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ACCEPTANCE

This dissertation, THE BENEFITS OF YOGA THERAPY FOR HEART FAILURE PATIENTS by PAULA REI PULLEN, was prepared under the direction of the candidate's Dissertation Advisory Committee. It is accepted by the committee members in partial fulfillment of the requirements for the degree Doctor of Philosophy in the College of Education, Georgia State University.

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ABSTRACT

THE BENEFITS OF YOGA THERAPY FOR HEART FAILURE PATIENTS

by
Paula R. Pullen

STATEMENT OF THE PROBLEM

The number of patients living with heart failure (HF) is on the rise. Yoga has been found to improve physical and psychological parameters amongst healthy individuals. The effects of yoga on HF patients are unknown. The purpose of this study was to examine the effects of yoga on cardio-vascular endurance [functional capacity (FC)], flexibility, inflammatory markers, and quality of life (QoL) on medically stable HF patients.

METHOD

Forty HF patients with compensated systolic or diastolic HF participated in the study. A randomized control design created two groups, yoga (N=21). and control (N=19). The treatment intervention consisted of 16-yoga sessions conducted bi-weekly (YG) vs. standard medical care (control- CG) for two months. All participants were asked to follow a home walk program. Pre- and post-study measurements included a treadmill stress test to peak exertion, flexibility (FLEX), girth, interleukin-6 (IL-6), c- reactive protein (CRP), and extra-cellular dismutase (EC-SOD). Quality of life was assessed by the Minnesota Living with Heart Failure Questionnaire (MLwHFQ).

RESULTS

Forty patients were randomized to YG (N=21) or CG (N=19). The results were significant for favorable changes in the YG as compared to the CG for flexibility ($P=0.012$), treadmill time ($P=0.002$), $\sim\text{VO}_2\text{peak}$ ($P=0.003$), and all biomarkers (IL-6, CRP, and EC-SOD) of inflammation. Within the YG, pre- to post- test scores for the total and physical sub- scale of the MLwHFQ were significant ($P=0.02$ and $P<0.001$).

CONCLUSIONS

Yoga therapy offered additional benefits to the standard medical care of HF patients by improving QoL, exercise capacity, FLEX, and biomarkers of inflammation.

THE BENEFITS OF YOGA THERAPY
FOR HEART FAILURE
PATIENTS

by
Paula R. Pullen

A Dissertation

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ABBREVIATIONS

ACSM	American College of Sports Medicine
CRP	C-reactive protein
EC-SOD	Extracellular Superoxide Dismutase
ECG	Electrocardiogram
~VO ₂ peak	Estimated peak oxygen consumption
FC	Functional Capacity
FLEX	Flexibility
HF	Heart Failure
HR	Heart Rate
HTN	Hypertension
IL-6	Interleukin- 6
METs	Metabolic Equivalents
MLwHFQ	Minnesota Living with Heart Failure Questionnaire
MI	Myocardial Infarction
NYHA	New York Heart Association
THR	Target Heart Rate
QoL	Quality of Life

CHAPTER 1

A REVIEW OF HEART FAILURE, EXERCISE AND YOGA

INTRODUCTION

The number of patients living with heart failure (HF) has been increasing, especially among the economically disadvantaged. Once established, symptoms of the disease may be minimized by optimal medical therapy, but it is rarely cured. Heart failure is a chronic disease, imposing a substantial clinical and economic impact on health care. According to the American Heart Association's (AHA) 2008 statistical update, the U.S. prevalence of HF in adults was approximately 5.3 million in 2005 (5). Six years after a myocardial infarction (MI) the risk of developing HF for both men and women is one in five (84). The lifetime risk of HF occurring without an antecedent MI is one in nine for men and one in six for women (84). The incidence of HF is greater in men, until after age 80 years when more women have the diagnosis, likely due to the higher life expectancy of women (84). Sudden cardiac death occurs at six to nine times the rate of the general population when HF is the diagnosis. According to the AHA, the estimated direct and indirect cost of HF in the United States for 2008 was \$34.8 billion (5).

Hypertension (HTN) is a common risk factor for HF with 75% of all HF cases having HTN as an antecedent diagnosis. The lifetime risk of HF doubles

for people with blood pressure greater than 160/90mm Hg compared to those with blood pressure less than 140/90mm Hg (82). There are insufficient data available to determine relative risk for persons with a systolic blood pressure between 140 and 160mm Hg. According to a study conducted in Minnesota, the incidence of HF has not declined during the past two decades; survival after onset has increased overall, with less improvement among women and elderly persons (110). Increased survival may be due to improved medications and treatment alternatives that have evolved during the past couple of decades. Similarly, improved HF survival, likely due to improved treatment options, may be responsible for the increasing numbers of people with advanced chronic heart failure. The European Society of Cardiology published a position statement in 2007 that defines the characteristics and treatment options for advanced chronic HF (92).

One study that looked at the predictors of HF among women with coronary artery disease (CAD) found that diabetes was the strongest risk factor (17). The prevalence of diabetes is increasing among older persons with HF, and diabetes is a significant independent risk factor for death in these individuals. Mayo Clinic researchers found that the odds of having diabetes for those first diagnosed with HF in 1999 was nearly four times higher than for those diagnosed 20 years earlier (101).

Heart failure patients experience multiple symptoms including dyspnea, exercise intolerance, fatigue, pain, and clinical depression, which significantly reduce their quality of life (QoL) (103, 128). These symptoms limit functional

capacity in patients with both systolic and diastolic heart failure (27). The incidence, morbidity, and mortality of HF remain elevated, despite effective medications and increased treatment options (99). However, studies support that interventions aimed at treating chronic symptoms of HF may improve QoL and lead to an improvement in overall health-related outcomes (128).

Age is a risk factor for developing HF since incidence doubles approximately every 10 years of life (38). The number of people living with HF is also on the rise, which places an increasing burden on the Medicare system, according to a recent report from Duke University researchers (110). This large incidence of HF makes the investigation of the role of alternative therapies and primary prevention imperative. The addition of nontraditional treatment modalities may lead to better management of HF, with improved symptoms and QoL.

In addition to the pharmacologic treatment of HF, exercise rehabilitation programs improve exercise capacity in cardiac patients (50). Among unconventional forms of mind/body exercise, yoga has gained immense popularity (76) and appears to provide overall and specific benefit for cardiac patients (15, 50, 115). Currently, hundreds of medical centers in the United States offer yoga classes to their community members and patients. One of the reasons for yoga's widespread appeal is that it may be adapted to a range of physical fitness levels. A suitably trained yoga therapist can modify postures and techniques to meet individual patient needs. Despite its emerging popularity as a form of exercise, only one study provides pilot data on whether the addition of yoga therapy improves symptoms or health-related quality of life exclusively in

patients with compensated heart failure (107). No other studies were found in the medical literature that examined the effect of yoga on individuals with HF.

Yoga is an ancient form of mind-body therapy that combines specific physical postures, or *asanas*, with breathing techniques called *pranayama* and meditation, *dhyana*, to create a sense of well-being (51). *Asanas* range from simple to complex, combined with controlled breathing. *Pranayama* involves a variety of breathing exercises including; slow, deep inspiration, relaxation of the abdominal muscles and the diaphragm, followed by controlled, slow exhalation, involving conscious contraction of the abdominal muscles. A yoga session typically includes a period of relaxation and/or meditation to induce a calm state of mind. An improvement in baroreflex sensitivity, a reduction in heart rate variability, and a decreased catecholamine response to hypoxia and hypercapnia have all been implicated as possible mechanisms by which yoga may be beneficial in healthy individuals (13, 57, 85).

Pro-inflammatory markers have been associated with unfavorable cardiovascular outcomes in HF (104). The focus of the present study was on the effect of yoga on biomarkers of inflammation and vascular elasticity, specifically Interleukin-6 (IL-6), C-reactive protein (CRP), and extracellular superoxide dismutase (EC-SOD). Elevated levels of IL-6 and CRP have been associated adversely with HF and EC-SOD activity has been correlated with endothelium-mediated, flow-dependent vasodilatation (28, 80). Measuring biomarkers in conjunction with functional capacity (FC) could provide a basis of objective measures of QoL in HF patients.

A REVIEW OF HEART FAILURE

Heart failure defined. The definition of HF includes the inability of the heart to provide adequate blood supply to meet the metabolic demands of body organs and systems, or to do so only at abnormally high ventricular filling pressures (44). Heart failure ultimately results in organ hypoperfusion and venous congestion. Symptoms include fatigue, bilateral peripheral edema, orthopnea, and dyspnea during exertion, which may progress to occurring at rest. The increased discomfort during exertion begins a negative feedback loop that results in a decreased capacity for exercise. Interestingly, exercise capacity does not correlate well with ejection fraction or cardiac output (CO) (36). This phenomenon may be due a combination of effects between peripheral and neurohumoral factors that relate to the body's response to decreased blood flow rather than initial impairment of oxygen extraction capability, cellular mitochondrial size and enzyme availability (35). The progression of HF, in the absence of physical training, leads to a worsening of the condition and its symptoms that spiral downward to an eventual deterioration of peripheral oxygen extraction mechanisms. The etiology of heart failure is eloquently described by Jaski (68) as:

“...the cumulative outcome of all insults to the heart over time associated with changes in the peripheral vasculature. As patients survive manifestations of acute cardiovascular disease, late progression to heart failure becomes more common secondary to chronic ventricular enlargement and remodeling.” (pg 3)

Hemodynamics. The medical presentation of HF is an abnormally low CO, which results from a variety of underlying conditions. Cardiac output (CO) is defined as:

$$\text{CO} = \text{SV} \times \text{HR} \text{ (SV = stroke volume, HR = heart rate)}$$

Generally, HR issues are acute and can be treated promptly. Stroke volume is the component most often compromised with HF. There are four main determinates of low SV: preload (end-diastolic volume), contractility (end-systolic volume), afterload and the presence of regurgitant flow. Preload is the same as ventricular filling. When preload is low due to hypovolemia (low blood volume) the cause is usually due to something other than HF (e.g., dehydration or blood loss) (72).

Heart failure can result from either a reduction in preload or an increase in afterload. Reduced preload is the physiological state that occurs when the ventricle cannot fill properly despite a normal circulating blood volume, which leads to a reduced SV. A reduction in preload is most commonly caused by ventricular stiffness, pericardial constriction, or mitral valve stenosis. A less common cause of a reduced preload is the presence of an intracardiac mass (73). A state of reduced CO results in a decreased volume of blood being ejected to the peripheral circulation. Common causes of poor myocardial contraction include myocardial infarction, myocardial ischemia, and myocarditis, but infiltrative diseases are a rare cause of poor contractility (72). Reduced preload, from a prolapsed valve, interventricular or interatrial septal wall defect, may result in the backflow of blood. Left untreated, any of these conditions may result in irreversible HF.

Afterload is a term used to describe the resistance that must be overcome in order to eject blood from the ventricles. Increased afterload impairs ventricular

ejection and SV. Hypertension and aortic valve stenosis are common causes of abnormally high afterload. A chronic increase in afterload can lead to a hypertrophic cardiomyopathy, in which the heart muscle is thickened due to myocyte hypertrophy. In all of these circumstances, the flow of blood to the heart is inadequate, and HF eventually results (122).

Two types of HF (diastolic and systolic) are distinguishable based on muscle fiber physiology. Myocytes, muscle cells of the heart contract during systole and relax during diastole. Heart failure can be a result of systolic dysfunction, diastolic dysfunction or some degree of both. Systolic dysfunction decreases contraction and diastolic failure impairs relaxation of the ventricles. Diastolic failure creates a stiff chamber that does not allow a normal amount of blood into the ventricles resulting in a decrease in preload (27). The body compensates for this by increasing the filling pressure. Examining a chest x-ray alone would not differentiate between systolic dysfunction and diastolic dysfunction as both conditions result in an enlarged silhouette of the heart. To distinguish between the two conditions an echocardiogram is necessary to examine the thickness of the ventricular wall since diastolic HF results in hypertrophy (thickening) of the heart. The typical cause of diastolic dysfunction is a history of long-standing systemic hypertension. Hypertension precedes 75% of all heart failure cases, which underscores the importance of early diagnosis and treatment of high blood pressure (82).

Systolic HF results from a chronic volume overload that eventually dilates

the ventricle due to a process called remodeling. *Remodeling* describes changes in the shape or size of the heart that occur in response to prolonged, chronically increased pressure (afterload) or volume (preload). Another primary etiology of systolic HF is a history of a large or multiple myocardial infarctions. Risk reduction for systolic HF is the same as coronary artery disease (CAD), as myocardial infarction is the main cause of systolic HF (4).

Physiology. The normal heart meets the demands of circulation based on three control mechanisms that vary in response time. Most immediately, contraction to contraction, the heart adjusts to preload (venous return) and after load (arterial resistance) based on feedback from the myocardial fiber's stretch-dependent mechanisms. The Frank-Starling relationship, contraction strength of the myocardial fibers is a function of fiber length at the end of diastole (ventricular filling), explains why short-term changes in ventricular blood volume immediately effect HR and contraction strength. Ejection fraction (EF) represents the percent of blood ejected from the ventricles, as a function of the amount of blood ejected per contraction at the end of systole (stroke volume) divided by the end diastolic volume (EDV; the amount of blood in the ventricles at the end of diastole. At rest the normal physiological range for EF is >55% and it is a poor indicator of the heart's ability to contract (72).

The second mechanism involves biochemical processes that take longer to affect myocardial contraction. These pathways involve extracellular signals that initiate a cascade of intracellular reactions that, ultimately, influence individual myocytes and their contractile properties. Increased hemodynamic

demands may originate from exercise, emotions, digestion, or illness, to name just a few of the potential stimuli. Various physiological and psychological stimuli effect changes in ion pumps, ion channels, and exchanges that regulate the inotropic (contractile) aspects of the myocardium (73). The degree of inotropy refers to biochemical substances, endogenous to the body or prescribed medications, that affect the force of muscle contraction. For example, myocardial infarction may decrease the inotropic state causing a decrease in CO and in turn an increase HR and the potential for ventricular arrhythmias (122).

The third and most complex mechanism involves growth abnormalities that change gene expression within the cardiac cells in response to circulatory changes. Molecular changes take longer to occur and are due to chemical signals that change a diseased heart, contributing to remodeling of the myocardium and the chronic sequale that defines HF (73).

Treatment. Recently, there have been significant advances in the medical, surgical, pharmacological and assistive device management of HF. Despite these advances in treatment, one-third of all HF patients require hospitalization annually for exacerbation of their condition (5). Up to 30% of these patients require re-hospitalization for HF exacerbation less than three months after their first admission (110). Similar to several of the more aggressive cancers, the one-year mortality rate for patients with severe HF approaches 40% (5). The long-term prognosis is better for patients with less advanced HF; however, they still experience considerable morbidity, deterioration in functional status and decreased QoL (72).

Heart failure encompasses a collection of medical issues including high mortality, frequent hospitalizations, decreased QoL, a complicated therapeutic regimen and progressively worsening symptoms that limit exercise tolerance and pulmonary function. As a result, HF has become the focus of a growing body of research necessitating practice guidelines to keep HF treatment uniform among physicians (92). The guidelines emphasize that HF is a syndrome with many different etiologies and a variety of clinical presentations and symptoms.

Heart failure may be due to damage from a single large MI or multiple smaller MIs. Etiologies may also include uncontrolled hypertension, diabetes, pulmonary hypertension, vascular stiffness, impaired renal-sodium handling, heart disease or dysfunction, infectious diseases, genetic predisposition and chronic drug or alcohol induced cardiomyopathy. The diagnosis of idiopathic cardiomyopathy is used when the etiology is unknown or due to multiple precipitating conditions.

Approximately one third of all HF cases are cured by medical diagnosis and treatment. According to the Heart Failure Association of the European Society of Cardiology, two thirds of all HF patients are stabilized or advance to chronic HF (92). Medications currently recommended for the routine treatment of HF include angiotensin-converting enzyme inhibitors, or angiotensin receptor blockers, β -blockers and diuretics. Successful treatment of HF depends on severity, patient adherence to prescribed medications and compliance with lifestyle modifications that help minimize symptoms and may deter worsening of the disease. Early identification, primary and/or secondary prevention are critical

interventions that can minimize HF progression and complications (24, 44).

Increased survival usually leads to comorbid conditions, such as renal failure or atherosclerosis, which complicate the treatment of HF patients.

Psychosocial issues Comorbidities of the HF diagnosis often include psychological distress, reduced social functioning, and diminished QoL (10). This is not surprising, given that HF is associated with increased consequences of morbidity and mortality. These psychosocial factors precipitate hospital admissions in one third to one-half of patients with HF (24). Psychosocial issues can influence physiological outcomes in several ways. Serum catecholamine levels increase in the presence of uncontrollable stress, leading to deleterious effects of both cardiac and immune functions (33). There are other psychosocial factors, such as coping styles that influence the health behaviors of an individual. For example, denial can take the form of avoiding the reality of the severity of the illness leading to decreased compliance with prescribed treatments and behavior modification recommendations. In HF, a few of the psychological contributors that play a role in adverse disease-related events may include depression, anxiety, and coping styles. Depression has been shown to increase cardiac events and overall mortality in patients with HF, even after controlling for other factors such as age, gender, New York Heart Association (NYHA) class, ejection fraction and serum B-type natriuretic peptide (BNP) levels (1, 63). The NYHA functional classification system describes HF based on severity of HF symptoms (Table 1) (63).

TABLE 1. New York Heart Association (NYHA) Heart Failure Classification Scale

NYHA Class	Symptoms
Class I	No symptoms
Class II	Symptoms with moderate activity
Class III	Symptoms with light activity
Class IV	Symptoms at rest

Depression also plays a role in high readmission rates for patients with HF (60). Younger, chronically ill, disabled patients and elderly patients with major depression have been studied and found to have poor medical treatment compliance (23). Therefore, it is possible that noncompliance with treatment regimens may be a major factor that precipitates re-admission for HF patients (87).

The diagnosis of depression is common for HF patients, occurring in 25% of patients. In addition, almost half have symptoms consistent with dysthymia, a milder form of clinical depression (60). Identifying and treating HF patients' psychological issues in an accurate and timely manner may considerably increase their levels of functioning, leading to an improvement in physical health status (70, 78). Murberg and Furze (95) evaluated the long-term effects of depression on mortality risk among HF patients over a six-year period. Symptoms of depression were found to be a significant predictor of mortality. The remaining question, regarding mortality and depression, is whether treatment of depression reduces future risk or decreases morbidity (29). Yoga has been found

to improve ratings of depression and may have a beneficial effect on heart patients (75).

Anxiety is a condition that frequently presents in conjunction with depression. Patients with HF often experience considerable anxiety due to the physical symptoms of dyspnea, poor exercise tolerance, and concern regarding poor prognosis. Social, financial difficulty and the affects of their disease on family and work status, likely contribute to escalating anxieties for the HF patient.

Mental stress is clinically relevant since it can negatively affect sympathetic nerve activity, regional blood flow and endothelium-mediated muscle vasodilatation of patients with HF (93, 111). Stress can cause an increase in HR, which has a negative effect on coronary artery perfusion by decreasing the duration of diastole; therefore, lowering myocardial oxygen delivery time. Tachycardia reduces the supply of oxygen to the heart, while increasing myocardial oxygen demand. This can create a downward spiraling effect, where patients become increasingly concerned about their physical state, which feeds back to increased anxiety and lower CO. Concerns about physical capability and anxiety about taking part in physical activities may also interfere with cardiac rehabilitation attempts. The possible pathways of chronic stress and the mechanisms involved were reviewed by Innes et al. (64) (figure 1).

Chronic and debilitating illnesses such as HF may lead to stress that prompts the patient to seek a variety of coping strategies (126). Coping is defined as cognitive or behavioral attempts to either avoid a stressful situation or actively do something to alter or deal with the situation (91). The general definition of

coping style is the way in which the individual responds to stressful encounters.

Individuals cope with negative or stressful life events in different ways that

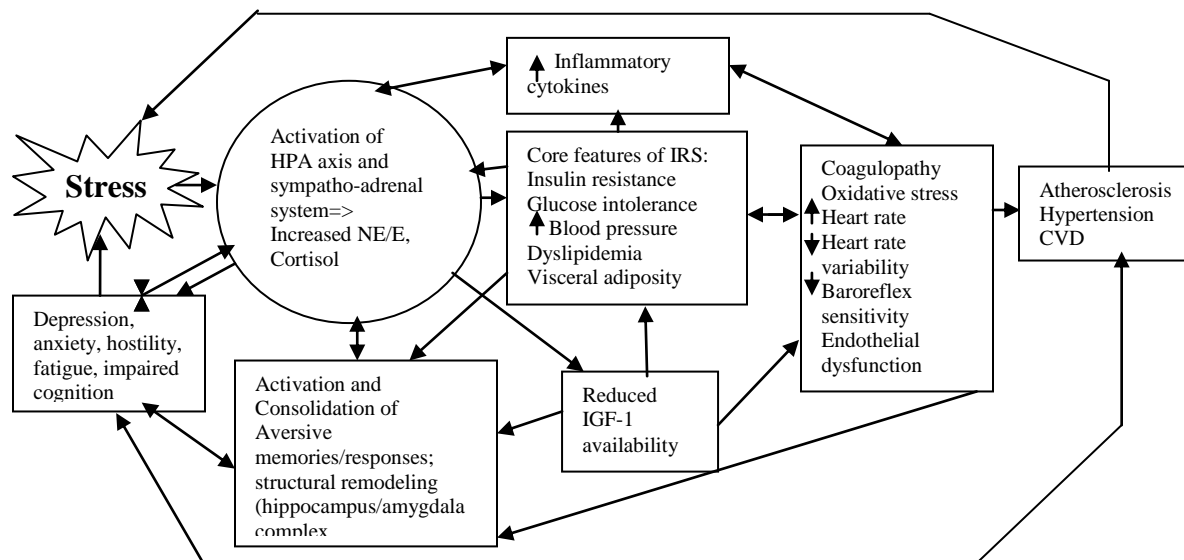


FIGURE 1- From: Pathological Sequellae of Chronic Stress: Possible Pathways. CVD indicates cardiovascular disease; E indicates epinephrine; HPA indicates hypothalamic pituitary axis; IGF indicates insulin-like growth factor; IRS indicates insulin resistance syndrome; NE indicates norepinephrine (64).

potentially can affect their physical and psychological well-being (47). Coping styles mediate between stressful life events and possible consequences such as depression and anxiety, which influence mortality in HF patients. In a study examining the association between coping styles and mortality in patients with HF, 119 outpatients were assessed on six subscales of the COPE inventory (94). A lower score on the proactive types of coping styles, and a higher score on the negative types of coping skills were significantly associated with increased morbidity and mortality, even when disease severity, gender, and age were controlled for using multivariate analysis (102).

Despite the difficulties of living with HF and the apparent success of educational programs following myocardial infarction, it is only recently that clinicians have begun to pay more attention to the psychosocial issues of HF. Some authors now suggest that interventions, which target the psychosocial factors involved in HF, may improve therapeutic compliance, reduce concomitant stressors and lead to an improvement in health-related quality of life (26).

QUALITY OF LIFE

Quality of life is an important factor when studying the effects of interventions in patients with HF, and numerous studies have evaluated the effects of various interventions on health related QoL in the HF population (52, 48). The accuracy of specific health related QoL measures in HF patients is an important consideration for research and clinical applications (30, 45).

One such study examined the relationships between exercise capacity, QoL, and different ways of assessing functional capacity in HF patients (62). Thirty-six patients with stable symptomatic HF and confirmed left ventricular dysfunction had their exercise capacity measured using three different methods: maximal treadmill stress test, self-paced hall walk, and home based pedometer. The researchers found that the different methods did not yield comparable results in their correlation to QoL and hemodynamic measures (non-invasive CO and left calf skeletal muscle blood flow). Home-based activity, as measured by pedometer step count, correlated well with QoL and calf blood flow. Interestingly, the corridor walk and treadmill test correlated with each other and not with QoL

or hemodynamic measures. The author suggested that pedometer scores might provide a more reliable indicator of the patient's own perception of their physical fitness. The patients with greater calf muscle blood flow likely had a better QoL because they were able to be more active. The fact that the pedometer scores were not related to the laboratory based exercise test supports the view that they measure different and complementary aspects of exercise capacity.

Quality of life may improve with interventions such as home-based walking programs. One preliminary study examined the effects of a home walk program on total sleep time, physical function and QoL in older women with NYHA class II and III diastolic heart failure (55). Patients were randomized to either a 12-week home-based walking intervention (n=13) or education-only program (control, n=10). Between-group differences were not found in women in either the intervention or the control groups regarding any of the outcome variables. Outcomes were compared within each group at baseline and at 12 weeks. Intervention-group patients had improvement in total sleep time ($P<0.01$) and heart failure-related QoL ($P<0.05$), however, depressive symptoms were not significantly decreased ($P<0.07$). Women randomized to the control group had no change in any of the outcome measures. Their preliminary findings suggest that a progressive walking program may improve total sleep time and QoL in older women with diastolic HF. Larger studies might evaluate the long-term benefits of a walking program on sleep patterns, QoL, and psychological function in this population.

In summary, QoL for the HF patient is a phenomenon influenced by

multiple psychological and physical components. Morbidity and mortality may be influenced in a positive manner by implementing alternative treatment strategies in addition to standard medical care. For example, improving a patient's coping strategy or providing supervised exercise instruction to improve QoL and decrease medical costs (Figure 2).

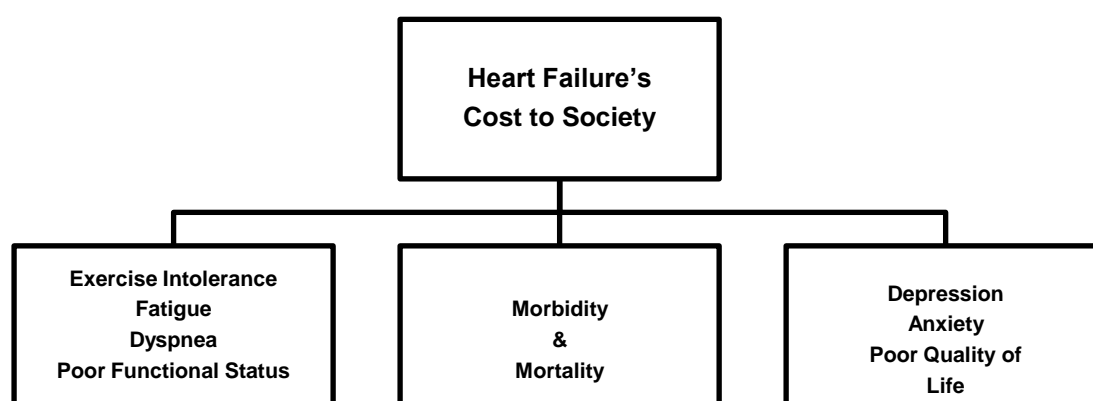


FIGURE 2- The burden of heart failure.

HEART FAILURE AND EXERCISE

Cardiac rehabilitation. Prevention of heart failure by lowering cardiac risk factors and treating the metabolic precursors of heart disease is the ideal treatment strategy for potential cardiac patients (6). However, for those patients that already have a HF diagnosis, cardiac rehabilitation programs offer a second chance to adopt positive lifestyle behaviors. Cardiac rehabilitation with an exercise prescription is an important component in the management of patients with HF, cardiac exertional symptoms, and exercise performance (32).

Improvements in peak oxygen consumption, CO and vascular function are a few of the clinical benefits gained by attending cardiac rehabilitation programs (125). The majority of patients referred to cardiac rehabilitation programs have a diagnosis of CAD. To attend a cardiac rehabilitation program a physician's referral is required. Typically, patients undergo an entry evaluation to measure their exercise capacity and to formulate an individualized exercise prescription. Supervised exercise training may take place three days per week for three to 12 months. Telemetry monitored electrocardiograms (ECGs) are utilized to establish a baseline during the first few weeks of exercise. The duration of continuous EKG monitoring depends on individual risk stratification and hemodynamic responses to exercise during training. Improved quality of life and cardiorespiratory function for HF patients have been reported after participating in aerobic exercise for 12 months (74). Currently, HF patients may not receive insurance reimbursement for cardiac rehabilitation.

Unfortunately, the logistics and practical aspects of attending a formal cardiac rehabilitation program prevent many patients from complying with a physician's recommendation or referral to attend a hospital based cardiac rehabilitation program. Financial, social, and family issues are among some of the obstacles of compliance. Cooper et al. (34) examined cardiac rehabilitation attendance and patient's beliefs toward cardiac rehabilitation. Patients' beliefs accounted for 65% of the variance found. Four barriers were identified and they differed significantly between attendees and nonattendees. The barriers were identified as perceived necessity, exercise concerns, practical barriers, and

personal suitability. In a similar study, interviews of post-MI patients were thematically analyzed which led to discovering that the determinants of cardiac rehabilitation relevance and adherence was influenced by financial, family, and social situations regardless of the encouragement they received toward attending the program. The researchers concluded that it might be unrealistic to anticipate 100% attendance in these programs.

Walking interventions. Adherence to any exercise program is difficult; factors that have been found to interfere in attendance to cardiac rehabilitation programs include financial, social, and family concerns (58). Based on the assumption that a large segment of the cardiac patient population will not attend supervised exercise sessions, home exercise may be a reasonable alternative pursuit. Ideally, a qualified health care professional prescribes exercise and follows the heart failure patient in a cardiac rehabilitation setting. For those who cannot attend formal programs, a practical and safe alternative may be a home or community based walking or exercise program. In this circumstance, a physician or Clinical Exercise Physiologist could develop the exercise prescription on an individual basis for home implementation. Home-based walking programs have been reported to be reasonably safe for HF patients and measures can be implemented to facilitate adherence (46).

Number of steps walked at home, as measured by pedometers worn by HF patients (N=84), were found to predict survival better than the laboratory-based exercise test in a study that examined the relationship between daily activity levels and long-term prognosis (127). Pedometer measured steps have

predicted exercise adherence and mortality in HF patients (49). The use of pedometers to study the activity level and exercise capability of HF patients, initially reported by Cowley et al. (36) in 1991, correlated poorly with treadmill stress test performance. However, in a second study where CO was measured indirectly using the Fick principle, CO correlated significantly ($p < 0.001$) with customary activity as assessed by the measurement of pedometer steps (35). Conversely, the relationship between treadmill stress test performance and CO was poor ($P = 0.245$). The authors concluded that CO is a reliable index for determining patients' exercise capacity when walking speed is self-directed, but not when undergoing laboratory treadmill tests.

Adherence to exercise is clinically important and relevant to the assessment of the effectiveness of interventions and their outcomes. Recently, the validity of pedometers for measuring exercise adherence during a 12-month home-based walking program in HF patients was studied (7). The validity of pedometer use in HF patients was determined by finding that patients who increased their steps at home by at least 10% (defined as adherers), also had significant increases in their functional status, as measured by the 6-minute walk and peak oxygen consumption tests. Considering the previous studies, the addition of pedometers to measure home activity and to encourage adherence to the home walk program seems reasonable.

Exercise benefits. Exercise is recommended and appears to be safe and beneficial for stable, well-compensated HF patients, although mortality benefits have not yet been determined (120). Compensated HF refers to the condition

where many of the accompanying symptoms of HF (e.g., fluid retention and pulmonary edema) have been stabilized or improved due to medical intervention. Studies show that exercise programs that are individually tailored to HF participants are well tolerated and yield positive adaptations on a muscular, metabolic and neurohormonal level (71, 77).

A relatively large (N=94) randomized trial that examined the effects of a one-year exercise intervention on HF patients (NYHA II- IV) concluded that long-term exercise training improved FC and QoL in chronic HF patients (9). Additionally, patients with left ventricular dysfunction decreased their symptoms, improved neurohormonal function and lowered vasoconstrictive hormones by participating in a physical conditioning program. Typically, HF patients gradually lose their ability to engage in physical exercise, especially activities involving dynamic large muscle mass movement, in response to symptoms of fatigue and dyspnea. To reverse the cycle of further exercise intolerance and peripheral muscle atrophy, the HF patient may benefit from medical guidance regarding safe exercise progression (31). Further benefits regarding muscle structure, endothelial function, catecholamine release, and peripheral oxygen extraction have been reported (39). The Committee on Exercise, Rehabilitation, and Prevention of the American Heart Association recommends that medical insurance companies support exercise training programs that follow their guidelines based on the existing evidence that HF patients benefit from exercise (106).

Exercise prescription. The American College of Sports Medicine

(ACSM) published guidelines that address some of the specifics of exercise prescription and physical conditioning for the HF patient (129). According to the ACSM, HF patients considered for exercise training should be clinically stable with an exercise capacity of at least 3 METs and under the care of a physician. The exercise prescription should be based on a symptom-limited stress test (treadmill or cycle ergometer). The exercise intensity is derived from a target heart rate (THR) that corresponds with 40 to 70% of peak oxygen consumption. The guidelines recommend that the exercise duration is between 20-40 minutes per session at a frequency of three to seven days per week. Additional medical test information, such as echocardiograms and heart catheterization results, add to the formulation of the exercise prescription. Longer warm-up and cool-down periods (10-15 minutes each) and avoidance of isometric exercise are advised. Initial exercise training time is increased gradually at intervals of two to six minutes, with one to two minutes of rest between bouts in order to stay below symptom thresholds. Exercise intensity should not provoke a worsening of dyspnea or other symptoms. Coincidentally, HF patients may have impaired chronotropic response making heart rate response to exercise a less reliable indicator of intensity. The ACSM guidelines conclude that perceived exertion and dyspnea may be better indicators of exercise intensity than heart rate alone for HF patients.

Moderate continuous verses aerobic interval training was studied in a group of postinfarction HF patients to examine which type of exercise yields greater benefits (131). Twenty-seven patients were randomized to either exercise

treatment or control group. The exercise treatment groups participated in a supervised exercise program, three times a week for 12 weeks. Maximal oxygen consumption improved significantly more in the aerobic interval training group than the continuous exercise group and was associated with reverse left ventricular remodeling. In the clinical setting, all of these recommendations are useful to consider when formulating an exercise prescription for a patient with HF.

YOGA

Yoga defined .Yoga is a system of physical and mental disciplines designed to foster the practitioner's mental and physical health (61). Yoga typically includes a triad of exercises; physical postures known as *asanas* (denoting a static physical position); breathing exercise called *pranayama*, and some form of relaxation or meditation. *Hatha* yoga is the generic term for the practice of the physical postures (*asanas*) intended to improve physical health by balancing strength and flexibility. The philosophical aim of yoga is to be comfortable enough to practice meditation without physical or mental disturbance. The word *Hatha* is a combination of two Sanskrit words *Ha* and *Tha*; meaning sun and moon. Many styles of yoga have developed, ranging from a focus on alignment of the body while holding static postures (for example, *Iyengar style*) (67), to a more dynamic and strenuous sequence of postures referred to as *Vinyasa*, *Ashtanga* or Power Yoga (18).

The popularity of yoga has increased tremendously over the past two decades in the United States. It has evolved from an eccentric and

misunderstood practice to a mainstream training available in most public and corporate fitness facilities. Approximately 15 million Americans have engaged in a yoga practice at least once for either wellness or specific health conditions (112). Yoga classes are offered in 75% of all health clubs in the United States and held in yoga studios, community centers, hospitals, colleges, schools, pre-schools, and senior citizen centers (76). There is some debate regarding whether or not the western version of yoga and its commercialization is consistent with the basic philosophical tenets of yoga (133). Some of the concern is on emphasis of *Hatha* yoga, the physical postures, over the many other components of yoga. The other aspects of yoga include the practice of abstinences (*yamas*), observances (*niyamas*), breath control (*pranayama*), sense withdrawal (*pratyahara*), concentration (*dharana*), contemplation (*dhyana*) and self-realization (*samadi*). The entire practice is known as the eight limbs of yoga.

Yoga therapy research. Claims regarding the health benefits of yoga are emerging in the scientific literature. In the past, most yoga research was conducted without the rigorous methods expected by the western scientific community. Currently, western standards and practices, include randomization and control groups, are being applied to yoga research around the world. The emerging research is legitimizing age old claims regarding the positive effects of yoga on stress reduction, anxiety, depression and a variety of other medical disorders including the management of hypertension (96, 116).

Studies of yoga therapy involving healthy subjects found that practicing various relaxing and calming yoga *asanas* blunted the normal physiologic

response to artificially induced physical stress, as measured by changes in HR recovery, HR variability, blood pressure, and respiratory rate (85, 12). Anxiety levels were lowered significantly in the yoga treatment group when 104 medical students were randomized to either yoga therapy or usual medical care (88). Anxiety was assessed utilizing the State Trait Anxiety Scale. Subjects in another study benefited from yoga therapy with a reduction in depressive symptoms according to the Beck Depression Inventory and subjective improvement in their sense of well being, feeling of relaxation, concentration, self-confidence, interpersonal relationships, and irritability levels, have also been reported following a yoga intervention (109).

The physiological effects of a regular yoga practice combined with breathing exercises lead to improved muscle strength, flexibility, cardiovascular endurance, and pulmonary function in human subjects. One study included fitness testing before and after an eight-week course of yoga training in previously sedentary individuals. The average improvements reported were 31% for muscle strength, 57% for muscle endurance, flexibility 88%, and aerobic capacity 7% (8).

The contribution of yoga to cardiovascular endurance and its metabolic requirement has been examined by researchers and is critical to consider before making recommendations for HF patients. A comparison of the metabolic requirements of a 32 minute *Hatha* yoga routine to 32 minutes of treadmill walking at 4.0mph was investigated (42). Ten healthy subjects 38- 47 years of age achieved an energy expenditure of 4.1 METs for the yoga routine, compared

with 5.4 METs required for the treadmill walking. In comparison, a similar study that measured the oxygen requirements of a more dynamic form of yoga routine (*Vinyasa* style) reported a metabolic demand of 6.7 METs (25). Clearly, the metabolic requirements vary considerably based on the type of yoga practiced.

Randomized controlled trials of yoga therapy in hypertensive individuals have demonstrated 15mmHg reductions of systolic blood pressure and 10mmHg reductions of diastolic blood pressure (117). They also reported a reduction in subjective symptoms of stress and anxiety with yoga. Improvement of such magnitude is comparable to what many hypertensive medications achieve.

Scientific studies that examined the mechanisms of how yoga works are also emerging in the medical literature. Several reviews have pooled yoga research studies and summarized their findings in an effort to examine the role of yoga on health (64, 65, 108). One of these review articles looked at 70 studies that met specific inclusion criteria between 1970 and 2004 (64). The selected studies were all concerned with the role of yoga and risk-reduction of the insulin resistance or metabolic syndrome and cardiovascular disease. Benefits of a yoga intervention were hypothesized to be synonymous with improved cardiovascular risk profiles, summarized by two physiological pathways (figure 3).

The mechanisms by which the practice of yoga can improve the insulin resistance syndrome related abnormalities and cardiovascular disease related outcomes are thought to involve two pathways. First, yoga may lead to down regulation of the sympathoadrenal system and hypothalamic pituitary adrenal axis, thereby shifting autonomic regulation towards the parasympathetic system

(Figure 3, Pathway 1). In effect, yoga may cause decreased perceived psychosocial stress and levels of depression, improved mood and sleep patterns, improved insulin sensitivity and glucose metabolism, reduced cholesterol and triglyceride levels and subsequent weight loss in the form of reduced visceral fat (79). Second, by stimulating the vagus nerve directly, yoga may promote additional parasympathetic activation thus leading to decreased heart rate and blood pressure, improved heart rate variability, and similar metabolic and psychological benefits as seen in pathway 2 (Figure 3, Pathway 2).

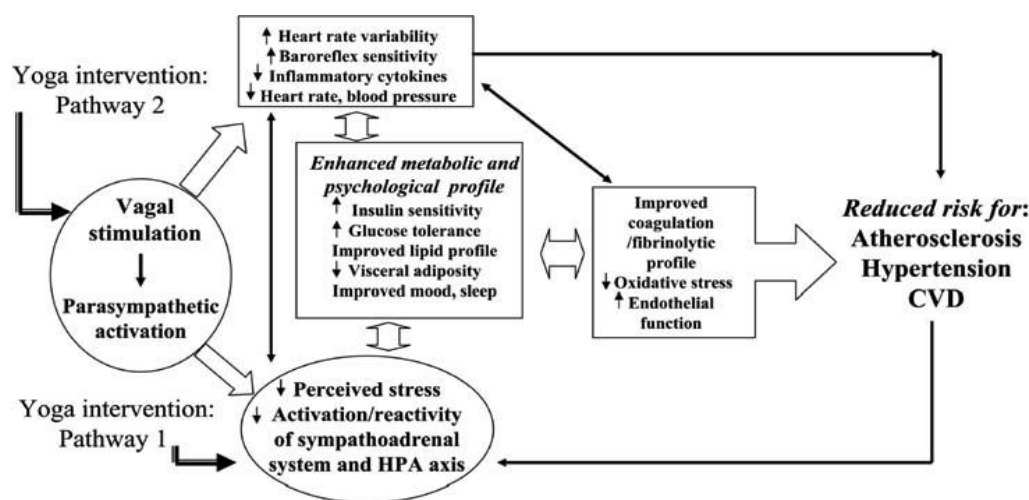


FIGURE 3- From: Hypothesized Pathways by Which Yoga Intervention May Enhance Cardiovascular Risk Profiles (64)

The effect of yoga on brachial artery reactivity in patients with coronary artery disease (CAD) or at high risk for CAD was studied in a 6-week pilot study (115). Impaired endothelial function is one of the mechanisms related to an increased risk of MI. Interestingly, the yoga intervention significantly improved brachial artery reactivity in the participants that had known CAD and had little association with the high risk group (119).

Collectively, these anthropometric, psychological and metabolic changes may lead to improved coagulation and inflammatory profiles. Yoga, therefore, may promote increased fibrinolysis, decreased free radical production and oxidative stress and improved endothelial function (107, 118). Understanding that atherosclerosis is an inflammatory process and cardiovascular events are in part dependent on endothelial function, lends physiological support to the literature showing yoga can reduce progression while improving management and clinical endpoints of atherosclerosis, hypertension, cardiovascular disease and risk factor reduction (40, 53, 89, 115).

Breathing research. The practice of yoga often includes breath awareness and specific breathing exercises called *pranayama*. Patients with HF who regularly practice breathing exercises derive an improvement in symptoms of dyspnea (22, 90). Breathing exercises teach patients to facilitate diaphragmatic breathing and inhibit excessive accessory muscle use, leading to decreased breathing work and energy expenditure. This is especially important to patients with pulmonary diseases. One randomized study of *pranayama*-type breathing exercises slowed the resting respiratory rate from 15 breaths per minute to six per minute. Fifteen HF patients had significant improvements in, peak oxygen consumption ventilation/perfusion mismatching, exercise tolerance, and perceptions of dyspnea after one month of therapy (16). Other studies using similar techniques for longer periods have shown improvements in chemoreflex activation, allowing for a greater tolerance to hypoxia and hypercapnia, and

increased arterial baroreflex sensitivity (14, 121). The latter is frequently impaired in HF and is associated with adverse prognosis.

The benefits of *pranayama*-type breathing exercises occur in healthy participants as well. In normal subjects, a combination of yoga therapy, including *pranayama*, for 12-15 weeks in a total of 347 volunteers was found to improve pulmonary function with increased forced vital capacity (FVC), forced expiratory ventilation in the first second of exhalation (FEV₁), and peak expiratory flow rate (19). The effect of a daily yoga practice on pulmonary function in 60 healthy women (age 17-28) was significant after 12 weeks, as compared to the first six weeks of practice (132).

The *pranayama* component of any yoga study is difficult to isolate since breathing instruction and awareness is often a part of the physical practice of yoga. The benefits of hatha yoga training alone might be controlled for if one arm of a study consisted of breath training alone. Theoretically, benefits beyond breath training alone could be contributed to the physical aspects of yoga.

INFLAMMATORY MARKERS AND ENDOTHELIAL DYSFUNCTION

A review by Braunwald in 2008, suggests that endothelial dysfunction is one of the hallmarks of cardiovascular disease (20). Endothelial cells line the inner most layer of the circulatory vessels and are responsible for the regulation of vascular tone. The production of nitric oxide (NO) takes place locally in the endothelial layer and is ultimately necessary for vasodilatation to occur. The nitric oxide production pathway involves several local substances that are referred to

as biomarkers. Many of the biomarkers have been studied in an effort to determine if they have prognostic, predictive or preventive value as clinical tools (figure 4) (59, 113).

Biomarkers are also examined in an effort to discover if complementary or alternative therapies for HF may exist since pharmacological therapies do not completely repair endothelial function. The increased availability of NO in the endocardium is thought to be the most important factor in restoring endothelial function (41). In contrast, exercise training corrects impaired circulatory vessel dilation by restoring levels of NO. Impaired endothelial-dependent vasorelaxation has been identified as an independent cardiovascular risk factor and a prognostic marker of cardiovascular disease (3, 97). Regular physical exercise is known to lower the risk of heart disease and the pro-inflammatory markers associated with unfavorable cardiovascular outcomes for HF patients. The reduction of inflammatory markers has also been reported to improve the oxidative capacity of skeletal muscle in HF patients which resulted in an increased exercise capacity (56). Three biomarkers, IL-6, CRP and EC-SOD were selected as indicators of a reduction in vascular inflammation (decreased IL-6 and CRP) and/or an improvement in vascular reactivity (increased EC-SOD) in HF patients.

Interleukin-6 is a low molecular weight pro- inflammatory cytokine that has a variety of related immune and inflammatory properties. Interleukin-6 is secreted by T-cells, macrophages, and by the smooth muscle cells of most blood vessels. The chronic over-production of IL-6 in the circulatory system makes it useful as a predictor of cardiovascular mortality and an important prognostic indicator for HF

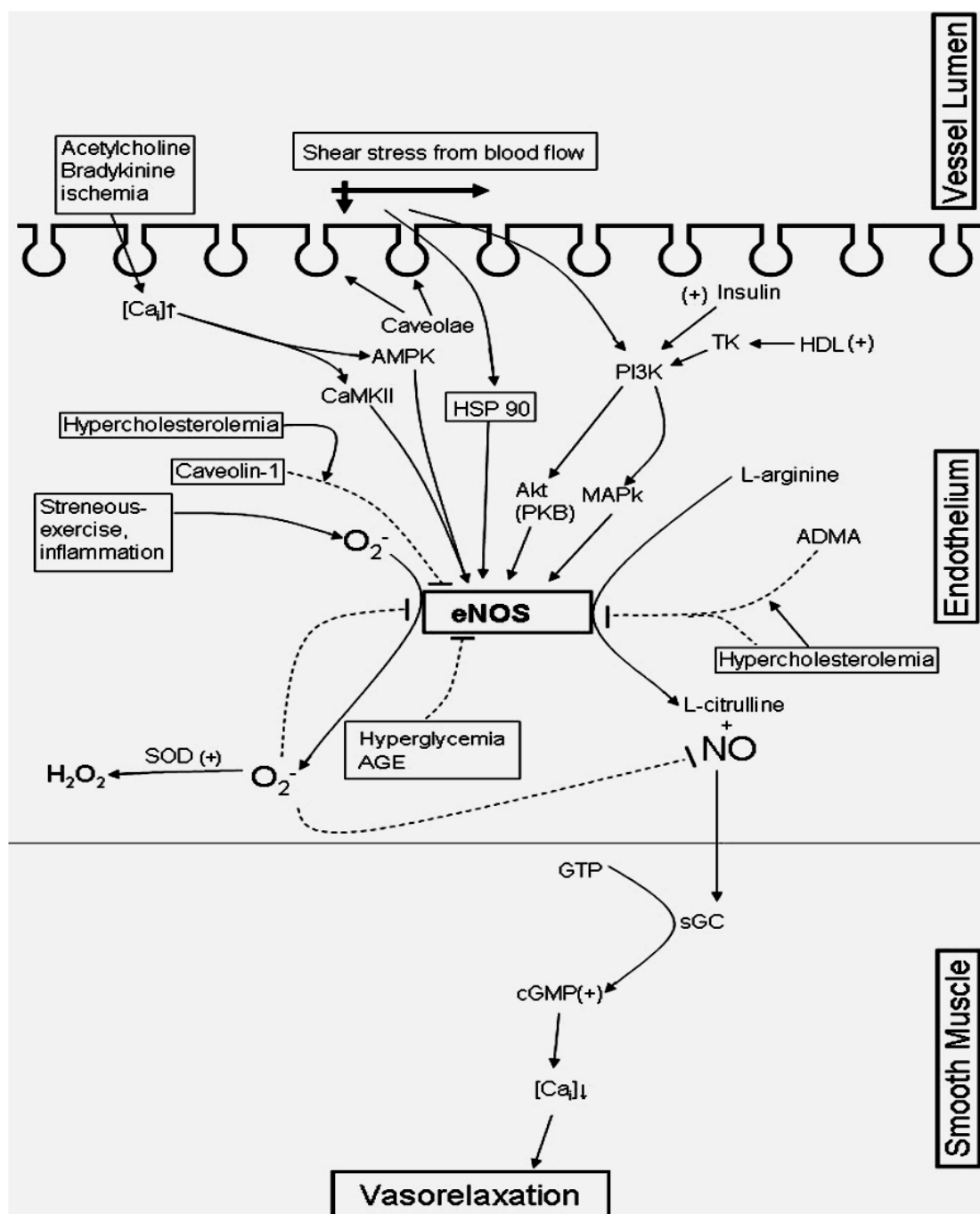


FIGURE 4- From: Factors influencing the bioavailability of nitric oxide (NO) in the endothelium, arrows define stimulating pathways, while bars define inhibitory pathway. See text for further details. AMPK, AMP-activated protein kinase; CaMKII, Ca²⁺-calmodulin-dependent protein kinase II; TK, tyrosine kinase; HDL, high density lipoprotein; PI3K, phosphatidylinositol 3-kinase; ADMA, asymmetric dimethylarginine; SOD, super oxide dismutase; O₂⁻, superoxide anion; MAPK, mitogen activated protein kinase; eNOS, endothelial nitric oxide synthase; AGE, advanced glycosylation end products; NO, nitric oxide; GTP, guanosine tri-phosphate; sGC, soluble guanosine cyclase; cGMP, cyclic guanylyl monophosphate; [Ca²⁺]_i, Ca²⁺ concentration; PKB, protein kinase B (Akt); HSP 90, heat shock protein 90; H₂O₂, hydrogen peroxide (59).

patients (124). C-reactive protein is an acute phase plasma protein whose levels rise dramatically during inflammatory reactions (2). Elevated levels of one or more of these biomarkers indicate an adverse association with HF and CAD (37, 123).

Extra cellular-superoxide dismutase is an enzyme with important antioxidant properties that catalyze the dismutation of superoxide (an isoform of oxygen, known to damage smooth muscle cells) into oxygen and hydrogen peroxide leading to an increase in NO levels (80). In addition, EC-SOD expression may be down-regulated in the presence of elevated homocysteine (98). This may explain why increased EC-SOD activity in the NO pathway correlates with improved endothelium-mediated, flow-dependent vasodilatation. Heart failure patients are known to have an impaired vasodilatory response which could be related to a reduction in EC-SOD and the presence of inflammatory cytokines.

A recent review of exercise training and its effect on inflammatory markers in HF patients concluded that abnormal levels of inflammatory markers are associated with left ventricular dysfunction, pulmonary edema, left-ventricular remodeling, and cardiomyopathy (97). Furthermore, they reported that routine exercise decreased these biomarkers (IL-6 and TNF α) and were associated with lowering oxidative stress, morbidity, hospitalization, and mortality.

Debate still exists regarding the most advantageous type, frequency and exercise intensity to prescribe for HF patients. To optimize the effects of exercise

on endothelial function and peak oxygen consumption, aerobic interval training may yield greater benefits than moderate continuous aerobic exercise (131). The authors suggest that the characteristic hypoperfusion of heart failure and resultant oxidative stress are the initial stimulators of the chronic inflammatory response. What remains to be answered is whether the reduction of the inflammatory response leads to improved morbidity and mortality in the HF population. Toward that end a large multi center study called the Heart Failure Action Trial (HF-ACTION) is underway and may yield important results regarding exercise, morbidity and mortality for HF patients (130). Preliminary results from the 2008 AHA national meeting, indicated that HF patients who exercised for two hours a week decreased mortality and heart failure hospitalization by 7% (100).

A recent and novel pilot study looked at the effect of aerobic training on vasodilatory capacity and proinflammatory markers in HF patients that had undergone heart transplant surgery eight weeks prior (105). After 12-weeks of aerobic training in a cardiac rehabilitation setting, inflammatory markers [CRP, IL-6, TNF α and soluble intercellular adhesion molecule-1 (sICAM-1)] remained the same in the exercise group and increased significantly in the control group. The exercise group also increased their treadmill test time significantly (52%) with a concurrent improvement in vasodilatation of a calf artery (22%). Neither of these parameters improved for the control group. Previous studies reported that vasodilatory changes are also due to systemic factors which would have resulted in improved forearm blood flow (83, 114). The exercise intervention in the heart transplant study did not include upper body training and there was a lack of

improvement in forearm blood flow. Future studies might include an upper body training regimen and contrast it with lower body exercise to examine this issue. Also, glucocorticoids and cyclosporine medications are known to cause endothelial dysfunction, a confounding issue when heart transplant subjects are involved (130).

Pilot study. Studies on both humans and rats have found that regular exercise maintains the absolute relaxation function found in the arterial vessels which may contribute to an increase in FC. Individuals with HF that exercised at moderate levels of intensity improved their endothelial function. The practice of yoga includes several of the components that have been found to benefit HF patients.

Research on stress reduction, breath training, and physical activity has been associated with a reduction in peripheral markers of inflammation and improved exercise tolerance in HF patients. This led to a pilot investigation of yoga as an exercise that might yield similar, if not greater benefits for HF patients. The research consisted of biweekly yoga classes at the hospital's Vascular Research Laboratory. Interleukin-6, CRP and EC-SOD were selected as biomarkers to measure the effects of yoga on the endothelium-mediated, flow-dependent vasodilatation in HF patients in a pilot study. The pilot study also examined the effect of yoga on HF patients' FC, flexibility and QoL (107). In a predominantly African-American (AA), out-patient cohort, measurements included a treadmill test to determine peak oxygen consumption, inflammatory markers and self-reported psychological well-being via the Minnesota Living with

Heart Failure Questionnaire (MLwHFQ). Twenty patients with NYHA class I-III symptoms of HF met inclusion criteria and were enrolled. All patients were medically stable, for at least six months prior to the study. The cohort included one patient with a diagnosis of diastolic HF who completed the study and was not included in any of the statistical analysis. Half the patients were randomized to the yoga treatment and the other half were randomized to usual medical care. The yoga group patients were placed in a program involving 60 minutes of yoga instruction and therapy twice a week, for an 8-week period. Measured variables included HR, blood pressure, flexibility, waist/hip ratio, and a ramp protocol treadmill test (TM) to peak oxygen consumption (i.e., symptom limited maximum) with a 12-lead continuously monitored ECG. Significant improvements for all inflammatory biomarkers (IL-6, CRP, and EC-SOD) and FC occurred in the yoga group (n=9) after 8-weeks of yoga training compared with the control group (n=10).

The patients who participated in the pilot study were encouraged by their improvements. The yoga group reported an increased ability in tasks of daily living and decreased symptoms from their HF which was congruent with the objective measures. Owing to the small sample size of the pilot study, further investigation with a larger number of patients was conducted.

The benefits of yoga, relaxation and yogic breathing on CAD risk factors have been documented in healthy and at risk subjects (11, 54). Heart failure therapy has improved resulting in the increased survival of HF patients. However, the medical management of HF remains challenging. Cardiovascular morbidity

and mortality remain high for HF patients, inviting the investigation of alternative therapies in an effort to improve QoL.

Exercise is routinely prescribed to cardiac patients for its multiple benefits, including improvement of inflammatory markers and vascular reactivity. Heart failure patients typically have comorbidities that prevent them from participating in traditional exercise. The lower metabolic demand of yoga is flexible, ranging from chair based to continuous flow, presenting an option for HF patients to participate in an exercise intervention with a sense of mastery, rather than difficulty. Yoga therapy may also be a safe and novel exercise alternative for HF patients if the metabolic and cardiovascular benefits are found to be similar to traditional exercise modalities.

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CHAPTER 2

THE BENEFITS OF YOGA THERAPY FOR HEART FAILURE PATIENTS

Heart failure (HF) is one of the most prevalent chronic illnesses of modern society with profound clinical and economic impact (29, 33). The manifestations of the disease significantly reduce quality of life (QoL) among those who live with HF (4, 7, 53, 54). In patients with systolic and/or diastolic HF, the symptoms of the disease usually limit functional capacity (36, 46). Previous studies have supported interventions aimed at treating the chronic symptoms of HF, QoL, and overall health-related outcomes (52). Physical exercise in the form of yoga has gained immense popularity (23) and may be beneficial in cardiac rehabilitation (11, 48). Despite yoga's widespread appeal, there is little data on whether the addition of yoga therapy improves symptoms or health-related QoL in patients with compensated, chronic HF (39).

Yoga combines structured physical exercises with breathing techniques and meditation to stimulate a sense of well-being. The breathing, relaxation and meditation components may lead to an improvement in baroreflex sensitivity and a reduction in heart rate variability (9, 10). A variety of beneficial effects for patients with cardiovascular disease has been reported. For example, studies have reported an improvement in lipid profiles (17), blood pressure (42) psychological well-being (26), and even regression of atherosclerosis when

combined with dietary and other life-style modifications (34, 35, 49). The clinical application of the previous studies may be limited by the lack of control groups, and the varied style, intensity, and duration of the yoga interventions. Pro-inflammatory markers have been associated with unfavorable cardiovascular outcomes in HF (38). Elevated levels of interleukin-6 (IL-6) and C - reactive protein (CRP) has been adversely associated with HF (12, 56); Extra-cellular super-oxide dismutase (EC-SOD) activity has been correlated with endothelium-mediated, flow-dependent vasodilatation (27). A randomized control group design was utilized to study the effects of an 8-week, low intensity, yoga program on the peak cardiovascular capacity, and biomarkers of inflammation, and QoL in patients with HF.

The present study was a continuation of the pilot study, with minor changes (40). In the second cohort, patients with diastolic HF were included, because similar changes with exercise training have been reported in the scientific literature (46). The aim of the present study was to further substantiate the findings of the pilot study and possibly illuminate additional effects by increasing the number of subjects in the control and treatment groups.

Hypothesis. Stable HF patients who participate in an 8-week program of yoga therapy classes will improve their exercise capacity, inflammatory markers of cardiovascular function and QoL measures as compared to a control group of HF patients that receive standard medical therapy alone.

METHODS

Patient selection. Forty patients were recruited prospectively from the

out-patient cardiology clinic at Grady Memorial Hospital in Atlanta, Georgia. All patients had systolic or diastolic HF of ischemic or nonischemic etiology. Patients were randomized to a supervised hospital-based yoga therapy group (YG) or a control group (CG), in addition to standard medical care. Patients were included if they had: 1) systolic or diastolic heart failure 2) New York Heart Association (NYHA) class I-III; 3) were able to walk without assistance; and 4) were on stable medical therapy for heart failure at least three months prior to enrollment.

Patients were excluded if they: 1) had significant co-morbidities with a life expectancy < 6 months; 2) were pregnant or breast feeding; 3) were unable to attend yoga sessions twice a week or 4) were currently addicted to alcohol or drugs. The study was approved by the Institutional Review Board (077-2004) at Emory University and by the Institutional Review Board of Georgia State University (H09015). Patients that were eligible for participation in the study were appropriately screened and enrolled after informed consent (Appendix A).

Pre- test and post- test assessment. Patients were scheduled for initial assessment at the Vascular Laboratory located at Grady Healthcare System's main hospital in Atlanta, Georgia. Pre-testing and subsequent appointments followed in a timely fashion (Figure 1).

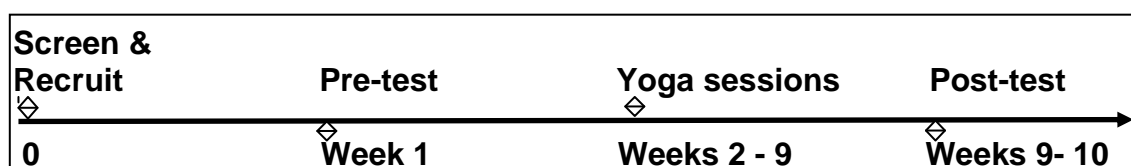


FIGURE 5- Time line for the study.

Cardiovascular parameters included resting systolic blood pressure in right and left arms, 12 lead EKG, and treadmill stress test. The sit and reach test

for flexibility (best of three), girth measurements for the waist/hip ratio, the Minnesota Living with Heart Failure Questionnaire (MLwHFQ), and venipuncture for serum biomarkers (IL-6, CRP, and EC-SOD) were also obtained during the assessment visits. Both groups received HF patient education, and a brochure with instructions for following a home walk progression. Documentation of current exercise behavior and exercise history was recorded during the initial visit and upon completion of the study. Investigators responsible for assessment of outcomes were blinded to the treatment assignment.

Yoga therapy. One hour yoga sessions were conducted twice a week in a quiet room located within Emory University's Vascular Laboratory. Patients randomized to yoga were given a yoga mat and strap for their personal use. Blood pressure and pulse were recorded before and after each class. Patients attended a total of 16 supervised sessions over an 8-10 week period. During each session, subjects completed the following: a five-minute warm-up phase including breathing exercises (*pranayama*), a 40-minute period of standing and/or seated yoga postures (*Asanas*) and finally, a 15-minute relaxation phase. Upon completion of the first four classes, patients were given a handout of the 18 yoga postures taught during class (Appendix B). The YG patients were asked to practice at home with a goal of three yoga sessions per week. The yoga sessions were conducted by a Registered Yoga Teacher (RYT-Yoga Alliance®) certified by the American College of Sports Medicine (ACSM; Registered Clinical Exercise Physiologist®), with over twenty years of experience in the field of cardiac rehabilitation. The yoga *asanas* for this study included traditional *hatha* yoga

postures including, combinations of forward and backward bends, twists and balance poses. Modifications were made on an individual basis, according to individual medical and orthopedic limitations. Chairs were utilized for patients unable to get up from the floor unassisted, and the wall was incorporated during the standing balance postures, as needed.

' Breathing exercises consisted of deep inhalation and exhalation in a 1:1 ratio, without breath retention. Inhalation was taught to begin with sequential involvement of the abdomen, lower chest, and then upper chest, with the same sequence in reverse, during exhalation. Meditation and relaxation was performed in a supine or seated position according to the patient's comfort level.

Exercise/fitness testing. All patients underwent a graded exercise test (GXT) at baseline and at the conclusion of the two month study period to determine exercise capacity (Marquette Electronics, Inc. Model: Case12 EKG and Marquette 2000 treadmill). Maximum oxygen consumption was estimated based on the work load at peak exertion utilizing the American College of Sports Medicine's standard formula for treadmill walking (55):

$$\text{VO}_2 (\text{mL/kg/min}) = 0.1 (\text{speed}) + 1.8 (\text{speed}) (\text{fractional grade}) + 3.5 \text{ mL/kg/min}$$

A one minute per stage, ramp protocol treadmill test was utilized for all pre and post treadmill tests (Table 2).

Additional baseline and post test measurements included EKG, blood pressure, flexibility (sit and reach test), and girth (waist and hip). Waist circumference was measured at the narrowest part of the torso and hip circumference was obtained

Table 2. *Heart Failure Ramp Protocol*

Time (Min.)	MPH	Grade	~METS
1	1	0	1.8
2	1.5	0	2.2
3	2	0	2.7
4	2.5	0	3.1
5	3	0	3.5
6	3	1	3.9
7	3	2	4.3
8	3	3	4.7
9	3	4	5.1
10	3	5	5.6
11	3	6	6
12	3	7	6.4
13	3	8	6.8
14	3	9	7.2
15	3	10	7.7
16	3	11	8.1
17	3	12	8.5
18	3.5	12	9

at the maximum extension of the buttocks, as described in the Anthropometric Standardization Reference Manual (28).

Measurement of soluble levels of IL-6, hsCRP, and EC-SOD.

Venipuncture was performed at baseline and at the conclusion of the study.

Plasma samples were centrifuged and stored at -80°C . An aliquot was drawn, and enzyme immunoassay (EIA – Cayman Chemical, Ann Arbor, Michigan) for serum IL-6, hsCRP, and EC-SOD was performed on each sample in triplicate. A total of 50 microliters of serum was used for analysis, and EIA was performed as previously described (21). The levels of total serum IL-6, hsCRP, and EC-SOD were determined on a plate reader at an optical density of 420 nm.

Quality of life. Quality of life was assessed with the MLwHFQ (14). This disease-specific questionnaire is the most widely used and validated assessment of quality of life in patients with HF. The MLHFQ is composed of 21 questions

addressing physical function, symptoms of heart failure, and psychosocial issues. The participants completed the questionnaire at enrollment and again at the end of the study. A decrease of five points in total score after a specific intervention is regarded as clinically significant (41).

Data analysis. Statistical analyses were conducted utilizing the Statistical Package for Social Sciences 16 (SPSS, Inc., Chicago Ill., USA). Means and standard deviations were computed for continuous variables, and *t*-test comparisons for within groups' analyses of pre- and post-test findings were conducted. A one-way analysis of variance was conducted on all measured variables between groups for comparisons of pre-to post-test differences. Confounding factors were adjusted for at baseline.

Success indicators were considered to be favorable changes in the treatment group, regarding inflammatory markers, ramp protocol treadmill test time to peak exertion in seconds, estimated peak oxygen consumption, flexibility, and QoL indicators that reached statistical significance ($\alpha < 0.05$), after the 16 bi-weekly yoga sessions.

RESULTS

Demographics. Ninety-one patients were interviewed initially regarding participation in the study. Fifty-one patients did not meet various eligibility criteria or declined to participate. Forty patients (17 females, 23 males) enrolled in the study, ages ranged from 31-76 years. Twenty-one patients randomized to the YG and 19 randomized to the CG. Three YG patients did not complete the study and three CG patients did not return for post- testing.

There were no significant differences between the groups in age, EF, resting heart rate, blood pressure, body weight, body mass index, flexibility, treadmill test time, VO₂peak, QoL scores, or biomarkers at baseline. Non-ischemic HF was the dominant etiology based on clinical history (Table 3).

TABLE 3. *Patients' Baseline Clinical Characteristics*

Total number of patients (n=40)	YOGA Group (n=21)	Control Group (n=19)
Age (years)	55.8 ±7.6	52.5±12.7
Men/Women, n (%)	10 (47.6)/11 (52.4)	13 (68.4)/6 (31.6)
BMI	35.7±10.1	32.6±9.5
Etiology		
-Systolic Heart Failure, n (%)		
Ischemic	7 (33.3)	2 (10.5)
Valvular	3 (14.3)	1 (5.3)
Non-Ischemic	10 (47.6)	12 (63.2)
Diastolic Dysfunction, n (%)		
NYHA Class, n (%)		
I	3 (14.3)	4 (21.1)
II	6 (28.6)	4 (21.1)
III	8 (38.1)	8 (42.1)
Ejection fraction by TTE, Mean (SD)	7 (33.3)	6 (31.6)
Medical History, n (%)		
CAD	31.2% (9.8)	27.1% (14)
Diabetes	8 (38.1)	6 (31.6)
Hypertension	8 (38.1)	3 (15.8)
Current Smokers	20 (95.2)	18 (94.7)
Aldosterone Blockers	2 (9.5)	3 (15.8)
ACEI/ARB	7 (33.3)	8 (42.1)
Statins	13/4 (61.9/19.0)	17/2 (89.5/10.5)
B-Blockers	15 (71.4)	12 (63.2)
	20 (95.2)	19 (100.0)

n=number, EF: ejection fraction, TTE: transthoracic echo, CAD: coronary artery disease

Exercise testing. Pre to post- test differences between the groups were significant for treadmill time and VO₂peak (P=0.002, P=0.003, Table 4). The YG increased their treadmill time by 22%, after the yoga intervention, while the CG's time decreased by 5% (Table 4).

Table 4. *Between Group Differences*

Test	Yoga (YG) % change from Baseline	Control (CG) % change from Baseline	P Value for Difference
Weight	1.68↑	4.64↓	0.983
Flexibility	17.22↑	7.67↑	0.012
Treadmill Time	19.28↑	5.3↓	0.002
~VO ₂ peak	15.08↑	3.95↓	0.003
MLHFQ-T	28.49↓	2.93↓	0.199
MLHFQ-P	28.17↓	0.58↑	0.128
MLHFQ-E	31.93↓	3.45↑	0.425
IL-6	18.82↓	1.61↑	0.001
CRP	24.49↓	2.46↓	0.001
EC- SOD	18.67↑	1.1↓	0.001

IL-6: interleukin-6 (pg/ml); CRP: C-reactive protein (mg/l); Ec-SOD: extracellular superoxide dismutase (U/ml); Treadmill time in seconds; VO₂peak: mL/kg⁻¹/min⁻¹; Oxygen consumption, MLHFQ: Minnesota living with heart failure questionnaire

Soluble inflammatory markers. There were clinically significant within group improvements in the plasma serum levels of the three biomarkers for YG patients (Table 5). Interleukin- 6 decreased from a mean value of 19.6 ± 2.5 to 16.0 ± 2.1 mg/dl ($P < 0.001$, $N=18$), CRP decreased from 2.4 ± 0.58 to 1.9 ± 0.4 Mg/dl ($P < 0.001$). Levels of EC-SOD increased from 509 ± 71.9 to 610 ± 86.2 U/ml ($P < 0.001$). Furthermore, between group comparisons from pre test to post test were significant for YG improvements (IL-6; $P < 0.001$, CRP; $P = 0.001$, EC-SOD; $P < 0.001$; Table 4).

Quality of life. There was a significant change from pre-test to post-test for the total scores and physical subscale scores for the MLwHFQ, within the YG (Table 5). No significant changes were found in the paired samples analysis for the CG. Other significant improvements within the YG from pre- to post- test were for improved flexibility ($P = 0.002$).

Table 5. *Within Yoga Group Differences*

Parameter pre- post	Time= 0 Months	Time= 2 Months	P- Value Time 0 vs. time 2-months
Flexibility	-1.4±5.6	0.29±4.5	0.002
Treadmill Time	441±208	565±222	0.001
VO ₂ peak	15.3±5.1	18.4±5.6	0.001
MLHFQ-T	41.55±21.82	30±15	0.02
MLHFQ-P	18.6±10.8	13.6±6.8	0.034
MLHFQ-E	7.8±4.6	5.4±5.4	0.192
IL-6 (pg/ml)	19.6±2.5	15.9±2.1	0.001
CRP (mg/l)	2.4±0.58	1.9±0.39	0.001
EC- SOD (U/ml)	509.1±71.8	610.1±86.2	0.001

Values are mean ± standard deviation; Flexibility in inches; IL-6: interleukin-6; CRP: C-reactive protein; Ec-SOD: extracellular superoxide dismutase; Treadmill time in seconds; VO₂peak: mL·kg⁻¹·min⁻¹; Oxygen consumption; MLHFQ: Minnesota living with heart failure questionnaire; T= total score; P= physical sub-scale; E= emotional sub-scale.

DISCUSSION

Despite significant advances in medical and surgical management of HF, the one-year mortality rate for patients with advanced HF remains approximately 35% (5). Prognosis may be better in patients within the early stages of HF but, they continue to experience considerable symptoms, deterioration in functional status, and a poor QoL (6). Psychosocial factors and reduced QoL contribute to recurrent HF exacerbations and hospitalizations (37, 57). The present study is unique in that there were no yoga studies in the medical literature that utilized a randomized control design while examining the clinical effects of yoga on HF patients. There is little data on the unconventional techniques of mind-body medicine specific to cardiac patients.

The addition of an organized program of yoga therapy for 8 weeks to standard medical treatment of HF led to an improvement in flexibility, exercise capacity, ~VO₂peak, and reduced inflammatory markers. Mechanisms by which

yoga therapy may have improved the clinical parameters in this study are speculative at this time. In addition to hemodynamic derangements, an increased neuro-hormonal activation via the sympathetic nervous system and the renin-angiotensin system has been implicated in the progression of HF (20, 43). Indeed, drugs such as beta-blockers and ACE-I/ARBs that block this neuro-hormonal activation lead to a reduction in morbidity and mortality in patients with HF (1, 2). Heart rate, blood pressure, and the respiratory rate interval are all influenced by input from both the parasympathetic and the sympathetic systems. Arterial baroreflex modulates vagal nerve traffic to the sino-atrial node. In post myocardial infarction (MI) patients, it has been observed that if the vagal baroreflex is abnormal, there is an increased risk of fatal events due to ventricular tachycardia (24). Furthermore, in patients with HF, the arterial baroreflex insensitivity may also lead to ventricular arrhythmias (25, 31). Combining yogic postures with breathing exercises and meditation attenuates sympathetic activation and could lead to a decrease in ventricular filling pressures. This may explain part of the improvement in exercise capacity that was found in this study (based on the significant improvement in treadmill time and estimated VO_{2peak} in the yoga group as compared to the control group).

Yoga postures, relaxation, and breathing practices may improve patient well-being and retard the pathogenic mechanisms observed in HF. Dyspnea in chronic HF results in muscle fatigue from decreased arterial CO_2 (18). Dyspnea requires increased ventilatory effort, driven by sympathetic activation, predisposes to ventricular arrhythmias. In addition to allowing for a

predominance of the parasympathetic state, yoga may also promote effective extraction of oxygen by peripheral tissues. When muscle is stretched, the O_2 consumption increases. Studies that examined the health related aspects of yoga found that an 8-week yoga training program increased muscular strength by 31%, increased muscular endurance by 57%, increased flexibility by 88%, improved oxygen uptake by 7% and a reduction in cardiovascular risk in healthy adults (15, 50). These data appear to support the current study's increase in exercise tolerance in the yoga treated group, as reflected by longer treadmill times and an increase in VO_{2max} . Flexibility increased significantly in the current study which was anticipated since the sit and reach test is a replication of one of the yoga postures in the routine. It was encouraging to find that, despite their comorbidities, age, and poor EF, the YG patients were able to improve their range of movement.

Several studies of yoga treatment in hypertensive patients have demonstrated mean reductions of systolic and diastolic blood pressure of 15 mmHg and 10 mmHg, respectively (32, 42). The insignificant blood pressure and heart rate changes in this cohort may have been influenced by medications, and the fluctuations in body weight noted throughout the study.

In addition to the proposed mechanism of yoga's ability to attenuate the derangements of the autonomic nervous system, and thereby improve symptoms, its effect on psychological well-being may be a benefit as well. Major depression occurs in 25% of patients with HF, and 50% report symptoms consistent with subclinical depression or dysthymia (19), which in turn affect

patient QoL and raise mortality (17). Increased serum catecholamine levels due to stress cause deleterious effects on cardiac health and immune function (13, 22, 51).

In this study, answers to the well-validated MLwHFQ indicated that patients who did yoga perceived it to be beneficial. Statistical significance was reached for total scores and for the physical improvement subscale which is congruent with a positive QoL effect. The emotional subscale failed to reach significance; possibly due to a few extraneous incidents that occurred to a couple of the YG participants during the study (one patient's brother died unexpectedly and another's husband was placed in intensive care).

The yoga treatment patients reported an improved tolerance for the activities of daily living. Another important factor to consider is that modified yoga postures can be practiced safely by the disabled, the elderly, and by patients with chronic debilitating illnesses like arthritis and HF, compared to the conventional aerobic forms of exercise which can be demanding. There were no adverse outcomes in patients in the YG, and they tolerated this form of non-aerobic exercise quite well. Interestingly, compliance for the yoga sessions and testing appointments was 85% for both the treatment and control subjects.

Increased levels of markers of inflammation such as IL-6 and CRP have been associated with higher mortality in cardiac patients (38). This data suggests that yoga therapy may improve endothelial function by decreasing inflammation and oxidative stress at the level of vasculature reactivity. The levels of all three biomarkers improved after 8 weeks of yoga therapy compared to the CG. These

results are noteworthy: CRP decreased by 20% in the YG compared to 1.6% in the control group; IL-6 decreased by 22% in the YG compared to minimal change from baseline in the CG (Table 4). This is consistent with the effect cardiovascular exercise has on markers of inflammation (16). Both forms of activity may also improve endothelial function by increasing levels of Ec-SOD and NO activity (3, 47). Recently, a pilot study demonstrated that after six weeks of yoga participation, brachial artery reactivity improved only in the CAD patients, as opposed to individuals at risk of CAD (44). Thus, in patients with HF, yoga therapy may improve functional capacity and QoL by lowering sympathetic response to physical activity, leading to a reduction in cytokines and oxidative stress resulting in improved vascular reactivity.

Limitations. The exclusive reliance on markers of inflammation as improvement indicators of HF severity may not be ideal. Additionally, estimations of peak aerobic capacity, rather than direct measurements of oxygen uptake were conducted (8). Furthermore, to clarify that the improvements were specific to the yoga therapy, a standardized home exercise or cardiac rehabilitation program may have been a better control to compare than medical therapy.

Conclusion. This study of the effect of yoga on exercise capacity, inflammatory markers and QoL in patients with HF indicates that yoga may provide a beneficial adjunctive therapy and may be safely added to standard medical care under similar circumstances. Markers of inflammation such as IL-6, hsCRP, and EC-SOD showed a significant improvement with an 8-week yoga based program in patients with compensated systolic and diastolic HF. Larger

patient groups and longer term studies that control for physical activity are needed to further delineate the mechanisms of improvement that are unique to yoga. Future investigation with additional measurements of brachial artery reactivity, myocardial contractility, accelerometer recordings, depression inventories and symptom rating scales, in a head to head comparison with exercise therapy may further delineate the benefits and mechanisms of yoga therapy as an adjunct treatment of HF. In conclusion, yoga offered additional benefits to HF patients in regards to FLEXIBILITY, exercise capacity, inflammatory markers, increased precursors of NO, and QoL when compared to a group of HF patients that received standard medical therapy.

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APPENDIXES

APPENDIX A

EMORY UNIVERSITY SCHOOL OF MEDICINE
DIVISION OF CARDIOLOGY
CONSENT TO BE A RESEARCH SUBJECT

TITLE: The Effects of YOGA in Congestive Heart Failure

INVESTIGATORS: Bobby V. Khan, MD PhD, Paula R. Pullen, M.Ed.

INTRODUCTION/PURPOSE:

You are being asked to volunteer to participate in a research study. Before agreeing to participate in this research study, read the following carefully and ask the study doctor any questions. Please take your time to make your decision. No guarantees or assurances can be made as to the result of the study. You have been asked to participate in this study because you have heart failure, a disease in which the heart cannot pump enough blood to meet the needs of the body. The research study will evaluate the effects of usual medical care (which will include heart failure education and home walk instruction) with or without supervised yoga sessions in people with heart failure. Several studies have shown that people with heart failure have higher amounts of depression and anxiety, as well as a lower quality of life, than people without heart failure. People with heart failure are also more likely to be hospitalized and have more difficulty doing their day to day activities due to failure, breathing difficulty, and weak muscles that their heart failure causes.

Yoga is a form of structured physical exercises called asanas, combined with breathing exercises called pranayama, and relaxation techniques that is an increasingly popular type of fitness exercise for well being in the US. Several studies have found that healthy people who do yoga have lower amounts of depression and anxiety, as well as a better quality of life than people who don't do yoga. In addition, they also have better muscle strength, endurance, and flexibility. Other studies have shown that people with heart failure who do yoga-type breathing exercises or pranayama have less trouble breathing and more endurance. This study looks at whether adding a program of regular yoga practice to usual medical care offers any advantage over medical care alone in people with heart failure. There will be 120 volunteers participating in this study which takes place at Grady Health System.

Consent Form Approved by Georgia State University IRB September 24, 2008 - August 20, 2009

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EMORY UNIVERSITY SCHOOL OF MEDICINE, DIVISION OF CARDIOLOGY

PROCEDURES: This study takes 10 weeks to complete with an initial pre-test the first week, eight weeks of yoga session visits to the Vascular Lab, twice a week and a post-test after yoga sessions are completed. The sessions will consist of yoga classes lasting approximately one hour. You will need to wear comfortable clothing that allows you to bend and stretch. Eat a light breakfast at least 2 hours prior to your yoga class time and take all prescribed medications as usual. The screening pre-test and post-test visits and a total of 16 yoga session visits will all take place at the Vascular Research Lab on the second floor (C-Hall room 233) at Grady Health System.

SCREENING AND PRE-TESTS:

You will be asked to come to the Vascular Research Lab for two study visits, one at the start of the study and again at the end. You will be required to fast (nothing to eat or drink but water, for 12 hours) prior to each of these visits. At the first “screening visit” and pre-test visit, the study doctor will determine whether you are eligible to take part in the study. During this first visit the study doctor or staff will explain the study to you and answer any questions you may have. If you agree to take part in this study, you will sign a consent form. The study doctor will then ask you about your medical history, your health, recent medications changes and will examine you. There are several procedures that you will be asked to complete during the first study visit and the last. This will consist of a couple of questionnaires, some blood will be drawn, height, weight hip and waist measurements, blood pressures, electrocardiograms, treadmill exercise tests and a flexibility test. The treadmill test allows us to evaluate your level of physical fitness. The treadmill will slowly increase in speed and steepness with electrodes attached to your chest to evaluate your heart rate and rhythm and capacity for exercise. The electrodes will be attached using sticky pads and will be removed after the test is over. In addition, you may be asked to wear a small mask that fits over your mouth and nose so that we can monitor the amount of oxygen you are using. The study doctor or Exercise Physiologist will measure your blood pressure every 2 minutes during the exercise test. The exercise test will be stopped whenever you want or when the study doctor feels it is proper to do so. During this visit, a study doctor or staff will talk with you about things you can do to help yourself manage heart failure. At the end of Visit 1, you will be assigned by chance (like drawing straws) to one of the following groups:

Group1: Heart Failure Education and home walking instruction only

You will be given a brochure today and instructions to guide your home walk program over the next 2 months. Use the recording section in the back of the brochure to track your progress. At the completion of the study, bring your That will complete your participation in the study. walking record back, in order to discuss your progress with the Exercise Physiologist. You will be contacted in about eight weeks to schedule your post-test visit will consist of the same tests and questionnaires as the pre-test visit.

Group 2: Heart Failure, home walk instruction and Yoga sessions

You will receive the same home walk instruction as group 1 with the addition of attending the yoga classes two times per week for an eight week period. The classes will meet in the Vascular Research Lab for one hour and you will be asked to arrive about 10 minutes before the class begins in order to put on a single chest strap and wrist watch type of pulse monitor and for the study staff to take your blood pressure and weight at each visit.

Run-In Period

After the screening visit, volunteers who are eligible to take part in the study will first be asked to complete a 2-week run-in period. This will allow you to see for yourself if this study is for you and also allows the study doctors to identify and correct problems that might keep you from participation in the study. You will be asked to complete at least 4 in hospital yoga sessions in 2 weeks. These sessions will involve learning how to do yoga. Volunteers who cannot complete all 4 sessions will not be allowed to participate in the study.

Study visits

If you complete the run-in period and want to continue with the study, you will be asked to come to the Vascular Research Lab for your first official study visit or Visit 1. These include giving you information about limiting the amount of salt and fluid you use, as well as ways to make sure you take your medicines properly and things to watch out for that could make you feel worse due to your heart. You will be asked to bring your spouse, significant other, or a family member to this study visit so they can also receive information about taking care of heart failure. You and your family members/friends will also be invited to join weekly cooking classes for people with heart failure.

Exercise treadmill test

Upon completion of the yoga session visits you will be asked to complete an exercise treadmill test similar to the one you completed during the screening visit. You can stop the exercise test whenever you want to or when your study doctor feels that it is proper to do so.

Physical Examination

A study doctor will examine you during the first and last study visits. In addition, we will check your blood pressure, heart rate and weight during each visit.

Blood Draw

During both testing visits, we will draw approximately 1-2 teaspoons of blood from a vein in your hand or arm. These samples will be used to measure certain compounds in the blood that are often higher in people with heart failure.

Pregnancy tests

If you are a woman who can bear children we will ask you to complete a urine pregnancy test at the beginning and the end of the study.

Yoga Sessions

If you complete the pre tests and want to continue with the study, you will be assigned by chance to one of two groups during visit 1: Group 1 (usual medical) You will be asked to come to the hospital 2 times a week for the in-hospital yoga

sessions. These exercise sessions take place in the Vascular Research Lab at Grady Health System. During the last 6 weeks of the study you will be asked to add on one home based yoga session per week for the remaining six weeks of the study. You must complete at least 80% of the in-hospital yoga sessions during the eight week study (at least 13 sessions) in order to qualify for the post-test visit. Every effort will be made to provide make-up classes in the event a yoga session is missed due to circumstances beyond your control. There will be an exercise physiologist/yoga teacher present at each in-hospital yoga session. Our exercise physiologist is trained in cardiac rehabilitation and yoga teaching. She can determine what yoga posture modifications are safe and monitor your response to the yoga. Your blood pressure, heart rate, and perceived exertion will be monitored while you are attending the yoga session and we will be able to help you if there are any medical problems during exercise. Your blood pressure and heart rate will be checked at the beginning and end of each yoga session. You may also be asked to wear a monitor on your chest and wrist to allow our exercise physiologist to monitor your heart rate while exercising. The exercising physiologist will use your heart rate, as well as your own feelings of how hard you are exercising, to adjust your yoga postures. You will also be given a logbook to record when you exercise or do the yoga series at home. The log will also include what type of exercise you did, for how long and how you felt. The exercise physiologist will collect these log books and review them with you. If you are hospitalized for a heart condition during the study, we may ask you to begin the study again, after you are medically cleared.

Yoga asanas for this study consist of 18 exercises designed to increase muscle strength, muscle flexibility, balance and relaxation. Volunteers in Group 2 will receive a *Yoga 4 Heart* handout that describes each posture, a *Yoga 4 Heart* video to use as a reference. during the home sessions.

Risks

People with heart failure can usually perform gently yoga without significant difficulty. However, like any exercise program, there may be risks caused by the exertion of exercise. Common side effects include tiredness, shortness of breath and muscle soreness, especially during the first few weeks of exercise. Less commonly (1 in 100), you may have problems with chest pain or angina that makes you stop exercising. This usually happens only in people with blockages in their heart arteries. Rarely (less than 1 in 5000), you may experience severe chest pain, heart attack, worsening of your heart failure, or an abnormal heart rhythm that requires further treatment and possible admission to the hospital. Your exercise physiologist will monitor your progress during the in-hospital yoga sessions for your safety. She will also teach you how to monitor yourself while you do the home-based yoga. You should stop exercising immediately if you develop chest pain; lightheadedness, significant shortness of breath or other significant symptoms develop and report them promptly to the exercise physiologist.

Blood draws

Blood samples will be collected during the first and last study visit. You may have discomfort, bruising, and /or bleeding at the site where the blood is taken. Localized blood clot formation and infections may occur but this is rare. We will place a small piece of gauze and a bandage over the site where blood is taken. There is a small chance of a reaction to the bandage that usually gets better once it is removed.

Exercise Treadmill test

You will be asked to undergo an exercise treadmill test to evaluate your level of fitness during the screening visit and at the completion of the study. A study doctor will monitor your progress and help safeguard against any potential problems. Risks of an exercise test include but are not limited to a 1 in 10,000 risk of falls, heart attacks, or abnormal heart rhythms that may require further treatment. You should notify your study doctors immediately if you notice any discomfort or unusual symptoms during the study visit or at any time during the study.

Benefits

Taking part in this study may not benefit you directly, but we doctors may learn new things that will help future patients.

Alternatives

You do not have to participate in this research study or yoga sessions. The alternative to participating in this study is not to participate.

Compensation

We will arrange for emergency care if you are injured by this research, the study doctors, the Vascular Research Lab, Emory University, Georgia State University and the Grady Health System have not set aside funds to pay for this care or to compensate you if a mishap occurs. Lab tests, physician fees, and costs for the Vascular Research Lab will pay for procedures done during each of the study visits. Financial compensation for such things as medical care lost wages, disability or discomfort due to injury or illness is not routinely available. You will be financially responsible for any additional treatment that may be required after participating in this study. You will not, however, give up your legal rights by signing this form. If you believe you have been injured by this research, you should contact Dr. Bobby Khan (phone 404-616-4440) promptly. You may keep the yoga mat if you complete the entire study successfully.

Confidentiality

All information concerning you will be kept private. People other than those doing the study may look at both medical charts and study record. Agencies that make rules and policy about how research is done have the right to review these records So do agencies that pay for the study. Those with the right to look at your study records include: Georgia State University, Emory University, The Institutional Review Board, and the Grady Research Oversight Committee and the Clinical Trials office of Emory University. Records can also be opened by

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court order. We will keep your records private to the extent allowed by law. We will do this even if outside review occurs. We will use a study number rather than your name on study record where we can. Your name and other facts that might point to you will not appear when we present this study or publish its results. People other than those doing the study may look at both medical charts and study

records. Agencies and Emory departments and committees that make rules and policy about how research is done have the right to review these records. So do companies and agencies that pay for the study. The government agencies and units within Emory responsible for making sure that studies are conducted and handled correctly that may look at your study records in order to do this job include The Institutional Review Board of Emory University, The Research Oversight Committee at Grady Health System, the FDA and the Clinical Trials Office of Emory University. Companies and other groups that pay for studies and that are listed in consent and authorization documents also will have the right to look at your records. In addition, records can be opened by court order or produced in response to a subpoena or a request for production of documents. We will keep any records that we produce private to the extent we are required to do so by law. We will use a study number rather than your name on study records where we can. Your name and other facts that might point to you will not appear when we present this study or publish its results. Some tests and procedures that may be performed during this study by Emory Healthcare or other facilities or persons may not be looked at or read for any healthcare treatment or diagnostic purposes. The specific types of tests or procedures, if any, that fall within this category are listed below: none

Contact Persons

Call Dr. Bobby Khan if you have any questions about this study or if you think you may have been harmed from being in this study. Call Dr. Colleen Dilorio, Chair of the Emory University Institutional Review Board at 404-616-0720 if you have any questions about your rights as a participant in this research study. If you are a patient receiving care from the Grady Health System and you have a question about your rights as a Grady patient, you may contact Dr. Curtis Lewis, Senior Vice President for Medical Affairs for Grady Health System at 404-616-4261. You may also contact the Georgia State University Office of Research Integrity (Susan Vogtner) at 404-413-3513.

Voluntary Participation and Withdrawal

Your participation is completely voluntary and you have the right to refuse to be in this study. You can stop at any time after giving your consent. This decision will not affect in any way your current or future medical care or any other benefit to which you are otherwise entitled.

Consent

The study doctor/investigator may stop you from taking part in this study at any time if they decide it is in your best interest, or if you do not follow study instructions. You will be given a copy of this consent to keep.

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I have read and understand this entire consent for. All my questions have been answered. I volunteer to participate in this study.

Signature of Volunteer Date and TIME

Printed Name of Volunteer

Name of Person Obtaining Consent Date and TIME

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APPENDIX B- Yoga Postures Handout

The goal of yoga is to relax the body and mind bringing one to a calmer state of being. This is done with 1) Breath awareness-keep the breath full and steady, 2) Balance of the body in the postures, and 3) Mind-focus on the present moment while going through the session. Each posture is held for 3-5 breaths. **Repeat the posture on the opposite side** when applicable. Each b) variation is a modified version of a).

The benefits of daily practice are 1) Decreased stress reactions 2) Lowered blood pressure 3) Increased feeling of well being and flexibility.

1. Seated Pose (Sukhasana)

- a) Sit cross-legged on the floor with support as needed.
- b) Seated in chair.



2. Staff Pose (Dandasana)

- a) On floor.
- b) On a chair placed against a wall. Legs extended toes up, feet together.



3. Forward Bend (Paschimottanasana)

- a) On floor.
- b) In a chair. Sit near the edge and bend down over the legs.



4. Mountain Pose (Tadasana)

- a) Stand with feet together weight evenly distributed over the feet.
- b) Stand with feet slightly separated and parallel to each other.
- c) Lift the sternum, shoulders at the sides.



5. Extended Triangle (Uthita Trikonasana) Separate the feet $3\frac{1}{2}$ to 4 feet apart, turn left foot in 15 degrees and right foot out to 90 degrees. Bend over the right leg. The right arm reaches down the leg. Look forward or upward

- a) Middle of the floor.
- b) Near the wall



6. Warrior Pose (Virabhadrasana) Separate legs 4-4½ feet wide.

- a) Bend to 90 degrees, turn to look over the hand of the bent leg
- b) Bend as close to 90 degrees as possible.



7. Awkward Chair (Utkatasana) Stand with feet together or slightly apart. Lower hips toward thighs parallel to the ground.

- a) Arms up, palms face each other or touch over head.
- b) Arms in namaste (prayer position at sternum)



8. Tree Pose (Vrksasana) Press the bent leg foot into the thigh and vise versa. Turn the knee out. Keep the shoulders parallel to the wall behind you.

- a) Middle of the floor, arms reach over head.
- b) Against the wall with hands in front of sternum in namaste.



9. Cobra Pose (Bhujangasana) Lying on the belly relax in savasana for a few breaths.

- a) On the belly, press hips downward, chest lifts in front of arms, look up as you lift.
- b) On wall press shoulders into the wall and look up.



10. **Downward Facing Dog (Adho Mukha Svanasana)** Extend legs, arms and back.
 a) On the floor.
 b) Table pose on wall.



11. **Child's Pose (Salaam Posture)**

Sit back on heels, lower head toward floor, arms over head. Arms extended or along sides.

- a) On the floor.
 b) In a chair release forward between knees.



12. **Wide Angle Pose (Upavistha Konasana)** Press thighs to the floor, feet straight up.
 a) On the floor.
 b) In a chair.
 c) Variations include sideways wide angle, turn to each side (Parsva).



13. **Tailor's Pose (Baddha Konasana)** The heels press together, the knees press downward.

- a) On the floor (or with your back against the wall for extra support).
 b) In a chair-feet on blankets or blocks to elevate the legs.



14. Cow Face Pose (Gomukhasana)

- a) Stretch one arm up, bend the elbow and walk the hand down the center of the back. Other hand reaches around hand down the center of the back. Other hand reaches around the back toward the first hand, try to touch finger tips or hold hands.
- b) Modify by keeping the second hand in front, pressing the elbow back, seated in a chair or cross leg position.



15. Half Spinal Twist (Maricyasana III)

- a) On the floor.
- b) On a chair.



16. Legs Up the Wall- Supported Inversion (Viparita Karani)

- a) Place a folded blanket up to the wall. Sit sideways to the wall and roll onto the back, bring the legs up the wall.
- b) Recline on a chair or bed with legs propped up with several pillows, toes above nose level.



17. Sponge Pose (Savasana)

Fifteen minutes of relaxation. Focus on the breath and try to quiet your thoughts. When finished, roll to the side and push with the arms to sit up.

- a) On the floor palms up.
- b) Reclining on a chair.



Namasté

(I bow to the light within you)

Paula R. Pullen, M.Ed., developed this handout.

