

Abstract

DOES MINIMALLY INVASIVE ROBOTIC SURGICAL TREATMENT ALTER EXERCISE TOLERANCE IN PATIENTS WITH ATRIAL FIBRILLATION AND MITRAL REGURGITATION AT SEVEN TO ELEVEN WEEKS POST-OPERATIVE?

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In the current study, we examined if exercise tolerance was going to be reduced in atrial fibrillation and mitral valve regurgitation patients post a minimally invasive surgery seven to eleven weeks when compared to pre-operative. Patients that participated in this study were diagnosed with atrial fibrillation or mitral valve regurgitation and were previously scheduled for minimally invasive corrective surgery. Subjects were maximally stress tested over two visits, before and after surgery. Oxygen consumption, maximal heart rate, and maximal treadmill time were measured. They also filled out a Physical Activity Scale for the Elderly (PASE) before and after surgery to determine their activity levels. A paired t-test with significance level set at $P \leq 0.05$ revealed that exercise tolerance and activity levels were not found to be significantly different. Subjects in this study were found to be asymptomatic, had mild-moderate atrial fibrillation or mitral valve regurgitation, were younger than previously studied subjects and were active in their daily activities up until the day of their surgery. The principle findings of this study are: 1) patients did not have reduced exercise tolerance after

surgery when compared to pre-operative, 2) when compared to age predicted data, VO_{2MAX} was not significantly different before or after surgery, and 3) there was no change in activity levels between pre and post surgery.

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DEDICATION

This thesis is dedicated to my parents and my brother, for their unconditional love and support in all my endeavors. I would not be where I am without their guidance.

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CHAPTER I

INTRODUCTION

The heart is one of the most important organs in the body. Proper functioning of the circulatory system ensures a high quality of life. When there are problems associated with the heart and its components, everyday activities become strenuous. Atrial fibrillation (AF) and mitral valve regurgitation (MR) are two major types of dysfunctions that can severely lower an individual's quality of life.

The prevalence of AF will increase as the elderly proportion of the population increases. It has been projected that the number of Americans with AF will increase to more than 5.6 million during the next 50 years (Go, Hylek et al., 2001). A more recent analysis has projected the number of adults with AF for the year 2050 to be 15.9 million, if a continuous rise in the incidence of AF persists (Miyasaka, Barnes et al., 2006). As individuals age, the heart begins to lose function and efficiency. When AF and MR are present concurrently, there is a significant decrease in an individual's quality of life, functional status, and cardiac performance, as well as higher medical costs and a higher risk of death (Go, Hylek et al., 2001). In many cases of AF and MR, surgical treatment is the only remaining option. Robotically-assisted minimally invasive surgery can correct AF and MR returning the heart to sinus rhythm and cardiac unidirectional blood flow. Individuals in sinus rhythm have a higher quality of life and higher exercise tolerance than AF and MR patients.

The purpose of this study was to investigate if exercise tolerance was returned to pre-surgical capacity at 7-11 weeks post-robotic surgery to treat AF, MR and AF + MR.

Problem Statement

Currently it is not known if exercise tolerance can be restored in asymptomatic patients 7-11 weeks post robotic surgery.

Hypothesis

It was hypothesized that exercise tolerance would be reduced at 7-11 weeks post-robotic surgery compared to pre-surgery in AF, MR and AF + MR patients.

Delimitations:

- 1) All subjects were men.
- 2) Sample size of 4 subjects.
- 3) Patients were not involved in a structured exercise program or participated in 30 minutes of vigorous exercise per week in the last 2 months.
- 4) All subjects were free of known pulmonary disease or any disease that would result in worsened exercise capacity independent of their cardiac disease.
- 5) Atrial fibrillation and mitral valve regurgitation were diagnosed by physician.
- 6) Patients were scheduled for AF or MR surgery.

Limitations:

- 1) Subjects may complete questionnaires, including the PASE and Modified Baeke, in a misleading or inaccurate manner.
- 2) Failure of maximal effort during VO_{2MAX} testing could lead to underestimation of exercise capacity workload and oxygen consumption.

Definition of Terms

Exercise Capacity: The maximum ability of the body to take up and use oxygen to do work

Maximal Oxygen Consumption (VO_{2MAX}): quantitatively expresses an individual's capacity for aerobic energy production

List of Acronyms

AF: Atrial Fibrillation

MV: Mitral Valve

MVR: Mitral Valve Regurgitation

MR: Mitral Regurgitation

BMI: Body Mass Index = body mass (kg) divided by height squared (kg/m^2)

PASE: Physical Activity Scale for the Elderly

NYHA: New York Heart Association

ECG: Electrocardiogram

HR: Heart Rate

BPM: beats per minute

TM: Treadmill

CHAPTER II

REVIEW OF LITERATURE

Normal Function of the Heart

The primary function of the heart is to supply blood and nutrients. In order for that to occur, a normal heart usually has a constant rhythm which beats between 60 to 100 times a minute. Athletes or highly trained individuals can have a resting rhythm as low as 40 beats per minute (bpm). During each beat, or contraction, the heart expels blood into the aorta. Each contraction is controlled by an electrical impulse traveling through the heart. In the normal heart, these impulses occur at constant and regular intervals. The rhythm of the heart is normally determined by a natural pacemaker called the sinoatrial (SA) node, which is located in the posterior wall of the right atrium near the superior vena cava. The SA node spontaneously generates action potentials at rates of 60-100 beats/minute (bpm). This intrinsic rhythm is influenced by the autonomic nerves, with sympathetic stimulation accelerating the sinus node rate of depolarization and vagal stimulation slowing it (Malcolm S. Thaler, 2007).

Sinus rhythm normally controls both the atrial and ventricular rhythm. Action potentials generated by the SA node spread through the atria, depolarizing this tissue and in turn cause atrial contraction. The impulse then travels into the ventricles via the atrioventricular node (AV node). The purpose of the AV node is to provide a pathway for impulses from the atria to the ventricles (Malcolm S. Thaler, 2007). There is a slight delay in conduction from the atria to ventricles, which allows the atria to contract first and the ventricles to fill with blood before the ventricles contract. The impulse is then

picked up by specialized conduction pathways, bundle branches and Purkinje fibers, to rapidly conduct the wave of depolarization through the ventricles to produce a ventricular contraction. Therefore, in a normal heart, the rhythm is controlled by the SA node.

The heart consists of 4 chambers, right atrium, right ventricle, left atrium, and left ventricle. The atriums are connected to the ventricles by valves. Between the right atrium and right ventricle is the tricuspid valve and between the left atria and left ventricle is the mitral valve. The right atrium collects de-oxygenated blood from the body (via the superior and inferior vena cava), pumps it through to the right ventricle via the tricuspid valve, and then pumps it through the pulmonary valve into the lungs. Oxygenated blood from the lungs then returns to the left atrium, pumps through the mitral valve into the left ventricle. Blood is then pumped to the rest of the body via the aortic valve. The muscle wall surrounding the left ventricle is thicker compared to the right ventricle due to the higher force needed to pump blood through the systemic circulation.

Arrhythmias

Variations in the heart rhythm are known as arrhythmias. There are many types of arrhythmias and they are classified according to where they originate in the heart. Those that do not originate from the ventricles are generally called supraventricular arrhythmias while those originating from the ventricles are called ventricular arrhythmias (Malcolm S. Thaler, 2007). Some general arrhythmias include supraventricular tachycardia, atrial flutter, ventricular tachycardia, and atrial fibrillation. However, these are not the only arrhythmias, just the most common ones.

Supraventricular tachycardia occurs when the atria or the AV node produces a regular but rapid discharge. The heart has a rate of over 100bpm (usually around 130-150bpm). Atrial flutter is generated by a reentrant circuit that runs largely around the annulus, the ring-like structure on a heart valve where the valve leaflets are anchored, of the tricuspid valve. Atrial depolarization occurs at such a rapid rate that discrete P waves separated by a flat baseline are not observed (Malcolm S. Thaler, 2007). Because the baseline continuously rises and falls, the effect produces a type of flutter wave. The rate is usually fast (250-350 bpm) and irregular. Ventricular tachycardia occurs when fast and regular impulses come from the ventricle and cause a very rapid heart rate. This arrhythmia can be life-threatening and requires immediate medical attention. Lastly, atrial fibrillation (AF), one of the most common chronic conditions (Benjamin, Wolf et al., 1998), is caused by electrical impulses discharged at a rapid rate from many different areas of the atria. Unlike atrial flutter, where there is a single constant signal responsible for the flutter waves, in AF multiple reentrant circuits are unpredictably occurring (Malcolm S. Thaler, 2007). In an ECG strip, no true P wave can be identified. This arrhythmia also causes fast and irregular heartbeats (usually between 120-180bpm).

Atrial Fibrillation

Based on research conducted in 1995, an estimated 2.23 million Americans have AF, with a median age of 75 years (Feinberg, Blackshear et al., 1995). The prevalence appears to double with each decade, from 0.5% in the population aged 50-59 years to almost 9% between ages 80-89 years, with prevalence being slightly higher in men than women (Conway, 2002) due to the decreased amount of estrogen found in men. It has

been noted that men are 50% more likely than women to develop AF (Kannel, Wolf et al., 1998). The incidence of AF increases with advancing age, with an annual incidence per 1000 person-years of about 3.1 cases in men and 1.9 cases in women 55 to 64 years; also rising to 38.0 and 31.4 cases in men and women 85 to 94 years of age (Benjamin, Levy et al., 1994).

Basic features of AF are great rapidity of atrial depolarization, irregularity of atrial depolarization, and absence of regular atrial activity on the surface ECG (Gallagher and Camm, 1998). Instead of one steady impulse, many impulses begin and spread through the atria to compete for a chance to travel to the AV node. This causes a rapid and disorganized heartbeat. Impulses in the atria can range from 300-600 bpm. The AV node then tries to limit the number of impulses that travel to the ventricles. Even before the ventricle has a chance to contract, another impulse may be sent. Irregular ventricular activity is usually the result of AF, but is not necessary to identify it (Gallagher and Camm, 1998).

There are known causes of atrial fibrillation but at times there can be no underlying heart disease. The most common causes of AF are hypertension, coronary artery disease, valvular disease, congestive heart failure, cardiomyopathy, and congenital heart disease (Benjamin, Levy et al., 1994); however, atrial fibrillation can also develop after cardiac surgery (Benjamin, Wolf et al., 1998). Obesity as a risk factor has been controversial in the past, but there is recent data suggesting an important risk relationship between BMI and AF development (Wang, Parise et al., 2004). Non-cardiac etiological factors associated with atrial fibrillation include high alcohol intake, thyrotoxicosis,

diabetes, chronic obstructive lung disease, infection and pulmonary embolism (Conway, 2002). Also, atrial fibrillation may be related to excessive caffeine use, stress, illegal drugs, electrolyte, or metabolic imbalances (Kannel, Wolf et al., 1998). In extreme cases, the cause is unknown.

Atrial fibrillation can be diagnosed through several tests. The most common tools used to diagnose AF include an electrocardiogram (ECG) or a holter monitor (24 hour test). An ECG records the electrical impulses traveling through the heart muscle. The holter monitor is a small external recorder that is usually worn for one to three days. This may be necessary because the condition often occurs sporadically.

The echocardiographic risk factors for non-rheumatic AF include left atrial enlargement, increased left ventricular thickness, and reduced left ventricular fractional shortening (Vaziri, Larson et al., 1994) For each of these echocardiographic predictors, AF risk increases in a continuous graded fashion (Kannel, Wolf et al., 1998). Because AF is usually associated with an underlying heart disease, other tests may need to be performed to fully diagnose the patient's condition including coronary angiography, stress test, or nuclear imaging tests.

Atrial fibrillation patients may be classified as acute or chronic, depending on whether the arrhythmia has been present for less than or more than 48 hours (Conway, 2002). Chronic AF can be further subdivided into paroxysmal (self-terminating and relapsing episodes), persistent (continuous episode, but susceptible to pharmacological or electrical cardioversion) and permanent (continuous AF despite attempts at cardioversion) (Conway, 2002). AF is highly associated with morbidity and mortality

(Gillinov, 2007) because of further complications and consequences that can occur such as systemic thromboembolism, tachycardia-induced cardiomyopathy, significant symptoms, and poor quality of life (Ad, 2007). Because the atria are beating rapidly and irregularly in chronic AF, blood does not flow quickly through them increasing the risk of a blood clot. The clot can then be pumped out of the heart and travel to other parts of the body, such as the brain. Circulating blood clots could result in a stroke. Atrial fibrillation patients are five to seven more times likely to have a stroke (Conway, 2002; Savelieva and Camm, 2008). Where most attributable stroke risk factors decline with advancing age, the attributable risks for stroke associated with AF increase with age, from 1.5% for those 50 to 59 years of age to 23.5% for those 80 to 89 years of age (Wolf, Abbott et al., 1991). In patients between the ages 80-89, AF is the single most important independent risk factor for stroke (Conway, 2002).

Because of the asynchronous electrical activity, there is a loss of atrial systolic function. The loss of atrial systolic function results in a decrease in stroke volume of about 10% in normal individuals and a greater fall at fast ventricular rates because of the reduction in diastolic filling time (Conway, 2002). Due to the decreased pumping ability of the heart, AF is an independent risk factor for increased mortality and it is also commonly associated with heart failure (HF) (Conway, 2002). The prevalence of AF among patients with HF ranges from 10% to 30% (Crijns, Tjeerdsma et al., 2000). AF is independently associated with a 50% to 90% increase in the risk of death in men and women consistently across the 4 decades of age studied (from 1948 to 1988) (Benjamin, Wolf et al., 1998).

Some patients have AF without any signs or symptoms, a condition known as silent AF. If symptoms occur, they include but are not limited to heart palpitations, fatigue, shortness of breath, exercise intolerance, dizziness, angina, and syncope (Hamer, Blumenthal et al., 1994; Luderitz and Jung, 2000). One study surveyed AF 147 patients and reported that 78% of patients had palpitations, 69% had fatigue, 68% had shortness of breath, 49% had exercise intolerance, 33% had dizziness, 29% had angina, and 14% had syncope (Jung and Luderitz, 1998).

Treatments for AF can range from pharmacological to surgical. Since there are intrinsic cardiac causes that predispose an individual to AF, simply decreasing the risk of cardiovascular events that induce AF will directly decrease the incidence of AF. Rhythm and rate control medications can help return the heart to its normal sinus rhythm (Ad, 2007; Savelieva and Camm, 2008). However, side effects include increased risk of other arrhythmias. Anticoagulants or antiplatelet therapy medications that are used to reduce the chance of blood clots and stroke can be contraindicated in the elderly because their use is often associated with significant morbidity (Kannel, Wolf et al., 1998). Lifestyle changes can also be beneficial. If a patient notices that certain activities trigger AF symptoms, such as smoking, then those activities should be limited and or avoided. Alcohol and caffeine should be taken in moderation if there is an excess usage or even better completely avoided. Also stimulants in cough and cold medications can promote irregular heart rhythms.

Mitral Valve Regurgitation

Atrial fibrillation is sometimes combined with other problems. One of the common problems associated with AF is mitral valvular disease or mitral regurgitation (MR) (Howes, Reid et al., 2001; Gillinov, 2007; Parthenakis, Patrianakos et al., 2007). The mitral valve permits the flow of blood from the atrium to the ventricle during ventricular diastole and prevents retrograde flow during ventricular systole. The mitral valve consists of valvar leaflets, the annulus, tendinous cords/papillary muscles, and subvalvar apparatus. The mitral valvar complex also includes the left atrial and left ventricle myocardium, left atrial and left ventricle endocardium, and the aorto-mitral curtain (Muresian, 2008). The mitral valve uses the tight systolic closure of the left atrioventricular orifice to prevent backflow of the blood from the left ventricle into the atrium. As blood fills the left atrium, the mitral valve remains closed until adequate pressure is generated to open the valve. The valve permissively allows for the atria to rapidly, forcefully, and efficiently eject the blood into the left ventricle and then the aortic root (Muresian, 2008).

Normally, the mitral valve opens due to pressure allowing blood to flow into the left ventricle during left atria systole. It closes at the end of atrial contraction to prevent blood from back flowing into the atria during left ventricular systole.

The mitral valve has two leaflets that guard the opening. The opening is surrounded by a fibrous ring known as the mitral valve annulus. These leaflets are prevented from prolapsing into the left atrium by the tendons attached to the posterior surface of the valve, chordae tendineae. The chordae tendineae are attached at one end to

the papillary muscles and the other to the valve cusps. When the left ventricle contracts, the intraventricular pressure forces the valve to close and prevent blood from flowing back into the left atria. During this time, the tendons prevent the valve from opening in the wrong directions. This prevents blood from flowing back to the left atrium. If damage occurs to any part of the mitral valvar complex, it can hamper emptying of the left atrium, incompetence of the mitral valvar, and/or ejection of the left ventricle (Muresian, 2008).

Mitral regurgitation (MR) is the second most common valve disease, representing nearly one-third of acquired left-sided valve disease (Iung, Baron et al., 2003). Mitral regurgitation is defined as a disorder in which the heart's mitral valve does not properly close, causing blood to flow backward into the upper heart chamber. This causes a decrease in forward blood flow, which in turn through negative feedback increases the forces of cardiac contraction (Libby, 2007). The main causes of mitral regurgitation include myxomatous (degeneration of the mitral valve), ischemic heart disease, coronary artery disease, and Rheumatic heart disease along with several others. Mitral regurgitation may also be caused by dysfunction or injury to the valve following a heart attack or infection of the heart valve (infective endocarditis) which may rupture the valve or surrounding structures, leaving an opening for blood to move backwards (Libby, 2007). The most common cause of mitral regurgitation is myxomatous degeneration of the valve. Degeneration is more common in males and with advancing age. There is a defect in the collagen that makes up the mitral valve which causes the leaflets and chordae tendineae to become stretched out. The stretched out valve leaflets and chordae

tendineae prevent the valve leaflets from closing properly, causing the valve leaflets to prolapse into the left atrium causing mitral regurgitation. The most common scenario that involved both MR and AF is found in rheumatic disease (Gillinov, 2007).

It is important to distinguish between primary and secondary (functional) MR. In primary MR, abnormalities of one or more components of the mitral valve cause it to leak and permit backflow which in turn results in left ventricular volume overload (Carabello, 2008). Severe prolonged primary MR can result in left ventricular remodeling, myocardial dysfunction, pulmonary hypertension, heart failure, and death. Correction of primary MR in a timely fashion can help to prevent these effects. In secondary MR, a damaged left ventricle causes the mitral valve to leak and as a result makes it harder to treat secondary MR (Carabello, 2008). In secondary MR, myocardial damage causes a normal valve to leak, so even if MR is corrected, the underlying muscle disease will still persist (Carabello, 2008).

Mitral regurgitation can become a chronic condition. Symptoms include but are not limited to chest pain, cough, rapid breathing, orthopnea, palpitations, fatigue, and light-headedness (Libby, 2007). People with mild to moderate chronic mitral valve regurgitation may be asymptomatic. Even moderate to severe disease may never display symptoms. If the heart weakens because of the mitral valve, symptoms of heart failure will occur: shortness of breath with activity, extreme tiredness and weakness, and/or edema. Acute mitral valve regurgitation is an emergency, causing severe shortness of breath at rest, coughing, and fast heart beat.

MR imposes a volume overload in the left ventricle (LV), but unlike aortic regurgitation, it does not cause an increase in systolic blood pressure (Wisnbaugh, Spann et al., 1984). Because of increased LV volume from MR, total stroke volume increases, and the resulting thin left ventricular wall enhances diastolic filling (Carabello, 2008). In acute MR, afterload is actually decreased; in chronic compensated MR afterload is normal, and in chronic decompensated MR afterload may actually be greater than normal (Corin, Monrad et al., 1987). If the damaged mitral valve is replaced, where some or all of the chordal attachments between the papillary muscles and valve leaflets are maintained, it can help preserve left ventricular function and improves exercise capacity (David, Burns et al., 1984; Madaric, Watripont et al., 2007).

To diagnose mitral valve regurgitation, one of the simplest ways is for a doctor to feel for a thrill (vibration) over the heart when feeling the chest area (Libby, 2007). While listening to the heart, an extra heart sound (S4 gallop) and a distinctive heart murmur may be heard (Libby, 2007). If fluid backs up in the lungs, crackles may be heard. Diagnostic tests include a chest x-ray, CT scan of the chest, ECG, echocardiogram, or a cardiac catheterization. Treatment depends on the severity of the condition symptoms. Antibiotics are prescribed for bacterial infection and to reduce the risk of infective endocarditis. Anti-hypertensive drugs and vasodilators reduce the strain on the heart. Anti-coagulants or anti-platelet medications prevent clot formation in patients that also have AF. Digitalis may be used to strengthen the heartbeat, and along with diuretics, remove excess fluid in the lungs (Libby, 2007). Patients with severe

symptoms may need to be admitted to a hospital for treatment, and for severe leakages emergency surgery may be necessary.

Exercise Capacity and Exercise Tolerance

Exercise is a physiological stress that in turn stresses the cardiovascular system. In the healthy population, heart rate (HR) and systolic arterial pressure (SAP) increase during exercise. Patients with AF fatigue rapidly and experience palpitations more frequently due to exertion. Gas exchange measurement for the determination of maximal oxygen consumption (VO_{2MAX}), as assessed during cardiopulmonary exercise testing, has become widely established in the routine evaluation and in risk stratification of patients. At sub maximal exercise levels, HR in patients with AF increases more than in those with sinus rhythm (Ueshima, Myers et al., 1993; Howes, Reid et al., 2001). Exercise tests in AF patients are performed predominantly in order to determine if the ventricular rate is under control by pharmacological treatment, to determine functional capacity, and to plan rehabilitation programs (Ueshima, Myers et al., 1993).

In patients with MR, echocardiographic findings at rest, such as systolic and diastolic left ventricular dimension, do not accurately reflect a patient's functional status or symptoms (Enriquez-Sarano, Tajik et al., 1994). Cardiopulmonary exercise testing is considered the standard tool for evaluating functional status, especially in AF and MR patients. Poor exercise capacity, reflected by a low peak oxygen consumption (peak VO_2) paired with an increased ventilatory response as indicated by a steeper slope of ventilation to carbon dioxide production rate (V_E/VCO_2 slope), are strong unfavorable predictors of outcome (De Feo, Franceschini et al., 2005).

Patients with AF have a significantly reduced exercise capacity (Agostoni, Emdin et al., 2008). One of the major characteristics of AF that decreases exercise performance is the irregular, rapid ventricular response at rest and during exercise which may reduce cardiac output by 10% or more (Vanhees, Schepers et al., 2000). Cardiac patients with concomitant AF may derive less benefit from traditional cardiac rehabilitation than other cardiac patients because of their greater reduction in exercise tolerance related to AF. Improving exercise tolerance is very important for these patients because their exercise capacity can be reduced from 15-20% (Atwood, Myers et al., 2007). At anaerobic ventilator threshold, AF patients have a higher VO_2 and heart rate, while sinus rhythm patients have a higher peak exercise VO_2 , O_2 saturation, and work load (Agostoni, Emdin et al., 2008). The reasoning for a lower VO_2 at peak but higher VO_2 at anaerobic threshold is likely related to the higher chronotropic response to exercise in AF patients likely due to an increased sympathetic drive activated to maintain cardiac output. Agostini et al. did not measure cardiac output during exercise; since O_2 saturation was lower, they argued it was likely that stroke volume was lower at peak exercise in AF patients. Despite the reduction in exercise tolerance, AF patients demonstrate similar increases in $\text{VO}_{2\text{MAX}}$ compared to controls (Vanhees, Schepers et al., 2000). In addition to improvements in exercise tolerance, exercise training also is associated with improved overall emotional health (Hegbom, Sire et al., 2006). Interestingly, men demonstrate greater improvements in peak VO_2 and peak cardiac output with exercise training than women (Mertens and Kavanagh, 1996).

The heart is a muscle and like any muscle, it gets stronger with exercise. Aerobic exercise strengthens the heart and makes it more efficient and is generally recommended for those with mitral valve regurgitation. Studies have shown that AF patients who engage in regular aerobic exercise report a decline in symptoms of chest pain, fatigue, dizziness and mood swings, and panic attacks (Bonow, Carabello et al., 2006). A person with mitral valve regurgitation should monitor their heart rate and other symptoms and slow down if they feel their heart racing, become lightheaded, or faint.

Mitral valve regurgitation is generally not considered to be a life threatening or a progressive condition. It may be the most benign of the various types of heart murmurs. However, over time, the added workload on the heart may cause shortness of breath with exercise or it may cause an abnormal heart rhythm (Bonow, Carabello et al., 2006). The abnormal rhythm feels like your heart is pounding, racing, or skipping in your chest. If a valve leaflet cord breaks, the sudden regurgitation may quickly cause heart failure. There are cases where even mild mitral valve regurgitation poses significant health problems and in these cases valve replacement would be considered.

Surgical Treatment

If medications are ineffective or not well tolerated by AF or MR patients, then more aggressive treatment would be required. Non-pharmacological approaches are usually offered to symptomatic patients, and can be done either by percutaneous catheter techniques or various surgical approaches (Ad, 2007). Procedures such as electrical cardioversion, catheter ablation, pulmonary vein isolation, or ablation of the AV node are the most common procedures performed. If these procedures are unsuccessful, even

more aggressive treatments may be necessary. Usually surgery is recommended for patients with chronic AF and MR since their symptoms cannot be relieved by medications or any other procedures. There are a few options for surgical treatment as well, but the most widely used are the robotically assisted minimally invasive mitral valve repair with the atrial cryo-maze procedure.

The original Cox-Maze procedure was developed by James Cox in 1987 to treat the atrial fibrillation and restore the atria to a more normal atria (Cox, 1991). Since then a series of improvements have been made, resulting in the Cox maze III procedure. Cox Maze III is associated with a higher incidence of sinus rhythm return, improved long-term sinus node function, fewer pacemaker implantations, and improved long-term atrial transport function (Ad 2007). Now considered the “gold standard,” Cox-Maze III is also technically less demanding than the Cox-Maze I and II procedures. During the procedure, a series of precise incisions are made in the right and left atria to interrupt the conduction of abnormal impulses (Cox, Jaquiss et al., 1995; Gillinov, 2007). A “maze” of new electrical pathways is created to allow electrical impulses to travel easily through the heart. This allows for a more normal sinus impulse to reach the AV node. A recent report demonstrated long-term results in patients having the Cox-Maze III procedure, either as an isolated or a combined procedure, with a success rate greater than 95% (Damiano, Gaynor et al., 2003; Prasad, Maniar et al., 2003). Another important impact of the Cox-Maze III procedure is a reduction in the rate of cerebrovascular accidents and transient ischemic events (Ad, 2007; Gillinov, 2007). There have been numerous revisions to the Cox-Maze III which have reduced the complexity of the procedure, but in

turn have sacrificed the completeness of the procedure and produced questionable outcomes (Kiser, Wimmer-Greinecker et al., 2007). According to Kiser et al. (2007), the best treatment for all types of atrial fibrillation remains the full Cox-Maze III, which addresses both the left and right atria; and is also associated with clinical benefits in patients with mitral valve disease (Gillinov, 2007).

Originally the Cox Maze procedure used the standard cut-and-sew method. Now there are a variety of devices that use different energy sources that permits the surgeon to rapidly perform corrective AF with very few suture lines (Gammie, Didolkar et al., 2009). One of the new methods uses argon-powered cryoenergy and is known as CryoMaze. As a treatment for atrial fibrillation, the CryoMaze procedure creates linear cryolesions (frozen scars) in the upper chamber of the heart by applying an argon-powered cold probe to freeze the tissue (Gammie, Laschinger et al., 2005). Freezing the tissue creates electrical barriers, which permanently block electrical activity, thus correcting for AF. Electrical barriers can be created in 60-90 seconds, minimizing the duration of the procedure. It has been suggested to be safer and more efficient for the treatment of AF (Gammie, Laschinger et al., 2005) or when combined with other cardiac operations (Gammie, Didolkar et al., 2009). Associated with the CryoMaze are lower stroke rates in long-term follow-up and results that are equivalent to those of the classic Cox Maze III (Gammie, Laschinger et al., 2005). Compared with other energy sources, collateral injury has never been reported, there is a long track record of safety, there is a greater likelihood of a contiguous lesion, and cryotherapy is associated with a lower endocardial thrombus volume (Gammie, Laschinger et al., 2005; Gammie, Didolkar et al., 2009).

With surgery time being reduced, recovery duration is the next stage. Minimally invasive mitral valve surgery continues to evolve as a treatment option. Studies have been conducted showing that mitral valve procedures could be performed with a small incision by modifying the standard sternotomy, or open chest method (Cohn, Adams et al., 1997; Cosgrove, Sabik et al., 1998). These studies have also reported large and successful series of endoscopic mitral valve repairs using various systems. But with the da Vinci® Robotic system, many of the concerns of minimally invasive mitral valve repair were addressed. The da Vinci® Robotic system allows three-dimensional visualization of the operative field and improved surgical manipulation by the use of the endowrists of the surgical arms (Tatooles, Pappas et al., 2004). With the introduction of the transthoracic aortic cross clamp and the da Vinci® Surgical System, mitral valve repair can be performed in the same manner as the standard sternotomy but with truly limited incisions (Tatooles, Pappas et al., 2004). Advantages of minimally invasive mitral valve surgery are reduced surgical trauma, decreased pain, fewer complications, improved cosmesis, shorter length of stay, less bleeding and fewer pulmonary complications, and earlier return to normal daily activity for the patient (Mohr, Onnasch et al., 1999; Reichenspurner, Boehm et al., 2000; Felger, Chitwood et al., 2001; Casselman, Van Slycke et al., 2003; Tatooles, Pappas et al., 2004).

On the day of surgery, electrodes are placed on the patient's chest. The electrodes are connected to an electrocardiogram machine which monitors the patient's heart rhythm and electrical activity. For the original procedure, the surgeons make an incision down the center of the chest and then split the breastbone. This facilitates complete

visualization of the heart and reduces the number of complications. However, using the Robotic-Assisted Maze surgery only small incisions are made between the ribs. The surgeon uses video guided instruments to manipulate a catheter and perform the ablations. The catheter directs cryo-freeze energy to the precise areas in the heart tissue to create lesions that block erratic electrical signals from traveling through the heart (Cox, Jaquiss et al., 1995; Savelieva and Camm, 2008). The patterns of the incision resemble a maze, which directs the heart's electrical impulses straight to the heart's lower chambers due to scar tissue that forms. The scar tissue cannot carry electrical impulses and thus creates a barrier to keep the electrical impulses on course.

Surgical correction of MR aims to preserve cardiac function and to improve function status and survival (Le Tourneau, de Groote et al., 2000). Chronic MR results in a progressive deterioration in left ventricle (LV) contractile function, although the LV ejection fraction (EF) is maintained over a relatively long period (Starling, 1995). After mitral valve surgery, LV contractile impairment has the ability to recover towards normal in most patients.

Exercise tolerance after surgery

In AF patients, Cox Maze does appear to effectively prevent exercise-induced AF (Hemels, Gu et al., 2006). In patients in whom sinus rhythm was established by Cox-Maze, exercise-induced initiation of AF was not observed.

Exercise capacity of patients with and without heart disease that underwent the Cox Maze procedure combined with mitral valve surgery do experience improvements in exercise tolerance in the late phase of their recovery hypothesized to occur through the

restoration of sinus rhythm (Yuda, Nakatani et al., 2004). Mitral valve surgery can improve exercise tolerance independent of sinus rhythm abnormalities (Le Tourneau, de Groote et al., 2000), though not all studies demonstrate such an effect (Kim, Ahn et al., 2004).

The proper timing of surgery in asymptomatic patients remains controversial (Madaric, Watrion et al., 2007). Usually, surgery was proposed when patients started having symptoms. However, it has been shown that patients operated on before the occurrence of symptoms have a better survival than patients operated on with severe symptoms (Enriquez-Sarano, Tajik et al., 1994; Tribouilloy, Enriquez-Sarano et al., 1999). Currently the effect of mitral valve repair (MVR) on exercise capacity and cardiopulmonary testing in patients with little or no symptoms is relatively unknown; however, studies have attempted to understand the mitral valve healing duration post surgery to better assess those effects.

One study looked at exercise tolerance 6 months after surgery and showed no change in exercise tolerance despite the mitral regurgitation correction, in absence of exercise reconditioning (Le Tourneau, de Groote et al., 2000). It is well known that physical training improves exercise performance in patients with coronary heart disease (Hambrecht, Walther et al. 2004) and heart failure (Belardinelli, Georgiou et al., 1999), but it is not known how long it takes for the mitral valve to heal after mitral regurgitation surgery in humans. Meurin et al. (2005) evaluated the safety and feasibility of early exercise training in patients after mitral valve repair. The 251 subjects were placed in an exercise training program that included calisthenics and endurance bicycle training for

about 8 weeks. Exercise training increased both peak VO_2 (22% increase) and anaerobic threshold (16% increase) (Meurin, Iliou et al., 2005). Exercise training appears to be safe in this population, does not have adverse effects on mitral valve function, and improves exercise tolerance.

Madaric et al. (2007) assessed the changes in cardiopulmonary functional capacity after minimally invasive video-assisted mitral valve repair in patients with mitral regurgitation with mild to no symptoms. All patients were in sinus rhythm and had a normal ejection fraction, and 80% claimed to be completely asymptomatic. They focused on testing patients one week before surgery and 4 months after surgery and were tested using a ramp protocol. The patients' quality of life was also assessed during testing time by the Euro Quality of life (EuroQol) questionnaire (Dolan, 1997). The questionnaire was composed of 5 items: mobility, self-care, usual activity, pain or discomfort, and anxiety or depression. Four months after surgery they found significant improvements in $\text{VO}_{2\text{MAX}}$, maximal workload, and peak oxygen pulse. Patients increased their overall health status also. They concluded their study stating that the minimally invasive repair improves exercise capacity of patients with severe mitral regurgitation with none to mild symptoms.

Conclusion

Aging increases the risk of developing AF and MR, both which decrease exercise capacity and exercise tolerance. It is imperative to examine exercise capacity post surgery to gain a better understanding of how quickly patients can return to normal daily activity and improvements in exercise capacity. There is no documented evidence

examining the exercise capacity in patients 7-11 weeks post surgery. The aim of this study is to measure the patients' VO_{2MAX} pre and 7-11 weeks post surgery to see if there is a difference in exercise tolerance. Insight into exercise tolerance changes 7-11 weeks post surgery can lead to quicker return to daily activity and ability to increase exercise capacity post surgery.

CHAPTER III

METHODS

Prior to testing, approval of methods was given by the University and Medical Center Institutional Review Board, and conformed to the University, State of North Carolina, and Federal mandates for standard operating procedures (Appendix A).

Subjects

Subjects diagnosed and already scheduled for treatment of AF, MR or AF+MR by minimally invasive surgery were recruited by their physician. Any patient who was involved in a structured exercise program or participated in 30 minutes of vigorous exercise per week in the last 2 months was excluded. Also any other medical conditions that would prevent patients from safely participating in this study or would result in worsened exercise capacity independent of their cardiac disease were excluded. Once participants were selected they had the following procedures performed before and 7-11 weeks post-surgery. Four male subjects volunteered for this study (mean age 57 years).

Testing Protocol

The testing of these patients was covered over two visits. All testing was performed at Brody room 3S08. After informed consent was signed, on each testing day Physical Activity Scale for the Elderly (PASE) questionnaire and the Modified Baeke (Appendix C) was filled out by one on one interview, resting vitals were measured (height, weight, resting blood pressure, and resting heart rate), minimum waist circumference, and percent body fat was measured by skin folds. Skin fold locations include chest, axilla, triceps, subscapular, abdominal, suprailium, and thigh. All

measurements were done on the right side of the body and performed twice, three times if there is a more than 2 mm discrepancy in measurements.

The questionnaire was used to quantify the amount of activity each individual did before and after surgery. PASE questionnaire was used because it closely matched the literature for how patients function ability was with their condition. Patients were compared to themselves regarding changes in activity levels pre and post-surgery.

Following the resting measurements, subjects performed a physician supervised, symptom limited, graded exercise test using the Modified Naughton treadmill test (Table 1) for determination of maximal oxygen consumption (VO_{2MAX}). Exercise intensity increased while minute ventilation, inhaled oxygen and exhaled carbon dioxide concentrations of the subject were continuously monitored via ParvoMedics TrueMax 2400 Metabolic Cart (Consentius Technologies, Sandy, UT). VO_{2MAX} is the maximum capacity of an individual's body to transport and utilize oxygen during incremental exercise, which reflects the physical fitness of the individual. VO_{2MAX} is reached when oxygen consumption remains at steady state despite an increase in workload. Prior to and during exercise, subjects had their blood pressure measured and a 12-lead ECG monitored. Heart rate was monitored continuously and recorded every two minutes using a Polar Electro heart rate monitor (Polar Electro, Washington, NY). Subjects were encouraged to continue as long as possible. The exercise test was stopped if the subject felt dizzy, had chest pain, had serious shortness of breath, or verbally indicated they wanted the test to be ended. If the physician detected an abnormal heart function from the ECG, then the test was terminated. At the end maximum time was recorded.

Statistical Analysis

A paired *t*-test was used to determine differences in VO_{2MAX} pre- and post-surgery in between individuals. Significance was established at $P \leq 0.05$ and data reported are Mean \pm SE.

Table 1: Modified Naughton Treadmill Protocol

<u>Time (min)</u>	<u>Stage</u>	<u>Speed (mph)</u>	<u>Grade (%)</u>
0-2	1	1.0	0
2-4	2	1.5	0
4-6	3	2.0	3.5
6-8	4	2.0	7.0
8-10	5	2.0	10.5
10-12	6	3.0	7.5
12-14	7	3.0	10.0
14-16	8	3.0	12.5
16-18	9	3.0	15.0
18-20	10	3.5	15.0

Time (min), time in minutes of the treadmill test. Speed (mph), speed, measured in miles per hour, for each stage. Grade (%), percent incline for each stage.

CHAPTER IV

RESULTS

Subject Characteristics

Subject characteristics are in Table 2. Four male patients completed both the pre- and post-surgery exercise testing. Mitral valve disease was present in all patients and surgical repair was performed. One patient had combined MR and AF and also had the biatrial cryo-maze procedure performed. All patients had the minimally invasive robotic surgery performed. There were no differences in HR, % body fat, waist circumference, or treadmill time pre and post-operative (Table 4).

Exercise Tolerance

There was no change in exercise tolerance pre vs. 7-11 weeks post-operation, therefore showing that patients did not have a reduced exercise capacity after surgery (Table 4). Subjects also showed no significant changes in their activity levels, treadmill time to exhaustion and HR pre and post surgery (Table 4). When compared to Houmard et al.'s (1998) age predicted data, the subjects' VO_{2MAX} were not significantly different before or after surgery (Figure 1). However, when compared to ACSM age predicted VO_{2MAX} , subject's had a significantly lower post-surgery VO_{2MAX} (Medicine, 2005) (Figure 2).

Table 2: NYHA Classification

Class	Patient Symptoms	Patients
Class I (Mild)	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, or dyspnea (shortness of breath).	4
Class II (Mild)	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitation, or dyspnea.	0
Class III (Moderate)	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes fatigue, palpitation, or dyspnea.	0
Class IV (Severe)	Unable to carry out any physical activity without discomfort. Symptoms of cardiac insufficiency at rest. If any physical activity is undertaken, discomfort is increased.	0

In order to determine the best course of therapy, physicians often assess the stage of heart failure according to the New York Heart Association (NYHA) functional classification system. This system relates symptoms to everyday activities and the patient's quality of life.

Table 3: Individual Data Pre and Post surgery

<u>Record Number</u>	<u>Age (yrs)</u>	<u>Pre % Fat (%)</u>	<u>Height (cm)</u>	<u>Weight (kg)</u>	<u>Waist (cm)</u>	<u>TM Time (min)</u>	<u>Max HR (bpm)</u>	<u>Pre-VO_{2MAX} (L/min)</u>	<u>Pre-VO_{2MAX} (mL/kg/min)</u>
MR001	59	N/A	175.3	75.9	n/a	20:00	189	2.21	29.1
MR002	49	24.2	172.7	89.5	98.0	13:40	149	2.04	22.7
MR003	64	18.4	188.0	78.6	94.0	12:36	157	1.89	24.1
MR005	56	20.5	170.2	84.5	100.3	21:10	164	2.91	34.5

<u>Record Number</u>	<u>Age (yrs)</u>	<u>Post % Fat (%)</u>	<u>Height (cm)</u>	<u>Weight (kg)</u>	<u>Waist (cm)</u>	<u>TM Time (min)</u>	<u>Max HR (bpm)</u>	<u>Post-VO_{2MAX} (L/min)</u>	<u>Post-VO_{2MAX} (mL/kg/min)</u>
MR001	59	24.8	175.3	72.1	97.8	19:22	180	2.12	28.0
MR002	49	26.1	172.7	90	97.8	15:24	167	2.15	23.9
MR003	64	18.7	188.0	77.5	92.2	12:42	150	1.68	21.7
MR005	56	27.6	170.2	84.5	101.6	15:40	110	2.14	25.3

% Fat, percentage body fat taken using 7 site skin folds on the right side of the subject pre- and post-operation. TM, Treadmill time to maximum exercise. Max HR, heart rate at maximum exercise. VO_{2MAX}, maximal oxygen consumption.

Table 4: Demographic and Exercise Data

	Pre-Op	Post-Op	P Value
Age, yrs	57 ± 3		
Height, cm	176.0 ± 4.3		
Mass, kg	82.2 ± 3.1	81.1 ± 3.9	0.321
Waist, cm	97.5 ± 1.5	97.3 ± 2.0	0.762
%BF	21.0 ± 1.5	24.3 ± 1.9	0.520
PASE Scores	255 ± 100	194 ± 103	0.171
TM time, sec	1012 ± 131	947 ± 82	0.539
Max HR, bpm	164.8 ± 8.6	151.8 ± 15.2	0.449
Absolute VO_{2MAX}, (L/min)	2.26 ± 0.23	2.023 ± 0.11	0.293

Pre (Pre-Op) and post-operative (Post-Op) data. %BF, percentage body fat. PASE Scores, Physical Activity Scale for the Elderly. TM time, maximum treadmill time to exhaustion. Max HR, heart rate at maximum exercise. VO_{2MAX}, absolute maximal oxygen consumption. * - significantly different ($p \leq 0.05$). Mean ±SE.

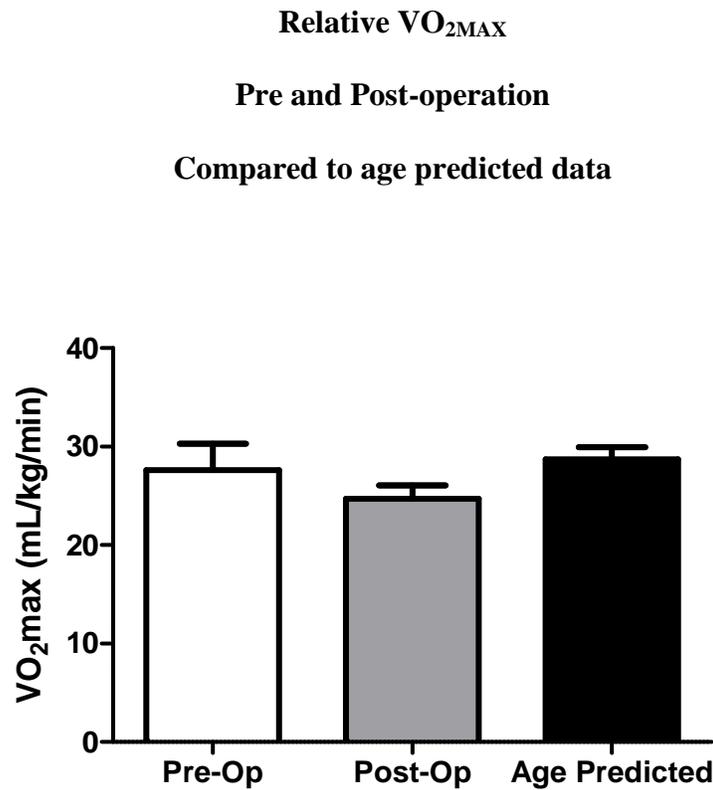


Figure 1: Relative VO₂MAX pre (Pre-Op) and post-operative (Post-Op) and age predicted (Houmard, Weidner et al. 1998). One way repeated measures Anova was used to analyze relative VO₂MAX pre (Pre-Op) and post-operative (Post-Op) and age predicted data (Houmard, Weidner et al. 1998). There were no significant differences in relative VO₂MAX between Pre-Op, Post-Op, or Age Predicted. # - significant difference between groups. Mean \pm SE.

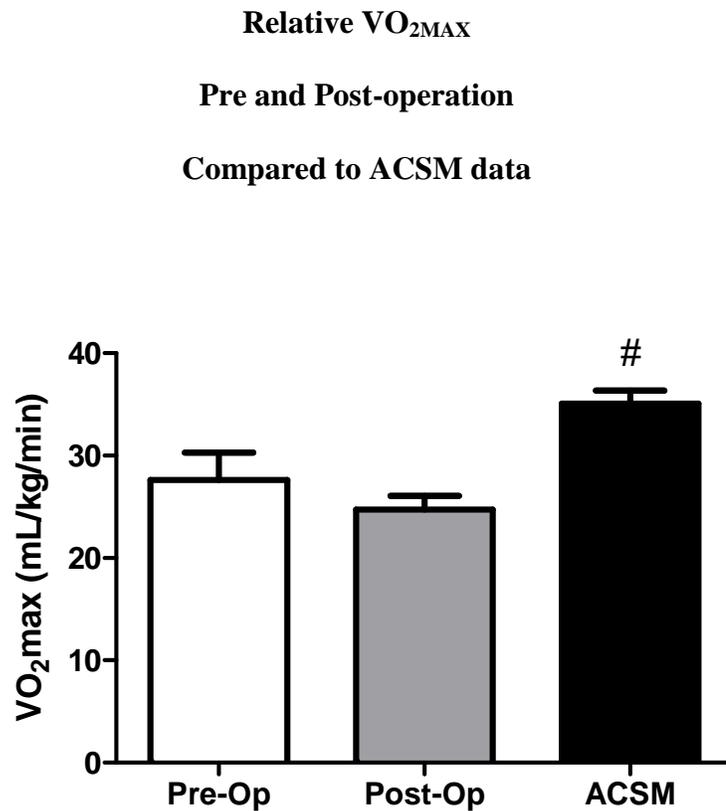


Figure 2: Relative pre (Pre-Op) and post-operative (Post-Op)VO₂MAX values compared to ACSM age predicted (Medicine 2005). One way repeated measures Anova was used to analyze relative VO₂MAX pre (Pre-Op) and post-operative (Post-Op) and ACSM age predicted data (Medicine 2005). ACSM age predicted VO₂MAX was found to be significantly higher than post-operative values. # - significantly different than all other groups ($p \leq 0.05$). Mean \pm SE.

CHAPTER V

DISCUSSION

Findings

The principle findings of this study are: 1) patients did not have reduced exercise tolerance after surgery when compared to pre-operative, 2) when compared to age predicted data (Houmard, Weidner et al. 1998), VO_{2MAX} was not significantly different before or after surgery (Figure 1), and 3) there was no change in activity levels between pre and post surgery (Table 4). The findings of the current study do not support the hypothesis that exercise tolerance would be reduced 7-11 weeks post-operation.

Subject Characteristics

Patients were recruited by their physician and in this study were asymptomatic and functional in their daily living up until the day of surgery. The NHYA classifications, which are a functional and therapeutic classification for prescription of physical activity for cardiac patients, showed the subjects were not in a severe condition. All four patients were NHYA I classified, meaning they had no limitation of physical activity and ordinary physical activity does not cause undue fatigue, palpitation, or dyspnea (shortness of breath). They were not assisted in their daily living, those that worked still went to work, and their daily activities were not affected by their heart condition.

Patients came in one week to as little as 3 days before their surgery. Patients are not seen far in advance before surgery and get surgical treatment soon after their first exercise visit. Their post-operation stress test was done at approximately 7-11 weeks

post-op, usually during their follow-up with the surgeon. Unlike previous studies that tested severely de-conditioned patients who were unable to perform their daily activities, the patients in the current study were completely functional and were younger (mean age 57 ± 3 compared to studies with mean ages of 70+). The current study specifically tested patients that were not severely de-conditioned and had a very good NYHA classification. Another study, that investigated severely de-conditioned patients who were unable to perform their daily activities, showed that after surgery their activities levels did increase and they were able to perform majority of their daily activities without fatigue (Le Tourneau, de Groote et al., 2000).

Given that the current patients were sedentary post-operation and still healing from surgery, their exercise capacity did not drop significantly from pre-operations values. When compared to Houmard et. al's (1998) age predicted data, there was no significant difference. The subjects' VO_{2MAX} were closer to Houmard et. al's (1998) age-predicted data than when compared to ACSM's age predicted VO_{2MAX} . This is due to the fact that as an individual ages, their VO_{2MAX} decreases linearly and a prediction that takes that into account is more accurate. ACSM's data classifies individuals based on a 10 year age predicted VO_{2MAX} (Medicine 2005). A 50 year old male's VO_{2MAX} will not be the same when he turns 59 years old and thus cannot be compared. ACSM's data is an average of national VO_{2MAX} for a 10 year age range. Houmard et. al's (1998) study closely matches the population in this study because it represents Eastern North Carolina's VO_{2MAX} values and eliminates the age gap represented in ACSM's data. Although the subject's VO_{2MAX} were closely matched with another study (Houmard,

Weidner et al., 1998), only 2 subjects (MR002, MR003) had lower than normal values. However there was no significant difference when compared to pre-operation values. Treadmill times varied with individuals: MR001 and MR005 had lower post-operation treadmill times, while the other two subjects MR002 and MR003 had higher post-operation treadmill times. Overall the mean treadmill time for the subjects were no different post-operation compared to pre-operation. All subjects continued testing until they indicated they wanted the test to be terminated. Also subjects reached their 60% heart rate max, which showed a true max for the patients in the current study.

There were a few factors that were controlled in this study. First patients enrolled were already diagnosed with valvular disease, AF, or both. Second, these patients were scheduled to have minimally invasive corrective surgery. Lastly, patients were not to have a NYHA class of III or IV, thus causing them increased discomfort with stress testing. Whether or not patients returned to their daily activities or if they exercised post-surgery was not controlled.

Effects of AF and MR on Exercise Tolerance

Severe AF and MR patients have reduced exercise tolerance and an inability to increase it due to the palpitations and fatigue associated with the disease (De Feo, Franceschini et al. 2005; Agostoni, Emdin et al. 2008). Typically these patients cannot perform their usual daily activity, are greatly fatigued by minimal exertion, and have a severely reduced exercise tolerance (Agostoni, Emdin et al. 2008). Compared to previous studies (Lewis, Irvine et al. 1988), the current subjects were asymptomatic and did not have a severe disease progression nor a severely reduced exercise tolerance.

Unlike previously treated patients that were in severe condition (Lewis, Irvine et al. 1988), the current patients were still active and performing their daily activities with little to no help. When compared to age predicted data with no signs of CHF or other known cardiac problem (Houmard, Weidner et al. 1998), there was no significant differences in VO_{2MAX} .

Effect of Minimally Invasive Surgery on Exercise Tolerance

Studies have shown that Minimally Invasive Robotic Surgery does return a patient to normal sinus rhythm (Gammie, Laschinger et al., 2005; Gammie, Didolkar et al., 2009) and return a patient to their daily activities 2 weeks quicker than a normal sternotomy (Mohr, Onnasch et al., 1999; Reichenspurner, Boehm et al., 2000; Felger, Chitwood et al., 2001). It has also been shown that treating MR and AF early, before the condition becomes severe enough to decrease an individual's daily activities, can return the patient to a condition capable of increasing their exercise tolerance (Meurin, Iliou et al., 2005). However, it is not known how soon surgical treatment should be given in MR and AF patients. It is also unknown how soon improved exercise tolerance can be observed (with no training).

Historically, exercise tolerance is reduced in AF and MR patients (De Feo, Franceschini et al., 2005; Agostoni, Emdin et al., 2008) and surgical treatment improves exercise tolerance (Le Tourneau, de Groote et al., 2000; Meurin, Iliou et al., 2005). In AF and MR patients with reduced exercise tolerance, surgical intervention improved exercise tolerance by 11.2% at 4 mo post-surgery (Madaric, Watripont et al., 2007). When surgical treatment is followed with formal exercise training, peak oxygen

consumption and anaerobic threshold increased 22% and 16% respectively 8 weeks post surgery (Meurin, Iliou et al., 2005). Compared to those results, the current study found that 7-11 weeks after surgery, with patients being sedentary, there was no difference in exercise capacity.

Limitations

A limitation that could not be controlled was the time the patient was tested for their post-operative visit. Because of scheduling patients coming from out of town and unseen factors such as illness, patient's post-operative visits varied. The post-operative visit was between 7-11 weeks post-surgery. Three patients came in 7 weeks after surgery with one coming in 11 weeks after surgery.

Since all testing was done at Brody, there was a limitation with measuring body fat percentage. Instead of using a Dual Energy X-Ray Absorptiometry (DEXA) to measure body fat, a 7-site skinfold was taken on the right side of every subject. While the accuracy of predicting percent fat from skinfolds is approximately plus or minus 3.5% assuming that appropriate techniques and equations have been used (Medicine, 2005), DEXA has an accuracy of plus or minus 1-3%.

Inexperience in treadmill usage was an issue for some patients. Some patients felt very comfortable on the treadmill, keeping hands by their sides and swinging them; while others patients were not as accustomed to the incline of the machine and holding the side handle bars. This could have biased exercise tolerance during the initial test toward lower exercise tolerance pre-surgery.

Future Projects

In order for a stronger finding to occur, more subjects need to be recruited and tested. Since the patients in this study were treated fairly early in their disease progression (NYHA classification Stage 1), a 6 month follow up in combination with an exercise training may demonstrate significant increases in VO_{2MAX} . If these patients underwent an exercise training program and follow up evaluations could be done, perhaps their VO_{2MAX} would be higher.

Conclusions

At 7-11 weeks following minimally invasive surgery to treat MR and AF, exercise tolerance is unchanged compared to pre-surgery. While not tested in the current investigation, it is likely that surgical treatment involving a sternotomy would have decreased exercise tolerance at 7-11 weeks post-op suggesting that minimally invasive surgery does provide significant outcomes for patients by maintaining exercise tolerance. Historically, surgical treatment for MR and AF is associated with an improvement in exercise tolerance which was not observed in the current investigation, however when patients with MR and AF are tested early in disease progression (NYHA class I) there is no significant decrement in exercise tolerance compared to age normative data and so surgery would not be expected to improve exercise tolerance. Since the patients in the current study were treated fairly early, they can return to daily activities quicker post surgery and they have the potential to increase their exercise tolerance and be above age normative data. The results of this study do not support the hypothesis that subjects' exercise capacity and tolerance will be reduced 7-11 weeks post-operation.

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APPENDIX A:
UMCIRB APPROVAL


University and Medical Center Institutional Review Board

East Carolina University

Ed Warren Life Sciences Building • 600 Moye Boulevard • LSB 104 • Greenville, NC 27834

 Office 252-744-2914 • Fax 252-744-2284 • www.ecu.edu/irb

Chair and Director of Biomedical IRB: L. Wiley Nifong, MD

Chair and Director of Behavioral and Social Science IRB: Susan L. McCammon, PhD

TO: Evalio Rodriguez, MD, Dept of Cardio Vascular Sciences, ECU—363 Ward Sports Medicine Building

FROM: UMCIRB *zz*

DATE: July 10, 2008

RE: Full Committee Approval of a Study

TITLE: “Mitochondrial Dysfunction in Cardiac Muscle of Patients with Mitral Regurgitation and/or Atrial Fibrillation, and Impact of Surgical Intervention on Exercise Capacity and Mitochondrial Function in Skeletal Muscle”

UMCIRB #08-0380

The above referenced research study was initially reviewed by the convened University and Medical Center Institutional Review Board (UMCIRB) on **6.11.08**. The research study underwent a review and approval of requested modifications on 7.8.08 by W. Nifong. The UMCIRB deemed this **unfunded** study **more than minimal risk** requiring a continuing review in **12 months**. Changes to this approved research may not be initiated without UMCIRB review except when necessary to eliminate an apparent immediate hazard to the participant. All unanticipated problems involving risks to participants and others must be promptly reported to the UMCIRB. The investigator must submit a continuing review/closure application to the UMCIRB prior to the date of study expiration. The investigator must adhere to all reporting requirements for this study.

The above referenced research study has been given approval for the period of **6.11.08** to **6.10.09**. The approval includes the following items:

- Internal Processing Form
- Protocol (received 7.8.08)
- Informed Consent (dated 7.8.08)
- COI Disclosure form (dated 5.30.08)

The following UMCIRB members were recused for reasons of potential for Conflict of Interest on this research study:
None

NOTE: The following UMCIRB members with a potential Conflict of Interest did not attend this IRB meeting:
None

The UMCIRB applies 45 CFR 46, Subparts A-D, to all research reviewed by the UMCIRB regardless of the funding source. 21 CFR 50 and 21 CFR 56 are applied to all research studies under the Food and Drug Administration regulation. The UMCIRB follows applicable International Conference on Harmonisation Good Clinical Practice guidelines.

APPENDIX B:
INFORMED CONSENT

Unique Identifier: MR/A-Fib and effects on skeletal muscle function

INFORMED CONSENT

Title: Mitochondrial Dysfunction in Cardiac Muscle of Patients with Mitral Regurgitation and/or Atrial Fibrillation, and Impact of Surgical Intervention on Exercise Capacity and Mitochondrial Function in Skeletal Muscle

Principal Investigator: Evelio Rodriguez, M.D.

Institution: Brody School of Medicine, Pitt County Memorial Hospital

Address: Teaching Annex PCMH 277

Telephone #: (252) 744-4536

This consent form document may contain words that you do not understand. You should ask the study doctor or the study coordinator to explain any words or information in this consent form that you do not understand.

INTRODUCTION

You have been asked to participate in a research study being conducted by Evelio Rodriguez, M.D. and fellow researchers at East Carolina University designed to determine if surgery that corrects mitral valve regurgitation (MR) (abnormal leaking of blood on the valve) and/or atrial fibrillation (AF) (abnormal heart rhythm) improves exercise capacity by reversing abnormalities in cardiac and skeletal muscle function. You have been asked to volunteer for this study because you are scheduled for surgery to treat your MR and/or AF. We know that surgery to treat MR and AF improves exercise capacity in individuals such as yourself and we are investigating how these surgeries improve cardiac and skeletal muscle structure and function. Approximately 75 individuals will be enrolled in this study.

PLANS AND PROCEDURES

Following successful recruitment and completion of this informed consent, you will have the following procedures performed. These exercise testing and Skeletal muscle biopsy procedures will occur prior to your surgery and again at 6 weeks post-surgery.

Exercise Testing

You will arrive at the Brody School of Medicine - 3S-08 in the morning where you will meet a doctor that will be overseeing this experiment. Please report at least 2 hour after your most recent meal. This testing will take approximately 1.5 hours to complete. The following procedures will occur in the order indicated:

1. Determination of fat-free and fat mass. Body composition will be determined by DEXA (a type of x-ray that scans the body and measures fat). Fat-free and fat mass will be calculated from body mass and body fat percentage.
2. Muscle biopsy. In this procedure, a small amount of anesthesia (3cc of 1% Lidocaine) will be injected in a ½ inch area under the skin of your thigh. A small (1/4 inch) incision will then be made through the skin, fat, and fibrous layer, which lies over the muscle. A biopsy needle (about ½ the width of a pencil) is then inserted through the incision ½ to 1 inch into the muscle. A small (½ the size of an eraser at the end of a pencil) piece of muscle is then clipped out with the biopsy needle. The needle is withdrawn and the muscle sample will be

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Subjects initials _____

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used for the determination of muscle fiber type, mitochondrial content, muscle blood vessels, and characteristics of the muscle performance capacity. Timothy Gavin, PhD; Evelio Rodriquez, MD; or Alan Kypson, MD will perform the muscle biopsies. You will then have pressure applied to the biopsy site for 10 minutes and a cold pack applied for 5 minutes. The incision will be closed with a steri-strip and a Band-Aid; a temporary pressure wrap will also be applied to your leg. The needle muscle biopsy technique is a research procedure designed to investigate phenomena in skeletal muscle; it has been performed on over 3000 occasions at ECU. The total time for this procedure is 30 minutes.

Exercise test. You will begin by walking on a tread mill at a slow speed and slight inclination, which will progressively increase with time. We will continue the test until you feel that you can no longer walk because of discomfort. You will probably exercise for 5 to 15 minutes, depending upon your fitness level. We will record the maximum speed and incline that the treadmill reached. During this test you will be fitted with a mouthpiece through which we can measure the oxygen and carbon dioxide levels that you breathe and the size of the breaths that you take while exercising. Your heart rate and heart tracings (ECG) will also be monitored during exercise and recovery.

Atrial tissue recovery

At the time of your heart surgery, your doctors will take a small piece of your atrial tissue. This piece of atrial tissue would normally be discarded as part of your heart surgery. There is nothing unusual or modified about your heart surgery in order to obtain this tissue and the taking of this tissue does not increase your risks in any way.

POTENTIAL RISKS AND DISCOMFORTS

Maximal and Sub-maximal Exercise Testing - Risks associated with the exercise to be completed in the current study are dizziness, ventricular arrhythmia (odd heart beats), and in very rare instances death. These risks are very small, with an occurrence of fewer than 1 in 10,000 deaths in patients who are known to, or suspected of, having heart disease. To minimize this risk, a Physician will conduct the maximal exercise test. The maximal exercise test will be stopped if you feel dizzy, are having chest pain, are having serious shortness of breath, or ask that the test be ended. The test will also be stopped if it is detected (from the ECG) that heart function is not normal.

Muscle Biopsy Procedure - Possible risks are a slight chance of fainting, a small risk of infection, injury to a blood vessel or nerve, and muscle soreness with bruising. You may have an allergic response to the injected anesthetic used in the current study if you do possess an allergy. You will also feel a stinging sensation during the injection of the anesthetic and may feel a sensation of pressure when the needle is inserted into the muscle. You understand that no stitches are required to heal the incision, but that you will be left with a small scar at each site.

EXCLUSIONS

To your knowledge, you are not allergic to Novocaine (Lidocaine). For example, you have not had an allergic reaction to an injection at the dentist's office. In the last two months, you have not participated in a structured exercise program. You do not perform vigorous physical activity for more than 30 minutes per week.

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POTENTIAL BENEFITS

The information gathered from this study may provide valuable insight into findings on the causes and potential treatments for mitral valve regurgitation and atrial fibrillation. There will be no direct benefits to you from this research.

TERMINATION OF PARTICIPATION

Your participation in this research study may be terminated without your consent if the investigators believe that these procedures will pose unnecessary risks to you. You may also be terminated from participation if you do not adhere to the study protocol.

COST AND COMPENSATION

You will receive \$100 for your time and inconvenience of participation at each test time point (prior to and at 6 weeks post-operatively) for a total of \$200 if you complete the pre- and post-surgery testing. The checks will be mailed out within 4 weeks of completing each phase of the study. The policy of East Carolina University and Pitt County Memorial Hospital does not provide for compensation or medical treatment for subjects because of physical or other injury resulting from this research activity. However, every effort will be made to make the facilities of the School of Medicine available for treatment in the event of such physical injury.

CONFIDENTIALITY

Only the investigators associated with this study will have access to the data obtained. However, the University Medical Center Institutional Review Board (UMCIRB), governmental, or university officials may require access to the data to determine if the research outlined here complies with all university and governmental statutes. Your identity will be protected by numeric coding. In the reporting of the results, no identifying information will be released.

VOLUNTARY PARTICIPATION

You understand that your participation in this study is voluntary. Refusal to participate will involve no penalty or loss of benefits to which you are otherwise entitled. Furthermore, you may stop participating at any time you choose without penalty, loss of benefits, or without jeopardizing your continuing medical care at this institution.

PERSONS TO CONTACT WITH QUESTIONS

The investigators will be available to answer any questions concerning this research, now or in the future. You may contact the primary investigator Evelio Rodriquez, MD at 252-744-4536 (days), Timothy P. Gavin, PhD at 252-737-4684 or 252-737-4688 (days) or 252-353-9969 (nights and weekends), Alan Kypson, MD at 252-744-3552 (days), Darrell Neuffer, PhD at 252-744-2780 (days), and Ethan Anderson, PhD at 252-744-2718 (days). If questions arise about your rights as a research subject, you may contact the Chairman of the University and Medical Center Institutional Review Board at phone number 252-744-2914 (days). You may contact Risk Management & Quality Programs at 252-328-2380. If you have a question about injury related to this research, you may call the ECU Brody School of Medicine Risk Management Office at 252-744-1857 (days).

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Exclusion Criteria Checklist

To the best of your knowledge you:

- Are not allergic to Novocaine (Lidocaine).
 Are not participating in a structured exercise program.
 Are not performing vigorous physical activity for more than 30 minutes per week.

RESEARCH PARTICIPANT AUTHORIZATION TO USE AND DISCLOSE INFORMATION

Federal laws require that researchers and health care providers protect your identifiable health information. Federal laws also require that researchers get your permission to use collected health information for research. The identifiable information we will collect from subjects in this research project will include: medications, blood levels of insulin, glucose, lipids, and other compounds related to diabetes and cardiovascular disease risk.

The members of our research team that will have access to your information will include the Principle Investigator, co-investigators, as well as technical and nursing personnel involved in this project. Information about you will be used and released in such a way that will protect your identity as much as possible; however, confidentiality cannot be absolutely guaranteed. We will only share your information with those individuals listed above. If we need to share information with other individuals other than those listed, we will request your permission a second time.

You will be given a signed copy of your authorization to release medical information for your records. You can limit the amount and type of information that is shared and you must make this request in writing; however, the researcher is able to use any and all information collected prior to the request not to disclose information. Although you can limit the release of your medical information, withholding some information may cause you to become ineligible for this research project. Because research information continues to be looked at after a study is finished, it is difficult to say when the use of your information will stop. There is currently not an expiration date for the use and disclosure of your information for this study. If a commercial product is developed from this research project, you will not profit financially from such a product.

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APPENDIX C:
ACTIVITY QUESTIONNAIRE

Id number or Name: _____

Visit: 1 or 2 (circle)

Date:

Physical Activity Scale for the Elderly

➤ INSTRUCTIONS:

Please complete this questionnaire by either circling the correct response or filling in the blank. Answer all items as accurately as possible. All information is strictly confidential.

➤ LEISURE TIME ACTIVITY

Q1. Over the past 7 days, how often did you participate in sitting activities such as reading, watching TV or doing handcrafts? (circle one answer)

- 0. NEVER (**go to Q2**)
- 1. SELDOM (1-2 DAYS)
- 2. SOMETIMES (3-4 DAYS)
- 3. OFTEN (5-7 DAYS)

1a. What were these activities?

1b. On average, how many hours per day did you engage in these sitting activities? (circle one answer)

- 1. Less than 1 hour
- 2. 1 but less than 2 hours
- 3. 2-4 hours
- 4. More than 4 hours

Q2. Over the past 7 days, how often did you take a walk outside your home or yard for any reason? For example, for fun or exercise, walking to work, walking the dog, etc.? (circle one answer)

- 0. NEVER (**go to Q3**)
- 1. SELDOM (1-2 DAYS)
- 2. SOMETIMES (3-4 DAYS)
- 3. OFTEN (5-7 DAYS)

Id number or Name: _____

Visit: 1 or 2 (circle)

Date:

2a. On average, how many hours per day did you spend walking? (circle one answer)

1. Less than 1 hour
2. 1 but less than 2 hours
3. 2-4 hours
4. More than 4 hours

Q3. Over the past 7 days, how often did you engage in light sport or recreational activities such as bowling, golf with a cart, shuffleboard, fishing from a boat or pier or other similar activities? (circle one answer)

0. NEVER (**go to Q4**)
1. SELDOM (1-2 DAYS)
2. SOMETIMES (3-4 DAYS)
3. OFTEN (5-7 DAYS)

3a. What were these activities?

3b. On average, how many hours per day did you engage in these light sport or recreational activities? (circle one answer)

1. Less than 1 hour
2. 1 but less than 2 hours
3. 2-4 hours
4. More than 4 hours

Q4. Over the past 7 days, how often did you engage in moderate sport and recreational activities such as doubles tennis, ballroom dancing, hunting, ice skating, golf without a cart, softball or other similar activities? (circle one answer)

0. NEVER (**go to Q5**)
1. SELDOM (1-2 DAYS)
2. SOMETIMES (3-4 DAYS)
3. OFTEN (5-7 DAYS)

4a. What were these activities?

Id number or Name: _____

Visit: 1 or 2 (circle)

Date:

4b. On average, how many hours per day did you engage in these moderate sport and recreational activities? (circle one answer)

1. Less than 1 hour
2. 1 but less than 2 hours
3. 2-4 hours
4. More than 4 hours

Q5. Over the past 7 days, how often did you engage in strenuous sport and recreational activities such as jogging, swimming, cycling, singles tennis, aerobic dance, skiing (downhill or cross-country) or other similar activities? (circle one answer)

0. NEVER (**go to Q5**)
1. SELDOM (1-2 DAYS)
2. SOMETIMES (3-4 DAYS)
3. OFTEN (5-7 DAYS)

5a. What were these activities?

5b. On average, how many hours per day did you engage in these strenuous sport and recreational activities? (circle one answer)

1. Less than 1 hour
2. 1 but less than 2 hours
3. 2-4 hours
4. More than 4 hours

Q6. Over the past 7 days, how often did you do any exercises specifically to increase muscle strength and endurance, such as lifting weights or pushups, etc.? (circle one answer)

0. NEVER (**go to Q7**)
1. SELDOM (1-2 DAYS)
2. SOMETIMES (3-4 DAYS)
3. OFTEN (5-7 DAYS)

6a. What were these activities?

Id number or Name: _____

Visit: 1 or 2 (circle)

Date:

6b. On average, how many hours per day did you engage in exercises to increase muscle strength and endurance? (circle one answer)

1. Less than 1 hour
2. 1 but less than 2 hours
3. 2-4 hours
4. More than 4 hours

➤ **HOUSEHOLD ACTIVITY**

Q7. During the past 7 days, have you done any light housework, such as dusting or washing dishes? (circle correct answer)

1. NO
2. YES

Q8. During the past 7 days, have you done any heavy housework or chores, such as vacuuming, scrubbing floors, washing windows, or carrying wood? (circle correct answer)

1. NO
2. YES

Q9. During the past 7 days, did you engage in any of the following activities? Please circle YES or NO for each item.

	<u>NO</u>	<u>YES</u>
a. Home repairs like painting, wallpapering, electrical work, etc.	1	2
b. Lawn work or yard care, including snow or leaf removal, wood chopping, etc	1	2
c. Outdoor gardening	1	2
d. Caring for another person, such as children, dependent spouse, or another adult	1	2

Id number or Name: _____

Visit: 1 or 2 (circle)

Date:

➤ **WORK-RELATED ACTIVITY**

Q10. During the past 7 days, did you work for pay or as a volunteer? (circle correct answer)

0. NO (**End of survey**)

1. Yes

10a. How many hours per week did you work for pay and/or as a volunteer?

_____ Hours

10b. Which of the following categories best describes the amount of physical activity required on your job and/or volunteer work? (circle correct answer)

1. Mainly sitting with slight arm movements.
[**Examples:** office worker, watchmaker, seated assembly line worker, bus driver, etc.]
2. Sitting or standing with some walking.
[**Examples:** cashier, general office worker, light tool and machinery worker.]
3. Walking, with some handling of materials generally weighing less than 50 pounds.
[**Examples:** mailman, waiter/waitress, construction worker, heavy tool and machinery worker.]
4. Walking and heavy manual work often requiring handling of material weighing over 50 pounds.
[**Examples:** lumberjack, stone mason, farm, or general laborer.]

Modified Baecke Questionnaire for Older Adults

➤ INSTRUCTIONS:

Please complete this questionnaire by either circling the correct response or filling in the blank. Answer all items as accurately as possible. All information is strictly confidential

➤ HOUSEHOLD ACTIVITIES

Q1. Do you do the light household work? (dusting, washing dishes, repairing clothes, etc.)? (circle correct answer)

- 0. Never (< once a month)
- 1. Sometimes (only when partner or help is not available)
- 2. Mostly (sometimes assisted by partner or help)
- 3. Always (alone or together with partner)

Q2. Do you do the heavy housework? (washing floors and windows, carrying trash disposal bags, etc.)? (circle correct answer)

- 0. Never (< once a month)
- 1. Sometimes (only when partner or help is not available)
- 2. Mostly (sometimes assisted by partner or help)
- 3. Always (alone or together with partner)

Q3. For how many persons do you keep house? (including yourself; fill in "0" if you answered "never" in Q1 and Q2.)

_____ number of people

Q4. How many rooms do you keep clean, including kitchen, bedroom, garage, cellar, bathroom, ceiling, etc.? (fill in "0" if you answered "never" in Q1 and Q2.) (circle correct answer)

- 0. Never do housekeeping
- 1. 1-6 rooms
- 2. 7-9 rooms
- 3. 10 or more rooms

Q5. If any rooms, on how many floors? (fill in "0" if you answered "never" in Q4.)

_____ number of floors

Q6. Do you prepare warm meals yourself, or do you assist in preparing? (circle correct answer)

0. Never
1. Sometimes (once or twice a week)
2. Mostly (3-5 times a week)
3. Always (more than 5 times a week)

Q7. How many flights of stairs do you walk up per day? (one flight of stairs is 10 steps.)

0. I never walk stairs
1. 1-5
2. 6-10
3. More than 10

Q8. If you go somewhere in your hometown, what kind of transportation do you use? (circle correct answer)

0. I never go out
1. Car
2. Public transportation
3. Bicycle
4. Walking

Q9. How often do you go out for shopping? (circle correct answer)

0. Never or less than once a week
1. Once a week
2. Twice to four times a week
3. Every day

Q10. If you go out for shopping, what kind of transportation do you use? (circle correct answer)

0. I never go out
1. Car
2. Public transportation
3. Bicycle
4. Walking

➤ **SPORT ACTIVITIES**

In the past year, what sports have you participated in? (ex: baseball, basketball, golf, shuffle board, bowling, tennis, water aerobics, swimming...etc)

Sport 1: Name _____

Hours per week: _____ (indicate the letter for the time spent)

- a. Less than 1h/wk
- b. 1 - <2h/wk
- c. 2 - <3h/wk
- d. 3 - <4h/wk
- e. 4 - <5h/wk
- f. 5 - <6h/wk
- g. 6 - <7h/wk
- h. 7 - <8h/wk
- i. 8 or more h/wk

Period of the year: _____ (indicate the correct letter for months)

- a. Less than 1 mo/yr
- b. 1 - 3 mo/yr
- c. 4 - 6 mo/yr
- d. 7 - 9 mo/yr
- e. More than 9 months/yr

Sport 2: Name _____

Hours per week: _____ (indicate the letter for the time spent)

- a. Less than 1h/wk
- b. 1 - <2h/wk
- c. 2 - <3h/wk
- d. 3 - <4h/wk
- e. 4 - <5h/wk
- f. 5 - <6h/wk
- g. 6 - <7h/wk
- h. 7 - <8h/wk
- i. 8 or more h/wk

Period of the year: _____ (indicate the correct letter for months)

- a. Less than 1 mo/yr
- b. 1 - 3 mo/yr
- c. 4 - 6 mo/yr
- d. 7 - 9 mo/yr
- e. More than 9 months/yr

➤ **LEISURE TIME ACTIVITIES**

Do you have any other physically active activities? (ex: walking, gardening, knitting, sewing, crocheting, fishing, dancing, etc.)

Activity 1: Name _____

Hours per week: _____ (indicate the letter for the time spent)

- a. Less than 1h/wk
- b. 1 - <2h/wk
- c. 2 - <3h/wk
- d. 3 - <4h/wk
- e. 4 - <5h/wk
- f. 5 - <6h/wk
- g. 6 - <7h/wk
- h. 7 - <8h/wk
- i. 8 or more h/wk

Period of the year: _____ (indicate the correct letter for months)

- a. Less than 1 mo/yr
- b. 1 - 3 mo/yr
- c. 4 - 6 mo/yr
- d. 7 - 9 mo/yr
- e. More than 9 months/yr

Activity 2: Name _____

Hours per week: _____ (indicate the letter for the time spent)

- a. Less than 1h/wk
- b. 1 - <2h/wk
- c. 2 - <3h/wk
- d. 3 - <4h/wk
- e. 4 - <5h/wk
- f. 5 - <6h/wk
- g. 6 - <7h/wk
- h. 7 - <8h/wk
- i. 8 or more h/wk

Period of the year: _____ (indicate the correct letter for months)

- a. Less than 1 mo/yr
- b. 1 - 3 mo/yr
- c. 4 - 6 mo/yr
- d. 7 - 9 mo/yr
- e. More than 9 months/yr

Activity 3: Name _____

Hours per week: _____ (indicate the letter for the time spent)

- a. Less than 1h/wk
- b. 1 - <2h/wk
- c. 2 - <3h/wk
- d. 3 - <4h/wk
- e. 4 - <5h/wk
- f. 5 - <6h/wk
- g. 6 - <7h/wk
- h. 7 - <8h/wk
- i. 8 or more h/wk

Period of the year: _____ (indicate the correct letter for months)

- a. Less than 1 mo/yr
- b. 1 - 3 mo/yr
- c. 4 - 6 mo/yr
- d. 7 - 9 mo/yr
- e. More than 9 months/yr

APPENDIX D:
TESTING PROTOCOLS

PRELIMINARY EVALUATION

Student Name: _____

Date: _____

Client Check-In

- Check that your client has a purple FITT parking pass
- Collect your client's Personal History Form and Know Your Number Questionnaire
- Have client complete a HIPPA form and Informed Consent located in the client's folder
- Lead your client to the locker room area and offer them a lock for their personal items

Personal Information

- Client Name: _____
- Age: _____ DOB: ____/____/____
- Resting Heart Rate: _____ Resting Blood Pressure: ____/____
- Height: _____(in.) Weight: _____ Minimum Waist: _____(in.)

Skinfold Measurement

	T-1	T-2	T-3
Chest			
Axilla			
Triceps			
Subscapular			
Abdominal			
Suprailium			
Thigh			

Skinfold % Fat: _____ %

Modified Naughton Treadmill Test

Subject: _____ Age: _____ Date: _____

Age-Predicted Maximum HR: _____ 85% _____ 100%

Supine: HR _____ BP _____ / _____ Sitting: HR _____ BP _____ / _____

Standing: HR _____ BP _____ / _____

Stage	Minute (min)	Speed (mph)	Grade (%)	METS	Heart Rate	Blood Pressure	RPE	COMMENTS
0	REST	0.0	0.0	1.0				
1	0:00	1.0	0.0	1.2	_____			_____
	1:00				_____	_____/_____	_____	
2	2:00	1.5	0.0	2.3	_____			_____
	3:00				_____	_____/_____	_____	
3	4:00	2.0	3.5	3.3	_____			_____
	5:00				_____	_____/_____	_____	
4	6:00	2.0	7.0	4.5	_____			_____
	7:00				_____	_____/_____	_____	
5	8:00	2.0	10.5	5.5	_____			_____
	9:00				_____	_____/_____	_____	
6	10:00	3.0	7.5	6.5	_____			_____
	11:00				_____	_____/_____	_____	
7	12:00	3.0	10.0	7.5	_____			_____
	13:00				_____	_____/_____	_____	
8	14:00	3.0	12.5	8.5	_____			_____
	15:00				_____	_____/_____	_____	
9	16:00	3.0	15.0	9.5	_____			_____
	17:00				_____	_____/_____	_____	

10	18:00	3.5	15.0	10.5	_____	_____
	19:00				_____/____	_____
11	20:00	4.0	15.0	11.5	_____	_____
	21:00				_____/____	_____
12	22:00	4.5	15.0	12.5		
	23:00					

Reason for ending test: _____

Max HR: _____

Max BP: ____/____

<u>Time</u>	<u>HR</u>	<u>RECOVERY</u>		<u>Comments</u>
		<u>BP</u>		
1:00	_____	_____/____		
2:00	_____	_____/____		
3:00	_____	_____/____		
4:00	_____	_____/____		
5:00	_____	_____/____		
6:00		_____/____		

Post-Test Gas Values

O2 values: 16.0 % _____

CO2 values: 4.0% _____

APPENDIX E:
PASE SCORING FORM

TABLE 1

PASE SCORING FORM

PASE Item	Type of Activity	Activity Weight	Activity Frequency	Weight times Frequency
2.	Walk outside home	20	a.	
3.	Light sport / recreational activities	21	a.	
4.	Moderate sport / recreational activities	23	a.	
5.	Strenuous sport / recreational activities	23	a.	
6.	Muscle strength / endurance exercises	30	a.	
7.	Light housework	25	b.	
8.	Heavy housework or chores	25	b.	
9a.	Home repairs	30	b.	
9b.	Lawn work or yard care	36	b.	
9c.	Outdoor gardening	20	b.	
9d.	Caring for another person	35	b.	
10.	Work for pay or as volunteer	21	c.	

PASE SCORE:

Activity Frequency Values:

- Use hours per day conversion table below
- 1 = activity reported in past week, 0 = activity not reported
- Divide work hours reported in Item 10.1 by seven; if no work hours or if job involves mainly sitting with slight arm movements (Item 10.2 = 1), then activity frequency = 0.

ACTIVITY TIME TO HOURS PER DAY CONVERSION TABLE

Days of Activity	Hours Per Day of Activity	Hours Per Day
0. Never		0
1. Seldom	1. Less than 1 hour	.11
	2. 1-2 hours	.32
	3. 2-4 hours	.64
	4. More than 4 hours	1.07
2. Sometimes	1. Less than 1 hour	.25
	2. 1-2 hours	.75
	3. 2-4 hours	1.50
	4. More than 4 hours	2.50
3. Often	1. Less than 1 hour	.43
	2. 1-2 hours	1.29
	3. 2-4 hours	2.57
	4. More than 4 hours	4.29

VALIDITY AND RELIABILITY OF THE PASE

The validity and reliability of the PASE were established in a random sample (N = 222) of individuals aged 65-100 years. PASE scores were validated through comparisons with physiologic and health status data measured in the home. In this sample, PASE scores were significantly correlated with balance, grip strength, leg strength, self-assessed health status, and Sickness Impact Profile scores. PASE scores also exhibited temperature-related seasonal variation. The reliability of PASE scores was evaluated by stability over repeated administrations three to seven weeks apart. The test-retest reliability coefficient was .75 (95% CI = .69 -.80). Reliability for mail administration (r = .84) was higher than for telephone administration (r = .68). A detailed description of the development of the PASE as well as reliability and validity results may be found in Appendix D.

PRELIMINARY NORMS

Preliminary norms for PASE were established in a general population of older adults. In this sample scores ranged from 0 to 361. The mean score was 102.9 (standard deviation = 64.1); the median was 90. Mean scores (and standard deviations) by age and gender were as follows:

	AGE GROUP		
	65-69 yrs.	70-75 yrs.	76-100 yrs.
MEN	144.3 ± 58.6	102.4 ± 53.7	101.8 ± 45.7
WOMEN	112.7 ± 64.2	89.1 ± 55.5	62.3 ± 50.7

