in this retrospective design. Subjects were defined as hypertensive (HYP) if at least two of the criteria were met: 1) SBP $\geq$ 140 mmHg or DBP $\geq$ 90 mmHg; 2) current use of antihypertensive medications; or 3) history of hypertension. Normotensive subjects (NORM) were defined as absence of the above criteria. Data for the ECG and ECHO variables were obtained simultaneously in association with treadmill exercise studies. In each test, ECG measures were taken at peak exercise while the ECHO data were taken within 90 seconds immediately post exercise to obtain images. ECG response was considered abnormal if the ST shifted $\geq$ .1 mV from baseline at J_{60}. The 2-D ECHOs were recorded with the subject in the left lateral decubitus position, and parasternal long- and short-axis apical two and four chamber views were recorded for qualitative determination of wall motion abnormalities. Eleven of the 37 subjects also underwent angiography. Significant disease was defined as $\geq$ 50% stenosis in at least one main coronary artery.

Results. Chi-square analysis demonstrated that high blood pressure status did not increase the frequency of abnormal test results for the ECHO (X^2= 0.00009, DF = 1, $p > .05$), the exercise ECG (X^2= 0.07, DF = 1, $p > .05$) nor for the angiography (X^2= 0.69, DF = 1, $p > .05$). There was also no significant differences between the ECG and ECHO in the occurrence of abnormal findings for NORM subjects (X^2=2.43E-015, DF = 1, $p > .05$) nor HYP subjects (X^2=0.13, DF = 1, $p > .05$). The ECHO showed 80% true-positive results compared to the angiography findings and the ECG showed 60% compared to the angiography findings. Both the ECG and ECHO had the same percentage of true-negatives (33%) compared to the angiography results.

Conclusion: These results indicate that resting blood pressure does not influence the occurrence of abnormal vs normal ECG and ECHO findings nor angiography findings. Nor did it indicate any significant differences between the ECG and ECHO in detecting abnormal findings in the NORM or HYP groups. There was however, a higher percentage of ECHO true-positive results compared to the angiography then the ECG. This may indicate that the ECHO is comparable to the angiography findings and may be a better predictor in determining disease than the ECG. However, these data warrant further evaluation studies .

Key Words: hypertension, exercise electrocardiography, exercise echocardiography, angiography.

INTRODUCTION

Treadmill exercise testing with electrocardiogram (ECG) monitoring is the most common screening tool for CAD. It is relatively inexpensive and simple and can be fairly accurate in most patients[1]. The electrocardiogram is used to determine ischemic changes and to diagnose CAD by observing changes on the ECG and the symptoms the patient exhibits during exercise. One of the disadvantages of the ECG is the high frequency of false-positive and false-negative test found[2]. Other research demonstrates that by adding additional parameters, such as test duration, sensitivity of the ECG improves[3].

In recent years, exercise echocardiography has gained acceptance in diagnosing CAD and has demonstrated high sensitivity and specificity[4-9]. Its accuracy has been compared to the thallium perfusion imaging technique in detecting CAD[10-11]. Echocardiography is noninvasive, cost-effective , and it gives cardiologists the ability to view the hearts chambers and blood flow for a more accurate diagnosis of CAD. It also has a high sensitivity in detecting wall motion abnormalities during exercise[6,10,12].

Exercise echocardiography has also been used for studying hypertension, a major risk factor for CAD. Hypertension has a number of effects on the heart including increased afterload on the left ventricle causing left ventricular hypertrophy (LVH) and an increased development of CAD[13]. Previous studies have shown that silent ischemia, changes seen on the echocardiogram without clinical symptoms, is common at rest and during daily activities in patients with hypertension and LVH[13-14]. Echocardiography has been shown to be a more accurate predictor in diagnosing LVH among the hypertensive population because it allows the observer to see regional wall motion abnormalities and systolic thickening which are consistent in patients with chronic CAD[15-16]. Therefore, the purpose of this investigation was to determine whether hypertensive subjects are more likely to show signs of ischemia during exercise when measured by both electrocardiography and echocardiography and comparing these measures to angiography.

METHODS

Patients

A retrospective design was used for subject selection. A letter of approval was given to the researcher by the Montgomery Regional Hospital Bioethics Advisory Committee as well as an Internship Statement of Understanding before research was permitted. Thirty-seven subjects who had been referred to Montgomery Regional Hospital in Southwest Virginia for treadmill exercise echocardiography testing were studied. The subjects gave informed consent as per hospital policy prior to exercise testing. Of the 37, eleven subjects also had angiography performed. Of these eleven, four were hypertensive and seven were normotensive. The four hypertensive subjects were all female.

Subjects were divided into two groups: those with normal resting blood pressure (NORM) and those with resting hypertension blood pressure (HYP). Those subjects with resting hypertension met at least two of the following criteria: 1) systolic blood pressure $\geq$ 140 mmHg or diastolic blood pressure $\geq$ 90 mmHg, 2) currently taking blood pressure medication, or 3) having a past history of hypertension, denoted as a current risk factor on hospital testing forms. Normotensive is defined as the absence of the above criteria.

Subjects were excluded who had known CAD, had taken medication the morning of the test which may have altered blood pressure responses to exercise (beta or calcium channel blockers) or which may have altered the ECG (digitalis), or who showed ST segment shift with hyperventilation ECG. In addition, those subjects who showed signs of left ventricular hypertrophy with strain, left bundle branch block, valvular stenosis or regurgitation, dyskinesis, aneurysm, known previous myocardial infarction or evidence of clinically significant Q waves >.04 sec were also excluded.

General Protocol

Exercise testing. Treadmill exercise testing was performed on each subject using the Bruce protocol. During each 3 minute stage, a 12 lead ECG and exercising blood pressure measures were recorded while three leads (II, avF, V_5) were continuously monitored. In accordance with the supervising physician, exercise endpoints were: 1) development of limiting chest pain and/or dyspnea, 2) fatigue, 3) subjects request to stop the test or, 4) subject reached over 85% maximal age predicted heart rate.

Electrocardiography: Resting 12 lead ECGs and blood pressure readings were performed on each subject prior to exercise testing in the supine positions. The electrodes for ECG monitoring were placed on the chest so as not to overlie the marked sites for the acoustic echocardiography window. Specifically, lead V_2 was placed on the sternum at the level of the second or third intercostal space, and leads V_4-V_6 were lowered to the 6th intercostal space.

The exercise ECG was determined by the investigator to be normal or ischemic. An ischemic response to exercise was defined as meeting one of the following criteria: 1) horizontal or downsloping ST segment depression of $\geq$1 mm 60 ms after the J point in a lead with a normal ST segment at rest , 2) ST segment elevation of 1 mm or more than the resting tracing 60 ms after the J point, 3) in the presence of ST depression in the resting tracing, an additional depression of 1mm or more is required. ST segment deviation was automatically calculated during the test by the computer (Q4500, Quinton Instrument

Company, Bothell, Washington) as well as reviewed by the supervising physician[17]. In addition, three concurrent complexes were measured for ST deviation and slope 60 ms after the J-point[18].

Echocardiography: Two dimensional M-mode echocardiograms were recorded with standard commercially available equipment (Hewlett Packard Sonos 1000, Andover, Massachusetts). Parastermal long and short axis and apical two and four chamber views were recorded with the subject in the left lateral decubitus position at rest. The acoustic echocardiography window for both the parasternal and apical positions were marked on each subject's chest using a washable felt tip marker for reference. Immediately after cessation of exercise, the subject resumed the left lateral decubitus position, and the standard four views were repeated (within 90 seconds of cessation of exercise).

The echocardiography studies were digitized on-line into a quad-screen, continuous loop format for analysis (Nova Microsonics ImageVue DCR, Mahwah, New Jersey). Images were recorded on ¾ inch VHS videotape as well as digitally on a 3 ½ inch floppy diskette. Data were reviewed with resting and immediate post-exercise images placed side-by-side. Images were assessed for ejection fraction, left ventricular mass, and for the presence of normal regional wall motion. Normal peak exercise shows a decrease in ventricular size with an increase in ejection fraction. Abnormal studies were defined as having regional wall motion abnormalities, such as hypokinesia, akinesia, or dyskinesia at rest or immediately after cessation of exercise as described by previous investigators[19-20]. These changes occur in conjunction with an increase in ventricular size and a decrease in ejection fraction. Ejection fraction was measured by the computer (Nova Microsonics ImageVue DCR, Mahwah, New Jersey), by calculating stroke volume and dividing by diastolic volume[21]. Left ventricular mass was defined by the investigator as normal or abnormal as recorded by the interpreting physician. The distribution of CAD was approximated by studying the area in which the wall motion abnormalities occurred, as adopted by the American Society for Echocardiography[22]. Thus, the left ventricular was divided into 16 segments utilized to develop a wall motion score.

Angiography: The patient was given .5 mg of Xanax and was taken to the catherization lab. The right groin was prepped and draped and 1% Xylocane was infiltrated into the operative field. Using a Potts Cournand needle, the right femoral artery was punctured using the Seldinger technique and a sterile guide-wire was passed. A French introducer was than advanced into the arterial system and used. The patient had a left heart catheter, a left ventriculogram, left and right coronary angiography utilizing the Judkins technique. A diagnosis of significant coronary artery disease was defined as a stenosis of $\geq$50% in at least one of the main coronary arteries (left anterior descending, right coronary artery and/or left circumflex artery).

Statistical Analysis

Independent t-tests were used for contrasting demographic data between the NORM and HYP groups. Chi-square analysis (X^2) was used to evaluate the distribution of normal vs. abnormal clinical findings for ECG in the NORM and HYP groups, ECHO in the NORM and HYP groups, and the CATH in the NORM and HYP groups. Chi-square (X^2) was also used to determine the occurrence of abnormal findings for the NORM and HYP groups between the ECG and ECHO. A percentage calculation was also done to determine the number of true-positive and true-negative results in the ECG and ECHO when compared to the angiogram results.

RESULTS

Table 1 presents demographic information for the subjects. Of the population sampled 54% if the subjects were normotensive and 46% of the subjects were hypertensive. No significant differences existed between the groups for age, gender, maximum heart rate or METS achieved during exercise. There were significant differences between hypertensive and normotensive blood pressure during exercise for both systolic and diastolic. There was also a significant difference between the normal and hypertensive group during rest in the diastolic blood pressure readings but not the resting systolic readings. However, even though there were significant differences in the blood pressures for the two groups, the HYP group was not extremely hypertensive as would be expected. There were significant differences between the groups but the HYP group was not very high with mean resting values of 141 systolic and 83.1 diastolic and exercise systolic and diastolic values of 184 and 93, respectively.

Chi square analysis indicates that there are no significant differences between hypertensive and normotensive subjects for the echocardiogram, electrocardiogram and the angiogram in finding abnormal results. For the ECHO, the findings were X^2= 0.00009, DF = 1, p>. 05, ECG X^2=0.07, DF = 1, p>. 05 and the angiogram showed a statistical value of X^2= 0.69, DF = 1, p>. 05.

There were also no significant differences between the ECG and ECHO in the occurrence of abnormal findings for NORM subjects (X^2=2.43E-015, DF = 1, p>.05) nor HYP subjects (X^2= 0.13, DF = 1, p>.05).

The subjects who also underwent the angiography, the percentage of true positives for the ECHO compared to the angiogram results was 80% compared to the ECG, 60%.

The ECG and ECHO both showed the same percentage of true-negatives, 33%. However, of the eleven subjects who underwent angiography, three were excluded when calculating a percentage due to the subject having abnormal ECHO results at rest and remaining the same immediate post-exercise (Table 2).

DISCUSSION

Since the present study did not demonstrate significant differences in the results obtained between the ECHO, ECG, and the angiogram during exercise for both the normotensive and hypertensive subjects, this suggests that the ability of these protocols to assess ischemia is not different for various patient populations. These findings do not agree with other studies that have found that ischemia is common during maximal exercise in hypertensive patients[13,23]. This study's findings were not consistent with the data in the current study where the hypertensive subjects were more likely to show signs of ischemia than the normotensive population.

Studies have found that the ECG has demonstrated a low sensitivity in detecting ischemia. Devereux et al.[15] found that the ECG for detecting LVH has a lower specificity and a higher rate of false positive findings and are less useful than the ECHO in findings especially for high and low risk subgroups due to the low sensitivity it produces. Devereux et al. points out that past studies show that the standard ECG criteria detected only 20-50% of instances of LVH.. Pringle et al.[13] found an exercise ECG sensitivity of 50% and specificity of 71% for ischemia in hypertensive subjects with known LVH. Otterstad[23] found that the ECG underestimated the prevalence of LVH as well as myocardial ischemia in patients with LVH (24%) and the thallium scintography showed positive ischemic results in only 14%. The ECHO found LVH in 68% of the 205 patients.

Other studies have confirmed these results in the usefulness of the exercise ECG and found that false-positives were frequent in patients with coronary artery disease and in asymptomatic patients[2,24]. Therefore, the lack of ischemic results for the ECG could be related to the presence of LVH but cannot be determined in this study due to insufficient measuring of LVH among subjects.

The ECHO has limitations as does the ECG. Popp et al[25] suggests that how accurately the ECHO is read depends on the technical and clinical understanding of the operator as well as the knowledge of the interpreter. Robertson et al[7] found that the ECHO performed immediately after exercise can be a useful clinical tool in evaluating coronary artery disease. However, one of the disadvantages of this procedure is the difficulty in obtaining echocardiogram images during peak exercise. Therefore, ECHOs are more easily recorded in the immediate post-exercise period than during exercise[6]. This delay in recording could result in inaccurate measures[6].

To determine the ECHO's diagnostic value during post-exercise, Limacher et al[26] found that wall motion abnormalities are still apparent for at least 90 seconds before resolving in patients with coronary artery disease. Other studies suggest that ischemia in two and three vessel disease frequently lasts for 3-4 minutes after exercise during ECHO imaging[12]. Therefore, echocardiography has high diagnostic accuracy in multi-vessel disease. However, ischemia in single-vessel disease may often disappear 30-60 seconds after exercise decreasing the sensitivity of detecting patients with single-vessel disease[12]. The procedure in the present study obtained images within a 90 second time period immediately following exercise. Therefore, the heart rates of the subjects were assumed to not be at maximum when the ECHO images were obtained which may effect the amount of ischemia present immediate post exercsie as compared to peak exercise. According to Ginzton,[12] obtaining ECHO images 90 seconds after exercise could be too long to determine disease in single-vessel patients. This could have been a factor leading to the results in this study which showed there were no differences in the ECG and the ECHO in determining CAD in the NORM and HYP groups. But, overall, most studies have confirmed the use of post exercise ECHO as a valuable addition to diagnosing coronary artery disease even considering its disadvantages[1,9].

Studies have compared the two techniques, ECHO and ECG, to determine their diagnostic value. The ECHO has been found to be the procedure of choice due to its accuracy when compared to the ECG. The ECHO has been proven to have a higher sensitivity and specificity in determining single and multi-vessel coronary disease[4,5]. However, there were no statistical differences between the exercise ECG and the exercise ECHO in the occurrence of abnormal findings for NORM subjects nor HYP subjects suggesting that the ECG and the ECHO are comparable as diagnostic tools in determining CAD.

Compared to the angiography results, the ECHO demonstrated a higher percentage of true-positive results (80%) then the ECG (60%). Both the ECG and ECHO showed the same percentage of true-negatives (33%) when compared to angiography. This finding may suggest that the ECHO is comparable to the angiography and may be a better predictor of CAD than the ECG in obtaining true-positive results.

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Table 1. Comparison of clinical and demographic findings between normotensive and hypertensive subjects.

MEASURE	NORM (n=20)		HYP (n=17)	
	Mean	SD	Mean	SD
Age (yr)	54.8	13.8	60.5	11.5
Male/Female	10/10		9/8	
Angiography Male/ Female Distribution	4/3		0/4	
Medication:				
Antihypertensive	2 (10%)		16 (94%)	
Antianginals	3 (15%)		4 (24%)	
Other	12 (60%)		9 (53%)	
Resting Blood Pressure (mmHg)				
Systolic	129.2	23.2	141	23.3
Diastolic	75.9	7.03	83.1 *	9.9
Exercise Blood Pressure (mmHg)				
Systolic	170.9	21.9	184.1 *	18.7
Diastolic	82.9	8.3	93 *	12.6
Maximum Heart Rate Achieved (bpm)	159.6	13.8	152.8	14.5
METS Achieved	7.6	2.1	6.55	1.8
Reason for Stopping Test				
Fatique	1 (5%)		0 (0%)	
Chest Pain	3 (15%)		3 (17.6%)	
Shortness of Breath	14 (70%)		11 (65%)	
Per Patient's Request	1 (5%)		0 (0%)	
Per Physician's Request	1 (5%)		3 (17.6%)	

Unless otherwise indicated by a percent % symbol, values are mean and standard deviation, respectively.
** indicates significance at $p \leq .0095$*

Table 2. Comparison of findings for hypertensive and normotensive groups

Distribution of ECG, ECHO, and CATH findings among HYP and NORM							
Variable	Positive		Negative		X^2	P Value	*DF
	NORM	HYP	NORM	HYP			
ECHO (n=37) %	7 35%	5 25%	13 65%	12 71%	0.00009	0.99 p> .05,	1
ECG (n=37) %	8 40%	7 41%	12 60%	10 59%	0.07	0.79 p > .05	1
CATH (n=11) %	4 57%	4 100%	3 43%	0 0%	0.69	0.41 p > .05	1

Comparison of ECG and ECHO in the occurrence of abnormal findings in NORM							
Procedure	Positive		Negative		X^2	P Value	*DF
	NORM	HYP	NORM	HYP			
ECG (n=20) %	8 40%	*NA	12 60%	*NA	2.43E-015	1.0 p > .05	1
ECHO (n=20) %	7 35%		13 65%				

Comparison of ECG and ECHO in the occurrence of abnormal findings in HYP							
Procedure	Positive		Negative		X^2	P Value	*DF
	NORM	HYP	NORM	HYP			
ECG (n=17) %	*NA	7 41%	*NA	10 59%	0.13	0.720 p > .05	1
ECHO (n=17) %		5 29%		12 71%			

ECHO rest and exercise abnormal findings in NORM and HYP				
	NORM		HYP	
	Normal	Abnormal	Normal	Abnormal
Rest ECHO (n = 37)	18	2	14	3
Exercise ECHO (n = 37)	13	7	12	5
	Worse w/ Exercise	No Change from rest	Worse w/ Exercise	No Change from rest
Abnormal Rest ECHO made worse or no change with exercise	2	0	0	3

* **DF** = Degree of Freedom
* **NA** denotes **Not Applicable**

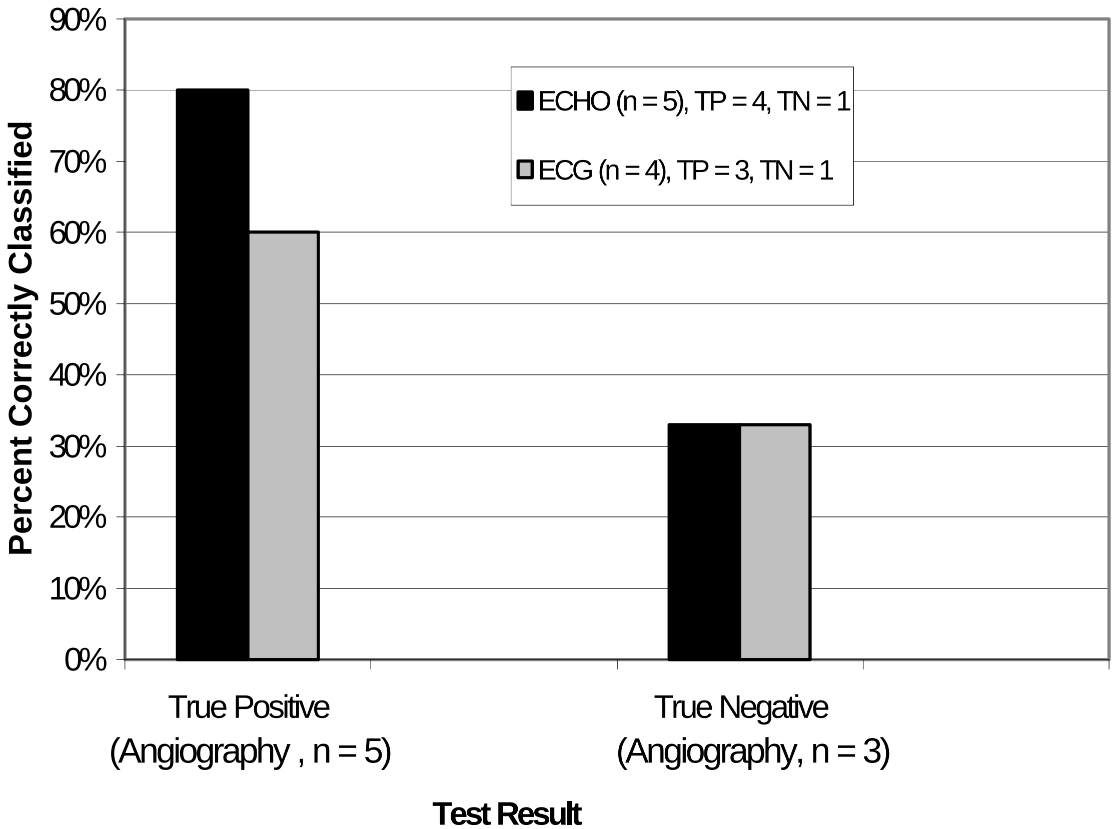

Figure 1. Correct Classification of Presence or Absence of Angiography Confirmed CAD by Exercise ECG vs ECHO

CHAPTER IV

SUMMARY

Hypertension is the most common cardiovascular disease and one of the most powerful predictors of coronary artery disease (Pollock & Wilmore, 1990). Extensive research has been done regarding the effects of this disease and cardiovascular testing. Most of the research has been determined by using electrocardiography (ECG) technique.

Even with the popularity of the exercise echocardiography on the rise, less research has been done using this technique especially with hypertensive patients. The echocardiography is the most common imaging procedure used for the diagnosis of coronary artery disease (Popp et. al. 1990). It is designed to view the heart chamber and blood flow for more accurate diagnosis of CAD. This is extremely beneficial to hypertensive patients who are more probable to also have left ventricular hypertrophy (LVH). Since echocardiography (ECHO) measures regional wall motion abnormalities, it can easily detect LVH as well as detect silent ischemia in patients without symptoms. The present investigation compared the frequencies of abnormal findings from exercise electrocardiography, post-exercise echocardiography and angiography in normotensive and hypertensive subjects. It specifically examined the ST segment shifts at 60 ms after the J point to determine ischemia as well as wall motion abnormalities exhibited on the ECHO at rest and immediately following exercise. The research problem was to determine if hypertensive subjects were more likely then normotensive subjects to show abnormal responses to exercise observed by the noninvasive ECG and ECHO techniques and comparing to the invasive technique, angiography.

Thirty-seven cases were included in this retrospective study. Each underwent maximal treadmill exercise testing with ECG and ECHO measures taken simultaneously during testing. Only eleven of the thirty-seven subjects also underwent angiography. Further details of the methodology are included in Appendix A.

In examining the results of exercise testing, there was no significance between hypertensive and normotensive subjects for signs of ischemia during the ECHO, ECG and angiography. Therefore, this study shows that the hypertensive subjects were not more likely to show signs of ischemia than the normotensive subjects on any of the procedures.

Since the present study does not demonstrate significant differences in the results between the ECG and ECHO suggests that the ability of these two protocols to assess ischemia is not different for this hypertensive population. Other studies have found different in which ischemia is common during maximal exercise in hypertensive patients (Pringle et. al 1991, Yurenev et al, 1990). These findings were not consistent in the current study. Hypertensive subjects were not more likely to show signs of ischemia than the normotensive population. This lack of ischemic results in the ECG could be related to the presence of LVH. Otterstad (1993) found that the ECG underestimated LVH in hypertensive subjects when compared to the ECHO studies. Pringle et al. (1991) found an exercise ECG sensitivity of 50% and a specificity of 71% for ischemia in hypertensive subjects with known LVH**.** However, LVH was not measured directly by the investigator and was not recognized as a major component in this study.

Additionally, the ECG has been known to produce a high number of false-positive results in patients without coronary artery disease and asymptomatic patients (Froelicher et al, 1973). This lack of specificity produced more false-positive results. In the current study, only 15% of the normotensive and 17.6% of the hypertensive had chest pain during exercise.

When the ECG is compared to the exercise ECHO, studies show that the ECHO rates a higher specificity in determining multi and single vessel disease (Popp et al, 1990, Crouse et al, 1991). But even with its advantages, the ECHO has limitations as well. One of the disadvantages is not being able to read images during exercise but instead immediately post-exercise. Robertson et al. (1983) found that the ECHO performed immediately following exercise can still be a useful clinical tool in evaluating CAD but Berberich et al. (1984) states that this delay in recording could result in inaccurate measures.

Limacher et al. (1983) found that wall motion abnormalities are still apparent for at least 90 seconds before resolving in patients with CAD. Other studies suggest that ischemia in 2 to 3 vessel disease frequently lasts for 3-4 minutes in imaging (Ginzton, 1989). However ischemia in single vessel disease may disappear in 30-60 seconds after exercise (Ginzton, 1989). The procedure in the present study obtained images within less than 90 second time period immediately following exercise. Therefore, the heart rates of the subjects were assumed to not be at maximum when the ECHO images were obtained which may effect the amount of ischemia present immediate post exercsie as compared to peak exercise. According to Ginzton, obtaining images 90 seconds after exercise could be too long to determine disease in single-vessel patients. Overall, most studies confirm that the post-exercise ECHO even with its limitations is a valuable addition in diagnosing CAD (Armstrong et al, 1986; Ryan et al, 1988)

IMPLICATIONS FOR FURTHER RESEARCH

The primary objective of this study was to determine if hypertensive subjects are more likely to have abnormal results for both exercise ECG and exercise ECHO and compared to angiography results. There were no differences in the NORM or HYP groups to have abnormal results for the exercise ECG and ECHO nor the angiography. The secondary objective was to determine if there are differences between the two noninvasive techniques (ECG and ECHO) to determining abnormal results in both hypertensive and normotensive subjects. These differences were not found in the present study. Therefore, exercise ECHO nor ECG were preferred one over the other as preferable in determining CAD in hypertensive subjects. However, the ECHO did find a higher percent of true positive results when compared to the angiography findings then the ECG. This may suggest that the ECHO could be a better predictor in determining CAD when compared to the angiography. Both the ECG and ECHO showed the same percent of true-negative findings.

Below are recommendations for further research necessary in the areas of hypertension and the evaluation of CAD via exercise electrocardiography and exercise echocardiography.

1. Since research has shown that hypertensive subjects are more likely to show signs of ischemia and therefore CAD, angiographic studies performed after the exercise testing would be beneficial. The current study included angiographic information on only 11 of the 37 subjects included.

Unfortunately, not all angiography tests were done after the exercise testing. Some where done before the exercise ECHO and ECG. If results were available from the cardiac catherization (angiography) before the exercise ECG and ECHO were performed, this information could have influenced the interpretations of the ECHO and ECG. Therefore, it would be beneficial to repeat the current study with more angiography tests performed on a larger population as well as have all angiography studies performed after the ECG and ECHO testing.

2. Another important consideration is whether the modification to electrodes V_2 and V_4-V_6 cause modification to the ST segment shifts both at rest and during exercise. This could likely have an effect on the accuracy of the ECG tracing during ECHO studies. It would be beneficial to study the two techniques on different test days, followed by angiography.

3. Since ischemic changes are sometimes lost from peak exercise to immediate post exercise, further research is needed to evaluate the magnitude of change for echocardiography in hypertensive patients. Utilizing an upright bicycle test with echocardiography during peak exercise instead of post-exercise may be a consideration.

4. Investigator should directly measure LVH to determine the possible impact it may have on the procedures and results.

5. Since the sample of HYP who underwent the CATH, ECG and ECHO was only four female subjects, a larger sample size may effect the results of future studies.

6. The HYP group did not have extremely high blood pressure values even though they were significantly different from the NORM values. It may be beneficial to have a more hypertensive population to determine the effects of abnormal results for this group.

7. Since positive angiography stenosis is not well defined ($\geq$50% or $\geq$70% in at least one coronary artery), it may be beneficial to compare the two definitions to determine the extent of disease and future procedures performed. Defining disease as $\geq$ 50% may not be enough stenosis to perform surgery but what are the future effects on the patient? Should surgical procedures be done for a stenosis of $\geq$50% and in how many arteries must this be seen to perform additional procedures? Does a definition of $\geq$70% stenosis have more value in prognosis?

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APPENDIX A

METHODOLOGY

METHODOLOGY

Subjects

A retrospective design was used for subject selection. A letter of approval was given to the researcher by the Montgomery Regional Hospital Bioethisc Advisory Committee as well as a n Internship Statement of Understanding before research was permitted. Thirty-seven subjects who had been referred to Montgomery Regional Hospital in Southwest Virginia for treadmill exercise echocardiography testing were studied. The subjects gave informed consent as per hospital policy prior to exercise testing. Of these, eleven subjects also had angiography performed. Three of the eleven were excluded in the percentage calculation due to having abnormal ECHO findings at rest and not changing or becoming worse with exercise.

Subjects were divided into two groups: those with normal resting blood pressure (NORM) and those with resting hypertension blood pressure (HYP). Those subjects with resting hypertension met at least two of the following criteria: 1) systolic blood pressure $\geq$ 140 mmHg or diastolic blood pressure $\geq$ 90 mmHg, 2) currently taking blood pressure medication, or 3) having a past history of hypertension, denoted as a current risk factor on hospital testing forms. Normotensive is defined as the absence of the above criteria.

Subjects were excluded who had known CAD, had taken medication the morning of the test which may have altered blood pressure responses to exercise (beta or calcium channel blockers) or which may have altered the ECG (digitalis), or who showed ST segment shift with hyperventilation ECG. In addition, those subjects who showed signs of left ventricular hypertrophy with strain, left bundle branch block, valvular stenosis or regurgitation, dyskinesis, aneurysm, known previous myocardial infarction or evidence of clinically significant Q waves >.04 sec were also excluded.

General Protocol

Exercise Testing: 12 lead ECG's and blood pressure readings were performed on each subject prior to exercise testing in both the supine and standing positions. The electrodes for ECG monitoring were placed on the chest so as not to overlie the marked sites for the acoustic echocardiography window. Specifically, lead V_2 was placed on the sternum at the level of the second or third intercostal space, and leads V_4-V_6 were lowered to the 6th intercostal space (Appendix D).

Treadmill exercise testing was performed on each subject using the Bruce protocol. During each 3-minute stage, a 12 lead ECG and exercising blood pressure measures were recorded while leads II, avF, and V_5 were continuously monitored. In accordance with the supervising physician, exercise test endpoints were: 1) development of limiting chest pain and/or dyspnea, 2) fatigue, or 3) subjects request to stop the test.

The exercise ECG was determined by the investigator to be normal or ischemic. An ischemic response to exercise was defined as meeting one of the following criteria: 1) horizontal or downsloping ST segment depression of $\geq$ 1 mm, 60 ms after the J point in a lead with a normal ST segment at rest, 2) ST segment elevation of 1 mm or more than the resting tracing 60 ms after the J point, 3) in the presence of ST depression in the resting tracing, an additional depression of 1 mm or more is required. St segment deviation was automatically calculated during the test by the computer (Q4500, Quinton Instrument Company, Seattle, Washington) as well as reviewed by the supervising physician. In addition, three concurrent complexes were measured for ST deviation and slope 60 ms after the J point.

Echocardiography. Stress echocardiography measures were done immediately following the stress electrocardiography test. Two-dimensional echocardiograms were recorded with standard commercially available equipment (Hewlett Packard Sonos 1000, Andover, Massachusetts). Parasternal long- and short- axis and apical two- and four-chamber views were recorded with the subject in the left lateral decubitus position at rest. The acoustic echocardiography window for both the parasternal and apical positions were marked on each subject's chest using a washable felt tip marker for reference. Immediately after cessation of exercise, the subject resumed the left lateral decubitus position, and the standard four views were repeated (within 90 seconds of cessation of exercise) as performed by previous researchers (Berberich et al, 1984; Marwick et al, 1992). All of the echocardiographic studies were done by the guidelines set by the American Society of Echocardiography (Henry et al, 1980).

The echocardiography studies were digitized on-line into a quad screen, continuous loop format for analysis (Nova microsonics ImageVue DCR, Mahwah, New Jersey). Images were recorded on ¾ inch VHS videotape as well as digitally on a 3-½ inch floppy diskette. Data were reviewed with resting and immediate post-exercise images placed side-by-side. Images were assessed for ejection fraction. Left ventricular mass, and for the presence of normal regional wall motion. Normal peak exercise shows a decrease in ventricular size with an increase in ejection fraction. Abnormal studies were defined as having regional wall motion abnormalities, such as hypokinesia, akinesia, or dyskinesia at rest or immediately after cessation of exercise. These changes occur in conjunction with an increase in ventricular size and a decrease in ejection fraction. Ejection fraction was measured by the computer (Nova Microsonics ImageVue DCR, Mahwah, New Jersey), by calculating stroke volume and dividing by diastolic volume. Left ventricular mass was defined by the investigator as normal or abnormal based on the physician's statement.

The distribution of CAD was approximated by studying the area in which the wall motion abnormalities occurred, using standards adopted by the American Society for Echocardiography. In general, disease of the left anterior descending artery was attributed to abnormalities in the apical, anterior and anteroseptal regions of the heart. Involvement of the left circumflex artery was attributed to abnormalities in the lateral and posterior walls of the heart. In addition, involvement of the right coronary artery was attributed to abnormalities in the inferior and basal septal regions of the heart. The cardiologist (s) interpreting the results of echocardiography studies maintain clinical competence as stated by the American College of Cardiology (Popp et al, 1990, Crouse et al., 1991).

Cardiac Catherization (Angiography): An angiography measure was done before or after the stress testing on different days. The patient was given .5 mgs of Xanax and was taken to the catherization lab. The right groin was prepped and draped and 1% Xylocane was infiltrated into the operative field. Using a Potts Cournand needle, the right femoral artery was punctured using the Seldinger technique and a sterile guide-wire was passed. A device (French introducer) was than advanced into the arterial system and used. The patient had a left heart cath, a left ventriculogram, left and right coronary angiography utilizing the Judkins technique. A diagnosis of significant coronary artery disease was defined as a stenosis of >50% in at least one of the main coronary arteries (left anterior descending, right coronary artery and/or left circumflex artery).

Statistical Analysis

Independent T-Tests was used for contrasting demographic data between the NORM and HYP groups. Chi-square analysis (X^2) was used to evaluate the distribution of normal vs abnormal clinical findings for ECG in the NORM and HYP groups, CATH in the NORM and HYP groups, and ECHO in the NORM and HYP groups. A chi-square analysis was also measured to determine the frequency of positive and negative CAD findings in the ECG and ECHO compared to the angiography results. A percentage of the ECG and ECHO true-positive and true-negative results was used to compare the precision of each to the angiography results.

The results showed that there was no statistical difference in the occurrence of abnormal findings for the NORM and HYP groups during exercise ECG (X^2= 0.07, DF=1, p>.05). There were also no statistical differences in the occurrence of abnormal findings for the NORM and HYP groups during post exercsie ECHO (X^2= 0.00009, DF=1, p>.05) nor angiography results (X^2= 0.69, DF=1, p>.05). Therefore, this study failed to reject the null hypothesis.

There was no difference between the exercise ECG and ECHO in the occurrence of abnormal findings for NORM subjects (X^2=2.43E-015, DF=1, p > .05) nor HYP subjects (X^2= 0.13, DF=1, p > .05). Therefore, this study failed to reject the null hypothesis.

The additional research question statistics showed the ECHO had 80% true-positive and the ECG 60% true-positive when compared to the angiography results. Both the ECG and ECHO had the same percentage of true-negatives (33%) when compared to the angiography results.

These results indicate that resting blood pressure does not influence the occurrence of abnormal vs normal ECG and ECHO findings nor angiography findings. Nor did it indicate any significant differences between the ECG and ECHO in detecting abnormal findings in the NORM or HYP groups. There was however, a higher percentage of ECHO true-positive results compared to the angiography then the ECG. This may indicate that the ECHO is comparable to the angiography findings and may be a better predictor in determining disease than the ECG.

APPENDIX B

MONTGOMERY REGIONAL HOSPITAL RESEARCH APPROVAL

INTERNSHIP STATEMENT OF UNDERSTANDING

MONTGOMERY REGIONAL HOSPITAL

An affiliate of Columbia/HCA Healthcare Corporation

18 December, 1995

Ms. Angie Gaddy
3347 Forest Ridge Rd.
Roanoke, VA 24018

Dear Ms. Gaddy:

This letter serves to inform you about our decision regarding your research proposal entitled, *The Relationship Between Resting Blood Pressure & Myocardial Ischemia During Maximal Exercise Echocardiography, Electrocardiography & Arteriography.*

In keeping with hospital policy your proposal has been reviewed by the Chair of the Bioethics Advisory Committee as well as by managers in charge of departments that would be involved in your proposed study.

I am pleased to inform you that we have no objections to your research project as defined in the materials presented for our review. As such, your proposal has been approved provided your compliance with a few administrative requirements.

In order to ensure the safety of our patients and provide you with the help you need, we ask that you abide by the following:

1. Sign a copy of the hospital's Statement of Understanding/confidentiality agreement.
2. Work with our Cardio-Pulmonary Dept. to identify potential participants.
3. Provide our Medical Records department with at least one week's notice prior to your chart review session(s).
4. No patient chart, or component of a chart, can be taken outside of the hospital at any time.
5. Notify us of any changes to the protocol or study design.
6. Provide us with a copy of your final report.

Should you have any questions, or require additional information, please do not hesitate to contact myself directly at 540/953-3524.

Once again, that you for your consideration and good luck with your research.

Sincerely,

Ian W. Watson
Chair, Bioethics Advisory Committee

cc. Bob Brannigan, CNO
Susan Richards, Mgr. of HIM
M.J. Bean, Mgr. of Cardio-Pulmonary

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MONTGOMERY REGIONAL HOSPITAL
An affiliate of Columbia/HCA Healthcare Corporation

Internship
Statement of Understanding

CONFIDENTIALITY
As an intern, I may have access to patient, employee, and/or administrative information. I understand that all hospital information is to be treated as confidential.

As a student, I may not use any information obtained from the hospital in my school projects or research without prior approval from the hospital administration. If approval is given, I understand the hospital administration reserves the right to review all relevant information.

STATUS
I understand that I am not an employee of the hospital and therefore, am not entitled to any of the terms and conditions granted to regular employees. This also means that I absolve Montgomery Regional Hospital and its parent company, Columbia/HCA from any and all liability that might occur during my internship.

I understand that either I or the hospital may absolve our relationship at any time during the internship.

STIPEND
I understand that I will not be paid on an hourly basis nor receive a regular salary. In exchange for the work and educational experience gained, I will be paid a monthly stipend of ________.

RULES OF CONDUCT
Although I am not an employee of Montgomery Regional Hospital, I agree to abide by the same rules, guidelines, and professional standards established for hospital employees.

______________________________ ____________________
Intern Printed Name **Date**

____
Intern Signature

____
Witness

P.O. Box 90004
3700 South Main Street
Blacksburg, VA 24062-9004
Telephone 540/951-1111
Fax 540/953-5295

APPENDIX C

INFORMED CONSENT

INFORMED CONSENT FOR PARTICIPATING IN CARDIAC & PULMONARY REHABILITATION PHASE II PROGRAMS

1. Explanation of Program

The cardiac and pulmonary rehabilitation programs include physical exercises, dietary counseling, psychological services and health education activities.

The level of exercise you perform will be based upon the exercise stress test you took prior to entering this program. The exercise level will be adjusted gradually and progressively as tolerated by you, the participant. You will participate in this program three times per week. You are expected to attend every session and to follow your physician's and the staff's instructions with regard to any medications, exercise limitations, dietary considerations, smoking cessation and stress management.

During the exercise session your heart rate, blood pressure and rating of perceived exertion will be monitored. All cardiac participants will be monitored by telemetry. Pulmonary participants who have exhibited EKG changes during the preliminary stress test will also be monitored by telemetry. Oxygen levels will be checked by oximetry in all pulmonary patients and supplemental oxygen will be administered if the oxygen level is low.

Upon completion of the cardiac or pulmonary rehabilitation program you will undergo a discharge exercise test.

2. Benefits to be Expected from Cardiac & Pulmonary Rehabilitation Program

Participation in this program may or may not benefit you directly in any way. The results obtained should help evaluate what type of activities you might engage in safely. No assurance can be given that this program will increase your ability, endurance or stamina, although there is widespread evidence which indicates that improvement is usually achieved provided the participant follows the program guidelines.

3. Confidentiality

The information obtained from the Cardiac & Pulmonary programs at Montgomery Regional Hospital is treated as privileged and confidential. It will not be released to anyone without your expressed written consent. This information will be used only for statistical and scientific purposes with your right to privacy retained.

4. Release

I hereby release Montgomery Regional Hospital and all of their employees from all liability and responsibility for any injury, illness or complication, including heart attack, which might arise out of or as a result of my participation in the Cardiac & Pulmonary Rehabilitation Program.

5. Inquiries and Freedom of Consent

I understand that my participation in the Cardiac & Pulmonary Rehabilitation Program at Montgomery Regional Hospital is voluntary and that I am free to withdraw at any time. I have read this form and understand the therapy program. I consent to participate in this program.

____________________________ ____________________________

Participant's Signature *Witness*

____

Date

APPENDIX D

CONTINGENCY TABLES

Table 3. Distribution of abnormal echocardiography findings and hypertension among subjects.

	Result of Echocardiography		
Subjects	*Negative*	*Positive*	*Total*
Normotensive	13	7	20
Expected	13.5	6.49	19.99
Hypertensive	12	5	17
Expected	11.5	5.51	17.01
Total	25	12	37

Note. X^2= .00009, DF=1, p>0.05

Table 4. Distribution of abnormal electrocardiography findings and hypertension among subjects

	Result of Electrocardiography		
Subjects	*Negative*	*Positive*	*Total*
Normotensive	12	8	20
Expected	11.9	8.11	20.01
Hypertensive	10	7	17
Expected	10.11	6.89	17
Total	22	15	37

Note. X^2= .0693, DF = 1, p > 0.05

Table 5. Distribution of abnormal angiography findings and hypertension among subjects.

	Result of Angiography		
Subjects	*Negative*	*Positive*	*Total*
Normotensive	3	4	7
Expected	1.91	5.09	7
Hypertensive	0	4	7
Expected	1.09	2.91	4
Total	3	8	11

Note. X^2=.692, DF=1, p > 0.05

Table 6. Comparison of ECG and ECHO in the Occurrence of Abnormal Findings for NORM Subjects

Result of ECG and ECHO for NORM Subjects				
Exercise Test		*Positive*	*Negative*	*Total*
ECG		8	12	20
	Expected	7.5	12.5	
ECHO		7	13	20
	Expected	7.5	12.5	
Total		15	25	40

Note: X^2=2.429 E-015, DF = 1, $p>0.05$

Table 7. Comparison of ECG and ECHO in the Occurrence of Abnormal Findings for HYP Subjects

Result of ECG and ECHO for HYP Subjects				
Exercise Test		*Positive*	*Negative*	*Total*
ECG		7	10	17
	Expected	6	11	
ECHO		5	12	17
	Expected	6	11	
Total		12	22	34

Note: X^2=.129, DF= 1, $p>0.05$

Table 8. Correct classification of presence or absence of angiography confirmed CAD by Exercise ECG vs ECHO

Procedure Result	*Angio + (N=5)*	*Angio - (N=3)*	Total
ECHO +	***4**	2	6
ECHO -	1	***1**	2
Total	5	3	8
ECG +	***3**	2	5
ECG -	2	***1**	3
Total	5	3	8

ECHO: Number of True positive + True negative = 5 correctly classified compared to angiography
ECG: Number of True positive + True negative = 4 correctly classified compared to angiography

* The numbers in bold represent true-positive and true-negative results of each procedure

APPENDIX E

MEASURES AND DEFINITIONS FOR COMPUTER DATA CODING

DEFINITIONS FOR COMPUTER DATA CODING:
(Definitions for analysis of Patient Raw Data found in Appendix J)

Patient Identification Number (PATIENT ID): Each subject was identified using their seven-digit Montgomery Regional Hospital patient ID number.

Date (ECHO/EKG DATE); (CARDIAC CATH DATE): The date the exercise test was performed; MM/DD/YY and the date the cardiac catherization was performed; MM/DD/YY.

Age (AGE): The actual age in years of each subject at the time of the testing.

Sex (SEX): Each subject's gender was recorded; M=male, F=female.

History (HISTORY): The presenting complaint of each subject for which the exercise test and cardiac catherization was performed; 1- rule out/ evaluate CAD, 2= chest pain/angina, 3= abnormal ECG, 4= shortness of breath, 5= other.

Medications: It was recorded whether each subject was regularly taking Blood Pressure Medications (BPMEDS), Antianginals (ANTIANG), and/or any other medications (OTHERMEDS); 0=no, 1=yes for each type of medication.

Hypertension Risk (HTNRISK): Each subject was categorized as having (1=yes) or not having (0=no) hypertension as a risk factor for coronary artery disease by family history.

Resting Blood Pressure: Each subject's blood pressure (mmHg) was measured prior to the exercise test in the supine position. (RSBPSUP) represents resting supine systolic blood pressure, while (RDBPSUP) represents resting supine diastolic blood pressure.

Hypertensive Subject (HTN): Each subject was categorized into whether they were (-1=yes) or whether not (0=no) hypertensive by the study criteria.

Blood Pressure at Maximum Exercise: Each subject's blood pressure (mmHg) was measured at peak exercise during the exercise test. (EXSBP) represents exercise systolic blood pressure, while (EXDBP) represents exercise diastolic blood pressure.

METs Achieved (METS): The maximum METs achieved by each subject at peak exercise.

Heart Rate at Maximum Exercise (EXHR): The actual heart rate in beats per minute at peak exercise.

Reason for Stopping Test (RFST): The reason for which the exercise test was stopped for each subject: 1=fatigue, 2=chest pain, 3=shortness of breath, 4=per patient request, 5= per MD request.

Resting ST Depression (RST): If there was significant ST depression at rest (1=yes) or there was not significant ST depression at rest (0=no) .

ST Depression at Maximum Exercise (EXST): If there was significant ST depression at maximum exercise (1=yes) or if there was not significant ST depression at maximum exercise (0=no).

Ischemia (ISCHEMIA): Whether or not ischemia was present by study criteria during exercise for each subject (1=no, 2=yes).

Chest Pain During Exercise (PAIN): Whether the patient exhibited chest pain during the exercise test (0=no, 1=yes)

Resting Wall Motion Abnormalities (RWMA): Whether wall motion abnormalities were present at rest:

0= normal

1= hypokinetic

2= akinetic

Resting Wall Motion Abnormality Location (RWMALOC): The location the resting wall motion abnormality was observed. Each abnormality was classified by segments and listed by corresponding number :

0=	no segment wall motion abnormality present		
1=	mid-anterior septal		
2=	basal anterior septal	10=	apical septal
3=	mid posterior	11=	apical lateral
4=	basal posterior	12=	basal lateral
5=	mid septal	13=	basal inferior
6=	mid inferior	14=	apical inferior
7=	mid lateral	15=	apical anterior
8=	mid anterior	16=	basal anterior
9=	basal septal		

Additional segments included by researcher for interpretation (not included as part of the 16 segment wall motion locations listed above)

17= inferior wall region

18= apical region

Exercise Wall Motion Abnormality (EXWMA): Whether wall motion abnormalities were present during peak exercise:

0= normal

1= hypokinetic

2= akinetic

Exercise Wall Motion Abnormality Location (EXWMALOC): The location the peak exercise wall motion abnormality was observed. Each abnormality was classified by segments and listed by corresponding number :

0= no segment wall motion abnormality present

1= mid-anterior septal

2=	basal anterior septal	10=	apical septal
3=	mid posterior	11=	apical lateral
4=	basal posterior	12=	basal lateral
5=	mid septal	13=	basal inferior
6=	mid inferior	14=	apical inferior
7=	mid lateral	15=	apical anterior
8=	mid anterior	16=	basal anterior
9=	basal septal		

Additional segments included by researcher for interpretation (not included as part of the 16 segment wall motion locations listed above)

17= inferior wall region

18= apical region

Location of Wall Motion Abnormalities by Coronary Vessel: Whether wall motion abnormalities were present (0=no, 1=yes) at rest or peak exercise in the three main coronary vessels: Left Anterior Descending (LAD), Left Circumflex (LCX), and/or Right Coronary Artery (RCA).

Others: Ejection Fraction at Peak Exercise (EXEFRAC) measured as 0=no change, 1=increase, -1= decrease from rest; Left Ventricular Mass (LVMASS) as considered 0=normal or 1=with hypertrophy.

Catherization Disease (CATHDISEASE): Does the cardiac catherization show significant coronary artery disease (≥50% in one or more coronary artery); 0=no, 1=yes.

Location of Coronary Artery Disease as Observed by Catherization Study (CATHLOC): Whether coronary artery disease was present (o=no, 1=yes) by the cardiac catherization in the three main arteries; Left Anterior Descending (LAD2), Left Circumflex Artery (LCX2), Right Coronary Artery (RCA2)

APPENDIX F

RAW DATA

Patient ID	ECHO/EKG Date	Cardiac Cath Date	Age (yrs)	SEX	History
1130828	5/10/93	4/13/93	56	M	1
1136957	5/25/93		59	F	2
1152507	9/22/93	10/22/93	71	F	2
1203239	6/20/94		54	F	2
2173970	4/5/93	5/5/93	66	F	2
2188111	4/29/93		71	M	2
2194796	5/11/93		50	M	2
2201200	5/24/93		30	M	2
2217556	6/24/93		80	M	5
2222228	7/6/93		49	F	2
2229412	7/20/93		50	M	2
2245240	8/18/93		34	M	5
2247484	8/24/93		49	M	5
2279772	10/18/93		70	F	2
2318283	12/20/93		29	M	2
2323741	1/5/94		67	M	5
2353879	5/3/93		65	F	4
2358059	3/7/94		36	M	2
2360092	3/16/94		67	F	5
2410126	6/1/94		77	F	2
2434657	7/15/94		50	M	2
2438376	7/21/94		57	F	2
2477936	9/28/94		51	F	2
2484993	10/10/94	3/29/95	65	F	4
2513453	11/22/94	10/6/94	61	F	2
2517398	11/30/94	12/21/94	69	F	2
2531437	12/21/94	1/5/95	57	F	2
2550401	1/25/95	12/1/94	45	M	2
2559170	2/9/95		61	F	5
2577786	3/9/95		75	F	2
2593475	4/3/95		51	M	5
2604228	4/18/95	4/26/95	57	F	2
2629838	5/30/95		75	M	2
2639257	6/14/95		54	M	2
2653714	4/27/94	4/29/94	42	M	5
2653904	7/12/95		65	M	2
2712722	10/16/95	4/5/95	59	M	2

Patient ID	BPMEDS	ANTIANG	OTHERMEDS	HTNRISK	RSBPSUP (mmHg)	RDBPSUP (mmHg)	HTN
1130828	1	0	1	0	128	80	0
1136957	1	1	1	1	108	70	-1
1152507	0	1	1	0	120	60	0
1203239	0	0	1	0	122	64	0
2173970	0	0	0	0	118	78	0
2188111	0	0	1	0	170	80	0
2194796	1	0	1	1	140	82	-1
2201200	0	0	0	0	120	68	0
2217556	1	0	0	1	180	70	-1
2222228	0	0	1	0	150	90	0
2229412	1	0	1	1	128	92	-1
2245240	0	0	0	0	118	76	0
2247484	0	0	0	0	132	80	0
2279772	1	0	0	1	158	86	-1
2318283	0	0	0	0	100	76	0
2323741	0	0	1	0	102	78	0
2353879	1	0	1	1	140	80	-1
2358059	1	1	1	0	150	80	-1
2360092	0	0	1	0	178	79	0
2410126	0	0	1	1	132	78	0
2434657	1	0	0	1	120	72	-1
2438376	0	0	0	0	130	72	0
2477936	0	0	0	0	102	68	0
2484993	1	1	0	1	160	70	-1
2513453	0	1	1	0	180	76	0
2517398	0	0	1	1	154	78	-1
2531437	1	0	1	1	130	80	-1
2550401	0	1	1	1	120	86	0
2559170	0	0	1	0	120	80	0
2577786	1	0	0	1	134	90	-1
2593475	1	0	1	1	140	100	-1
2604228	1	1	0	1	187	88	-1
2629838	1	0	0	1	110	94	-1
2639257	1	0	0	1	106	80	-1
2653714	0	0	1	0	124	72	0
2653904	1	0	1	1	152	100	-1
2712722	1	0	0	0	118	76	0

Patient ID	EXSBP (mmHg)	EXDBP (mmHg)	METs	EXHR (bpm)	RFST	RST	EXST
1130828	140	82	7.6	162	3	0	0
1136957	150	70	7.6	165	3	0	0
1152507	182	94	5.6	147	2	1	0
1203239	0	0	7.6	162	3	0	0
2173970	170	80	5.6	167	2	0	1
2188111	206	92	5.6	142	3	0	1
2194796	196	93	9.7	153	3	0	0
2201200	178	82	9.7	168	3	0	0
2217556	200	90	5.6	157	3	0	0
2222228	190	80	7.6	160	3	0	1
2229412	189	80	7.6	168	3	0	0
2245240	140	74	9.7	175	5	0	0
2247484	188	90	9.7	168	3	0	0
2279772	188	100	5.6	157	3	0	1
2318283	154	70	11.7	170	3	0	0
2323741	140	80	9.7	143	3	0	0
2353879	166	88	5.6	158	3	0	0
2358059	226	100	9.7	160	2	0	1
2360092	192	80	7.6	184	3	1	1
2410126	160	86	3.6	160	3	1	1
2434657	200	90	7.6	180	3	0	1
2438376	189	98	5.6	148	3	0	0
2477936	140	86	7.6	152	3	0	0
2484993	164	74	3.6	132	2	0	1
2513453	190	70	5.6	140	1	0	0
2517398	180	84	5.6	129	3	0	1
2531437	196	120	3.6	147	2	0	0
2550401	190	78	7.6	147	3	0	0
2559170	168	74	5.6	158	3	0	0
2577786	170	100	5.6	144	5	0	0
2593475	170	110	7.6	167	3	0	1
2604228	200	88	7.6	130	3	1	1
2629838	190	90	5.6	145	3	1	1
2639257	164	104	7.6	142	5	0	0
2653714	176	96	7.6	149	4	0	1
2653904	180	100	5.6	164	5	0	0
2712722	142	84	10.1	189	2	1	1

Patient ID	ISCHEMIA	PAIN	RWMA	RWMALOC	EXWMA	EXWMALOC	LAD	LCX
1130828	1	0	0	0	1	14	0	0
1136957	1	0	0	0	0	0	0	0
1152507	2	1	1	10	2	10	0	0
1203239	1	0	0	0	0	0	0	0
2173970	2	0	0	0	1	17	0	0
2188111	2	1	0	0	1	18	0	0
2194796	1	0	0	0	0	0	0	0
2201200	1	0	0	0	0	0	0	0
2217556	1	0	0	0	0	0	0	0
2222228	2	0	0	0	0	0	0	0
2229412	1	0	0	0	0	0	0	0
2245240	1	0	0	0	0	0	0	0
2247484	1	0	0	0	0	0	0	0
2279772	2	0	0	0	0	0	0	0
2318283	1	0	0	0	0	0	0	0
2323741	1	0	0	0	1	4	0	0
2353879	1	0	0	0	0	0	0	0
2358059	1	1	0	0	1	2	1	0
2360092	2	0	0	0	0	0	0	0
2410126	2	0	0	0	0	0	0	0
2434657	2	0	0	0	0	0	0	0
2438376	1	0	0	0	0	0	0	0
2477936	1	0	0	0	0	0	0	0
2484993	2	1	2	11,15	2	11,15	0	1
2513453	1	0	0	0	0	0	0	0
2517398	2	1	0	0	1	11,17	0	0
2531437	1	1	1	17	1	17	0	0
2550401	1	0	0	0	0	0	0	0
2559170	1	0	0	0	0	0	0	0
2577786	1	0	0	0	0	0	0	0
2593475	2	0	0	0	0	0	0	0
2604228	2	1	1	17	1	17	0	0
2629838	2	0	0	0	0	0	0	0
2639257	1	0	0	0	0	0	0	0
2653714	2	0	0	0	2	18	1	0
2653904	1	0	0	0	0	0	0	0
2712722	2	0	1	1,2	2	1,2	1	0

Patient ID	RCA	EXEFRAC	LVMASS	CATHDIS	LAD2	LCX2	RCA2
1130828	0	1	0	1	0	1	1
1136957	0	1	0	0	0	0	0
1152507	0	1	0	1	1	0	1
1203239	0	1	0	0	0	0	0
2173970	1	1	0	0	0	0	0
2188111	0	0	0	0	0	0	0
2194796	0	1	0	0	0	0	0
2201200	0	1	0	0	0	0	0
2217556	0	1	0	0	0	0	0
2222228	0	1	0	0	0	0	0
2229412	0	1	0	0	0	0	0
2245240	0	1	0	0	0	0	0
2247484	0	1	0	0	0	0	0
2279772	0	1	0	0	0	0	0
2318283	0	1	0	0	0	0	0
2323741	0	1	0	0	0	0	0
2353879	0	1	0	0	0	0	0
2358059	0	0	1	0	0	0	0
2360092	0	1	1	0	0	0	0
2410126	0	1	0	0	0	0	0
2434657	0	1	0	0	0	0	0
2438376	0	1	0	0	0	0	0
2477936	0	1	0	0	0	0	0
2484993	0	0	0	1	0	1	0
2513453	0	0	0	0	0	0	0
2517398	0	1	0	1	1	1	1
2531437	0	0	0	1	1	1	1
2550401	0	1	0	1	1	0	0
2559170	0	1	0	0	0	0	0
2577786	0	1	0	0	0	0	0
2593475	0	1	1	0	0	0	0
2604228	1	1	0	1	0	0	1
2629838	0	1	1	0	0	0	0
2639257	0	1	0	0	0	0	0
2653714	0	1	0	1	0	1	1
2653904	0	1	0	0	0	0	0
2712722	0	1	0	0	1	0	0

VITA

Angela G. Gerni, was born in Lynchburg, Virginia in 1969. She attended Radford University where she received her Bachelor's Degree in Sportsmedicine. Immediately after her BS, she attended VA Tech in pursuit of her Master's Degree in Exercise Science. She has worked in both the health club setting as well as the hospital setting and is currently working in the field she enjoys the most, Cardiac Rehabilitation. She is married to a wonderful husband and now resides in Vinton, Virginia.