

A comparison of exercise response variables
among smokers and non-smokers.

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Dedication

This thesis is dedicated to my husband, Dr. Greg Bonikowske.

Abstract

Heart rate recovery and chronotropic incompetence are two prognostic variables that have been examined as predictors for CAD and all-cause mortality (Cole et al., 1999). Abnormal heart rate recovery is defined as failure of the heart rate to decrease by greater than or equal to twelve beats per minute within the first minute of recovery (Cole, et al., 1999). Chronotropic incompetence is identified as an impaired heart rate response to exercise (Lauer, 2004) and failure to reach 85% of age-predicted heart rate maximum (Lauer et al., 1996). This study examined the effect of an acute bout of exercise on heart-rate recovery in smoking and non-smoking men and women (n=32). Participant's mood and urge to smoke were also examined with two questionnaires before and after. Pearson's chi-square revealed no significant differences in chronotropic incompetence between the two groups (p=0.833). None of the participants exhibited abnormal heart rate recovery. The within-subjects ANOVA analyzing the Urge to Smoke Questionnaire revealed no significant differences between pre and post exercise urge to smoke among the smoking individuals (n=9; p=0.537). The within-subjects ANOVA revealed no significant differences between pre and post POMS scores among all participants (p=0.517). The findings indicate no effect of smoking status on heart rate recovery or chronotropic response. The findings also indicate no effect of exercise on urge to smoke or mood. Additional studies with larger sample sizes are needed to discover these relationships.

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Introduction

Heart disease is the number one cause of death in the United States with Coronary Artery Disease (CAD) accounting for one third of these deaths. (Lloyd-Jones, et al., 2009). Risk factors for CAD include diabetes mellitus (DM), hypertension (HTN), family history, dyslipidemia, gender, age, physical inactivity, overweight and obesity, diet and cigarette smoking (Lloyd-Jones et al., 2009). Heart rate recovery and chronotropic incompetence are two prognostic variables that have been examined as predictors for CAD and all-cause mortality (Cole et al., 1999). Abnormal heart rate recovery is defined as failure of the heart rate to decrease by greater than or equal to twelve beats per minute within the first minute of recovery (Cole, et al., 1999). Heart rate recovery was even found to be predictive of mortality independent of coronary angiography findings (Vivekananthan et al., 2003). Chronotropic incompetence is identified as an impaired heart rate response to exercise (Lauer, 2004) and failure to reach 85% of age-predicted heart rate maximum (Lauer et al., 1996).

The previously mentioned risk factors for CAD are classified as modifiable and non-modifiable. Family history, gender and age are examples of non-modifiable risk factors. Physical inactivity, diet and smoking are modifiable risk factors than can be altered through lifestyle and behavioral changes. Smoking is the number one preventable cause of death with rates of smoking adults declining over the years to 19.8% in 2007 (Thorne et al., 2008). Abnormal heart rate recovery is emerging as another modifiable risk factor demonstrated in a study of patients completing a phase II cardiac rehab program (Hao et al., 2002). Heart rate recovery, when adjustments were made for all

other risk factors, was statistically the strongest predictor of mortality (adjusted RR, 2.0; 95% CI 1.5-2.7; $P < 0.001$; Cole et al., 1999).

The purpose of this study was to examine the effect of a single bout of exercise on heart rate recovery and chronotropic competence among smoking and non-smoking men and women referred for a treadmill stress test at North Memorial Heart and Vascular Institute. Because the above risk factors are associated with mortality, this study focused on the effects of smoking and the prognostic variables heart rate recovery and chronotropic incompetence. The primary hypothesis was that smokers would have a higher incidence of abnormal heart rate recovery and chronotropic incompetence than non-smokers. The secondary aim of the study was to evaluate the effect of an acute session of exercise on mood and urge to smoke using the Profile of Mood States (POMS) and Urge to Smoke questionnaires. The secondary hypothesis was that among smokers, their urge to smoke would decrease following exercise and mood would improve after exercise among all participants.

Literature Review

Risks of Smoking

The risks of smoking are widely advertised and known throughout the public. Regrettably, smokers continue to smoke and others still begin to smoke knowing the risks. Generally smoking rates are higher among those with a lower socioeconomic status and education level (Jackson et al., 2008). A study conducted on 737 smokers found that 60 percent of these current smokers did not think that smoking is harmful to them and did not think that they were at an increased risk of myocardial infarction (Ayanian et al.,

1999). As stated previously, smoking is a known and independent risk factor for coronary heart disease, cerebrovascular disease and atherosclerotic cardiovascular disease (Jackson et al., 2008). Cigarette smoking is also known to increase all-cause as well as cardiovascular mortality (Qiao et al., 2000). Research indicates that individuals who are able to quit smoking and maintain cessation do not have an increased mortality risk compared to nonsmokers (Jackson et al., 2008).

Numerous studies indicate that smoking plays a role in the development of atherosclerosis. The Atherosclerosis Risk in Communities (ARIC) study was conducted on 10,914 patients. Carotid artery intimal-medial thickness was measured by ultrasound over three years. Current smokers had a 50 percent increase in atherosclerosis progression in the three year study period compared to the nonsmokers (Howard et al., 1998). This study also found that there was no difference between progression of atherosclerosis between current and previous smokers, thus suggesting some of the negative effects of smoking may not be reversible through cessation. Despite these findings, the relationship between smoking and the development of atherosclerosis is not completely understood and is likely due to several different factors.

Smokers and Heart Disease

Factors that influence the relationship between smoking and heart disease are the effects of smoking on the lipid profile and factors that lead to endothelial dysfunction. Lipid levels are adversely affected by smoking causing a rise in low-density lipoproteins (LDL) and triglycerides and a reduction of the good cholesterol, high density lipoprotein (HDL) (Craig et al., 1989). Smoking has also been found to be associated with insulin

resistance (Facchini et al., 1992). The sympathetic nervous system is activated by cigarette smoking which in turn produces an increase in heart rate and blood pressure along with possible vasoconstriction (Narkeiwicz et al., 1998). A prothrombotic state is created with smoking due to the inhibition of tissue plasminogen activator released by the endothelium (Newby et al., 1999). An increase in platelet activity is also seen and is thought to be attributed to the previously mentioned increased sympathetic activity (Fusegawa et al., 1999).

Smoking poses another threat to the normal function of the endothelium. Whether smoking the cigarette or simply being exposed to the smoke, endothelium-dependent vasodilation is impaired in normal coronary arteries along with a reduction in the coronary flow reserve (Celermajer et al., 1993). Endothelial dysfunction may also result via oxidative stress from enhanced oxidation of LDL along with a reduction in the production of nitric oxide (Barua et al., 2001). Although the relationship is not completely understood between smoking and the development of atherosclerosis, much of the research continues to point to the negative effects of smoking on substances in the body and their reaction with the endothelium. Ultimately, these reactions lead to possible endothelial dysfunction followed by plaque accumulation and adverse cardiac events.

The potential risks of smoking and their relationship with atherosclerosis has been outlined by numerous research studies, although incompletely understood, appear quite clear. There are numerous benefits of smoking cessation including reduction in the harmful effect of smoking on the vascular system. Another benefit to smoking cessation is that the cardiac risks are reduced fairly quickly following cessation and continue to

decrease the longer the individual is abstinent (Surgeon General's Report, 1990).

Smoking cessation also has a significant effect on mortality. For example, Critchley and colleagues (2003) conducted a meta-analysis of 20 prospective cohort studies which included 12,603 smokers who had an MI, coronary artery bypass grafting or known CHD over a 2 year follow-up period. Of those included, 5,659 had quit smoking and 6,944 had continued to smoke. The relative risk for those who quit compared to those who continued to smoke was 0.64 (95% CI 0.58-0.71). The benefit from smoking cessation was not affected by the type of coronary event, age, gender, country or the year the study was begun.

Exercise, Urge to Smoke, and Mood

To better understand why people continue to smoke despite the harmful effects, researchers have examined the effects of exercise on urge to smoke and mood. In the review conducted by Taylor et al., 2007, the acute effects of exercise on cigarette cravings, withdrawal symptoms, affect and smoking behavior were analyzed. This review included fourteen relevant studies with twelve of the fourteen comparing a single bout of exercise to some form of a passive condition and the effects on smoking. The general findings of the review include an improvement of mood and affect both during as well as after exercise. In this pilot study this same outcome was desired through the use of the Urge to Smoke Questionnaire as well as the Profile of Mood States. The other general finding of the review was that exercise decreased the ratings of the participants desire to smoke and also had a more prompt effect than when compared to the use of oral anti-smoking agents. A limitation of the review is the number of outcome variables used by

the researchers. To obtain a clear picture of the acute effects of exercise on smoking urges and behaviors future research is needed using the same outcome variables to create a possible exercise treatment to aid in smoking cessation. The implications of the review include the creation of a smoking cessation program focusing on an exercise regimen rather than oral anti-smoking agents.

Heart Rate Recovery and Chronotropic Incompetence

A prospective cohort study was conducted by Cole and colleagues (1999) at the Cleveland Clinic Foundation. Adults (n=2,428) were followed for six years following initial nuclear stress testing. The focus of the study was to use heart rate recovery to predict mortality in this cohort. In this study abnormal heart rate recovery was defined as failure of the heart rate to decrease twelve beats within the first minute. Chronotropic response was used to evaluate heart rate response to exercise. Chronotropic response was defined as the percent of heart rate reserve obtained at peak exercise. If a participant failed to achieve at least 80% of heart-rate reserve there was evidence for an impaired chronotropic response to exercise.

The study found a median value of 17 beats per minute for heart-rate recovery and a range of 12 to 23 beats from the 25th to 75th percentile. The low value of 12 beats per minute as the cut-off was found to maximize the log-rank test statistic which provides the rationale for using 12 beats as the abnormal value in this study. Of the 2,428 included, 639 or 26% of the patients had an abnormal heart-rate recovery. Those with an abnormal heart-rate recovery were also more likely to have other co-morbidities. There were 213 deaths at the six year follow-up from all causes with 120, or 56 percent, of these people

having an abnormal heart-rate recovery. The incidence of abnormal heart-rate recovery was thus strongly predictive of death. The researchers conducted a Multivariate Cox Regression analysis and when all adjustments were made for multiple co-morbidities, a poor heart-rate recovery continued to come forward as the strongest predictor of mortality.

The study also identified subgroups, other than men, that a low value for heart-rate recovery was predictive of mortality. These groups included women, the elderly, patients with a normal chronotropic response to exercise and those on beta-blocker therapy. The study reported that the mechanism which associates an abnormal heart-rate recovery to an increased risk of death is still not clear. However, it has been demonstrated previously by Imai et al. that vagal reactivation is the primary determinant of the decrease in heart rate for the first 30 seconds following exercise. The study found an inverse relationship between exercise capacity and heart-rate recovery which leads to the theory of heart-rate recovery emerging as a predictor of mortality. The proposed study will build on this theory by analyzing a known major risk factor for all-cause mortality and CHD and the emerging risk factor, abnormal heart-rate recovery. Both appear to be modifiable but require lifestyle and behavioral changes. Another limitation of their study was the absence of left ventricular function as a prognostic variable that would have been helpful in their analysis.

Heart-rate recovery and chronotropic response to exercise are both easily obtained figures during a treadmill stress test. Lauer and colleagues (1997) used members from the Framingham Offspring study to further investigate the relationship between cigarette

smoking and the occurrence of chronotropic incompetence in this healthy cohort of mostly middle-aged men and women. Again, the focus was the prognostic capacity of these variables for heart disease and all-cause mortality. Chronotropic incompetence as defined in the introduction is the failure to achieve the target heart rate during exercise. This study also chose to calculate chronotropic incompetence by using the ratio of heart rate reserve used to metabolic reserve at stage 2 of exercise and termed this “chronotropic index.” This calculation accounts for the effects of age, physical fitness and resting heart rate thus could also be used in this study to assess the accuracy of chronotropic incompetence.

One limitation is that in everyday practice this would be difficult to implement since many patients fail to exercise into the second stage of the protocol but could still serve as a useful tool in reporting prognosis. A low value for the chronotropic index ratio is <0.8 . They were unable to perform outcome analyses on women due the low number of events. A gap in the literature is clearly defined here as the lack of data on women who smoke and the incidence of chronotropic incompetence. In this prospective cohort, smokers had a higher rate of failure to achieve target heart rate compared to the nonsmokers and had a higher incidence of low chronotropic index. These findings persisted even after adjustments were made for confounders. A limitation of this study was a primarily white cohort therefore the results may not be generalizable to other populations. A second limitation was that the stress test was ended at target heart rate rather than continued until symptom-limited which was previously found to correlate strongly with coronary events (Ellestad, 1996).

A similar study was conducted on a cardiovascularly healthy cohort of individuals taken from the Lipid Research Clinics Prevalence Study. Cole and colleagues (2000) evaluated heart rate recovery following submaximal exercise testing as a predictor of mortality in this cohort. Adults (n=5,234) without evidence for cardiovascular disease were included. In comparison to the other studies, Cole and colleagues defined abnormal heart-rate recovery as the change from max to the value at two minutes into recovery. They were unable to use this value to compare with previous studies. Even with this finding, the study is valuable to the literature in that it offers a new perspective on heart rate-recovery data.

The primary new information reported from the above study was that heart-rate recovery values may be used as a clinically relevant prediction of risk for patients completing an exercise screening test. This study also found a similar relationship between abnormal heart-rate recovery and fitness levels. A possible use of this value could be for physicians to evaluate how much exercise a patient may actually be performing. A limitation is that the collection of the heart rate occurred at two minutes, therefore the data could not be compared to their previous study. The study does support the use of heart-rate recovery data in the interpretation of exercise testing. The advantage is that heart-rate recovery is simple to measure and is emerging as a powerful predictor of mortality.

Myers and colleagues (2007) conducted a prospective cohort study at the Veterans Affairs Palo Alto Medical Center between 1992 and 2002. The study consisted of male veterans (n=1,910) who were referred for symptom-limited exercise testing. The

primary aim of the study was to compare the predictive value of cardiovascular mortality of chronotropic response and heart rate recovery. This study utilized the heart rate value at two minutes into recovery and defined abnormal as failure to decrease greater than 22 beats within the two minutes of recovery. Chronotropic incompetence was identified as failure to achieve 80 percent of heart rate reserve. Interestingly, results indicated that chronotropic incompetence was the strongest predictor of mortality rather than heart-rate recovery, as typically found in other research studies. They also found that the presence of both chronotropic incompetence and abnormal heart-rate recovery was an even stronger predictor of cardiovascular death with a relative risk of 4.2 when compared to these two values being normal (Myers et al., 2007).

Limitations of this study included a solely male cohort, thus the findings cannot be generalized to women. They report the lack of using the chronotropic index to evaluate chronotropic response as a limitation but this value is not always applicable due to the necessity of reaching the second stage of the Bruce protocol. A final limitation was that they defined abnormal heart-rate recovery at the two minute mark of recovery rather than the one minute mark. The literature more widely supports the use of the one minute value rather than the two minute value as the data can be compared to the large studies using the one minute value.

Another prospective cohort study was conducted by Nishime and colleagues (2000), in which heart rate recovery and treadmill exercise score were analyzed as predictors of mortality. Consistent with the previously reported studies, an attenuated heart rate response in recovery has been shown to be an independent predictor of

mortality (Nishime et al., 2000). This study consisted of 9,454 consecutive patients scheduled for a symptom-limited treadmill exercise test. Abnormal heart-rate recovery was present in 20 percent of the patients and an intermediate or high risk Duke Treadmill Score was present in 21 percent of the patients. The Duke Treadmill Score is based on the combination of exercise duration, ST segment changes and the occurrence of angina during the treadmill test. This study is unique from the others in that it incorporated the use of the Duke Treadmill Score for predicting outcomes.

Similar to the previous studies, abnormal heart-rate recovery as well as an intermediate-high risk treadmill score were predictive of death however there was no interaction between these two predictors. The data from this study may be compared to previous data since they used the one minute heart rate value and set an abnormal value at 12 beats per minute. Chronotropic incompetence was set at failure to achieve 80 percent of heart rate reserve at peak exercise calculated by $220 - \text{age} - \text{resting heart rate}$.

These patients were then followed for a median of 5.2 years with the primary endpoint being all-cause mortality. In the follow-up period there were 312 deaths and an abnormal heart-rate recovery was again strongly correlated with death. As the beat per minute decrease in heart rate in the first minute drops lower than 12 the risk for death increases. Once again this study found abnormal heart-rate recovery to be an independent predictor of death (adjusted HR, 2.30; 95% CI, 1.41-3.77; $P < .001$). Another important finding of the study was the lack of difference in the predictive properties of heart rate recovery between the group simply performing the test as a screening and the symptomatic group. This is important because screening asymptomatic individuals is

considered controversial but the data may suggest otherwise as the predictive findings were the same for both groups. The study reports its limitations as being an observational and single site study.

Rationale

Heart-rate recovery values are simple for the physicians to interpret and report to their patients following exercise stress testing. Physicians could utilize these values in reporting results to patients and encouraging smoking cessation. This study was not evaluating mortality, rather an acute bout of exercise and the associations of smoking with abnormal heart rate values. Morbidity and mortality reduction is the ultimate goal in heart disease prevention. This study aimed to find a relationship between smoking and two predictors of morbidity and mortality to consequently provide more information on the necessity of smoking cessation.

Multiple risks have been associated with smoking yet approximately 20% of the adult population continues to smoke. Additional research is needed to establish strategies to assist this 20% to quit smoking. Cost of smoking cessation programs are high and therefore will always be an issue which is why the simple use of a single exercise session to aid in smoking cessation would be so beneficial. The commonly cited issue of weight gain associated with smoking cessation could theoretically be eliminated if exercise, along with an appropriate diet, was used as the cessation tool. In this study the participants urge to smoke and mood was assessed both before and immediately following exercise to examine the effect of the acute bout of exercise as well as to

analyze how these two measures change and compare with each other following an acute bout of exercise.

The POMS and Urge to Smoke questionnaires have been previously studied; however, the majority of the studies have included mostly young people. We will add to the literature by examining a higher age range (30 to 70 years old). Taylor and colleagues (2007), conducted a review on smoking withdrawal symptoms and reported that studies have found an improvement of mood and affect both during and after exercise. The second relevant finding to support the study was the decreased ratings of the participants urge to smoke from pre to post exercise. This study aimed to report similar findings with the two questionnaires.

Methods

Participants

The study was a quasi-experimental group design. The study was conducted as a pilot with the population consisting of 32 consecutive patients scheduled for a symptom-limited treadmill exercise test at North Memorial Heart and Vascular Institute. The participants were obtained from patients referred to the clinic by their physician for this exam. The participants were evaluated for inclusion and exclusion criteria and informed consent was obtained. A total of 49 were approached for the study. Seventeen participants did not participate due to refusal (n=13) and inadequate echocardiographic images (n=4). The remaining 32 participants took part in the study, which consisted of 17 male (n=6 smokers), and 15 female (n=3 smokers) participants. The mean age of the participants was 53 ± 9.56 years.

The indications for stress testing included chest pain or chest discomfort, dyspnea, dyspnea on exertion, palpitations, risk factors (specifically HTN and family history), fatigue, near syncope, bradycardia, abnormal EKG, and diaphoresis. On the day of testing, participants were fasting for two hours, did not smoke four hours prior to testing, did not ingest caffeine for 24 hours, did not take beta or calcium channel blockers for 24 hours, and did not exercise 24 hours before testing.

Inclusion and Exclusion Criteria

Inclusion criteria were men and women ages 30-70 who were performing a stress test for the first time. Exclusion criteria included history of heart failure or valvular abnormalities, having smoked within four hours of the test, took beta blockers within twenty four hours of the test, digitalis use, a resting blood pressure greater than 200/110 mmHg, have a history of myocardial infarction, reperfusion therapy, coronary artery bypass grafting and other criteria that excludes participants from completing a treadmill stress test. These exclusion criteria aimed to reduce confounding factors. Current smokers were defined as smoking at least 10 cigarettes a day.

Measures

A symptom-limited stress test was performed by the participants. Allowing the individual to exercise beyond 85% of heart-rate maximum is what has been done in previous studies, and is strongly correlated to coronary events rather than subjectively ending at 85% of heart rate maximum (Ellestad, 1996). Participants were asked to complete three questionnaires; Urge to Smoke, POMS, the Lipid Research Clinic Physical Activity questionnaire and a demographics sheet. The Urge to Smoke and

POMS questionnaires have been shown to be valid and reliable. Internal consistency of the POMS has a Cronbach alpha rating of 0.63 to 0.96 (McNaire et al., 2003). The POMS has also been correlated with the Functional Assessment of Cancer Therapy scale along with the Psychological Well-Being Scale with a rating of -0.68.

The POMS measures an individual's transient mood using a sixty five item questionnaire that the participant rates the item on a one to five scale of "not at all" to "extremely". This questionnaire identifies six different factors: tension-anxiety, depression-dejection, anger-hostility, fatigue-inertia-vigor-activity, and confusion-bewilderment. Based on these factors, their Total Mood Disturbance (TMD) score was calculated (McNair et al., 1971). The Profile of Mood States assessment will be used in this pilot to assess both smoking and nonsmoking participants' mood before and after exercise. The POMS "Identifies and assesses transient, fluctuating affective mood states," (McNair et al., 1971). The POMS is a 65 item self-report assessment for adults over the age of 18 and takes approximately five to ten minutes to complete. This assessment was originally created in 1971 and has continued to prove valid and reliable among various groups. The assessment items included are easy for participants to understand which aids in the timely completion of the inventory. Participants rate the inventory factors on a five point likert scale from "Not at all" to "Extremely."

The Urge to Smoke questionnaire is a shortened version of the Questionnaire on Smoking Urges (QSU) (Tiffany, Drobles, 1991). When studied, the QSU-Brief demonstrated reliability with a Cronbach alpha rating of 0.97 (Cox, Tiffany & Christen,

2001). This ten question survey assesses urge to smoke using a seven point likert scale from “definitely not” to “definitely”.

Apparatus

The exercise tests were conducted on Mortara Xscribe treadmill and computer systems. Blood pressure was taken manually with a Welch-Allyn sphygmomanometer and a Littman stethoscope. The echocardiographic images were performed on Sequoia ultrasound machines.

Procedure

Upon informed consent, participants recorded demographic information and completed the pre-exercise POMS and Urge to Smoke questionnaires. Then the participant was hooked up to the computer and resting data was collected on each participant including heart rate, blood pressure, resting electrocardiogram (EKG), oxygen saturation, resting echocardiogram and current symptoms if any. The resting echocardiogram was completed once all resting data had been collected. The resting information was presented to the physician prior to starting the exercise portion of the test.

The participant then exercised on the standard Bruce Protocol to at least 85% of predicted heart rate maximum calculated with the equation $220 - \text{age}$ for heart rate maximum. The participants hung onto the siderails of the treadmill throughout the test. They were asked to rate their perceived exertion using the Borg rating of perceived exertion (RPE) scale. When the participant was fatigued and requested to stop they returned to the supine position for the peak echocardiogram pictures for approximately

one minute and continued to lay for the remaining four minutes. Heart rate recovery and blood pressure values were recorded at minutes one through five into recovery and until the EKG and vitals returned to normal. Following five minutes of recovery the participant completed the post-exercise Urge to Smoke and the POMS questionnaires. Upon return to resting values the participant was disconnected from the equipment and their information was given to the physician for review. The participant received a twenty dollar gift card to Target to thank them for their participation.

Human Subjects Approval

Institutional Review Board (IRB) approval was obtained from the University of Minnesota IRB as well as the IRB at North Memorial Medical Center. Patient information was de-identified and all HIPAA policies were followed.

Data Analysis

To examine the effect of a single bout of exercise on heart rate recovery and chronotropic incompetence Pearson's chi-square test was conducted. The independent variable was smoking status and the dependent variables were heart rate recovery and chronotropic incompetence. None of the participants exhibited abnormal heart rate recovery so Pearson's chi-square was not conducted for this variable. To examine the pre-exercise and post-exercise effects on urge to smoke, within-subjects ANOVA was conducted only among the smoking participants. Finally, to examine the pre- and post-exercise effect on the POMS, within-subjects ANOVA was conducted among all participants.

Results

Demographics

Demographic data for the sample is summarized in Table 1. Specifically, a majority of the participants were employed and married. Approximately half of the participants graduated from college or were doing post-graduate work. Over half of the participants had a total annual household income of greater than \$50,000. The percentage of current smokers was roughly eight percent higher than the general population.

Table 1
Demographics

Age (yrs), mean (SD)	53.3 (9.6)
Employed (%)	71.9%
Married (%)	71.9%
Education Level	
- College graduate (or doing post-grad work) (%)	43.7%
- Some college	28.1%
- High School Graduate	18.7%
- < High School Graduate	9.4%
Total annual household income	
> \$50,000 (%)	65.6%
- \$40-50,000	12.5%
- \$30-39,000	6.3%
- \$20-29,000	9.4%
- \$10-19,000	3.1%
- <\$10,000	3.1%
Current Smoker (%)	28.1%

Table 2 summarizes the prevalence of the primary risk factors for CAD broken down by gender and smoking status. The prevalence of diabetes and dyslipidemia was much higher among women smokers. The male participants had a higher rate of family history compared to the women.

Table 2
Coronary Artery Disease Risk Factors by Gender and Smoking Status

Gender	n	Age (yrs), mean (SD)	Family History of CAD (%)	Diabetes (%)	Hypertension (%)	Dyslipidemia (%)
Male - S	6	46.2 (12.3)	50.0%	0.0%	16.7%	33.3%
Male - NS	11	54.7 (9.5)	45.5%	0.0%	45.5%	27.3%
Female - S	3	58.0 (2)	33.3%	33.3%	33.3%	66.7%
Female - NS	12	54.4 (8.3)	25.0%	8.3%	41.7%	41.7%

S = Smoker, NS = Non-smoker

Table 3 summarizes the physical activity level of the participants broken down by gender and smoking status. Very few of the participants fell into the highly active category. The majority of the participants were sedentary in the low active category.

Table 3
Physical Activity Category by Gender and Smoking Status

Gender & Condition	High Active	Moderately Active	Low Active	Very Low Active
Smoking Males	1	2	1	2
Non-Smoking Males	1	0	10	0
Smoking Females	1	1	1	0
Non-Smoking Females	1	4	1	6

Primary Findings

Pearson's chi-square test revealed no significant differences between the two groups for chronotropic incompetence ($p=0.833$). None of the participants exhibited abnormal heart rate recovery. Table 4 summarizes the incidence of chronotropic incompetence by smoking status.

Table 4
Incidence of Chronotropic Incompetence by Smoking Status

Smoking Status	+ Chronotropic Incompetence	- Chronotropic Incompetence
Smokers	1	8
Non-smokers	2	21

The mean value for heart rate recovery among all subjects was 32 beats within the first minute of recovery with a minimum of 13 and maximum of 74 beats. Table 5 summarizes the mean values for heart rate recovery by gender and smoking status. No significant differences were found between smokers and non-smokers.

Table 5
Heart Rate Recovery

Gender & Condition	Mean Heart Rate Recovery (SD)
Male Smoker	34.5 (8.5)
Male Non-smoker	30.7 (10.6)
Female Smoker	27.3 (7.2)
Female Non-smoker	35.2 (15.3)

RPE values were only obtained on 18 of the 32 participants. The mean RPE for all of the participants was 16.1 (SD=2.3). The mean RPE of the smokers was 16.6 (SD=2.9, n=5) and the mean for non-smokers was 15.9 (SD=2.3, n=13). The difference in RPE ratings between the two groups was not statistically significant ($p=0.603$).

Secondary Findings

The within-subjects ANOVA to analyze the Urge to Smoke Questionnaire revealed no significant differences between pre and post exercise urge to smoke among the smoking individuals ($p=0.537$). Table 6 summarizes the mean values for pre and post urge to smoke scores by gender. The male participants had higher scores for pre and post-exercise urge to smoke but this difference was not statistically significant.

Table 6
Urge to Smoke

Gender	Pre-exercise Urge Score (SD)	Post-exercise Urge Score (SD)
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Male (n=6)	31.3 (12.2)	28.5 (8.9)
Female (n=3)	17.3 (6.1)	19.0 (13.9)

The within-subjects ANOVA revealed no significant differences between pre and post POMS scores among all participants ($p=0.517$). When scores were tested among males alone, there were no significant differences ($p=0.407$). There were also no significant differences among the women ($p=0.212$). Table 7 summarizes the mean Total Mood Disturbance values pre and post-exercise.

Table 7
POMS – Total Mood Disturbance (TMD) Score

Gender	Pre-exercise TMD (SD)	Post-exercise TMD (SD)
Male	52.3 (28.7)	56.3 (30.3)
Female	51.0 (27.0)	44.9 (14.3)

Discussion

This study failed to find an effect of smoking status on heart rate recovery and chronotropic incompetence. Previous studies that have found an effect were sufficiently powered to detect differences and included thousands of participants (Cole, et al. 1999). Unfortunately, this pilot was not sufficiently powered to detect significance given the small sample size. None of the participants had an abnormal heart rate recovery which is not surprising given our small sample size and the inclusion of as close to healthy

individuals. This assumption is verified by a study conducted on a larger cohort which indicated that individuals with abnormal heart rate recovery were generally older, had diabetes or hypertension, and had a prior history of myocardial infarction (Vivekananthan et al., 2003).

Three individuals demonstrated chronotropic incompetence, two of which were non-smokers and one a smoker. One of these individuals, a non-smoking male, was taken for immediate coronary angiography and bypass to treat his CAD. This participant's inability to attain heart rate was clearly attributed to his underlying CAD. The incidence of chronotropic incompetence among this small cohort may not be surprising as Myers and colleagues (2007) found chronotropic incompetence to be more predictive of cardiovascular mortality rather than heart rate recovery. As previously stated, the majority of studies found heart rate recovery to be more predictive of cardiovascular mortality however in this study one of the three individuals with chronotropic incompetence did in fact have underlying CAD. The fact that this gentleman required coronary artery bypass grafting does not suggest cardiovascular mortality however a correlation appears to exist between chronotropic incompetence and the existence of atherosclerosis. This is not suggesting that every individual have a coronary angiogram if they are unable to achieve target heart rate during a stress test, rather suggesting that failure to achieve target heart rate is not always simply due to deconditioning. The remaining two participants were a non-smoking female and a smoking female who had no evidence of CAD as the cause of chronotropic incompetence.

One secondary aim of the study was to analyze pre and post urge to smoke among the smoking participants. Again, the study was not powered to detect differences in urge to smoke. The studies examined in the review done by Taylor and colleagues (2007), did not include thousands of participants. The majority of the studies recruited less than 100 participants and were able to detect significant differences in the effect of exercise on urge to smoke. They even found that short duration and low intensity exercise had an effect on urge to smoke. The participants performed a very short bout of exercise in this pilot which was previously shown to be effective in reducing urge to smoke. When compared to the sample sizes of the studies in the review, the ability to detect significant differences would have been possible with only a few more participants. However, similar results may not have been found due to the difference in age of the participants. The average age of the participants in this pilot was approximately 20 to 30 years higher (53 ± 9.56 years) compared to the studies included in the review.

The other secondary analysis of the study was the effect of exercise on mood. No significant differences were found between pre and post Total Mood Disturbance (TMD) scores among all participants. When controlled for gender, the female participant's TMD scores were closer to significance than the male participants. Although significance was not detected, this may suggest that women's mood is more affected by exercise than men's. In the review by Taylor and colleagues (2007), mood was assessed up to 20 minutes after exercise. This study assessed mood less than 10 minutes after exercise. This may have been a factor in the ability to detect the effect of exercise on mood. Another possible factor affecting the participant's mood could have been the reason for having the

stress test. The results of the test were unknown to the patient throughout this process and may have played a role in the way they responded to the questionnaire after exercise. The previous studies were not conducted in an already stressful situation so this could account for the inability to detect differences related to exercise.

The study experienced a few recruitment issues. It was already known that the general population continues to smoke at a rate of 20%. This made it difficult to recruit smoking participants. Another reason was the high refusal rate of female smoking participants who met the criteria for inclusion. Finally, smoking individuals can be difficult to obtain echocardiographic images on requiring them to perform a nuclear stress test instead.

Limitations

As with all of the studies included on heart-rate recovery and chronotropic response, a primary limitation is that these patients are referred for stress testing rather than randomly sampled. However, it is not common practice to refer individuals for a stress test when asymptomatic. Another limitation is the nature of the study in that it was conducted as a pilot. Therefore, the sample size was not large enough to detect significant differences between the groups. A third limitation is that the sample may not be a representative sample in that the participants were patients referred for a stress test at North Memorial Heart and Vascular Institute. The majority of the participants were college graduates, married, and had a total annual income greater than \$50,000. Despite these limitations, the design and results of this pilot can be used to inform future studies that can be adequately powered.

Future Directions

This pilot study could be replicated in the future with a larger population to further examine the relationship between smoking and the heart's ability to respond to exercise. Left ventricular function is another variable that could be incorporated and used to compare groups as it could easily be included from the data gathered during a stress echocardiogram. A study that compares heart-rate recovery and endothelial function as prognostic variables for mortality would also provide beneficial information on whether or not a relationship exists between the incidence of abnormal heart rate recovery and endothelial dysfunction. The results could be used to create another non-invasive test for CAD risk-stratification. Heart rate could also be analyzed in a nonlinear fashion to detect functional differences and abnormalities suggestive of chronic disease among different groups over time. These results may also be used to create an intervention examining the effects of exercise and smoking cessation on heart rate recovery.

Conclusion

Previous studies including larger sample sizes were able to detect significant differences in the effect of exercise on heart rate response variables as well as urge to smoke and mood. Our study was unable to detect significance in this smaller sample. Further research is needed to examine the effect of exercise on these variables. Exercise could be a useful tool in risk factor reduction and primary prevention of heart disease.

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Appendices

Appendix A

Protocol

- Participant past medical history compiled and recorded on exam sheet
 - Participant called 48 hours prior to appointment
 - Instructions given:
 - NPO 6 hours prior to appointment
 - No caffeine, decaf, chocolate, or alcohol for 24 hours
 - No smoking at least 4 hours prior
 - Beta-blockers, Calcium Channel blockers, Alpha-Beta blockers, Nitrates, Anti-arrhythmics held for 24 hours
 - Current medications recorded, if any
- Participant checks in for appointment at front desk
- Participant brought back to exam room – informed consent signed
- Surveys and exercise test explained – questions answered
 - Participant prep verified – NPO, no caffeine, no smoking, no meds
- Surveys completed
 - Demographic information completed
 - POMS Survey
 - Urge to Smoke Questionnaire
 - Lipid Research Clinics Physical Activity Questionnaire
- Participant prepped and hooked up to 12-lead ECG monitor
 - Resting blood pressure taken
 - Oxygen saturation recorded
 - Heart and lung sounds examined
 - Resting ECG printed
- Resting echocardiogram completed
- Test presented to physician and permission to begin received from physician
- Participant begins walking on the BRUCE protocol
 - 3 minute stages
 - Blood pressure measured each stage
 - Rating of Perceived Exertion obtained each stage
- Participant exercises until they must stop
 - 85% of heart rate max is desired
- Participant requests to stop exercising or other reason for stopping (> 2 mm horizontal or down-sloping ST segment depression, cardiac symptoms necessitating termination, abnormal blood pressure response >230/120, cardiac arrhythmia)
- Exercise echocardiogram completed and patient remains in the supine position for 5 minutes
 - ECG printed at 1, 2, 3, 4 and 5 minutes into recovery to measure heart-rate recovery
 - ECG monitored until vitals return to resting – at least 5 minutes

- Participant completes Urge to Smoke Questionnaire and POMS after recovery
- Participant unhooked and dismissed
- ECG tracings and paperwork given to physician once completed

Appendix B

Urge to Smoke Scale +

	Definitely Not				Possibly				Definitely					
1.	<input type="checkbox"/>	1	<input type="checkbox"/>	2	<input type="checkbox"/>	3	<input type="checkbox"/>	4	<input type="checkbox"/>	5	<input type="checkbox"/>	6	<input type="checkbox"/>	7
If you could smoke freely, would you like a cigarette this minute?														
<hr/>														
2.	<input type="checkbox"/>	1	<input type="checkbox"/>	2	<input type="checkbox"/>	3	<input type="checkbox"/>	4	<input type="checkbox"/>	5	<input type="checkbox"/>	6	<input type="checkbox"/>	7
Do you have an urge for a cigarette right now?														
<hr/>														
3.	<input type="checkbox"/>	1	<input type="checkbox"/>	2	<input type="checkbox"/>	3	<input type="checkbox"/>	4	<input type="checkbox"/>	5	<input type="checkbox"/>	6	<input type="checkbox"/>	7
Do you miss a cigarette?														
<hr/>														
4.	<input type="checkbox"/>	1	<input type="checkbox"/>	2	<input type="checkbox"/>	3	<input type="checkbox"/>	4	<input type="checkbox"/>	5	<input type="checkbox"/>	6	<input type="checkbox"/>	7
I crave a cigarette right now.														
<hr/>														
5.	<input type="checkbox"/>	1	<input type="checkbox"/>	2	<input type="checkbox"/>	3	<input type="checkbox"/>	4	<input type="checkbox"/>	5	<input type="checkbox"/>	6	<input type="checkbox"/>	7
I am going to smoke as soon as possible.														
<hr/>														
6.	<input type="checkbox"/>	1	<input type="checkbox"/>	2	<input type="checkbox"/>	3	<input type="checkbox"/>	4	<input type="checkbox"/>	5	<input type="checkbox"/>	6	<input type="checkbox"/>	7
All I want right now is a cigarette.														
<hr/>														
7.	<input type="checkbox"/>	1	<input type="checkbox"/>	2	<input type="checkbox"/>	3	<input type="checkbox"/>	4	<input type="checkbox"/>	5	<input type="checkbox"/>	6	<input type="checkbox"/>	7
I want to smoke now?														
<hr/>														
8.	<input type="checkbox"/>	1	<input type="checkbox"/>	2	<input type="checkbox"/>	3	<input type="checkbox"/>	4	<input type="checkbox"/>	5	<input type="checkbox"/>	6	<input type="checkbox"/>	7
I have a desire for a cigarette now.														
<hr/>														
9.	<input type="checkbox"/>	1	<input type="checkbox"/>	2	<input type="checkbox"/>	3	<input type="checkbox"/>	4	<input type="checkbox"/>	5	<input type="checkbox"/>	6	<input type="checkbox"/>	7
Nothing would be better than smoking a cigarette right now.														
<hr/>														
10.	<input type="checkbox"/>	1	<input type="checkbox"/>	2	<input type="checkbox"/>	3	<input type="checkbox"/>	4	<input type="checkbox"/>	5	<input type="checkbox"/>	6	<input type="checkbox"/>	7
Smoking a cigarette would be pleasant.														

How many years have you smoked? _____

How many cigarettes do you smoke per day? _____

Appendix C

Profile of Mood States

Subject's Initials _____

Birth date _____

Date _____

Subject Code No. _____

Directions: Describe HOW YOU FEEL RIGHT NOW by checking one space after each of the words listed below:

FEELING	Not at all	A little	Mod.	Quite a bit	Extremely
Friendly	1	2	3	4	5
Tense	1	2	3	4	5
Angry	1	2	3	4	5
Worn Out	1	2	3	4	5
Unhappy	1	2	3	4	5
Clear-headed	1	2	3	4	5
Lively	1	2	3	4	5
Confused	1	2	3	4	5
Sorry for things done	1	2	3	4	5
Shaky	1	2	3	4	5
Listless	1	2	3	4	5
Peeved	1	2	3	4	5
Considerate	1	2	3	4	5
Sad	1	2	3	4	5
Active	1	2	3	4	5
On edge	1	2	3	4	5
Grouchy	1	2	3	4	5
Blue	1	2	3	4	5
Energetic	1	2	3	4	5
Panicky	1	2	3	4	5
Hopeless	1	2	3	4	5
Relaxed	1	2	3	4	5
Unworthy	1	2	3	4	5
Spiteful	1	2	3	4	5
Sympathetic	1	2	3	4	5
Uneasy	1	2	3	4	5
Restless	1	2	3	4	5
Unable to concentrate	1	2	3	4	5
Fatigued	1	2	3	4	5
Helpful	1	2	3	4	5

Annoyed	1	2	3	4	5
Discouraged	1	2	3	4	5
Resentful	1	2	3	4	5
Nervous	1	2	3	4	5
Lonely	1	2	3	4	5
Miserable	1	2	3	4	5
Muddled	1	2	3	4	5
Cheerful	1	2	3	4	5
Bitter	1	2	3	4	5
Exhausted	1	2	3	4	5
Anxious	1	2	3	4	5
Ready to fight	1	2	3	4	5
Good-natured	1	2	3	4	5
Gloomy	1	2	3	4	5
Desperate	1	2	3	4	5
Sluggish	1	2	3	4	5
Rebellious	1	2	3	4	5
Helpless	1	2	3	4	5
Weary	1	2	3	4	5
Bewildered	1	2	3	4	5
Alert	1	2	3	4	5
Deceived	1	2	3	4	5
Furious	1	2	3	4	5
Effacious	1	2	3	4	5
Trusting	1	2	3	4	5
Full of pep	1	2	3	4	5
Bad-tempered	1	2	3	4	5
Worthless	1	2	3	4	5
Forgetful	1	2	3	4	5
Carefree	1	2	3	4	5
Terrified	1	2	3	4	5
Guilty	1	2	3	4	5
Vigorous	1	2	3	4	5
Uncertain about things	1	2	3	4	5
Bushed	1	2	3	4	5