OBJECTIVELY MEASURED PHYSICAL ACTIVITY LEVELS AND THEIR RELATIONSHIP TO PHYSICAL FITNESS/FUNCTION IN HEART FAILURE PATIENTS

BY

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DEDICATION

I would like to dedicate this thesis to my loving and supportive parents, Karen and David Goodman. Both of you have taught me to be who I am today, and for that I am forever grateful. All that you both have sacrificed for me is beyond words. The life lessons I have learned by having you two as my parents are gifts from God. I know that a simple thank you is not enough for all that you two have done for me, and I hope that I can repay a small portion of what you both have done for me as we continue down this road called life.
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LIST OF ABBREVIATIONS

6MW: Six-Minute Walk Distance

6MWT: Six-Minute Walk Test

ACE – inhibitors: Angiotension-Converting Enzyme - inhibitors

ACSM: American College of Sports Medicine

ALVD: Asyptomatic Left Ventricular Dysfunction

AS: Activity Score

a-vO$_2$ difference: Arterial-Venous Oxygen Difference

BMI: Body Mass Index

BNP: Brain Natriuric Peptide

bpm: Beats per Minute

BRFSS: Behavioral Risk Factor Surveillance System

CAD: Coronary Artery Disease

CDC: Center for Disease Control and Prevention

CF: Cystic Fibrosis

CHAMPS: Community Health Activities Model Program for Seniors

CLIP: Cooperative Lifestyle Intervention Program

CO: Cardiac Output

COPD: Chronic Obstructive Pulmonary Disease

CPET: Cardiopulmonary Exercise Test

CRC: Colorectal Cancer

CRP: Cardiac Rehabilitation Program

CVD: Cardiovascular Disease
DEE: Daily Energy Expenditure
DEXA: Dual Energy X-ray Absorptiometry
EDV: End-Diastolic Volume
EE: Energy Expenditure
EF%: Ejection Fraction
ESV: End-Systolic Volume
G: Gravitational Constant
HCS: Healthy Control Subject
HF: Heart Failure
HF-ACTION: Heart Failure and A Controlled Trial Investigating Outcomes of exercise Training
HFpEF: Heart Failure with a Preserved Ejection Fraction
HFrEF: Heart Failure with a Reduced Ejection Fraction
HR: Heart Rate
HTN: Hypertension
Hz: Hertz
IADL: Instrumental Activities of Daily Living
IPAQ: International Physical Activity Questionnaire
kcal: kilocalorie
kg: Kilogram
LPA: Light Physical Activity
LV: Left Ventricle
LVEF: Left Ventricular Ejection Fraction
m: Meters
max: Maximum
MET: Metabolic Equivalent
MI: Myocardial Infarction
min: Minimum
MLHF: Minnesota – Living with Heart Failure Quality of Life Questionnaire
mmHg: Millimeters of Mercury
MPA: Moderate Physical Activity
MVPA: Moderate-Vigorous Physical Activity
NHANES: National Health and Nutrition Examination Survey
NHW: Non-Hispanic White
NYHA: New York Heart Association
OR: Odds Ratio
PA: Physical Activity
PAAS: Physical Activity Analysis Software
PAD: Peripheral Artery Disease
PADL: Personal Activities of Daily Living
PAEE: Physical Activity Energy Expenditure
PARIS: Prospective Aerobic Reconditioning Intervention Study
PC: Computer
PCA: Principal Components Factors Analysis
PLP: Power Leg Press
QOL: Quality of Life
r: Correlation
RPE: Rating of Perceived Exertion
SD: Standard Deviation
SECRET: Study of the Effects of Caloric Restriction and Exercise Training
SEE: Standard Error of the Estimate
Slope: VE/VCO2 Slope
SPSS: Statistical Package for the Social Sciences
SV: Stroke Volume
TEE: Total Energy Expenditure
US: United States
VAT: Ventilatory Anaerobic Threshold
VO_{2} max: Maximum Oxygen Consumption
VO_{2} peak: Peak Oxygen Consumption
VPA: Vigorous Physical Activity
vs: Versus
WFUBMC: Wake Forest University Baptist Medical Center
yrs.: Years
ABSTRACT

Alesia Goodman

OBJECTIVELY MEASURED PHYSICAL ACTIVITY LEVELS AND THEIR RELATIONSHIP TO PHYSICAL FITNESS/FUNCTION IN HEART FAILURE PATIENTS

Thesis under the direction of Peter H. Brubaker, Ph.D., Department of Health and Exercise Science

PURPOSE: To describe levels of physical activity (PA) in those with heart failure and a preserved ejection fraction (HFpEF), examine the relationship of PA levels to other physical fitness/functional measures, and determine if there are significant differences between objectively measured PA levels and well-established prognostic measures in this population.

METHODS: Subjects were assessed at baseline of a RCT examining the effects of an exercise and/or weight loss intervention in older HFpEF patients. Inclusion for the RCT included: a HF Clinical Score of > 3, a normal ejection fraction (> 50%), a BMI of >30 kg/m², and > 60 years of age. Peak oxygen consumption (VO₂ peak) was obtained from a maximal effort exercise test on a motorized treadmill. Six-minute walk test was completed in a marked hallway using standard procedures. A uniaxial accelerometer (Lifecorder) was worn for 7 continuous days, and evaluated for adequate wear time and days. The average steps/day, physical activity energy expenditure (PAEE) in kcal/min, minutes of light (LPA) and moderate-vigorous physical activity (MVPA) were determined for each participant.

RESULTS: The 36 HFpEF subjects included in this study were older (mean age 68 yrs), mostly female (81%), and overweight/obese (mean BMI of 40.2 kg/m²). The only variables that were significantly different between males and females were % fat, % lean
body mass, leg press power, ejection fraction, and VO2 peak. No significant differences were seen between males and females for any of the PA measures. The average steps/day, PAEE, LPA, and MVPA were 3,475.0 ±1,303.4, 139.9 ± 58.6, 30.5 ± 11.1, and 8.8 ± 5.8 respectively. The 6-minute walk distance was significantly correlated with steps/day, PAEE, LPA, and MVPA (r = 0.52, 0.35, 0.45, and 0.38 respectively), and VO2 peak was significantly correlated with steps/day and LPA (r = 0.44 and 0.49 respectively). After prognostic clinical measures were dichotomized based on established criteria, the only significant difference was a greater number of steps/day for patients with a VO2 peak > 14 ml·kg·min⁻¹.

CONCLUSION: These older, overweight, and mostly female HFpEF patients have very low levels of PA and are comparable to other chronic disease populations. The moderate correlations observed between physical fitness (VO2 peak and 6MW) and PA measures suggest that current levels only partially explain the functional differences observed in HFpEF patients. Finally, other than steps/day and VO2 peak, PA levels are not significantly different when compared on well-established dichotomous prognostic measures. Future studies should focus on the change in PA and change in physical fitness/function measures after exercise and/or weight loss interventions in this population.
Overview of Heart Failure

Epidemiology of Heart Failure.

Chronic heart failure (HF) affects 5.8 million American adults, causing over one million hospitalizations per year and more than 282,000 deaths per year. The total cost of managing HF in 2010 is projected to reach $39.2 billion dollars (89). Over the past 25 years, HF is the only cardiovascular disease that has increased in prevalence, incidence, hospitalization rate, total burden of mortality, and cost (55, 63). The prevalence of HF in men and women ages 40-59 is 3.3 percent with the prevalence increasing to 27.5 percent in women and men over the age of 80 (89). The overall risk of developing HF, across the lifespan, of both men and women is 20 percent (90). The incidence of HF for 2006, in those over the age of 45, was 670,000 new cases per year thus adding to the prevalence rate over time (89). The astounding increase in incidence and prevalence rates over the past decades has been a result of an increase in life-expectancy and lower death rates from cardiovascular and other diseases and secondary improvements in the medical field. Of a greater concern, there are an estimated 77.2 million new cases of HF projected for 2040 (116). Despite improvements in technology, a better understanding of HF pathology, and improved medical treatments, the incidence of HF is projected to increase and will continue to be a major public health concern (55, 63).

Risk Factors for Heart Failure.

There are many risk factors associated with developing HF. Viral and idiopathic cardiomyopathy as well as valvular heart disease can result in HF, but are not very
common in the US. The most common causes of HF in the US are coronary artery disease (CAD), hypertension (HTN), and diabetes (90). According to 2010 statistics, HTN was a major risk factor for developing HF and it was found that 75% of HF patients have HTN (> 140/90 mmHg) (89). The Framingham Heart Study was conducted from 1971-1996 to evaluate potential risk factors for CAD (90, 100) and has provided important information regarding the development of HF. Framingham participants, free of HF at baseline, were followed to determine overall lifetime risk for developing HF and potential risk factors for HF. This research determined that the overall lifetime risk for developing HF over the age of 40 was 21 percent for males and 20.3 percent for females. Hypertension increased the lifetime risk of developing HF by two-fold in those with blood pressures at or above 160/100 mmHg compared to those with blood pressure below 140/90 mmHg. The presence of a previous myocardial infarction (MI) increased the lifetime risk of developing HF in persons over the age of 40 (90). These results from the Framingham Heart Study demonstrated that a history of HTN or MI significantly increases the risk for developing HF (90).

Bibbins-Domingo et al. (23) evaluated the risk factors of HF in 2391 postmenopausal women with coronary artery disease from 1993-2006. These investigators found diabetes to be the strongest predictor for the development of HF in these postmenopausal women. Women with diabetes and no additional risk factors for CAD had a 3% incidence of HF; however, women with diabetes and ≥ 3 risk factors for CAD had an 8.2% incidence of HF (23). After adjusting for possible covariates, those with diabetes and a fasting blood glucose of > 300 mg/dL had three times the risk of developing HF compared to those with controlled diabetes and fasting blood glucose
levels of 80-150 mg/dL (23). Research has also found that obesity (BMI ≥ 30 kg/m²) is associated with an increased risk of developing HF (76). The Physician’s Health Study (76) evaluated 21,094 men (mean age 53 years) with no CAD history. After adjusting for baseline variables of HTN, diabetes, and hypercholesterolemia, the relative risk for developing HF decreased from 3.38 to 2.80 in those that were obese compared to the lean men (RR = 1.49) (76). The Physician’s Health Study determined that HTN, diabetes, and hypercholesterolemia are responsible for a 24.4% increase in the risk of developing HF in obese individuals (76).

The aforementioned risk factors for HF can be changed by altering one’s lifestyle; however, age is a risk factor for HF that cannot be changed over time. The development of HF has been found to be related to an increase in age (62, 73, 75, 100, 126) The Framingham Heart Study followed 5,209 males and females between ages 30-62 to follow their development of cardiovascular disease (100). One study concluded that age is a major risk factor for HF development. By the age of 60, the incidence rate of CHF development among males was five times the incidence rate of those between 40-49 years old. The number of HF cases that developed in the males was 81, and the women developed 61 cases of HF. Women also demonstrate an increased incidence rate with an increase in age, however, the incidence rate generally is found to be higher in males than females. The rate/1,000/year was 2.3 in males compared to 1.4 in females (100).

Another study, looking at the Framingham Heart Study, followed 9,405 adults from 1948-1988, and found that the average age of HF development was 70.0 years. Again, the incidence rate of developing HF rose considerably as age increased. The incidence rate for men between the ages of 50-59 was 3 cases/1,000 and increased to 27
cases/1,000 for those between the ages of 80-89. An increase in the incidence rate for females was also noted, and the incidence rate was 2 cases/1,000 for those between 50-59 years and increased to 22 cases/1,000 for those between 80-89 years of age (62) thus demonstrating that age has an effect on the heart’s morphology within the left ventricle (LV) as a result of the pathophysiological “syndrome” of HF.

**Pathophysiology of Heart Failure.**

Heart failure is defined as the inability of the heart to provide adequate blood perfusion to the body. The reduced cardiac output (CO) from the heart results in a number of pathphysiological responses that further exacerbate the symptoms of heart failure. Thus, heart failure is often described as a “syndrome” (see Figure 1) (66, 70, 110).

Due to a lack of blood flow to the lungs, pulmonary mismatching occurs and the patient commonly experiences fatigue and shortness of breath on exertion. The kidneys are also affected by the lack of blood flow and subsequently the renin-angiotensin-aldosterone system and the sympathetic nervous system are activated. As a result of the neurohormonal activation of the renin-angiotensin-aldosterone system, the peripheral arteries undergo vasoconstriction and increase the afterload experienced by the heart. However, brain natriuretic peptide (BNP) produced by the ventricular myocardium attempts to counteract the physiological effects of angiotensin II and aldosterone, and cause vasodilatation of the arterioles. In addition, there is also a decrease in blood flow to the skeletal muscle, resulting from the activation of the sympathetic nervous system and neurohormones, thus impairing the vasodilatatory capacity of the arterioles in the active
skeletal muscle. The inability to decrease vascular resistance of the skeletal muscle is a major contributor to exercise intolerance in the HF population.

Figure 1. Pathophysiologic Syndrome of Heart Failure

Furthermore, HF is a progressive disease where pathologic remodeling of the heart further weakens the myocardium. As a result, the contractile function of the ventricles decreases and further impairs ejection fraction (26, 30, 55, 70). Due to the myriad of physiological changes presented above, the patient will ultimately present with exercise intolerance as well as fatigue and/or dyspnea on exertion (30, 77). The most common symptom among HF patients is exercise intolerance (26, 30, 65, 77, 120).

**Acute Exercise Responses in Heart Failure.**

Exercise intolerance in HF patients, best quantified by VO\(_2\) peak, can be evaluated by the Fick equation where the VO\(_2\) peak = cardiac output x arterial-venous
oxygen difference (a-vO$_2$ difference). The Fick equation evaluates the contribution of both central and peripheral hemodynamics to the VO$_2$ peak. In normal subjects, cardiac output (CO) increases 4-6 fold from resting to peak exertion due to increases in both heart rate (HR) and stroke volume (SV). During an acute bout of exercise in normal subjects, SV increases 20-50% due to an increase in end-diastolic volume (EDV), subsequent to an increase in venous return, and a decrease in end-systolic volume (ESV) due to increased myocardial contractility. In HF patients, the heart is inefficient and the CO achieved is $< 50\%$ than that achieved by normal healthy subjects. Thus decreased cardiac output is due to a decrease in SV and often an inadequate response in HR. A recent study has shown that chronotropic incompetence occurs in 20 – 25$\%$ of HF patients (35). In HF, SV fails to increase to normal levels due to inability of the LV to relax and/or contract normally.

In addition to changes in central hemodynamics, there are also changes in peripheral hemodynamics in HF patients. These changes in the periphery do not allow for a sufficient widening of the a-VO$_2$ difference and thus, adequate oxygen delivery to the working skeletal muscles diminishes over time (77). In HF, the skeletal muscles are inefficient at extracting oxygen from the blood and thus there is decreased oxygen supply to the working muscle. Subsequently, there is a decrease in oxidative enzymes and an increase in anaerobic enzymes in the skeletal muscle. The skeletal muscle adapts to the poor perfusion by decreasing the number and size of Type I muscle fibers and a decrease in mitochondria volume and density. Vasoconstriction is also present due to increased endothelial dysfunction and vasomotor activity (30). While a-vO$_2$ difference increases
three fold, from rest to peak exertion, in normal subjects, in HF patients, the a-vO$_2$

difference only increases two fold from rest to peak exertion (71).

*Signs/Symptoms, Diagnosis, and Treatment of Heart Failure.*

The main signs and symptoms of HF are dyspnea, peripheral and/or pulmonary edema, and excessive fatigue, particularly with exertion. It should be noted that these symptoms are not “diagnostic” of HF as they can be symptoms for other medical conditions as well. Thus, the diagnosis of HF is difficult due to the overlap of symptoms with other medical conditions, and is often done by the exclusion of other medical conditions over a period of time due to the continued presence of symptoms despite treatment for other medical conditions (46, 70, 107). Heart failure patients are often categorized into subgroups based on functional capacity and symptoms using the New York Heart Association (NYHA) and/or the American College of Cardiology Scale (Appendices A and B).

Patients that present with HF undergo a multitude of clinical, physical, and diagnostic assessments. Cardiac function is commonly evaluated by measuring ejection fraction (EF%), which is calculated by stroke volume (SV)/end-diastolic volume (EDV). A normal EF% is generally defined between 55 - 65 percent. Recent investigations have determined that HF signs/symptoms occur when there is significant systolic and/or diastolic dysfunction of the left ventricle (LV). As a result of the aging process and increased angiotensin II production, the heart undergoes morphological changes that alter its ability to function properly. Patients that present with signs and symptoms of HF and considerable LV dysfunction, quantified as a reduced EF% of < 35 percent, are categorized as having HF with a reduced EF% (HFrEF). The aging HFrEF heart is
characterized by an enlarged LV size and poor LV contractility. Patients can also present with signs and symptoms of HF, but with a preserved or normal EF% (40% or greater) and are thus categorized as having HF with a preserved EF% (HFrEF). The aging HFrEF heart is characterized as having normal LV systolic function, but lower EDV due to reduced LV filling, impaired LV relaxation due to a lowered filling capability, and concentric hypertrophy in the LV resulting in a thick and stiffened heart. Impaired filling in HFrEF results in a reduced cardiac output and stroke volume that can also provoke the HF syndrome (26, 30, 70).

Ejection fraction, LV size, and LV contractility are used to evaluate the HF patient and can categorize the patient as having either HFrEF or HFrEF. The most useful tool for evaluating HF is the echocardiogram, which can be used to determine systolic or diastolic dysfunction. The standard 2-D echocardiogram can evaluate EF%, LV wall diameter and thickness, and wall motion (46, 55, 65). Moreover, the cardiac echo can be used to evaluate the LV filling chamber. Other assessments used to determine the presence and/or severity of LV dysfunction including nuclear myocardial perfusion imaging, positron-emission tomography, cardiac magnetic resonance imaging, pulmonary function tests, exercise tests to evaluate peak oxygen consumption, and cardiac catheterization (46, 55). These tests can be used to more definitively determine if the patient has HFrEF or HFrEF and if the former is due to ischemic versus non-ischemic causes. Ischemic HF is generally caused due to lack of blood flow to the myocardium as a result of coronary artery disease (CAD) or previous myocardial infarction and/or chronic myocardial ischemia. In contrast, non-ischemic causes of HF are usually the
result of heart valve dysfunction or infections of viral origin that affect the myocardium and/or myocytes (30).

Treatment for HF generally begins after the patient presents with signs, symptoms, or risk factors. However, it is preferred to begin treatment earlier in those with risk factors for developing HF. The American College of Cardiology scale (Appendix B) can be used to categorize patients in stage A-D. Patients in stage A do not have overt HF, thus the main goal of treatment at this point is to control the risk factors such as HTN, CAD, and diabetes mellitus to delay the incidence of future cardiovascular events. Successfully reducing blood pressure reduces the development of left ventricular hypertrophy as well as reducing cardiovascular mortality, lowering HF incidence rates by 30-50% (70, 86, 89). Patients with HTN can be prescribed ACE-inhibitors or angiotensin-receptor blockers to delay or prevent LV remodeling and disease progression (70). Patients that are already diagnosed with HF due to the presence of signs/symptoms are categorized as stage B, C, or D. The primary objectives for these patients are to slow the disease progression, diminish symptom severity, manage risk factors, and to increase life expectancy. These goals can be met by altering the lifestyle of the patient including lowering sodium intake, tracking body weight closely, and adhering to prescribed medications. Medications, such as ACE-inhibitors, beta blockers, and diuretics, are commonly prescribed to patients in stages B-D. Beta blockers are used to treat HTN, angina, and arrhythmias as well as to diminish the harmful effects of the sympathetic nervous system. Beta blockers have been shown to positively alter mortality, morbidity, LV remodeling, quality of life, hospital admission rates, and risk of sudden death in HF patients. The life-threatening ventricular arrhythmias that often occur in HF patients can
be managed with an implantable cardioverter defibrillator or pacemaker to control both heart rate and rhythm. Myocardial revascularization, either with bypass or angioplasty/stent, can also be beneficial to this HF population that suffers from CAD. Although extensive research over the past three decades has consistently demonstrated that exercise/PA is beneficial for stable HF patients, many guidelines do not yet include this potentially beneficial therapy (46, 65).

**Recommendation of Physical Activity**

It has been well documented that physical activity (PA) has numerous benefits and decreases the all-cause mortality rate in all age groups. There are a multitude of benefits associated with being physically active and exercise training can be utilized for both the primary and secondary prevention of a variety of chronic disease conditions (48). Appropriate amounts of physical activity have been shown to reduce the risk of premature death due to coronary artery disease, type 2 diabetes, metabolic syndrome, colon cancer, breast cancer, and for developing hypertension (64, 83, 88, 117, 130, 140, 141). Physical activity has been shown to benefit those already diagnosed with hypertension by lowering blood pressure, decreasing the feelings of depression and anxiety by improving mental health, mood, and quality of life as well as strengthening bones, muscles, and joints. Exercise can also benefit those that are overweight or obese by helping one to lose weight and lower body fat (3, 8).

The Centers for Disease Control and Prevention (CDC) states that men and women of all ages will show benefits from daily physical activity. The CDC and the American College of Sports Medicine (ACSM) recommend that adults participate in
aerobic exercise, such as 30 minutes of PA at a moderate intensity (i.e. brisk walking or cycling at less than 10 miles per hour) or 15-20 minutes of PA at a vigorous intensity (i.e. jogging, running, swimming laps, cycling at greater than 10 miles per hour) per day to reduce their risk of developing CVD (118). The United States Department of Health and Human Services suggests that the general population can significantly lower their risk for developing CVD and maintain overall health by accumulating at least 150 minutes of PA per week at a moderate intensity. Furthermore, research indicates that there is a dose-response relationship and adults can gain even more benefit if they increase PA levels to > 150 minutes/week. If weight loss is the primary goal, it is recommended that the individual should increase the total duration to at least 180 minutes/week of moderate intensity activity. A combination of PA as well as a reduction in caloric intake should result in weight reduction. It is recommended that some individuals may need to complete at least 300 minutes of PA per week to effectively lose weight (5). The Surgeon General’s Report on Physical Activity and Health recommends that participation in regular, moderate PA for at least 30 minutes/day that results in a physical activity energy expenditure of 150 kcals/day or 1000 kcals/week can result in overall health benefits (2).

While PA guidelines are well-established, most Americans do not fulfill these PA guidelines. In 2008, the National Health Interview Survey reported that only 14% of Americans over the age of 18 participated in vigorous leisure-time PA three to four times per week and only 11.5% of adults participated in vigorous leisure-time PA five or more times per week. It was also determined through the same survey that 36% of all adults were sedentary during their leisure-time, and that 59% of U.S. adults did no vigorous PA during their leisure-time (7). Furthermore, the National Health and Nutrition Examination
Survey (NHANES) found that only 5% of the adult population met the recommendation of at least 30 minutes/day of moderate PA (143).

While there are many benefits associated with PA in healthy individuals, there are also concerns about the potential risk for untoward events such as a heart attack and/or sudden cardiac death. Research suggests that heavy physical exertion is associated with acute myocardial infarctions (MI) and/or sudden cardiac death. Furthermore, it appears that there is a hazard period over which persons are most at risk for adverse events during or within one hour of completing heavy physical exertion (49, 105, 155). Mittleman et al. (105) found that 54% of those with an MI had taken part in heavy physical exertion within the previous hour prior to the cardiac event. Of those, 82% experienced some symptoms during this period of heavy physical exertion (105). In addition, Mittleman et al. and Willich et al. (105, 155) found that habitually sedentary individuals were most at risk for MI during the hazard period associated with physical exertion. The overall risk of sudden death in apparently healthy individuals varies from 0.01-0.20 cases per 10,000 hours (49). The risk of death is quantified as 0.03 cases per 10,000 hours in individuals that had been properly screened, as well as supervised, by competent medical staff (49). Therefore, the risk of cardiac complication and/or death throughout exercise is low with proper medical screening, well-qualified exercise leaders, under medical supervision, and with the availability of emergency equipment on site. Prescreening adults by reviewing their medical history is especially important in those beginning a new exercise program as well as those with risk factors for CVD and/or known cardiovascular history (49).

When looking at the risk of untoward events during exercise program in secondary prevention (i.e. cardiac rehabilitation programs), Haskell (59) found that MIs
are the most common cardiovascular complication, but there was just 1 MI per 32,593 patient hours of exercise. The overall risk of a cardiovascular complications during a cardiac rehabilitation exercise session is 0.45 per 10,000 hours (49, 59). The most current estimate of the cardiovascular complication risk during cardiac rehab exercise program is 0.08-0.15 cases per 10,000 hours (49). While there is some risk associated with exercise, regular physical activity helps reduce an individual’s risk of sudden cardiac death.

*Methods of Quantifying Physical Activity.*

Physical activity is a complex and multidimensional activity and thus an exact measure of PA is difficult to obtain. Physical activity is defined as a bodily movement that is resultant from skeletal muscle movement. Physical activity can be quantified in terms of intensity, frequency, type, and duration of activity. Subjective and objective measures have been used in research settings to measure minutes of light (LPA), moderate (MPA), and vigorous PA (VPA) (85). Furthermore, energy expenditure (EE) is used to quantify the amount of energy the body must produce to maintain a specific level of PA. Energy expenditure during physical activity (PAEE) (11-13, 42, 51, 61, 92, 102, 123-125, 136, 144, 154) is quantified in kilocalories (kcal) that occurs with PA (12, 85).

There are a variety of subjective measures that can be used to quantify PA including: logs, surveys, and PA recall/interview. The most commonly used subjective approach to evaluate PA levels is the recall questionnaires. These subjective measures attempt to quantify patterns of PA over a particular time period. The advantage of using one of these subjective measures is that they are relatively inexpensive and can easily assess the PA patterns in a large group. Physical activity diaries provide descriptive
feedback on common daily activities over the timeframe which they were completed. Physical activity questionnaires are easily distributed to a large group, target a particular population or ethnic group, inexpensive, and do not require as much time as PA logs and diaries. Physical activity logs are structured in the form of a checklist of activities that are commonly performed in a certain target population. However, the main drawbacks of PA records, logs, and recalls are that they are very time consuming to the participant as well as the researchers are subject to recall bias. Since epidemiological studies rely on these results to determine PA patterns, it is imperative the methods of data collection result in the least amount of individual bias as possible (85).

Objective measures of PA include doubly labeled water, heart rate monitoring, pedometers, and accelerometers. While the doubly labeled water method is the most accurate way of quantifying total EE, this method cannot evaluate the frequency, intensity, and time of the PA (85), thus has limited application.

Macfarlane et al. (92) found that the heart rate monitor significantly overestimated the average amount of light PA and significantly underestimated the average amount of moderate PA when compared to the International Physical Activity Questionnaire (IPAQ), PA log, pedometer, uniaxial accelerometer, and a triaxial accelerometer. The investigators suggest that these errors in estimation could be due to the percentage cut off points used for the heart rate reserve (92).

A pedometer uses “a horizontal spring-suspended lever arm that moves with the vertical acceleration of the hips” to measure PA (39). The user must enter stride length and body mass into the pedometer in order to achieve an estimation of total steps, distance covered, and EE (39). While the pedometer can provide immediate feedback and
potential for self-motivation, there are several important limitations to the pedometer (39, 85). Limitations of pedometers include; inability to quantify non-ambulatory activities, inability to store data for multiple days, inability to quantify the amount of time per day that the device was worn each day, and the inability to quantify the frequency, intensity, or time of the activity (39). As age and body mass index increase, the accuracy of the pedometer decreases (102). Pedometer accuracy is negatively affected by slow walking speeds of < 1.86 miles/hr (102) and running speeds of > 9.94 miles/hr (123). In 2003, Schneider et al. (125) compared ten different pedometers over a 400-meter walk, and found that eight of the pedometers tested were reasonably accurate. Three pedometers, the Kenz-Lifecorder, New Lifestyles-2000, and the Yamax Digiwalker, were the most accurate with values within ± 3% of the actual step counts. The least accurate of the ten pedometers in question were the Sportline 330 and the Omron HJ-105 with values that were ± 37% of the actual step counts (125). In 2004, Schneider et al. (124) studied a total of 13 motion sensors, including the Kenz-Lifecorder accelerometer, and compared the output from the 13 motion sensors to the criterion pedometer, the Yamax SW-200. When the 13 models were compared to the criterion, the mean difference scores significantly underestimated and overestimated step counts by as much as 25% and 45%, respectively. The Kenz-Lifecorder was one of the four models that produced accurate step counts and led these researchers to conclude that the Kenz-Lifecorder was an appropriate tool for assessing PA in research settings (124).

Various studies (16, 18, 40-42, 82) have also determined that the Kenz-Lifecorder is a valid tool for quantifying PA levels in a variety of populations. Kumahara et al. (82) investigated the ability of this device to accurately measure total energy expenditure
(TEE) and PAEE as well as the Lifecorder’s ability to accurately estimate exercise intensity. The correlations between TEE and PAEE, as measured by direct calorimetry and the Lifecorder, respectively, were significant ($r = 0.928$ and $0.564$, respectively). Furthermore, this investigation found a positive relationship between exercise intensity levels as measured by the Lifecorder and MET level ($r^2 = 0.929$) (82). This study also determined that the exercise intensity levels produced by the Lifecorder could be categorized into levels of $< 3.0$, $4.0 – 6.0$, and $> 7.0$ METs, which correlate well with light ($< 3.0$ METs), moderate ($4.0 – 6.0$ METs), and vigorous ($> 7.0$ METs) intensity. Since most PA occurs between 2-8 METs, the Kenz-Lifecorder accelerometer appears to provide an accurate measure of PAEE and evaluating patterns of PA in various populations (16, 18, 40-42, 82).

Quantifying Physical Activity Levels in Different Populations

*Healthy Adults.*

Tudor-Locke and Myers performed a literature review in PA patterns in American children, adults, and older adults in 2001 (147). These researchers determined that children attained a range of 12,000 – 16,000 steps/day while the healthy adult population ranged between 7,000 – 13,000 steps/day (147). Older adults attained a range of 6,000 – 8,500 steps/day (147). The 2003-2004 National Health and Nutrition Examination Survey (NHANES) collected accelerometer data in children (6-11 years), adolescents (12-19 years), and adults (20+ years) (143). Data was collected from 6,329 subjects that had at least 1 day of accelerometer data and 4867 subjects that had accelerometer data for four or more days (143). Age-related decline in activity was seen across all age groups until >
60 years. In addition, those suffering from chronic diseases were less active and ranged between 3,500 – 5,500 steps/day (147).

Tudor-Locke and Bassett have suggested a classification system for evaluating PA levels in adults: “sedentary” = < 5,000 steps/day; “low-active” = 5,000 – 7,499 steps/day; “somewhat active” = 7,500 – 9,999 steps/day; “active” = 10,000-12,499 steps/day; and “highly active” = ≥ 12,500 steps/day (145). While 10,000 steps/day is recommended for normal adults, this goal may not be attainable and/or appropriate for older adults and those with chronic diseases (9).

In 2004, Bassett et al. (19) investigated the impact of modern technology on physical activity levels by investigating the Old Order Amish in southern Ontario, Canada. The relationship between PA levels and chronic disease prevalence was also investigated. The researchers studied 98 Amish adults (18-75 years) by having each participant wear an electronic pedometer for a 7 day period as well as manually record their steps/day at the end of each day. Following the 7 days of wearing the pedometer, they completed an International Physical Activity Questionnaire (IPAQ) that was tailored to the Amish lifestyle. The Amish men took significantly more steps than the Amish female (18,425 vs 14,196 steps/day). Moreover, the Amish men reported 10.0 hours of vigorous PA/week, 42.8 hours of moderate PA/week, and 12.0 hours of walking/week. In contrast, Amish women reported 3.4 hours of vigorous PA/week, 39.2 hours of moderate PA/week, and 5.7 hours of walking/week (19). Twenty five percent of Amish men and 27% of Amish women were overweight (BMI ≥ 25) and 0% of Amish men and 9% of Amish women were classified as obese (BMI ≥ 30) (19). This study indicates the
negative impact modern technology has had on our PA levels as this population is significantly more active than normal American adults.

Elderly.

It has been well-established that regular PA at a moderate to vigorous intensity is beneficial for those of all ages (45, 98). Despite these benefits, not all American adults are sufficiently active. Older adults are often less active than middle-aged adults. The 2009 Behavioral Risk Factor Surveillance System (BRFSS) reported that 59.7% of 65+ year old Americans did not participate in at least 30 minutes of moderate PA, five or more days/week, or at least 20 minutes for three or more days/week (6).

Numerous research studies (24, 31, 44, 91, 101, 137) have evaluated the PA patterns of older adults and conclude that total duration of exercise tends to decrease with age. One study (137) found that the activities that were performed the most in the elderly rural Hispanic and non-Hispanic white (NHW) were walking, general household duties, and gardening. Men were more likely to participate in non-leisure activity and recreational activity than women. While non-leisure activity (housework, childcare, manual labor, etc.) in Hispanic and NHW men slowly decreased with age, both Hispanic and NHW men increased the amount of recreational activity until 63 years or age. Both older Hispanic and NHW women participated in non-leisure activity; however, the NHW women were able to continue non-leisure activity into an older age than their Hispanic counterpart. The NHW women showed a stronger decrease in recreational activity than the Hispanic women. These researchers were able to show that activity levels decreased with an increase in age, regardless of their respected ethnic association (137).
Lord et al. (91) evaluated the walking, postural transition, and sedentary behavior patterns of 56 older, community dwelling adults. The study participants wore an accelerometer for seven days from which four variables were quantified; volume, frequency, intensity, and variability of physical activity patterns. These community dwellers in older adults had an average step count/day of $6,343.2 ± 2,807.1$ (Range: $864.8 – 15,847.1$) (91). Using a principal components factors analysis (PCA), the researchers found that walking (39% variance), sedentary behavior (24.3% variance), and postural transition (16.7% variance) explained 80% of the overall variation seen between the four characteristics of physical activity patterns. The researchers found distinctive qualities, that explained walking and postural transition behaviors, that were of statistical significance. Younger age and lower BMI were significant predictors of physical activity and could account for 36% of the overall variance. A lower BMI accounted for 15% of the overall variance for postural transitions. These researchers concluded that walking, sedentary behavior, and postural transition are different from each other, yet, when used together, these behaviors help to clarify the complexity of daily function in an older community dwelling adult (91). This study also suggests that older adults are “somewhat active” based on the scale produced by Tudor-Locke and Bassett (145).

Bruce et al. (31) studied physically and mentally healthy women between the ages of 70 to 85 and found that 26% of those women did no recreational PA, whereas 39% achieved adequate PA from their recreational activities (31). Of the inactive women, 42.5% did not exercise because of a fear of falling (31). In contrast, twenty-seven percent of the physically active women in this study reported no fear of falling (31). This study suggests that fear of falling is a major barrier to PA in older adults (31).
Meijer et al. (101) quantified mean physical activity level (PAL) in older (mean age: 61 years) versus younger (mean age: 27 years) subjects. Mean physical activity level was calculated as the average daily metabolic rate (ADMR) divided by the basal metabolic rate (BMR). Physical activity was measured using a tri-axial accelerometer. Low intensity activities were defined by movement patterns of $\leq 200$ counts/min such as observed while lying, sitting, or standing ($< 3$ METs), whereas moderate intensity activities (such as walking at 3-6 METs) were quantified as 200-500 counts/min, and high intensity activities were defined as $\geq 500$ counts/min such as seen during domestic activities performed around the house, exercise, and/or sport ($> 6$ METs) (101). The PAL values were significantly correlated with activity counts obtained from the accelerometer ($r = 0.78$) and VO$_2$ max ($r = 0.59$) (101). Moreover, elderly subjects spent a significantly greater amount of time in low intensity activities versus moderate or high intensity activities (101). As expected, younger subjects participated in a significantly greater amount of time in moderate and high intensity activities compared to the elderly (101). Consequently, Meijer et al. (101) concluded that elderly subjects spent a significantly greater amount of time in low intensity activities and did significantly less moderate to high intensity activities than their younger counterparts.

*Overweight/Obese Individuals.*

Various studies have evaluated the PA levels of overweight/obese populations (10, 20, 146, 148) and have collectively found that this population is generally less physically active than their normal weight counterparts. Uthman et al. (148) reviewed 58 studies published within the past 40 years related to PA levels in overweight/obese
persons. Those classified as overweight showed lesser levels of PA compared to those classified as having a normal weight. An inverse relationship was seen between PA level and percent of body fat ($r = -0.5$ to $-0.16$) (148). One study (20) evaluated the steps/day in 1,136 adults using pedometers and found that, on average, adults took 5,117 steps/day. Males were shown to be significantly more active than females (5,340 vs 4,912 steps/day, respectively) and as BMI levels increased, the number of steps/day significantly decreased (Normal = 5,864, Overweight = 5,200, Obese = 4,330 steps/day, respectively) (20).

Adams et al. (10) evaluated PA levels in adults living in South Carolina by extracting data from the Centers for Disease Control and Prevention Behavioral Risk Factor Surveillance System (BRFSS). These researchers dichotomized individually based on BMI into lean ($< 25$ kg/m$^2$), overweight ($25-29.9$ kg/m$^2$), or obese ($\geq 30$ kg/m$^2$). Adams and colleagues, utilizing the PA recommendations of the Centers for Disease Control and Prevention (CDC) and the American College of Sports Medicine (ACSM), defined physical activity as doing $\geq 30$ minutes of PA at a moderate intensity on $\geq 5$ days per week or $\geq 20$ minutes of PA at a vigorous intensity on $\geq 3$ days per week (10, 118). Physical activity levels were dichotomized as inactive (no PA participation), insufficiently active (physically active, but did not meet CDC-ACSM recommendations for PA), or sufficiently active (met CDC-ACSM recommendations for PA) (10, 118). The researchers found that 23.6% of lean, 23.4% of overweight, and 31.9% of obese males were inactive, while 46.9% of lean, 48.8% of overweight, and 48.9% of obese males participated in insufficient activity. In contrast, 29.5% of lean, 27.8% of overweight, and 19.3% of obese were sufficiently active (10). The researchers also looked at the PA
levels of females, and found that 22.4% of lean, 32.3% of overweight, and 41.7% of obese women were inactive, while 48.1% of lean, 44.5% of overweight, and 41.9% of obese women were insufficiently active. Similarly, 29.4% of lean, 23.3% of overweight, and 16.4% of obese women were sufficiently active (10). This study demonstrated that both obese and overweight men and women participated in less leisure-time PA than their normal weight counterparts. It was also found that physical inactivity was more common in obese and overweight men and women than those of a healthy and normal weight. Overall, there was a consistent inverse relationship between levels of PA and BMI level (10).

Tudor-Locke et al. (146) examined the 2005-2006 National Health and Nutrition Examination Survey (NHANES) to evaluate BMI as well as PA and physical inactivity using accelerometer data. The BMI categories were dichotomized into normal (< 25 kg/m²), overweight (25-30 kg/m²), and obese (≥ 30 kg/m²). The normal, overweight, or obese subjects were evaluated to determine if they met the public health recommendation of attaining 30 minutes (or the equivalent in 10 minute intervals) of physical activity per day of moderate or vigorous intensity on 5 or more days per week (146). This study determined that only 3.2% of the adults in the United States met the Surgeon General’s recommendation for physical activity (146). The data also indicated that as BMI increased, a smaller percentage of individuals achieved recommended PA levels. There was also a significant difference in the distribution of a 24-hour period spent in sedentary, light, moderate, and vigorous activities in obese males (486.8 min/day, 142.4 min/day, 22.4 min/day, 3.7 min/day, respectively) versus the overweight (484.2 min/day, 155.4 min/day, 30.7 min/day, 5.3 min/day, respectively) and normal (466.9 min/day, 160.2
min/day, 34.6 min/day, 6 min/day, respectively) males (146). In females, the only significant difference in the distribution of PA during a 24-hour period spent in were in the moderate and vigorous categories for obese (13 min/day, 2.5 min/day) versus the overweight (17.5 min/day, 5.3 min/day) and normal (19.9 min/day, 8.7 min/day, respectively) women (146). This study demonstrates that there are differences in PA levels between men and women, and with BMI, as obese individuals are less active than those classified as normal or overweight (146).

Other Chronic Diseases.

Researchers in Spain evaluated the PA levels in 346 patients with chronic obstructive pulmonary disease (COPD) as well as the determinants of PA in this population (52). These COPD patients completed the Minnesota Leisure Physical Activity Questionnaire to measure PA. The sample of this study was predominantly male (92%), had an average age of 69 ± 9 years, and an average BMI of 26 ± 5 (52). Seventy-eight percent of this COPD population walked daily, 51% were able to participate in stair climbing, and 10% participated in other PA like swimming or dancing (52). Eighty-three percent of the total population participated in some kind of PA, but approximately 20% of the study population were inactive. The average PAEE for the COPD subjects was 109 kcals/day, most of which (98%) was explained by walking (52). Females were more apt to report lower levels of PA including those of an older age, higher socioeconomic status, diagnosed diabetes, a low physical or mental quality of life, and on long-term oxygen therapy use, were more apt to report lower levels of PA (52).
Irwin and colleagues collected data on 1,223 breast cancer survivors that participated in a population-based, multi-center, multi-ethnic prospective cohort study entitled Health, Eating, Activity, and Lifestyle (HEAL) study (67). Physical activity levels were assessed using a PA questionnaire based on the Modifiable Activity Questionnaire that was administered in an interview setting. These participants had an average age of 54.9 ± 10.5 years and a mean BMI of 27.8 ± 6.4 (67). An inverse trend was seen between BMI and duration of MPA, VPA, and sports/recreational activities. Obese breast cancer survivors participated in 28%, 64%, and 49% less MPA, VPA, and sports/recreational activity, respectively, than their lean breast cancer counterparts. Thirty-two percent of the population participated in at least 150 minutes/week of MVPA, however, when household and gardening activities were included in the PA definition the percentage increased to 73%. In regards to race, African-American breast cancer survivors participated in less MPA, VPA, and sports/recreational activity compared to their non-Hispanic white and Hispanic breast cancer survivor counterparts (67).

Using a cross-sectional survey design, Stephenson et al. (133) studied 67 colorectal cancer (CRC) patients (Age: 29 – 84 years; Mean: 60.4) undergoing chemotherapy. Physical activity information was collected through the Godin Leisure Time Exercise Questionnaire (GLTEQ). The PA criteria used in this study was ≥ 30 minutes of moderate PA, 4 or more times per week, an amount that corresponds with ≥ 10 MET hours/week. On average, these patients participated in 49.2 minutes of total PA for at least 4.4 times/week. This overall result can be divided into 11.7 minutes of MPA at least 1.1 times/week, and 5.4 minutes of VPA at least 0.3 times/week. While 12.3% of
this population participated in no PA, 26% of this population were meeting the recommended PA guidelines, even when undergoing chemotherapy (133).

Myers and colleagues (109) evaluated the PA patterns of 47 cardiac transplant patients with an average age of 47 years and an average time post-transplant of 4.8 years. Physical activity patterns were assessed using a questionnaire from the Harvard Alumni study and VO₂ peak was determined through symptom-limited exercise tests on a cycle ergometer. On average, these cardiac transplant patients expended an average of 1100 kcal/week through recreational activity during the past year. Absolute level of VO₂ peak (L·min⁻¹) was significantly correlated with the amount of EE through blocks walked and stairs climbed (r = 0.36) (109). However, VO₂ peak, when expressed as % age-predicted, was significantly related to the VO₂ at the ventilatory threshold (r =0.53), the amount of EE through blocks walked and stairs climbed (r = 0.39), and the amount of recreational activities over the previous year (r = 0.34) (109). Energy expenditure during recreational activities was significantly correlated with VO₂ at ventilatory threshold (r = 0.45) as well as EE through blocks walked and stairs climbed (r = 0.48) (109). This study demonstrates that post-transplant patients are able to maintain an active lifestyle. Researchers also found that physical fitness measures can be correlated to the most recent physical activity measures in cardiac transplant patients, however, these are modest correlations (109).

Several studies (17, 71) have evaluated the PA patterns of cardiac rehabilitation program (CRP) participants. Ayabe et al. (17) evaluated the PA patterns of 53 male and 24 female CRP participants (Age: 46-88 years) using a Kenz-Lifecorder EX accelerometer, which objectively quantified the PAEE and the duration of light (LPA) (< 3 METs), moderate (MPA) (3-6 METs), and vigorous (VPA) PA (> 6 METs) on both
CRP and non-CRP days (17). The average PAEE of the CRP participant was 1,597 ± 846 kcals/week (17). The average minutes of LPA, MPA, and VPA were 375.5 ± 124.5, 125.2 ± 109.4, and 5.7 ± 12.8 per week, respectively. (17). When comparing activity levels on CRP vs non-CRP days, this study determined that PAEE was significantly less on non-CRP days than on CRP days (177 ± 113 vs 299 ± 161 kcals/day) (17). In addition, the amount of LPA, MPA, and VPA were significantly less on non-CRP versus CRP days (49.3 ± 19.3 vs 59.7 ± 19.8; 10.5 ± 14.6 vs 26.4 ± 20.4; 0.4 ± 1.7 vs 1.4 ± 3.0 minutes/day, respectively) (17). These researchers concluded that on CRP days patients were close to the PA recommendation of 30 minutes of MVPA/day, however, on non-CRP days, the levels of PA were less than the recommended (17). Consequently, participation in just three days of CRP without any activity on non-CRP did not produce enough total activity to maintain cardiovascular health (> 1,600 kcals/wk).

Another study (156) evaluated the PA levels, using PA diaries, of 31 phase IV CRP patients that participated in an “active for life” class. This study found that there were no significant changes in PA patterns and fitness levels from phase III to phase IV CRP, even in those that did not attend the “active for life” classes after phase III (156). The estimated leisure-time PA energy expenditure averaged 1376 kcals/week (Range: 128 – 3,380 kcals/week), which is less than the level of PA typically allocated with increased fitness (1,400 kcals/week), decreasing progression of CAD (1,600 kcals/week), or causing regression of CAD (≥ 2,200 kcals/week) (156). In summary, the consensus of the aforementioned studies is that overweight/obese individuals, COPD, cancer, cardiac transplant, and CRP/CAD patients are not as physically active as those without disease, of younger age or of a normal weight. Moreover, numerous studies have reported that
men have significantly higher PA levels than women (2, 10, 17, 20, 31, 52, 67, 71, 101, 109, 133, 143, 146-148, 156).

Heart Failure.

Exercise and PA of a moderate intensity, once was considered contraindicated in those with HF, is becoming a more widely recognized therapy for HF patients. Despite the benefits associated with exercise training, many HF patients do not participate in exercise either because they are limited by symptoms of exercise intolerance, exercise may not be recommended by their health care provider, and/or that there is no reimbursement for the participation of HF patients in cardiac rehabilitation programs. Therefore, this HF population is more likely to be “inactive,” but there are a few studies that have attempted to quantify PA levels, either subjectively or objectively, in HF patients.

Walsh et al. (150) evaluated if exercise performance on a treadmill exercise test or physical activity during the daily life was a better predictor of long-term prognosis in HF patients. These researchers followed 84 subjects between the ages of 46 to 78 years with HF for an average of 710 days (150). The modified Bruce treadmill protocol, as well as a self-paced corridor walk, was utilized to measure exercise capacity. Physical activity during normal daily activity was measured using a Digiwalker pedometer during the same time span. This study indicated the duration of exercise tests were not significant predictors of long-term prognosis (150), but the pedometer scores (> 25,000 steps per week) were significant predictors of prognosis in both the univariate and multivariate analyses. These investigators showed that the reduced daily amount of PA of HF patients is an important measure of prognosis (150).
Oka et al. (113) used a treadmill exercise test to evaluate the relationship between exercise capacity and objective measures of daily PA levels in patients with HF. Vitalog activity monitors were used to evaluate the amount of PA of 45 HF patients (Age: 60±13 years, Mean VO$_2$ peak: 16.8 mL·kg·min$^{-1}$) taken over a two day period. Participants also recorded time spent in each activity, the rating of perceived exertion (RPE) of each activity, and the symptoms experienced (113). Forty-four percent of HF patients in this study participated in walking activity and 42% noted performing domestic activity around the house and yard (113). Of these participants, 50% were classified as NYHA Class I, 40% were NYHA Class II, and 47% were NYHA Class III (113). Daily PA produced a variety of HF symptoms in this HF population including: shortness of breath (SOB) = 22%, fatigue = 16%, and muscle/joint soreness = 13% (113). Forty-six percent of these patients did not report any HF symptoms during daily PA (113). This study suggests that daily PA levels of HF patients are reduced, likely to avoid further exacerbation of HF symptoms. These researchers found that the amount of daily PA performed by HF patients was of a fairly low amount thus these HF patients may gage their daily PA so that their symptoms are not exacerbated by too much activity (113).

Garet et al. (54) utilized a PA questionnaire to assess the PA of 105 patients with congestive HF (Age: 55.8 ± 12.4 years, Mean Left Ventricular Ejection Fraction (LVEF): 33.2 ± 6.1%, BMI: 25.8 ± 4.0 kg/m$^2$, VO$_2$ peak: 17.5 ± 4.8 mL·kg·min$^{-1}$) daily energy expenditure (DEE) in these patients. This study also evaluated the validity, reliability, and sensitivity of a PA questionnaire, as an accurate instrument in looking in HF populations. All participants underwent a symptom-limited exercise test on a cycle ergometer to determine VO$_2$ peak (54). Daily energy expenditure was from the product of
the duration of activity and the energy cost of the activity over a 24-hour period. The DEE and physical activity energy expenditure (PAEE) was adjusted for age, weight, and gender and estimated over a 24-hour period (54). Time at “rest” was quantified by measuring time in activities such as sleeping or periods of no activity (54). PA was dichotomized into 3 different categories: \( \text{PA}_{\text{low}} \) (< 3 METs), \( \text{PA}_{\text{high}} \) (3-5 METs), and \( \text{PA}_{\text{intensive}} \) (> 5 METs) (54). The investigators found there was no significant difference between measured work and the average DEE \((11,127.52 \pm 3,051.83 \text{ kJ/24-hr period})\), PAEE \((4,479.62 \pm 1,731.91 \text{ kJ/24-hr period})\), \( \text{PA}_{\text{low}} \) \((2,509.76 \pm 741.19 \text{ kJ/24-hr period})\), \( \text{PA}_{\text{high}} \) \((1,414.66 \pm 992.19 \text{ kJ/24-hr period})\), and \( \text{PA}_{\text{intensive}} \) \((113.49 \pm 269.79 \text{ kJ/24-hr period})\) \((1 \text{ kJ} = 0.24 \text{ kcals})\) (54). Daily energy expenditure was found to decline with age \((r = 0.71)\) as well as with NYHA functional class (54). The test-retest correlation coefficient for activities between 3-5 METs was 0.82. Indirectly this questionnaire provided a reproducible estimate of DEE (54). This study suggests that HF patients spent most of their energy in \( \text{PA}_{\text{low}} \) (< 3 METs) with less energy devoted to \( \text{PA}_{\text{high}} \) or \( \text{PA}_{\text{intensive}} \) (> 3 METs), probably to avoid the worsening of symptoms (54).

In 2010, Norberg et al. (111) investigated the relationship between levels of fatigue and activities of daily living (ADLs) in a convenience sample of 40 HF patients. Fatigue was subjectively assessed by each participant using the Multidimensional Fatigue Inventory (MFI-20), which included 20 phrases measured on a five-point scale (111). Fatigue was dichotomized over five different categories: general fatigue (Mean: 15.48 ± 3.97), physical fatigue (Mean: 15.10 ± 4.41), reduced activity (Mean: 14.7 ± 4.29), reduced motivation (Mean: 9.0 ± 3.02), and mental fatigue (Mean: 9.5 ± 4.48) (111). The greater the score was out of 20 total points, then the more fatigue experienced by the
Personal ADLs (PADL) such as bathing, dressing, toileting, transfers, and feeding as well as instrumental ADLs (IADL) such as cooking, transportation, shopping, and cleaning were evaluated using the MFI-20. The performance of each PADL and IADL was categorized as either independent (completed task on their own or with the use of an assistive device) or dependent (dependence on another person). Thirty-two participants were able to complete PADLs and IADLs independently, and eight participants were classified as dependent. The association between general fatigue (Median: 16.0, Range: 11.0 - 18.0), physical fatigue (Median: 14.0, Range: 11.0 - 18.75), and reduced activity (Median: 15, Range: 10.25 - 16.75) in those classified as “independent” for PADLs differed significantly from those classified as “dependent” for PADLs in general fatigue (Median: 19.5, Range: 16.25 - 20.0), physical fatigue (Median: 20.0, Range: 17.0 - 20.0), and reduced activity (Median: 20.0, Range: 19.0 - 20.0). Based on these scores, HF patients reported a greater degree of general fatigue, physical fatigue, and reduced activity, especially among the dependent participants (111). Both independent and dependent PADLs appeared to be significantly affected by general and physical fatigue as well as reduced activity. However, reduced activity reported by the dependent participants remained significantly different from the independent counterpart after adjusting for age (OR=1.62 (95% CI: 1.03 - 2.56) (111). These researchers conclude that there was a substantial amount of general fatigue, physical fatigue, and reduced activity in these HF patients and suggest that HF causes more physical rather than mental fatigue (111).
Comparison of Subjective and Objective Measures of Physical Activity.

Numerous studies (11, 14, 57, 92, 115, 127) have compared subjective measures, such as questionnaires, to objective measures of PA obtained from pedometers/accelerometers, and have generally concluded that subjective measures of PA tend to overestimate time spent in PA compared to objective measures.

Ainsworth et al. (11) compared three methods of assessing time spent in PA in 83 adults (38 men and 45 women) over a 21-day period. The participants wore a CSA accelerometer and completed a 48-item PA log to quantify the quantity of time doing household activity, occupational activity, mode of transportation, sports participation, and leisure time PA. Each subject also participated in a telephone survey to recall non-occupational walking, moderate intensity activity, and hard/very hard intensity activities over the previous week. There was a weak correlation ($r = 0.22$ and $0.36$) for moderate intensity activity and a weak correlation for hard/very hard intensity activity ($r = 0.31$ and $0.36$) using both the CSA and PA logs, respectively. The correlation between the telephone survey and the PA logs revealed variable results for moderate intensity and walking activities with correlations between 0.26 to 0.54. The correlation between phone survey and PA log for hard/very hard intensity activities was $r < 0.09$, which showed no significant difference between the reporting of hard/very hard intensity activities using subjective measures (11). These researchers concluded that all three assessment tools can reasonably determine levels of moderate and hard/very hard PA, but that there was generally poor agreement between the subjective and objective techniques used to measure PA (11).
In 2008, Amico and Brubaker (14) objectively quantified PA patterns in 184 sedentary, overweight and obese older adults with mobility disability and established CVD and/or metabolic syndrome participating in the Cooperative Lifestyle Intervention Program (CLIP) study. The researchers gathered PA measures using the Community Health Activities Model Program for Seniors (CHAMPS) PA questionnaire and the Kenz-Lifecorder accelerometer. The CHAMPS and Kenz-Lifecorder accelerometer measures were evaluated separately in regards to steps, PAEE, light PA (LPA), and moderate-vigorous PA (MVPA). This research indicated that there were no significant correlations between CHAMPS and accelerometer derived steps, PAEE, LPA, and MVPA (r = 0.002, 0.060, 0.063, and -0.028, respectively) (14).

Brubaker and Shedd (127) evaluated the baseline patterns of PA in a subset of participants (N = 34) from the Heart Failure and A Controlled Trial Investigating Outcomes of exercise traiNing (HF-ACTION) trial using the Kenz-Lifecorder accelerometer and International Physical Activity Questionnaire (IPAQ). There was no difference between the amount of moderate (178 ± 27 vs 441 ± 175) PA and total (1209 ± 83 vs 1406 ± 385) PA reported by these two methods (127). There was, however, a significant difference in the amount of light (1018 ± 69 vs 460 ± 124) and vigorous (12 ± 6 vs 400 ± 155) activities reported when comparing the accelerometer versus the IPAQ-derived MET min/wk, respectively, indicating that the IPAQ tended to underestimate light PA and overestimate of vigorous PA.
Relationship of Physical Activity Levels to Physical Fitness/Function Measures

Physical fitness contains multiple elements, and is determined by individual characteristics that related to the ability to perform physical activity (4). The five components of physical fitness are cardiovascular endurance, muscular strength, muscular endurance, flexibility, and body composition (4). On the other hand, physical function has been defined as the ability of an individual to perform physically and is indicative of overall health as well as the ability to perform everyday tasks (1). Physical function is commonly measured through six-minute walk distance (6MW), timed up-and-go, grip strength, repeated chair stands, standing balance test, maximal isokinetic knee extensor strength, leg muscle power, and timed sit-to-stand. Moderate to high correlations between physical fitness (VO2 peak, anaerobic threshold) and physical function measures (6MW) have been documented in numerous research investigations (33, 34, 47, 93, 106, 114, 131, 157). Moreover, the relationship between physical activity levels and physical fitness/function has been studied in normal healthy subjects and other chronic disease populations, but not in the HF population (35, 60, 132).

Healthy Adults.

Cao et al. (35) studied 148 Japanese women between the ages of 20-69 years to determine if PA intensity measures obtained from an accelerometer could predict VO2 max in this population. A maximal test on a cycle ergometer was used to objectively measure VO2 max. Physical activity variables of steps per day, minutes of moderate and vigorous PA (MVPA), and vigorous PA (VPA) were quantified with a Kenz Lifecorder accelerometer. There was a moderate to strong inverse correlation between VO2 max and BMI as well as waist circumference (r = -0.46 and -0.62 respectively) (35). Steps per day,
MVPA, and VPA were all significantly correlated to VO$_{2\text{max}}$ ($r = 0.43$, 0.52, and 0.58 respectively) (35). Since there was a large range in the age of the participants of this study, the researchers controlled for age in the analysis. After controlling for age, the correlations between VO$_{2\text{max}}$ and steps per day, MVPA, and VPA were all significantly strengthened ($r = 0.55$, 0.54, and 0.60 respectively) (35). This study shows that PA levels are significantly associated with VO$_{2\text{max}}$ in Japanese women of all ages (35).

Cao et al. (36) also objectively measured physical activity in 127 Japanese men (Age: 20-69). Physical activity was measured using the Kenz-Lifecorder and VO$_{2\text{max}}$ was calculated through a graded exercise test on a cycle ergometer. The accelerometer quantified step counts/day, minutes of moderate-vigorous PA (MVPA), and minutes of vigorous PA (VPA). After controlling for age, statistically significant correlations between VO$_{2\text{max}}$ and steps/day and VPA ($r = 0.58$ and 0.51, respectively) were observed (36). These researchers concluded that steps/day and VPA could be used to predict VO$_{2\text{max}}$ in healthy Japanese men (36).

**Other Chronic Disease Populations.**

Hebestreit et al. (60) investigated the correlation between PA levels and VO$_{2\text{max}}$ in 71 cystic fibrosis (CF) patients between the ages of 12-40. Maximum oxygen consumption was measured using cycle ergometry, and PA was objectively quantified by wearing an accelerometer for a 7-day period. All 71 patients wore the MTI/CSA 7164 accelerometer for 5 or more days and had at least 10 hours of wear time per day (60). The average number of steps per day as well as the amount of time spent in moderate and vigorous activity (MVPA) was determined for each subject (60). Moderate-vigorous PA
was quantitatively defined as the mean amount of minutes spent per day of at least 1000 steps per minute (60). There was a significant correlation between VO₂ max and steps/day as well as MVPA. When expressed relative to body weight (ml·kg·min⁻¹), VO₂ max was moderately correlated with steps/day and MVPA (r = 0.45 and 0.55, respectively). When VO₂ max was expressed as % pred, moderate correlations seen between VO₂ max and steps/day (r = 0.32) as well as VO₂ max and MVPA (r = 0.42) were observed (60). The study by Hebestreit et al. (60) indicates that physical fitness (VO₂ max) and amount of MVPA are moderately correlated in CF patients.

Steele et al. (132) studied 47 patients (Age: 48 – 80) with chronic obstructive pulmonary disease (COPD), aged 48-80 in a pulmonary rehabilitation program. The Tritrac R3D accelerometer was worn for a 4-day period before starting pulmonary rehabilitation (132). Functional exercise capacity was quantified using the longest of three 6-minute walk tests (6MWT). The average distance walked was 1152 feet (132). This study found a relationship between the PA levels at home and the 6MWT (r = 0.74) (132). This strong association between PA and 6MWT suggests that PA levels may reflect physical fitness/function (132).

Pitta et al. (121) objectively measured PA, using an accelerometer, in 25 healthy elderly subjects and 50 participants suffering from COPD. Cardiorespiratory fitness was measured using cycle ergometry. This study determined that the amount of time spent walking during the day was moderately correlated to the measured VO₂ peak and BMI in healthy older adults (r = 0.47 and -0.47, respectively). Walking time was also moderately correlated to VO₂ peak, isometric quadriceps force (% pred), and isometric handgrip force (% pred) in COPD patients (r = 0.33, 0.45, and 0.44, respectively). While the only
variable that was highly correlated to walking time was the six-minute walking distance (6MW) achieved by those with COPD ($r = 0.76$) (121). This study concluded that the functional exercise capacity of COPD patients significantly correlated to daily physical activity levels (121).

Mezzani et al. (104) evaluated the relationship between PA and peak exercise capacity in patients with clinical criteria of HF as well as those with asymptomatic left ventricular dysfunction (ALVD). One-hundred sixty seven HF patients (NYHA stage I to III), 40 persons with ALVD, and 52 healthy control subjects (HCS) (ages 57 ± 9, 55 ± 11, and 54 ± 8) were evaluated for levels of PA (104). Leisure time PA, occupational PA, and sedentary time over the past 6 months was estimated via an interview-based questionnaire. The intensity of each activity correlated to an approximate amount of energy used during the activity (Low: $\leq 2$ METs, Moderate: $> 2$ METs $\leq 4$ METs, Heavy: $>4$ METs $\leq 6$ METs, Very Heavy: $> 6$ METs) (104). The duration of any activity had to be at least 4 hours per week to qualify as that level of activity (104). The interview evaluated five different levels of physical activity per week, which corresponded to an activity score (AS) of 1 to 5, respectively (104). If a hospital stay occurred over the 6 month period, then the AS was reduced by 20% (if hospitalization occurred within the month before the exercise test) or 10% (if the hospitalization occurred within 1-4 months before the exercise test) to account for the decrease in peak exercise capacity that would have occurred during the hospital stay (104). Peak exercise oxygen consumption was measured through an exercise test conducted on a cycle ergometer (HF: $14.7 \pm 3.7$, ALVD: $20 \pm 4$, and HCS: $33.1 \pm 10$ ml·kg·min$^{-1}$, respectively). The AS reported by the questionnaire demonstrated that PA was an independent predictor of the peak exercise
capacity in those with clinical HF (r = 0.48), ALVD (r = 0.69), and HCS (r = 0.83) (104). The AS was significantly lower in the HF patients compared to the other two groups (HF: 1.6 ± 0.6, ALVD: 2.2 ± 0.7, HCS: 3.5 ± 1.1) (104). Both peak exercise capacity and AS decreased significantly by HF class (NYHA Class I: 2.1 ± 0.5, NYHA Class II: 1.7 ± 0.5, NYHA Class III: 1.3 ± 0.5) (104). After adjusting for AS, there was no longer a significant difference in the exercise capacity between the HCS, ALVD, and HF (21.3 ± 6, 16.6 ± 3.6, 14.8 ± 3.5 mL·kg·min⁻¹, respectively) (104). This study suggests that AS levels attributed to the difference seen in peak exercise capacity between symptomatic HF patients compared to ALVD and HCS (104). While most literature suggests that PA levels and measures of physical fitness/function are well correlated in healthy and several chronic disease populations, this relationship has not been studied in the HFpEF population.

Aims and Hypotheses

While heart failure with a preserved EF% (HFpEF) represents a significant public health problem, little is known about the physical activity levels in this population. Thus, the primary aim of this study is to objectively quantify PA using an accelerometer, the PA levels of HFpEF patients. We will descriptively compare the PA levels of the males and females that were included in this analysis. The second aim of this investigation is to evaluate the relationship between PA levels and important physical fitness/function measures in HFpEF; such as VO₂ peak, 6MW, and leg power. We hypothesize that all PA measures (steps/day, PAEE, LPA, and MVPA) will be significantly correlated with VO₂ peak, 6MW, leg power, and NYHA class. The third aim of this investigation is to
examine the differences between objectively measured PA levels and well-established
prognostic measures (VO₂ peak, 6MW, and NYHA class) in HFpEF. We hypothesize
that PA levels (steps/day, PAEE, and MVPA) will be significantly higher in HFpEF
patients with good vs poor prognosis, when categorized based on VO₂ peak (≤ 14
ml·kg·min⁻¹), 6MW (≤ 300 m), and NYHA class (class II vs III).
METHODS

Subjects

A portion of the participants from the Study of the Effects of Caloric Restriction and Exercise Training (SECRET), which was funded by the National Institute of Health (NIH), were utilized for this particular study. SECRET was designed to determine if exercise intolerance and quality of life (QOL) could be improved through exercise training and caloric restriction in elderly patients with heart failure with a preserved ejection fraction (HFpEF) (78). The participants that were eligible for SECRET were randomized into one of four groups: diet only, exercise only, diet and exercise combined, or an attention control group. Hypotheses for SECRET are described in Appendix C. The primary aim of this thesis was to objectively quantify physical activity levels in these HFpEF participants and to explore the relationships between measures of PA and physical fitness/function measures.

The recruitment goal for SECRET was to obtain 100 participants within the area of Wake Forest University Baptist Medical Center. Briefly, the inclusion criteria include; diagnosed with heart failure (clinical score > 3) and a normal ejection fraction of > 50% that was determined by echocardiography. In addition to the above criteria, the participant must have been at least 60 years of age, had a body mass index of > 30 kg/m², been managed for heart failure using the appropriate medical therapy, and able to perform exercise at a moderate intensity (78). See Appendix D for detailed inclusion and exclusion criteria for SECRET. The analysis for this thesis includes 36 of the participants from the SECRET study that participated in the accelerometry aspect of the study.
Testing Procedures

The testing procedures, for the entire SECRET study, took place over four different testing visits. During the first visit, each participant signed an informed consent and completed medical history forms. This visit also included a medical screening, anthropometric measurements (height and weight), a basic 2-D echocardiogram, and a dietary consult. Additional assessments during the next three visits included; resting metabolic rate, phlebotomy for biomarkers, lipoproteins, and brain natriuretic peptide (BNP), cardiac magnetic resonance imaging (MRI), dual energy x-ray absorptiometry (DEXA), echocardiography including doppler, maximal isokinetic knee extensor strength (KinCom), leg muscle power, a skeletal muscle biopsy, and administration of the Minnesota Living with Heart Failure Questionnaire (MLHF). Furthermore, the 6 minute walk test (6MWT) and cardiopulmonary exercise test (CPET) with breath-by-breath expired gas measurements were utilized to evaluate functional capacity. For this thesis, the variables of interest are VO\textsubscript{2} peak, ventilatory anaerobic threshold (VAT), VE/VCO\textsubscript{2} Slope (Slope), 6-minute walk distance (6MW), power leg press (PLP), and New York Heart Association (NYHA) functional classification.

The CPET has been shown to generate reproducible measures of VO\textsubscript{2} peak and ventilatory anaerobic threshold (VAT) in elderly patients with HF (95). The CPET was conducted on a motorized treadmill, using the modified Naughton protocol, to determine VO\textsubscript{2} peak, Slope, and VAT measures. The Medical Graphics (Minneapolis, MN) system was calibrated according to specification before testing so that expired gases could be analyzed. The SECRET participants were encouraged to give a maximal effort during the CPET. A maximal test was determined by an RER > 1.05, RPE > 15, and > 90% age
predicted maximal HR. The participant’s blood pressure, heart rate, and ECG were continuously monitored during the test. The CPET was overseen by a Master’s level exercise physiologist, and a board-certified cardiologist. Peak VO₂ was determined by calculating the average VO₂ over the last 15 seconds of the test. Ventilatory anaerobic threshold was determined with the Wasserman v-slope method by an experienced exercise physiologist who was blinded to the participant’s group assignment (78).

The 6MWT was administered in a long corridor and each participant was told to walk as many lengths as possible in 6 minutes. During the 6MWT, the participant was advised that they could stop and rest if needed, but the clock would still be running. The outcome measured during the 6MWT was the total distance (in meters) that was covered by the participant (78). The 6MWT has been shown to be a valid submaximal measure of exercise intolerance in those with HF (56, 69).

Dual energy x-ray absorptiometry (DEXA) was used to determine the body fat percentage as well as the percent of lean body mass present in these HFpEF subjects. If any subject presented with a body weight that was over the DEXA weight limit, then the subject was not able to complete this part of the investigation.

The NYHA functional classification scale was used to determine the extent of symptom exacerbation during physical exertion or rest (See Appendix A). New York Heart Association functional classification was determined by the attending cardiologist.

The leg muscle power was determined through using the Nottingham leg press to determine muscular power in the quadriceps of both the right and left legs. Each leg underwent five trials to determine muscular power (measured in Watts). Each participant was told to push as hard as possible during each trial. Of the five trials for each leg, the
lowest and highest values were noted, but the average of the three remaining values were averaged to determine average muscular power for each leg (78).

Collection and Analysis of Accelerometry Data

Accelerometry data and its relationship to other functional measures was the primary interest of this thesis. All eligible participants were given an accelerometer device, the Kenz Lifecorder Ex, prior to randomization on their second clinical visit and were instructed to wear for at least 7 days. Each accelerometer was programmed with the participant’s age, weight, height, gender, and time of day before being given to the participant to wear. Instructions on how to wear the accelerometer were verbally given to the participant. The device was sealed so the participant was unable to obtain any feedback about their activity level. The subject was told to consistently wear the device on either the left or right hip with the safety cord attached to clothing, to begin wearing the device as soon as they woke up, and to continue to wear the accelerometer during all waking hours except for when showering, swimming, or sleeping. The device should be worn between 7-10 days to obtain stable baseline measures of the participant’s physical activity levels. A slight variability in the number of days the device was worn occurred because the accelerometer could be returned in person during one of the other visits or through the mail in a protective envelope. Once the device was returned, the device was connected to a PC and the information collected by the device was downloaded.

The accelerometer that was utilized for this study was the Kenz Lifecorder Ex. This uniaxial accelerometer is 6 x 4.6 x 2.6cm and lightweight (40 grams) and analyzes vertical accelerations ranging from 0.06 to 1.94 G, where 1 G is equal to the acceleration
of earth’s gravity, at a frequency of 32 Hz. The movement intensity is determined by the
frequency and magnitude of the accelerations and recorded every 4 seconds. The
movement intensity is measured on a scale of 1 to 9, with 1 being the lowest intensity of
movement and 9 being the highest movement intensity. These intensity levels were
previously shown to correlate well to metabolic equivalents (METs) and have been
divided into categories of 1 to 3, 4 to 6, and 7 to 9 METs, for light, moderate, and
vigorous levels of PA, respectively (17, 84). It should be noted that light physical activity
may be underestimated with this device because the intensity level of 1 correlates to
approximately 2 METs (17, 84). Since this thesis is looking at HFpEF participants, then
light (LPA) PA was defined as 1-2 METs and moderate-vigorous PA (MVPA) was
defined as 3-9 METs.

Physical activity analysis software (PAAS) that comes with the Lifecorder is used
to download data from the accelerometer to the PC. Data is then viewed on a Microsoft
Excel CSV spreadsheet as well as in a customized report. The spreadsheet contains the
following information; dates of wear, the participant’s height, weight, gender, and age,
total daily energy expenditure (DEE) expended in kilocalories. Physical activity energy
expenditure (PAEE) expressed in kilocalories (kcal), daily step count, and minutes spent
in light, moderate, and vigorous activity levels are quantified for each day. The
customized report reflected the same information, but also includes graphs describing the
frequency of device usage and number of minutes at each movement intensity level.

From the customized report, each subject’s physical activity data was evaluated to
determine if he or she would be included or excluded from this investigation. The total
time for each day was determined for each day and had to meet or exceed 10 hours for
inclusion. When the participant fulfilled the first criteria of wear time (≥ 10 hrs.) for a particular day, the percent of wear time for each day was also calculated. If the participant did not wear the device for at least 80 percent of the total wear time, then that day was excluded from further analysis. To be included, the participant had to have at least three days that met the accelerometry inclusion criteria. These inclusion and exclusion criteria for the physical activity measures were based on previous research (37, 97). Thus for each participant in this aspect of the SECRET study we will be able to obtain the following measures: steps/day, minutes of light (LPA) and moderate/vigorous physical activity (MVPA), and physical activity energy expenditure (PAEE).

**Statistical Analysis**

All of the data were entered into SPSS Statistics 17.0 for Windows and analyzed for normality. Descriptive statistics, including mean, medians, standard deviations, and ranges, were run on all data sets. An independent-samples t-test was utilized to compare the mean steps/day, MVPA, and PAEE between males and females. The Pearson Product Moment Correlation was used to examine the relationship between PA levels (steps/day, LPA, MVPA, and PAEE) and other functional measures including; VO2 peak, ventilatory anaerobic threshold (VAT), 6-minute walk distance (6MW), VE/VCO2 Slope (Slope), leg strength/power (PLP), and NYHA functional class. Independent t-tests were used to determine if there were significant differences in PA levels, when important prognostic variables (6MW, NYHA class, and VO2 peak) are examined by established criteria. A P-value of < 0.05 was considered statistically significant for all analyses.
RESULTS

The primary aim of this thesis was to objectively quantify physical activity (PA) levels in those with heart failure and a preserved ejection fraction (HFpEF). The PA levels were evaluated at baseline of a single-blinded, randomized control trial using a Kenz Lifecorder Ex accelerometer. The second objective of this thesis was to explore the relationships between measures of PA and physical fitness/function in HFpEF patients. The PA measures obtained from the Kenz Lifecorder Ex accelerometer were steps/day, minutes of light (LPA) and moderate-vigorous (MVPA) PA, and physical activity energy expenditure (PAEE). The physical fitness/function variables examined in this thesis were VO₂ peak, ventilatory anaerobic threshold (VAT), 6 minute walk distance (6MW), power leg press (PLP), and New York Heart Association (NYHA) functional classification. The VE/VCO₂ slope (Slope) an important prognostic measure obtained for expired gas analysis, and body mass index were evaluated. Thirty-six participants from the SECRET study at Wake Forest University Baptist Medical Center were recruited for this investigation.

Participant Demographics

Descriptive statistics of the SECRET participants included in this investigation are listed in Table I. This sample included a greater number of females (N = 27) compared to males (N = 9). There was a higher percentage of whites (N = 22, 61.1%) compared to blacks (N = 13, 38.9%) and Hispanics (N = 1, 0.03%). Ninety-seven percent of these patients had a history of hypertension and 44.4% of these participants were diagnosed with type 2 diabetes. The only significant differences between males and females were in % fat (women significantly higher than men), lean body mass % (men
significantly higher than men), and ejection fraction (women significantly higher than
men).

Table II shows the measures from an exercise treadmill test performed at baseline
of the SECRET study. The first five variables are peak exercise values obtained from the
cardiopulmonary exercise test as well as the 6MW. The four variables that were
significantly different between males and females were VO2 peak (significantly higher in
males), right power leg press (PLP) (males significantly higher), left PLP (males
significantly higher), and VE/VCO2 Slope (males significantly higher).

Physical Activity Measures

Table III displays the accelerometer results for all 36 subjects included in this
analysis. The objectively quantified PA variables are; average steps/day, amount of
minutes spent in light (LPA) (1-2 METs) and moderate-vigorous (MVPA) (3-9 METs)
PA, as well as physical activity energy expenditure (PAEE) expressed in kilocalories/day
(kcals/day). There were no significant differences between males and females for any of
the PA measures.

Physical Activity Measures Versus Physical Fitness/Function Measures

The relationship between the accelerometer-derived PA measures (steps/day,
PAEE, minutes of light (LPA), and moderate-vigorous (MVPA) PA) and physical
fitness/function measures (VO2 peak, ventilatory anaerobic threshold (VAT), VE/VCO2
Slope (Slope), six minute walk (6MW), power leg press (PLP), and New York Heart
Association (NYHA) functional class) were determined using the Pearson Product Moment Correlations. The calculated r-values are shown in Table IV. Plots (with r and SEE) for all significant relationships are presented in Appendix E. The Pearson Product Moment Correlation classification was defined as: “no correlation” r = 0.0-0.3, “low correlation” r = 0.3-0.5, “moderate correlation” r = 0.5-0.7, and “high correlation” r = 0.7-1.0. Although of moderate strength, VO₂ peak was significantly correlated with steps/day and LPA. The 6MW was significantly correlated with all PA measures, although these relationships were also of moderate strength. No other significant correlations were observed between any other PA and physical fitness/function measures. There was no significant correlation between BMI and any PA measures.

Physical Activity Measures and Prognostic Variables

The relationship between physical activity measures and important prognostic variables (VO₂ peak, 6MW, and NYHA class) were also examined. Individual steps/day, minutes of light physical activity (LPA), minutes of moderate-vigorous physical activity (MVPA), and PAEE were plotted (and tested for significance) based on known prognostic criteria for selected variables (VO₂ peak: ≤ 14 ml·kg⁻¹·min⁻¹, 6MW: ≤ 300 m, and NYHA class: II vs III).

Figure 2 indicates that average steps/day were significantly lower in HFpEF patients when dichotomized based on VO₂ peak ≤ 14 ≥ ml·kg⁻¹·min⁻¹. Plots of other dichotomous prognostic variables (6MW, NYHA class) versus PA measures indicate there were no differences between PA levels when subjects are stratified into high/low risk categories. Small diamonds represent individual data, whereas large blue diamond is the group mean. These plots can be found in Appendix F.
Table I: Descriptive Characteristics of Study Participants

<table>
<thead>
<tr>
<th>Variables</th>
<th>ALL (N = 36)</th>
<th>Males (N = 7)</th>
<th>Females (N = 29)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td></td>
<td>Range: Min – Max</td>
<td>Range: Min – Max</td>
<td>Range: Min – Max</td>
</tr>
<tr>
<td>Age (Years)</td>
<td>68.1 ± 5.4</td>
<td>69.3 ± 3.9</td>
<td>67.7 ± 5.8</td>
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<tr>
<td></td>
<td>60.0 – 80.0</td>
<td>65.0 – 75.0</td>
<td>60.0 – 80.0</td>
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<tr>
<td>Wt (kg)</td>
<td>108.8 ± 20.5</td>
<td>115.7 ± 21.0</td>
<td>106.5 ± 20.2</td>
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<tr>
<td></td>
<td>79.0 – 154.0</td>
<td>100.5 – 151.5</td>
<td>79.0 – 154.0</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>40.2 ± 7.1</td>
<td>37.6 ± 4.9</td>
<td>41.0 ± 7.6</td>
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<tr>
<td></td>
<td>31.6 – 61.7</td>
<td>32.7 – 46.4</td>
<td>31.6 – 61.7</td>
</tr>
<tr>
<td>% Fat (N = 31)</td>
<td>44.0 ± 6.0</td>
<td>35.5 ± 5.1**</td>
<td>46.5 ± 3.5</td>
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<tr>
<td></td>
<td>29.5 – 52.5</td>
<td>(N = 7)</td>
<td>(N = 24)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>29.5 – 43.2</td>
<td>38.5 – 52.5</td>
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<tr>
<td>Lean Body Mass (%)</td>
<td>55.4 ± 5.7</td>
<td>63.4 ± 4.4**</td>
<td>53.0 ± 3.5</td>
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<td>(N = 31)</td>
<td>47.6 – 67.8</td>
<td>(N = 7)</td>
<td>(N = 24)</td>
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<td></td>
<td></td>
<td>55.4 – 67.8</td>
<td>46.7 – 58.7</td>
</tr>
<tr>
<td>Resting Systolic BP</td>
<td>135.9 ± 16.8</td>
<td>129.1 ± 15.7</td>
<td>138.2 ± 16.8</td>
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<tr>
<td>(mmHg)</td>
<td>104.0 ±182.0</td>
<td>104.0 – 154.0</td>
<td>112.0 – 182.0</td>
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<tr>
<td>Resting Diastolic BP</td>
<td>77.83 ± 9.54</td>
<td>77.56 ± 8.82</td>
<td>77.93 ± 9.93</td>
</tr>
<tr>
<td>(mmHg)</td>
<td>62.0 – 98.0</td>
<td>68.0 – 88.0</td>
<td>62.0 – 98.0</td>
</tr>
<tr>
<td>Resting Heart Rate</td>
<td>74.7 ± 10.5</td>
<td>77.4 ± 11.1</td>
<td>73.7 ± 10.3</td>
</tr>
<tr>
<td>(bpm)</td>
<td>56.0 – 97.0</td>
<td>61.0 – 97.0</td>
<td>56.0 – 91.0</td>
</tr>
<tr>
<td>Ejection Fraction (%)</td>
<td>59.4 ± 6.0</td>
<td>55.6 ± 4.1*</td>
<td>60. 7± 6.0</td>
</tr>
<tr>
<td></td>
<td>49.0 – 73.0</td>
<td>49.0 – 60.0</td>
<td>50.0 – 73.0</td>
</tr>
<tr>
<td>NYHA (N (%))</td>
<td>Class II: 23 (68%)</td>
<td>Class II: 6 (75%)</td>
<td>Class II: 17 (65%)</td>
</tr>
<tr>
<td>(N = 34)</td>
<td>Class III: 11 (32%)</td>
<td>Class III:  2 (25%)</td>
<td>Class III: 9 (35%)</td>
</tr>
</tbody>
</table>

*Significant Difference between Males and Females (P < 0.05)

**Significant Difference between Males and Females (P < 0.01)

NYHA = New York Heart Association Class
Table II: Physical Fitness/Functional Test Results

<table>
<thead>
<tr>
<th>Variables</th>
<th>ALL (N = 36)</th>
<th>Males (N = 7)</th>
<th>Females (N = 29)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Peak Heart Rate (bpm)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>138.6 ± 17.0</td>
<td>134.9 ± 20.0</td>
<td>139.8 ± 16.1</td>
</tr>
<tr>
<td>Range: Min – Max</td>
<td>98.0 – 165.0</td>
<td>98.0 – 161.0</td>
<td>99.0 – 165.0</td>
</tr>
<tr>
<td><strong>VO₂ peak (ml · kg · min⁻¹)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>14.7 ± 2.6</td>
<td>16.6 ± 3.2*</td>
<td>14.1 ± 2.2</td>
</tr>
<tr>
<td>Range: Min – Max</td>
<td>10.4 – 20.6</td>
<td>12.2 – 20.6</td>
<td>10.4 – 18.2</td>
</tr>
<tr>
<td><strong>Treadmill Test Time (seconds)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>610.8 ± 146.5</td>
<td>701.3 ± 191.5</td>
<td>580.6 ± 117.5</td>
</tr>
<tr>
<td>Range: Min – Max</td>
<td>346.0 – 1,031.0</td>
<td>346.0 – 840.0</td>
<td>440.0 – 1,031.0</td>
</tr>
<tr>
<td><strong>VE/VCO₂ Slope (ml · kg · min⁻¹)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>29.6 ± 3.8</td>
<td>31.6 ± 1.7**</td>
<td>29.0 ± 4.1</td>
</tr>
<tr>
<td>Range: Min – Max</td>
<td>21.5 – 36.0</td>
<td>28.6 – 33.5</td>
<td>21.5 – 36.0</td>
</tr>
<tr>
<td><strong>VAT (N = 30) (at VO₂ in ml · kg · min⁻¹)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>1,071.2 ± 250.0</td>
<td>1,214.2 ± 269.1</td>
<td>1,035.4 ± 236.7</td>
</tr>
<tr>
<td>Range: Min – Max</td>
<td>675.0 – 1,600.0</td>
<td>900.0 – 1,600.0</td>
<td>675.0 – 1,450.0</td>
</tr>
<tr>
<td><strong>6MW distance (meters)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>408.1 ± 72.9</td>
<td>444.8 ± 75.0</td>
<td>395.9 ± 69.3</td>
</tr>
<tr>
<td>Range: Min – Max</td>
<td>253.0 – 549.9</td>
<td>278.3 – 531.3</td>
<td>253.0 – 549.9</td>
</tr>
<tr>
<td><strong>R PLP _Average (Watts) (N = 34)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>118.3 ± 52.0</td>
<td>158.6 ± 54.3**</td>
<td>103.8 ± 43.7</td>
</tr>
<tr>
<td>Range: Min – Max</td>
<td>30.6 – 222.6</td>
<td>76.0 – 222.6</td>
<td>30.6 – 191.7</td>
</tr>
<tr>
<td><strong>L PLP _Average (Watts) (N = 34)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>114.4 ± 43.6</td>
<td>143.4 ± 47.0*</td>
<td>103.9 ± 38.0</td>
</tr>
<tr>
<td>Range: Min – Max</td>
<td>34.4 – 210.0</td>
<td>81.5 – 210.0</td>
<td>34.4 – 166.1</td>
</tr>
</tbody>
</table>

*Significant Difference between Males and Females (P < 0.05)

**Significant Difference between Males and Females (P < 0.01)

VAT = Ventilatory Anaerobic Threshold, NYHA = New York Heart Association

Functional Classification, R PLP = Right Power Leg Press, L PLP = Left Power Leg Press, 6MW = 6-Minute Walk Distance
### Table III: Accelerometer Data

<table>
<thead>
<tr>
<th>Variables</th>
<th>ALL (N = 36)</th>
<th>Males (N = 7)</th>
<th>Females (N = 29)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td></td>
<td>Range: Min – Max</td>
<td>Range: Min – Max</td>
<td>Range: Min – Max</td>
</tr>
<tr>
<td>Steps/day (# of steps)</td>
<td>3,475.0 ± 1,303.4</td>
<td>3,873.5 ± 1,506.1</td>
<td>3,342.2 ± 1,231.2</td>
</tr>
<tr>
<td></td>
<td>1,072.0 – 6,302.0</td>
<td>1,359.0 – 6,302.0</td>
<td>1,072.0 – 5,529.0</td>
</tr>
<tr>
<td>Amount of LPA/day (min)</td>
<td>30.5 ± 11.1</td>
<td>34.8 ± 14.1</td>
<td>29.0 ± 9.7</td>
</tr>
<tr>
<td></td>
<td>12.4 – 61.5</td>
<td>12.4 – 53.5</td>
<td>15.7 – 61.5</td>
</tr>
<tr>
<td>Amount of MVPA/day (min)</td>
<td>8.8 ± 5.8</td>
<td>8.5 ± 6.4</td>
<td>8.9 ± 5.7</td>
</tr>
<tr>
<td></td>
<td>0.3 – 23.7</td>
<td>0.3 – 19.1</td>
<td>0.6 – 23.7</td>
</tr>
<tr>
<td>Physical Activity Energy Expenditure (kcals/day)</td>
<td>139.9 ± 58.6</td>
<td>163.2 ± 58.9</td>
<td>132.1 ± 57.5</td>
</tr>
<tr>
<td></td>
<td>37.6 – 245.0</td>
<td>49.3 – 224.8</td>
<td>37.6 – 245.0</td>
</tr>
</tbody>
</table>

LPA/day = minutes of light PA/day

MVPA/day = minutes of moderate-vigorous PA/day
### Table IV: Correlation Matrix of Accelerometer Derived Physical Activity Measures vs Physical Fitness/Physical Functional Measures

<table>
<thead>
<tr>
<th>Variables</th>
<th>Steps/day</th>
<th>PAEE</th>
<th>LPA</th>
<th>MVPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO2 peak</td>
<td><strong>0.44</strong></td>
<td>0.31</td>
<td><strong>0.49</strong></td>
<td>0.13</td>
</tr>
<tr>
<td>VAT</td>
<td>0.14</td>
<td><strong>0.38</strong></td>
<td>0.10</td>
<td>0.16</td>
</tr>
<tr>
<td>VE/VCO2 Slope</td>
<td>-0.10</td>
<td>-0.27</td>
<td>0.01</td>
<td>-0.27</td>
</tr>
<tr>
<td>6MW</td>
<td><strong>0.52</strong></td>
<td><strong>0.35</strong></td>
<td><strong>0.45</strong></td>
<td><strong>0.38</strong></td>
</tr>
<tr>
<td>R PLP_Average</td>
<td>0.19</td>
<td>0.32</td>
<td>0.12</td>
<td>0.14</td>
</tr>
<tr>
<td>L PLP_Average</td>
<td>0.18</td>
<td>0.30</td>
<td>0.13</td>
<td>0.06</td>
</tr>
<tr>
<td>BMI</td>
<td>-0.18</td>
<td>0.14</td>
<td>-0.23</td>
<td>0.02</td>
</tr>
</tbody>
</table>

*Significant correlation with a P-value < 0.05

**Significant correlation with a P-value < 0.01

PAEE = Physical Activity Energy Expenditure, MVPA = Moderate-Vigorous Physical Activity, LPA = Light Physical Activity, MPA = Moderate Physical Activity, VPA = Vigorous Physical Activity, VAT = Ventilatory Anaerobic Threshold, 6MW = Six Minute Walk, R PLP = Right Power Leg Press, L PLP = Left Power Leg Press, BMI = Body Mass Index
Figure 2: Plot of Dichotomous Prognostic VO₂ Levels versus Steps/day

P < 0.05

x = 2,818.5

x = 3,803.4

≤ 14 ml·kg·min⁻¹

> 14 ml·kg·min⁻¹

Peak VO₂
A large number of studies have evaluated, either subjectively and/or objectively, the physical activity (PA) levels of healthy subjects (6, 19, 24, 31, 44, 91, 98, 101, 139, 145-147), those with heart (17, 43, 109, 156, 157) and/or lung disease (52) as well as subjects with heart failure and a reduced ejection (HFrEF) (15, 22, 29, 58, 72, 94, 112, 135, 149). However, no research has evaluated the PA levels of subjects with heart failure and a preserved ejection fraction (HFpEF). Thus the primary aim for this thesis was to objectively quantify the levels of PA in those with HFpEF. The secondary objective of this thesis was to explore the relationship between PA measures and physical fitness/function measures in these HFpEF patients.

Participant Demographics

The participants of this study consisted of 36 HFpEF patients that were entering the SECRET study at Wake Forest University Baptist Medical Center. As expected from this population, the EF% was approximately 60%. By definition, HFpEF is diagnosed when HF symptoms are present, but EF% is normal (≥ 50%). On average, the participants of this study were elderly (Mean: 68 ± 5.3 years), mostly female (75%), and mostly white (61.1%). The participants of this project had a mean weight of 108 ± 20.5 kg, a BMI of 40.2 ± 7.1 kg/m², and a % body fat of 44.0 ± 6.0 %. There was a significant difference in % fat between men and women, but no other significant difference in body weight/composition between the sexes in the present investigation.

There were more females than males in this trial, this was not surprising since most HFpEF trials report a similar disproportion of females (80). The reason why HFpEF is more common in women than men is not well understood, but may be due to the
absence of the “protective” role that estrogen plays in regards to the cardiovascular system after menopause (108, 134). Also cardiac remodeling appears to differ between males and females in response to pressure overload. In response to pressure overload, there is a greater amount of LV hypertrophy and less LV dilation in women compared to men (81).

There has only been one reported randomized controlled trial of exercise training in HFP EF, called PARIS (80). In general, the participants of the present study were similar to PARIS participants with regard to age, gender, EF%, and NYHA class. The only meaningful difference between the two RCTs was with regard to weight/body composition of the participants. Because SECRET is designed to decrease body weight with diet and/or exercise, the inclusion criteria included HFP EF patients with a higher BMI (> 30) versus PARIS participants (> 25).

Physical Fitness/Function Test Results

The participants of the present investigation are similar to those described in the PARIS study with regards to exercise capacity (80). The mean VO₂ peak of the present study was 14.7 ± 2.6 ml·kg·min⁻¹, which is only 32.5% of normal for healthy active older adults and 55.3% of healthy sedentary older adults (99, 103). HFP EF patients have reduced exercise levels and exercise intolerance due to a combination of a reduced cardiac output and decreased oxygen extraction in the peripheral tissue (30, 66, 70, 77, 112). The cardiac output is reduced in HFP EF due to a decreased EDV, SV, and potentially, a reduced peak HR. The mean peak HR in the present study was 138.6 ± 17 bpm, which represents 92% of the expected (220 – age). However, previous research has
described that approximately 20% of HFpEF patients have chronotropic incompetence (27), an impairment in HR response to exercise, which would greatly reduce VO$_2$ peak. In the present study, males had a significantly higher VO$_2$ peak than females. This is expected as male subjects in all populations generally have higher VO$_2$ peak due to greater muscle mass and decreased body fat percentage. The higher VO$_2$ peak for males versus females is expected and consistently reported in the literature (32, 139, 142, 151, 152).

The participants in the present investigation walked a slightly shorter 6MW distance than those described in the PARIS study (80). The mean 6MW distance in the present investigation was 408.1 m versus 442.9 m in PARIS. This difference of 8% could be due to a high BMI and body weight of those in the present investigation compared to those of the PARIS study (80). When compared to healthy community-dwelling elderly persons, the participants of this study performed 68% of predicted 6MW for normal healthy older adults (21). The reduced 6MW distance of HFpEF patients in the present investigation compared to normal healthy subjects could be explained by a greater body weight/composition as well as an overall lower functional capacity as VO$_2$ peak in the present study is only 58% of predicted. HFpEF patients recruited for this trial were NYHA class II and III indicating the presence of symptoms at lower levels of exercise thus it would not be surprising that these 6MW and VO$_2$ peak would be reduced compared to older normal subjects.

While the 6MW distance of approximately 400 m observed from the participants of this study is reduced compared to healthy older adults, it is above the 300 m level associated with increased mortality in HFrEF patients (25). Moreover, it is also higher
than values typically reported in COPD patients and patients with dilated cardiomyopathy (131, 157). Thus, while these HFpEF patients have both central and peripheral limitations, they do not appear to be as physically limited as other chronic disease populations.

The present investigation is the first to evaluate the power leg press (PLP) in the HFpEF population. The mean skeletal muscle mass in the present investigation was 55.4%, which is reduced from that of healthy elderly subjects (68.3%) (38). The average PLP levels observed in the present study (Males = 151 W, Females = 103.9 W), are less than reported for healthy elderly males and females (213 and 119 W, respectively) (96, 128, 129). The mechanism responsible for the reduced leg power in HFpEF is unknown, but may be related to the reduced skeletal mass and muscle blood flow that are part of the HF syndrome.

Other than VO2 peak, right PLP, left PLP, and VE/VCO2 Slope, there were no significant differences, with regards to gender, for the other physical fitness/function measures.

**Physical Activity Levels**

A uniaxial accelerometer was used in this investigation to objectively measure physical activity (PA) and quantify steps/day, minutes of light (LPA), moderate (MPA), vigorous (VPA), and moderate-vigorous (MVPA) PA per day, and physical activity energy expenditure (PAEE). This sample of HFpEF participants averaged 3,475 steps/day and ranged between 1,072 – 6,302 steps/day. According to the classification system of Tudor-Locke and Bassett, these HFpEF participants would clearly be classified as
“sedentary” (< 5,000 steps/day) (145). These results suggest that HFpEF participants only achieve about 50% of the steps of “active” healthy older adults (6,000 – 8,500 steps/day) (147). The HFpEF participants in this present investigation achieve step counts that are more consistent with older adults with disabilities and chronic diseases such as osteoarthritis (4,086 steps/day), peripheral artery disease (PAD) (3,149 steps/day), post-stroke (4,346 steps/day), and obesity (4,330 steps/day) (20, 53, 74, 138). While there are no reports describing PA levels HFpEF, several studies have reported objective PA levels in all HF and those HFrEF patients.

Walsh et al. (150) examined PA levels in a HFrEF population, and reported that a median pedometer score of at least 25,000 steps/week or 3,571 steps/day was a significant predictor of improved prognosis. The levels of steps/day reported by Walsh et al. (150) are similar to those found in the present investigation, and are likely due to the similarity in age and disease status of both groups. The healthy controls of Walsh et al. (150) averaged 8,800 steps/day. Thus subjects in the present investigation only achieved 39.5% of the steps/day achieved by the healthy controls, which clearly shows that the HFpEF participants in the present investigation are limited in their daily PA due to exercise intolerance and the manifestation of their disease.

Shedd (127) objectively quantified the PA levels of HFrEF participants that were in HF-ACTION by using a Kenz-Lifecorder accelerometer, the same device used in the present investigation. These HFrEF participants averaged a greater number of steps/day (4,858 ± 1,895 steps/day) than the HFpEF subjects in the present study. The 28% higher step counts in Shedd et al. (127) may be related to the difference in age (58 vs 68 yrs), lower BMI levels (30 vs 40.2 kg/m²), and a higher functional capacity (VO₂ peak = 15.8 vs 14.7 ml·kg·min⁻¹) compared to the participants in the present study.
On the other extreme of the physical activity continuum, Amish men and women have been shown to average 16,310 steps/day (19) which easily exceeds the recommended 10,000 steps/day. While the average age of the Amish (19) studied was significantly younger than those studied in the present investigation (33.0 vs 68.1, respectively), the range in age was larger than the present investigation (18-75 years). Bassett et al. (19) reported that the Amish were more active than non-Amish healthy younger adults (16,310 vs 10,000 steps/day) and more active than non-Amish healthy older adults (16,310 vs 7,250 steps/day) (147). In comparison, the Amish took 4.7 times more steps/day than the HFpEF participants in the present investigation (3,475 steps/day). While the Amish represent an extreme cohort of active adults, it does provide some indication of how inactive these HFpEF patients in this investigation. Obviously, physical activity levels are greatly reduced in these HFpEF patients because of their inactivity, increased body weight, and symptoms associated with HF.

Physical activity energy expenditure (PAEE) was also used in this investigation to quantify PA levels in the HFpEF patients in this investigation. The amount of PAEE that is generally recommended by the CDC – ACSM and Surgeon General is at least 150 kcals/day or 1,000 kcals/week. Participants of the present investigation expended an average of 140 kcals/day or 980 kcals/week in PAEE. While this appears to be close to the desired level, the actual range for individuals was large (38 – 245 kcals/day or 266 – 1,715 kcals/week), thus many patients were well below the goal. It is also important to note that the HFpEF patients used in this investigation had higher body weight and therefore would have an easier time achieving those caloric levels due to the energy expenditure required to move a larger mass. Furthermore, very few in the present
investigation reached or exceeded the level of PAEE (> 2,000 kcals/week) that has been associated with CAD regression and/or weight loss (17).

Physical activity energy expenditure has not been evaluated in any HFrEF population, but has been studied in the HFrEF population. Shedd et al. (127) found that these HFrEF subjects achieved a PAEE of 1,134 kcals/week, which is different than the HFpEF participants in the present investigation. One would expect similar findings in the two HF groups due to similarity in age and disease status HF (79). Furthermore, the higher body weight in HFpEF vs HFrEF should result in a greater PAEE in the former population.

There are several reports in the literature suggesting that other cardiac populations including; CAD (1,487.5 kcals/wk), PAD (1,148 kcals/wk), and cardiac transplant (1,100 kcals/wk) have greater levels of PAEE than the HFpEF patients (980 kcals/wk) used in the present investigation (17, 43, 109, 156). Those suffering from other chronic diseases such as COPD (784 kcals/wk) and stroke (784 kcals/wk) patients are reported to have decreased PAEE/week levels compared to the HFpEF participants of the present study (980 kcals/wk) (52, 74). Although not as low as COPD and stroke patients, the HFpEF patients used in this investigation have, on average, very low levels of PAEE and will need to increase to > 2000 kcals/wk, if CAD regression and/or weight loss are the goal (28).

The number of minutes/day of light (LPA) and moderate-vigorous (MVPA) PA were also quantified to assess the levels of PA in the present investigation. The average amount of time spent in LPA was 30.5 ± 11.1 min/day with a range of 12.4 to 61.5 min/day. The amount of time spent in MVPA averaged 8.8 ± 5.8 min/day with a range of
0.3 to 23.7 min/day. While there are no specific recommendations for the amount of LPA, the CDC recommends $\geq 30$ min/day of MVPA. It is clear the HFpEF patients used in the present investigation did not come close to these levels.

Shedd et al. (127) quantified objectively measured LPA and MVPA in a small group of participants from the HF-ACTION study, and found that HFrEF patients participated in 37.2% (41.8 vs 30.5 min/day, respectively) more LPA compared to those in the present study. The higher amount of LPA observed by Shedd et al. (127) may be due to the fact that their participants were younger (Mean: 58 vs 68 yrs, respectively), had a lower BMI (30 vs 40.2, kg/m$^2$, respectively), and a higher VO$_2$ peak (15.8 vs 14.7 ml·kg·min$^{-1}$, respectively) compared to the HFpEF participants in the present investigation. Similar reduced levels of MVPA were found in HFrEF patients (127) and those of the present investigation (Mean: 6.3 vs 8.8 min/day, respectively). This reduced amount of MVPA in both groups is not surprising given the pathophysiological syndrome induced by HFrEF and HFpEF (79).

It was not surprising that the participants of the present study had low levels of PA compared to healthy normal adults as they are older, deconditioned, and overweight. It is somewhat surprising that HFpEF patients in this investigation have lower PA levels than HFrEF patients of Shedd et al. (127). The latter form of HF is generally thought to be more physically limiting. The lower PA levels seen in HFpEF vs HFrEF could be explained, at least in part, by the advanced age and higher body weight/body fat of the HFpEF patients.

It was interesting to observe in the present investigation that there were no significant differences in any of the PA measures between male and female HFpEF
patients. While there are some conflicting reports, most studies of healthy adults suggest that males generally have higher PA levels than females (35, 36).

**Physical Activity Measures versus Physical Fitness/Function Measures**

The relationship between PA measures (steps/day, PAEE, minutes of LPA, and minutes of MVPA) and physical fitness/function measures (VO₂ peak and other expired gas measures, leg power, and 6MW) was also evaluated. Significant correlations would be expected between all PA measures and all physical fitness/function measures. There were non-significant relationships between PA and leg power, NYHA class, and BMI. The literature generally indicates that there is a modest to strong positive association between peak leg power and walking behaviors (steps, walking speed, and walking distance) in older adults with functional limitations (122). The present investigation in HFpEF patients did not produce a significant correlation between any PA levels and leg power. The lack of a significant correlation between PA levels and leg power in these HFpEF patients could be due to a homogenous sample with minimal variability in both PA levels and leg power, which could weaken the correlation.

To date, there have been several studies that have evaluated the association between BMI and PA levels, and have found there to be an inverse relationship between the two variables (10, 20, 50, 68, 87, 119, 146, 148, 153). In adults, one study indicated that obesity leads to a decrease in PA, and does not support the idea that a lack of PA over the long term would result in obesity (119). Therefore, the lack of a significant correlation between the PA and BMI could be due to the small range of values observed in these HFpEF patients for each measure.
Shedd et al. (127) did note a positive correlation between BMI and PAEE (r = 0.38) in HFrEF subjects versus 0.14 in the present study. The difference in the two studies could be explained by the greater homogeneity of the HFrEF sample (i.e. all older and overweight) versus the HFrEF patients that had a wide range of age and BMI.

In the present study, there were significant, albeit modest, correlations between VO2 peak and 6MW and most PA measures. The relationship appears strongest for physical function (measured by VO2 peak and 6MW) versus steps/day or minutes of LPA. Again, the lack of significant correlations between other PA measures, such as MVPA, and physical fitness/function could be explained by the very small range of MVPA reported in these patients (range = 0.3 – 23.7 min/day).

The relationship between PA measures and physical fitness/function has been examined in several different populations including healthy subjects, stroke patients, and HFrEF patients. In healthy subjects, there are reports indicating that VO2 max is significantly (r = 0.51) correlated with steps/day (35, 36). The HFrEF participants in the current study had a similar moderate correlation (r = 0.44) between VO2 peak and steps/day (35, 36). In stroke patients, Katoh et al. (74) found a significant correlation between daily walking steps and VO2 peak (r = 0.61), which is higher than what was found in the present investigation (r = 0.44). It is unclear why the correlation between steps/day and VO2 peak would be higher in stroke than HF patients. Shedd et al. (127) observed a similar correlation (r = 0.43) between steps/day and 6MW.

While moderately significant correlations, defined as r = 0.5-0.7, between VO2 peak and MVPA has been reported, in healthy females (r = 0.54) (35), the present investigation did not reveal a relationship between VO2 peak and MVPA. This difference
between the two studies could be the older age (20-69 years) and functional capacity range in healthy vs HFP EF (35). In contrast, one study evaluated the correlation between VO₂ peak and low-intensity leisure-time PA in healthy adults and determined that there was no significant correlation between the two variables (139). In contrast, the present investigation did find a significant, albeit low to moderate, correlation between VO₂ peak and LPA ($r = 0.49$), which suggests that the amount of LPA maybe more of a determinant of physical function in HFP EF patients vs normal healthy individuals.

It appears that physical activity levels only moderately relate to objective physical fitness/function measures in HFP EF. Since the amount of variance explained by current PA levels is relatively small other factors such as disease severity/status, genetics, and/or previous history of PA are likely to also contribute to their fitness/functional measures.

Physical Activity Measures and Prognostic Variables

The final interest of the present investigation was to explore the relationship between PA levels and variables that are known to have prognostic significance; VO₂ peak, 6MW, and NYHA class. Generally, there was no significant difference between PA activity levels when compared above and below the established prognostic levels. The only variable that was significantly different was steps/day at VO₂ peak above and below 14 ml·kg·min⁻¹. However, there was still significant overlap of subjects in the two categories. It appears that objectively measured levels of PA do not accurately stratify at-risk patients and should not be used as surrogate measures for well-established prognostic variables such as: VO₂ peak and 6MW.
Future Research Recommendations

One limitation of the present investigation is the small sample size. The SECRET study is ongoing, thus when the study is complete there will be PA and physical fitness/function data on nearly 100 HFpEF patients. The findings of the present study will need to be verified on the larger sample. The SECRET study is a weight-loss and PA intervention, and the inclusion criteria required the participants to be “inactive” and “overweight” at baseline, which would likely decrease PA levels of these patients. While it is not likely, more physically active and/or normal weight HFpEF may have been excluded for this investigation, which could negatively skew baseline levels of PA. Thus PA levels of this study may underestimate the PA levels of all HFpEF patients. It is also possible that the participants of the study may have favorably altered their PA levels because of the study measures, particularly in response to wearing the accelerometer. It has been shown that wearing a pedometer/accelerometer may actually increase PA levels (40, 86). However, these HFpEF patients are so physically limited and inactive, it is unlikely that wearing the accelerometer would have a major impact. Finally, this study recruited a very homogenous group of overweight and inactive HFpEF patients, therefore, the results of this investigation cannot be generalized to other populations.

Conclusions

This is the first investigation to objectively evaluate PA levels of HFpEF patients. It is obvious that these older, overweight, HFpEF patients have very low activity levels that are comparable or less than other chronic disease populations. These inactive patients will clearly benefit from lifestyle interventions designed to increase their activity levels. While, PA measures were well correlated with steps/day, the correlations were only
moderate and most of these measures did not correlate significantly with other important physical fitness/function measures including VO₂ peak and leg press power. Other than a significant difference in steps/day with prognostic levels for VO₂ peak, there were no significant differences found between other PA measures (LPA, MVPA, and PAEE) and other prognostic measures (6MW and NYHA). While accelerometry provides an objective amount of PA levels in HFpEF, these measures appear to add very little to the other fitness/functional measures typically obtained in these patients. Consequently, current PA levels, only explain a small amount of the variance seen in these physical fitness/function levels suggesting there are other variables that must contribute to these outcomes. Further studies will focus on evaluating the change in the PA and fitness/function measures after an exercise/weight loss intervention.
APPENDIX A

New York Heart Association Functional Classification

Class I: Patient that has heart disease and symptoms are exacerbated at physical activity
levels that would inhibit normal individuals

Class II: Symptoms are exacerbated at levels of ordinary exertion

Class III: Symptoms are exacerbated at exertion levels that are less than ordinary

Class IV: Symptoms are exacerbated at rest
APPENDIX B

American Heart Association and American College of Cardiology Heart Failure Classification System

Stage A: Patients who have no structural disease or disorder of the heart, but are at high risk of developing heart failure

Stage B: Patients who have structural disease or disorder of the heart, but have not yet developed symptoms of heart failure

Stage C: Patient who has underlying heart disease, which is associated with past or present heart failure symptoms

Stage D: Patient in end-stage heart failure which requires a specialized treatment regimen such as mechanical circulatory support, cardiac transplantation, continuous inotropic infusions, or hospice care
APPENDIX C

SECRET Study Hypotheses

**Primary Hypothesis:** Both weight loss and exercise training will improve exercise intolerance and quality of life in older, obese patients with heart failure with a preserved ejection fraction.

**Secondary Hypothesis:** Weight loss and exercise training combined will produce complementary effects on body and thigh muscle composition and additive improvements in exercise intolerance in patients with heart failure with a preserved ejection fraction.

**Tertiary Hypothesis:** Improvements in exercise tolerance will correlate with improvements in lean body mass, reversal of adverse thigh muscle remodeling, and increased thigh muscle capillarity.
APPENDIX D
SECRET Inclusion and Exclusion Criteria

Inclusion Criteria:

HF Clinical Score (>3)

<table>
<thead>
<tr>
<th>Clinical Variables</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea/difficulty breathing</td>
<td></td>
</tr>
<tr>
<td>Trouble with breathing (SOB)</td>
<td>1</td>
</tr>
<tr>
<td>Hurrying on the level or up slight hill</td>
<td>1</td>
</tr>
<tr>
<td>At ordinary pace on the level?</td>
<td>2</td>
</tr>
<tr>
<td>Do you stop for breath when walking at own pace?</td>
<td>2</td>
</tr>
<tr>
<td>Do you stop for breath after 100 yds on the level?</td>
<td>2</td>
</tr>
</tbody>
</table>

Physical Examination

<table>
<thead>
<tr>
<th>Heart Rate (bpm)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>91 to 110</td>
<td>1</td>
</tr>
<tr>
<td>111+</td>
<td>2</td>
</tr>
</tbody>
</table>

Rales/Crackles

<table>
<thead>
<tr>
<th>Either lower lung field</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Either lower and either upper lung field</td>
<td>2</td>
</tr>
</tbody>
</table>

Jugulovenous Distention

<table>
<thead>
<tr>
<th>Alone</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Plus Edema</td>
<td>2</td>
</tr>
<tr>
<td>Plus Hepatomegaly</td>
<td>2</td>
</tr>
</tbody>
</table>
Chest X-Ray Film

- Cephalization of pulmonary vessels 1
- Interstitial edema 2
- Alveolar Fluid plus Pleural Fluid 3
- Interstitial Edema plus Pleural Fluid 3

Normal EF (>50%)

- >60 years of age
- BMI >30 kg/m²

Exclusion Criteria:

Medical

- Valvular heart disease as the primary etiology of CHF
- Significant change in cardiac medication <4 weeks
- Uncontrolled hypertension as defined according to current JNC guidelines
- Uncontrolled diabetes
- Evidence of significant COPD; assessment may be made by pulmonary function test
- Recent or debilitating stroke
- Cancer or other non-cardiovascular conditions with life expectancy less than 2 years
- Anemia (<11 grams Hgb) determined by CBC
- Significant renal insufficiency (creatinine >2.5mg/dl) determined by CMP
- Pregnancy—women of child bearing potential are excluded from participation
Psychiatric disease- uncontrolled major psychoses, depressions, dementia, or personality disorder

Other

Plans to leave area within 1 year

Refuses informed consent

Screening Echocardiogram

Left ventricular ejection fraction < 50%

Significant valvular heart disease

Familiarization/Screening Exercise Test

Evidence of significant ischemia

ECG: 1mm flat ST depression (confirm with echocardiogram wall motion)

Echo: Wall motion abnormality or decrease in global contractility

Stopped exercising due to chest or leg pain or any reason other than exhaustion/fatigue/dyspnea

Exercise SBP > 240 mmHg, DBP > 110 mmHg

Unstable hemodynamics or rhythm

Unwilling or unable to complete adequate exercise test

Magnetic resonance imaging

Indwelling metal-containing prosthesis (orthopedic, valvular, other)

Pacemaker or defibrillator

History of welding occupation (ocular metal debris)

Uncontrollable claustrophobia

Any other contra-indication to MRI
Thigh muscle biopsy

- History of bleeding disorder
- Current anticoagulation
- Contraindication to stopping aspirin for 1 week
- Allergy to topical anesthetic
APPENDIX E

Physical Activity Levels vs Physical Fitness/Function Measures

Steps/Day vs VO₂ peak

\[ r = 0.44 \]

\[ \text{SEE} = 2.40 \text{ ml·kg·min}^{-1} \]
Light PA vs VO₂ peak

\[ r = 0.49 \]

\[ \text{SEE} = 2.34 \text{ ml·kg·min}^{-1} \]
Steps/Day vs 6 Minute Walk Distance

$r = 0.52$

SEE = 63.3 meters
Physical Activity Energy Expenditure vs 6 Minute Walk Distance

$r = 0.35$

$SEE = 69.14$ meters

Physical Activity Energy Expenditure (kcal/day) vs 6 Minute Walk Distance (meters)
Light PA vs 6 Minute Walk Distance

$r = 0.45$

SEE = 65.86 meters
Moderate-Vigorous PA vs 6 Minute Walk Distance

Moderate-Vigorous PA (min/day)

6 Minute Walk Distance (meters)

$r = 0.38$

SEE = 68.27 meters
APPENDIX F

Physical Activity Energy Expenditure vs VO₂ Peak

\[ P = 0.14 \]

\[ x = 119.4 \quad x = 150.1 \]
Moderate-Vigorous Physical Activity vs VO₂ peak

P = 0.28

Peak VO₂

Moderate - Vigorous PA (min/day)

≤ 14 ml·kg·min⁻¹  > 14 ml·kg·min⁻¹

x = 7.3  x = 9.5
Steps/day vs NYHA Class

$P = 0.45$

$x_1 = 3539.4$

$x_2 = 3168.9$
Physical Activity Energy Expenditure vs NYHA Class

P = 0.65

x = 135.0

x = 145.0
Moderate-Vigorous Physical Activity vs NYHA Class

![Moderate-Vigorous PA vs NYHA Class](image)

- Moderate-Vigorous PA (min/day)
- NYHA Class II
- NYHA Class III

P = 0.63

\[ \bar{x} = 8.2 \]
\[ \bar{x} = 9.3 \]
Steps/Day vs 6 Minute Walk Distance

![Graph showing the relationship between steps per day and 6-minute walk distance. The x-axis represents 6-Minute Walk Distance, with categories for < 300 meters and ≥ 300 meters. The y-axis represents steps per day. The graph includes data points and annotations indicating \( P = 0.14 \), with values \( x = 2403.3 \) and \( x = 3564.4 \).]
Physical Activity Energy Expenditure vs 6 Minute Walk Distance

P = 0.57

Physical Activity Energy Expenditure (kcal/day)

< 300 meters

≥ 300 meters

6-Minute Walk Distance

x = 121.2

x = 125.7
Moderate-Vigorous Physical Activity vs 6 Minute Walk Distance

P = 0.25

x = 5.1

x = 9.1

6-Minute Walk Distance
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SCHOLASTIC VITA

ALESIA GOODMAN

PERSONAL INFORMATION

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Birth date: February 11, 1987

UNDERGRADUATE STUDY

2005-2007 Greensboro College
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Concentration in Sports Medicine

GRADUATE STUDY

2009-2011 Wake Forest University
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M.S. Health and Exercise Science
Advisor: Peter H. Brubaker, Ph.D.
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PROFESSIONAL EXPERIENCE

2010-2011 PM Coordinator
Healthy Exercise and Lifestyle Programs (HELPS)
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Wake Forest University Baptist Medical Center
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2009-2011 Exercise Leader
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2009-2011  Research Assistant
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Winston-Salem, North Carolina

PRESENTATIONS

May 2011, ACSM Annual Meeting
Alesia Goodman BS; Peter H. Brubaker PhD FACSM; Joel Eggebeen MS;
Dalane W. Kitzman MD. Patterns of Physical Activity in Heart Failure Patients
with a Preserved Ejection Fraction

October 2009, Biomechanics Presentation
Head Impact and Concussion in American Football

MEMBERSHIPS

2008-2011  American College of Sports Medicine

CERTIFICATIONS

2010-2013  ACSM Certified Clinical Exercise Specialist
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