Effect of Yoga on Early Recurrence of Atrial Tachyarrhythmia after Atrial Fibrillation Ablation

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ABSTRACT

Background: Atrial fibrillation (AF) is the most common sustained cardiac rhythm disturbance, increasing in prevalence with age. Today, medical treatment involving catheter ablation is the well-accepted management strategy; however, failure of this therapy is common, with only two-thirds or less of the patients treated remaining free of AF on long-term follow-up. Given the role that stress, anxiety, inflammation, and autonomic nervous system imbalance plays in AF, the complementary health-enhancing therapy of yoga could potentially prevent episodes of AF. Although, to date, two studies have assessed the impact of yoga on paroxysmal AF, no studies have investigated the effect of yoga on early recurrence of atrial tachyarrhythmia (ERAT) after AF ablation.

Objective: The two specific aims for this study were: (1) to examine the feasibility and acceptability of a Viniyoga intervention for individuals with AF and (2) to test whether or not a 6-week Viniyoga intervention in persons age 18 to 65 years with paroxysmal or persistent AF prior to ablation will decrease AF symptoms, stress, depression, anxiety, prevent ERAT after AF ablation, and improve overall health-related quality of life (QOL) during the 6-month post-ablation period if these participants continued to practice yoga post-ablation at least twice a week for 50 minutes. A secondary aim was to capture all the participants' perceptions of health-related QOL, using semi-structured interviews, and for the yoga intervention group participants, their experiences with yoga as well.

Design and Methods: A sequential mixed methods, prospective, quasi-experimental, two-group design informed by a psychoneuroimmunology theoretical framework guided the study design to investigate the effect of a twice-weekly 6-week Viniyoga intervention and continued practice of yoga at home in prevention of ERAT after AF ablation. Self-

report questionnaires were completed at 8 different time points, including baseline and at the 6-month post-AF ablation time period. All participants participated in a semi-structured interview during their 6-month post-ablation clinic visit.

Results: The recruitment rate for the yoga intervention plus usual care (YI) group was very low at 16.67% and 50% for the usual care alone (UC) group, with recruitment for the UC group having been stopped because of less recruitment to the YI group. A total of 4 UC group participants and 2 participants in the YI group completed the study. Two major reasons for participants declining participation in the study were travel distance and challenges in attending twice-weekly YI sessions. Other reasons included current practice of yoga or mindfulness meditation, lack of a smart phone or iPad to download the Alivecor™ app, and questions about the affiliation of yoga with a religion that the participants did not practice. No statistical significance was achieved for any of the study outcome measures given the small sample size, although clinically meaningful improvements were noted in the Atrial Fibrillation Effect on QualiTy-of-Life questionnaire overall score and symptom score in the YI group compared with the UC group participants. The study also showed that ERAT in the two YI participants was 0% but it was 75% in the four UC group participants. Minimal decrease in stress, depression, and anxiety scores were noted, although qualitative data analysis showed that the participants identified stress, depression, and anxiety as triggers and manifestations of their AF. The reason for no significant change in the anxiety scores may be related to the fact that a new diagnosis of AF is compounded with much anxiety about the disease course, and at post-ablation these participants continued to be worried about recurrences, with this impacting their QOL.

Conclusion: This study did not show any statistical significance in the outcome measures, which may be because of the small sample size, but it did show clinically meaningful improvements in a few of the study outcomes as described above. These preliminary findings support the need for future randomized controlled studies to determine the impact of yoga on prevention of recurrent atrial arrhythmias.

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CHAPTER ONE: INTRODUCTION

Atrial fibrillation (AF), the most common sustained cardiac arrhythmia, is associated with increased cardiovascular risk factors such as stroke, heart failure, dementia, and death (Savelieva & Camm, 2004). One of the largest U.S. epidemiological studies, the Framingham Heart Study, predicted that AF prevalence doubles with each advancing decade of age, from 0.5% at age 50-59 years to almost 9% at age 80-89 years, independent of the increasing prevalence of known predisposing conditions (Kannel et al., 1998). Cumulative lifetime risk estimates demonstrate that AF is largely a disease of aging. In U.S. and European community-based cohort studies, the estimated lifetime risk of AF is 22% to 26% in men and 22% to 23% in women by age 80 years old (Magnani et al., 2011).

Regarding management of AF, the American College of Cardiology Foundation, American Heart Association, and Heart Rhythm Society (ACCF/AHA/HRS) task force recommend that AF management involve three non-mutually exclusive objectives: rate control, prevention of thromboembolism, and correction of the rhythm disturbance. Thus, the focus of treatment for AF is to maintain the heart rate or rhythm either through medical management or ablation procedures, with catheter ablation being an accepted management strategy for AF (Kumar & Mounsey, 2012). However, failure of this therapy is not uncommon, with only two-thirds or less of the patients treated with catheter ablation remaining free of AF at long-term follow-up (Kumar & Mounsey, 2012). It has been recognized that early recurrence of atrial tachyarrhythmia (ERAT), usually defined as arrhythmia recurrence within the first 3 months following ablation, is frequently associated with late recurrence of atrial tachyarrhythmia (Themistoclakis et al., 2008;

Choi et al., 2010). Consequently, many of these individuals experience poor health-related quality of life (QOL).The most common AF symptoms include palpitations, shortness of breath, fatigue, dizziness, and anxiety. In a study of 100 randomly selected AF patients, 88% reported palpitations on exertion, 86% reported palpitations at rest, 70% reported shortness of breath on exertion, 87% reported reduced physical ability, and 59% reported anxiety (Hansson et al., 2004). Adults with worsened severity of depression, anxiety, or somatization disorder symptoms had an associated increase in the severity of the AF symptoms (Gehi, et al., 2012).

Psychological stressors and imbalance in the autonomic nervous system (ANS) are the most common triggers for paroxysmal AF (Hansson et al., 2004; Mattioli et al., 2005). Acute life stressors affect the development and spontaneous conversion of AF and are thought to be mediated by the sympathetic nervous system. This hypothesis is supported by the increase in circulating catecholamine in the aftermath of acute life stress and by observation that beta-adrenergic blockade prevent the arrhythmogenic effects (Choi et al., 2010). Lower overall heart rate variability as well as increased sympathetic/parasympathetic tones were associated with a higher risk of AF (Agarwal et al., 2017).

The mind-body therapy yoga has been shown to reduce stress, anxiety, inflammation, and maintain autonomic nervous system balance (Kiecolt-Glaser et al., 2010; Streeter et al., 2012; Telles et al., 2013), which could potentially prevent AF. In particular, the breath can have a major influence on physiology, especially the balance between sympathetic and parasympathetic tone in the autonomic nervous system. This is the prime focus in Viniyoga, the style of yoga used in this dissertation study. Varying the

respiratory rate, depth, and ratio of inhalation to exhalation can refine this effect. Similarly, the choice and sequence of poses can be used to modulate this balance and influence physical structures affected by stress.

To date, two studies have assessed the impact of yoga on AF. One, a proof-of-concept study (Lakkireddy et al., 2013), revealed that 60-minute Iyengar yoga sessions at least twice a week for 3 months improved symptoms, arrhythmia burden, heart rate, blood pressure, anxiety and depression scores, and several domains of QOL in adults with paroxysmal AF. A second study (Whalstrom et al., 2017) using Mediyoga as the intervention showed that this style of yoga might potentially lower blood pressure and heart rate in patients with paroxysmal AF and improve QOL compared to a control group. To date, no studies were identified that documented the effect of yoga in preventing ERAT in adults with AF after ablation.

This dissertation is the synthesis of a scholarly process that began with a review of the literature on effect of yoga on stress and autonomic nervous system and progressed through the design, implementation, analysis, and interpretation of a study using Viniyoga as an intervention in prevention of ERAT after AF ablation with a sample of adults diagnosed with paroxysmal and persistent AF. In accordance with the 2012-2013 PhD Student Handbook for Academic Policies and Procedures of the University of Virginia School of Nursing, this dissertation follows the manuscript dissertation design.

Chapter Two: *Effect of Yoga on the Autonomic Nervous System: Clinical Implications in the Management of Atrial Fibrillation* is a manuscript that examines the original studies published in English, evaluating the effects of yoga as a complementary

health approach on stress and ANS. It further attempts to describe how this mind-body modality, if added to conventional treatment, might contribute importantly to reducing or eliminating recurrent episodes of AF. To address the deficit in the literature regarding theoretical or conceptual frameworks in the studies reviewed, a psychoneuroimmunology theoretical framework was identified to depict the electrical, mechanical, and structural changes in the heart that lead to a stress-related imbalance in the ANS resulting in AF. It further explains how an appropriate yoga intervention for cardiac patients can help in reducing stress, decrease inflammation, and modulate the ANS towards parasympathetic dominance, which is a key factor in prevention of tachycardia.

Chapter Three: *A Feasibility Protocol to Assess the Effect of Yoga on Early Recurrence of Atrial Tachyarrhythmia after Atrial Fibrillation Ablation* provides the research design and detailed methods of the study conducted, including the description of the theoretical framework that was used to inform the study design and data analysis.

Chapter Four: *Effect of Yoga on Early Recurrence of Atrial Tachyarrhythmia after Atrial Fibrillation Ablation: Results of a 6-week Viniyoga Intervention* presents the results of the 6-week Viniyoga intervention on stress, anxiety, depression, AF episodes and symptoms, ERAT after AF ablation, and health-related QOL in study participants. It also provides information related to feasibility of the intervention and the study participants' perceptions of the experience of participating in the study. Also, adherence to the yoga intervention is reported.

Chapter Five: *Conclusion* incorporates the components of the dissertation into a cohesive document providing lessons learned, implications for nursing, and future directions related to research and theory development for symptom management using

complementary health-enhancing approaches for individuals with AF and other cardiovascular diseases.

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CHAPTER TWO: REVIEW OF THE LITERATURE

Manuscript One

Effect of Yoga on the Autonomic Nervous System: Clinical Implications in the Management of Atrial Fibrillation

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Abstract

Atrial fibrillation (AF) affects about 1.5% of the U.S. population, especially aging persons, resulting in substantial morbidity and mortality. Although catheter ablation is the accepted treatment for AF, failure of this therapy is common. Given that the onset of AF is preceded by a primary increase in the sympathetic drive followed by marked modulation towards vagal pre-dominance, it is likely that stress precipitates and exacerbates AF. The authors searched the databases of Ovid MEDLINE, PubMed, APA PsycNET, Alt Health Watch via EBSCOhost, and CINAHL to evaluate the effects of yoga as a complementary health approach on the autonomic nervous system and how this mind-body modality, if added to conventional treatment, might contribute importantly to reducing or eliminating stress as a trigger for AF. Articles written in English and published in peer-reviewed journals between 2003 and 2017, reporting on research of yoga on autonomic nervous system, were identified. Twenty articles met the inclusion criteria, revealing that yoga resulted in a significant shift in autonomic balance towards vagal dominance; reduction in heart rate and blood pressure; reduction in indices of ventricular repolarization dispersion in patients with ventricular arrhythmias; significant reduction in stress, anger, depression, and anxiety; and improvements in neuroendocrine release, emotional processing, and social binding. Given these literature review findings, the authors provide an integrative overview of biological mechanisms and substrates that mediate AF, which can be targets for future research evaluating how the practice of selected styles of yoga can mitigate the onset of AF.

Key words:

Yoga, heart rate variability, stress, autonomic nervous system, atrial fibrillation

Introduction

Atrial fibrillation (AF), the most common sustained cardiac arrhythmia, is seen in approximately 1.5% of the U.S. population[1] and results in substantial morbidity and mortality.[2] One of the largest U.S. epidemiological studies, the Framingham Heart Study, predicted that AF prevalence doubles with each advancing decade of age, from 0.5% at age 50-59 years to almost 9% at age 80-89 years, independent of the increasing prevalence of known predisposing conditions.[2] Although medical treatment involving catheter ablation has become a well-accepted management strategy for AF[3] failure of this therapy is common, with only two-thirds or less of the patients treated remaining free of AF on long-term follow-up.[3] Early recurrence of atrial tachyarrhythmia, usually defined as arrhythmia recurrence within the first 3 months following ablation, is frequently associated with late recurrence of atrial tachyarrhythmia.[4,5] Acute myocardial injury and the subsequent inflammatory response, as well as modifications of the cardiac autonomic nervous system, provide an early and potentially reversible pro-arrhythmic substrate because of altered atrial myocardial conduction and refractoriness.[3] Research has shown that psychological stressors and imbalance in the autonomic nervous system (ANS) are the most common triggers for paroxysmal AF.[6, 7] The mind-body therapy yoga has been shown to reduce stress and maintain autonomic nervous system balance[8]: hence, use of complementary health approaches such as yoga, which are low-cost interventions, might contribute importantly to reducing stress, help individuals maintain balance in the ANS, and thereby prevent recurrence of AF. In this article, the authors provide an overview of AF, the effects of yoga on lessening stress and maintaining ANS balance, and suggest

through a psychoneuroimmunology framework the possible mechanisms by which the practice of yoga could mitigate AF episodes and symptoms.

Atrial Fibrillation and Associated Symptoms

Cumulative lifetime risk estimates reveal that AF is primarily a disease of aging. In U.S. and European community-based cohort studies, the estimated lifetime risk of AF is 22% to 26% in men and 22% to 23% in women by age 80 years.[9] The effects of heart failure, valvular disease, myocardial infarction, and ischemic stroke on AF are substantial. Heart failure increases the risk of AF by a 4.5-fold in men and a 5.9-fold in women. Valvular heart disease increases the risk of AF by a 1.8-fold in men and a 3.4-fold increase in women, with myocardial infarction significantly increasing the risk of AF by 40% in men.[2] Likewise, AF is a potent risk factor for ischemic stroke, increasing the risk of stroke 5-fold, thus leading to about 15% of all strokes nationally.[10]

The most common AF symptoms include palpitations, shortness of breath, fatigue, dizziness, and anxiety. In a study of 100 randomly selected patients with AF, 88% reported palpitations on exertion, 86% reported palpitations at rest, 70% reported shortness of breath on exertion, 87% reported reduced physical ability, and 59% reported anxiety.[6] Adults with major depression, anxiety, or somatization disorder generally have an associated increase in the severity of their AF symptoms.[11]

Quality of Life in Individuals with AF

AF contributes to increased morbidity in the elderly by adversely affecting their quality of life (QOL) and by deterioration in myocardial function, increasing susceptibility to heart failure, stroke, hospitalization, and mortality.[12] Evaluation of QOL in a group of 264 female patients with AF enrolled in the Canadian Trial of Atrial

Fibrillation (*N* = 403) showed that women had significantly more impaired QOL than men, specifically related to physical rather than emotional functioning.[13] In another study, outpatients with documented AF (*N* = 152) reported substantially poorer QOL than healthy controls.[14] Three of the four well-known randomized controlled trials (STAF, PIAF, RACE) comparing rate versus rhythm control demonstrated a greater improvement in QOL in patients receiving rate control[15] than those in the rhythm control group. However, the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial revealed a similar improvement in QOL for both rate and rhythm control groups.[15]

Health Care Costs associated with AF

A national survey estimated that direct medical costs were 73% higher in patients with AF compared with matched control subjects, representing a net incremental cost of $8705 per patient per year and a national incremental cost between $6 and $26 billion.[16] Retrospective analyses of three federally funded U.S. databases using 2001 data[17] found that approximately 234,000 hospital outpatient department visits, 276,000 emergency room visits, 350,000 hospitalizations, and 5 million office visits were attributable annually to AF. The total annual medical cost for the treatment of AF in the inpatient, emergency department, and hospital outpatient settings estimated at $6.65 billion is likely an underestimate as costs for long-term anticoagulation, stroke prevention, inpatient drugs, and hospital-based physician services were not included.[17] Patients with AF enrolled in the Fibrillation Registry Assessing Costs, Therapies, Adverse events, and Lifestyle (FRACTAL) study who were managed with cardioversion and pharmacotherapy incurred AF and other cardiovascular-related health care costs of $4000

to $5000 per year.[18] Among patients with recurrent AF, the frequency of recurrence was strongly associated with higher resource use, with each recurrence increasing annual costs by an average of $1600.[18] The cost-effectiveness of catheter ablation is difficult to determine because of differences in the experience levels of centers treating these patients, use of technology, and rates of reimbursement, each of which affects cost calculations.[19] Researchers evaluating the cost-effectiveness of AF ablation compared with rhythm control or antiarrhythmic agents have shown that ablation treatment results in improved quality-adjusted life expectancy, although at a higher cost.[18, 19]

Atrial Fibrillation and Stress

Researchers have shown that psychological stressors and imbalance in the autonomic nervous system are the most common triggers for paroxysmal AF.[6, 7] Acute life stressors affect the development and spontaneous conversion of AF and are thought to be mediated by the sympathetic nervous system. This hypothesis is supported by increased circulating catecholamines following an acute life stress and by observation that beta-adrenergic blockade prevents abnormal heart rhythm disturbances triggered by acute life stress.[5] In a study of 100 randomly selected patients with idiopathic paroxysmal atrial fibrillation, 54% reported psychological stress as the most common triggering factor for AF.[6] In another study of 116 patients with AF without an obvious cause, acute life stress significantly affected the development and spontaneous conversion of AF.[7]

Atrial Fibrillation and the Autonomic Nervous System

The autonomic innervation to the heart from the brain, the spinal cord (extrinsic system), and the ganglia plexi of the heart itself comprise the local ANS (intrinsic system).[20] This intrinsic cardiac ANS of the heart and the pericardium serves as more

than a relay station for the intrinsic projections of the vagal-sympathetic system from the brain and spinal cord to the heart. Supporting this theory is the fact that ablation of the major ganglion plexi at the pulmonary vein atrial entrances either eliminates or markedly diminishes AF inducibility. Also, this intrinsic cardiac autonomic system can act independently to modulate numerous cardiac functions, including automaticity, contractility, and conduction.[20]

In addition to the sympathetic component of the ANS, the parasympathetic component has been shown to play a role in AF.[21] Amar et al., (2003) [22] showed that the onset of AF was preceded by a primary increase in the sympathetic drive followed by marked modulation toward vagal pre-dominance. The physiologic studies by Patterson et al., (2005) [23] further indicate that sympathetic stimulation plays an important modulatory role in the emergence of focal drivers for AF in the presence of an increased vagal tone. The ANS is involved in the genesis of both AF triggers (i.e., ectopic foci that result from interaction between vagal and sympathetic stimulation) and the creation of a more established AF substrate that is needed for the maintenance of AF and is enhanced in the presence of structural heart disease.[21] It has been shown that the abnormal electrical conduction within the pulmonary veins could be sustained only in the presence of isoproterenol or acetylcholine, indicating that sympathomimetic or cholinergic stimulation appears to be necessary to promote the development of sustained focal activity in the pulmonary veins.[21]

Relationship between Autonomic Nervous System and Measurement of Heart Rate Variability

Heart rate variability (HRV), the variance between the R-R intervals or complete

cardiac cycle on the electrocardiogram, can be used to assess the balance between the sympathetic and parasympathetic branches of the ANS.[24] Efferent sympathetic and parasympathetic activity is integrated in and with the activity occurring in the heart's intrinsic nervous system. Thus, HRV is considered a measure of neurocardiac function that reflects heart-brain interactions and ANS dynamics.[25] HRV is assessed with various analytical approaches, although the most commonly used are frequency domain (power spectral density) analysis and time domain analysis.[25] The European Society of Cardiology and the North American Society of Pacing and Electrophysiology Task Force Report on HRV divided heart rhythm oscillations into 4 primary frequency bands: high-frequency (HF), low-frequency (LF), very-low-frequency (VLF), and ultra-low-frequency (ULF). [24] It is often assumed that a low LF: HF ratio reflects greater parasympathetic activity relative to sympathetic activity. [25] In contrast, a high LF:HF ratio may indicate higher sympathetic activity relative to parasympathetic activity as can be observed when people engage in meeting a challenge that requires effort and increased sympathetic activation.[25]Alternatively, it can indicate increased parasympathetic activity as it occurs during slow breathing. Time domain indices quantify the amount of variance in the inter-beat-intervals using statistical measures.[25] The three most important and commonly reported time domain measures are the standard deviation of normal-to-normal (SDNN), the SDNN index, and the root mean square of successive differences (RMSSD).[25] The modulation of vagal tone helps maintain the dynamic autonomic regulation important for cardiovascular health. Reduced parasympathetic (high frequency) activity has been found in cardiac pathologies and in patients under stress or suffering from panic, anxiety, or worry.[24]

Yoga as a Complementary Health Approach in Treating Atrial Fibrillation

Yoga, an ancient discipline from India, is a mind-body exercise in which both physical and mental disciplines are brought together to achieve peacefulness of mind and body, resulting in a relaxed state that is useful in managing stress and anxiety. To date, two studies have assessed the impact of yoga on AF. One, a proof-of-concept study, [26] revealed that 60-minute Iyengar yoga sessions at least twice a week for 3 months improved symptoms, arrhythmia burden, heart rate, blood pressure, anxiety and depression scores, and several domains of QOL in adults with paroxysmal AF. A second study[27] using mediyoga as the intervention, showed that this style of yoga might potentially lower blood pressure, lower heart rate in patients with paroxysmal AF, and improve QOL compared to a control group.

Given the potential positive impact of yoga on decreasing AF episodes and symptoms as shown in Table 1 (page 34), the authors conducted an extensive computerized search of diverse databases (Ovid MEDLINE, PubMed, APA PsycNET, Alt Health Watch via EBSCOhost, CINAHL), using key terms of heart rate variability and autonomic nervous system, to assess the effect of yoga on the ANS. These computerized searches yielded 230 studies (Ovid MEDLINE = 25, PubMed = 31, APA PsycNET = 16, Alt Health Watch = 153, CINAHL = 5), which were then reviewed for eligibility. Inclusion criteria were English language articles reporting on studies that (a) enrolled subjects 18 years and older and (b) were published between 2003 and 2017 in peer-reviewed scientific journals. The 20 articles that met the inclusion criteria are shown in Table 2 (page 36). Seventeen were interventional studies with 14 of these using random sampling; 3 used non-randomized sampling techniques. One of the studies

included a discussion of the effect of yoga on the parasympathetic and GABA systems[8] and the other study reviewed the health impacts of yoga and pranayama.[28] The review also identified two relevant articles that provided additional information on the impact of yoga on the ANS. One of the articles, provided a review of the health impacts of yoga and pranayama[28] and the second proposed a neurophysiologic model to clarify the mechanisms by which Sudharshan Kriya yogic breathing balance the autonomic nervous system activity.[29]

Sample characteristics

The participants in all 17 interventional studies were adults aged 18 years or older. Three studies included only male participants, with the rationale for excluding females being the tendency in variation of the autonomic variables with the phases of the menstrual cycle in females. However, Markil et al., (2012)[30] included 15 women in their study, completing the study during the follicular phase of the menstrual cycle given that the luteal phase causes increase in sympathetic activity. One study did not mention the sex of the participants. Of the 17 interventional studies, 8 were completed in India, 5 within the United States, 1 in each completed in Australia, Germany, Brazil, and Nepal. Women and ethnic minorities were under represented in these studies. Most of the studies except for Dabhade et al., (2012)[31] excluded patients with arrhythmias and those on any medications such as beta-blockers and anti-arrhythmic medications that have significant effect on heart rate and rhythm.

The studies reviewed showed that participation in a yoga intervention resulted in a significant shift in autonomic balance towards vagal dominance; a reduction in heart rate and systolic, diastolic, and mean blood pressure; a reduction in the indices of ventricular

repolarization dispersion (QTd, JTd) in patients with ventricular arrhythmias; significant reduction in stress, anger, depression, anxiety, and neurotic symptoms; and improvements in neuroendocrine release, emotional processing, and social binding. Both time and frequency domain indices of heart rate variability showed significant changes towards parasympathetic modulation. Bidwell, et al., (2012)[32] found that yoga training for females with mild to moderate asthma decreased parasympathetic activity and increased sympathetic modulation as assessed by isometric forearm exercise. Yoga not only causes increased parasympathetic tone but when needed decreases the highly active parasympathetic nervous system to maintain a balanced autonomic nervous system activity.

Right nostril yoga breathing can increase sympathetic tone and cardiac sympathetic activity, resulting in increased blood pressure and heart rate. Left nostril yoga breathing can decrease systolic and mean blood pressure while alternate nostril breathing can decrease both systolic and diastolic blood pressure.[33] Slow breathing exercises can improve sympathetic and parasympathetic reactivity.[34] Slow pace Bhastrika pranayama exercise has shown a strong tendency towards improving function of the ANS through enhanced activation of the parasympathetic system.[35] Yoga practice of cyclic meditation during the day appears to shift sympatho-vagal balance in favor of parasympathetic dominance during sleep on the following night which promotes improved quality of sleep.[36] Four months of respiratory training in Bhastrika pranayama increased respiratory function and improved cardiac parasympathetic modulation in a group of healthy elderly subjects.[37] The changes during Dhyana (meditation)[38] and guided relaxation[39] resulted in reduced activity of the sympathetic nervous system

showing a shift in autonomic balance towards vagal dominance. Laughter yoga therapy for individuals awaiting heart transplant showed improvement in vigor-activity, friendliness, and long-term anxiety. It also improved HRV measures within or close to normal ranges from being low at baseline perhaps related to reduced vagal stimulation.[40] Integrated yoga practice reduced perceived stress and improved adaptive autonomic response to stress in healthy pregnant women.[41]

The styles of yoga reported on in the research reviewed include Hatha yoga, viniyoga, Isha yoga, Iyengar yoga, laughter yoga, integrated yoga, yoga nidra relaxation, meditation (cancalata, ekagrata, dharana, dhyana), pranayama (Bhastrika, Kapalbhati, Anilom-vilom, Bhramari, Udgit), cyclic meditation, guided relaxation and yoga breathing practices. Yoga postures, breathing exercises, pranayama, and meditation reportedly led to a significant shift in autonomic balance towards vagal dominance, which can prevent tachycardia, an important goal in the management of AF.

Only 4 studies mentioned the number of participants who completed the studies, with attrition rates ranging from 3.3% to 54.06%. The primary reasons for participants not completing a study were drop outs, irregular attendance at intervention sessions, and relocation following study enrollment. Higher attrition occurred in ‘in-person’ mindfulness therapy groups (27.3%) compared to the ‘online’ mindfulness meditation groups (3.8%),[42] giving rise to the need to consider the format and location of yoga interventions. Also, the studies reviewed did not provide an explicit theoretical or conceptual framework to explain the basis for the yoga interventions used with the study population.

A Psychoneuroimmunology Framework to Explain Effects of Yoga on AF

To address the deficit in the literature regarding theoretical or conceptual frameworks in the studies reviewed, the authors identified a psychoneuroimmunology framework (adapted from McCain et al., 2005)[43] shown in Figure 1 (page 59) to depict the electrical, mechanical, and structural changes in the heart that lead to a stress-related imbalance in the ANS resulting in AF. Yoga interventions can potentially foster the electrical stability of the heart by maintaining ANS balance and lessening AF episodes, AF symptoms (palpitations, shortness of breath, dizziness, and fatigue), stress, depression, and anxiety, thus improving the participants' health-related QOL. Modulating factors such as stress can cause imbalance in the ANS, which, in turn, can lead to AF. Persistent AF causes inflammation and fibrosis of the atria, resulting in a fixed substrate for re-entry and consequent sustained episodes of AF,[21] making treatment options to break this re-entrant cycle challenging. Triggers for atrial fibrosis include the activation of the renin-angiotensin-aldosterone system, inflammation, and oxidative stress.[44] The combination of normal and diseased atrial fibers in conjunction with local fibrosis results in spatial dispersion of atrial refractoriness and causes localized conduction abnormalities, including intra-atrial conduction block and slow conduction.[44] Thus, the interplay of stress (psycho), imbalance in the ANS (neuro), activation of the renin-angiotensin-aldosterone system, inflammation and oxidative stress resulting in atrial fibrosis (immuno) triggers AF and creates a substrate for persistent AF. Mind-body approaches use the concept of body and self-awareness to promote rechanneling of energy within the body thereby maintaining an internal balance. This mind-body balance

can further reduce psychological stressors that are important modulating factors in AF and modulate the ANS to parasympathetic dominance in maintaining a stable myocardium, thereby preventing arrhythmias.

Conclusion

Even though the time span of the yoga interventions reported in the studies reviewed ranged from a few minutes to months, all the studies demonstrated some beneficial effect in maintaining autonomic balance and significant impact on selected physiological and psychological factors, thereby improving the participants' overall QOL. Given its impact on modulating autonomic system balance and reducing psychological stress, selected styles of yoga might be considered as cost-effective complementary health approaches in managing AF episodes and symptoms. Further rigorous study is warranted to clarify further the specific mechanisms involved in the use of yoga in patients diagnosed with AF.

Conflict of Interest

The authors declare that no economic interest or any conflict of interest exists.

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Table 1: Studies Reporting Effects of Yoga on Atrial Fibrillation[1]

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
Lakkireddy, et al., (2013)	Purpose to examine the impact of yoga on AF burden, QOL, depression, and anxiety scores	103 consecutive eligible paroxysmal atrial fibrillation patients screened; 52 enrolled and 49 completed study. Age: 60.6 SD ± 11.5 23 males and 26 females	Inclusion criteria: Patients with paroxysmal AF between 18 and 80 yrs of age Exclusion criteria: Patients with a history of AF ablation within 3 months, contraindications for yoga training, life expectancy <1 year, advanced heart failure, and those who practiced any form of yoga in preceding 6 months	Structured Iyengar yoga training at least twice weekly; 60 min training sessions were conducted in groups of 15-20 people in a yoga studio by a certified professional yoga instructor; During each yoga session, 10 min of *prana-yamas*, 10 min of warm-up exercises, 30 min of *asanas*, and 10 min of relaxation exercises performed; An educational DVD provided to guide home yoga practice; Compliance reinforced with biweekly phone calls	Single-center, prospective, self-controlled pre-post study	AF symptoms and episodes using self-reported diary and cardiac non-looping monitor; SF-36; Zung self-rated anxiety scale and Zung self-rated depression scale	Yoga training reduced symptomatic AF epi-sodes ($p < 0.001$), symptomatic non-AF epi-sodes ($p < 0.001$), asymptomatic AF episodes ($p < 0.001$), depression and anxiety ($p < 0.001$; improved QOL parameters of physical functioning, general health, vitality, social functioning, and mental health domains on SF-36; Significant decrease in heart rate, systolic and diastolic blood pressure before after yoga ($p < 0.001$)	In patients with paroxysmal AF, yoga improves symptoms, arrhythmia burden, heart rate, blood pressure, anxiety and depression scores, and several domains of QOL

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
Wahlstrom, M et al., (2017)	To investigate whether yoga can improve QOL and decrease blood pressure and heart rate in patients with PAF	80 partici-pants with a new diagnosis of PAF were randomized to either a yoga intervention group and a control group; Intervention group: mean age 64 SD ± 7, n = 33 (16 males, 17 females); Control group: mean age 63 SD± 8, n = 36 (26 males, 10 females)	Inclusion criteria: New diagnosis of PAF necessi-tating pharma-cological treat-ment for at least 3 months Exclusion criteria: Patients with difficulties understanding Swedish language, patients with multiple concurrent medical conditions (i.e., cancer, heart failure, and renal failure with symptoms) or cognitive dysfunction	Mediyoga 1 time/week X 12 weeks in group sessions specifically designed for people with cardiac diseases; Each session started with deep breathing for 5–10 min followed by three movements (back flex, back roll, and Sat Kriya) that included two breathing techniques; Subsequent meditation (10 min) and relaxation (10 min)	Randomized controlled design	Two generic health-related QOL question-naires: - Short- Form Health Survey (SF-36) - VAS-scale from EuroQOL-5D (EQ-5D) used	At end of 12-week interven-tion, yoga group averaged higher on SF-36 mental health scores but no differences in EQ-5D VAS-scale and physiological health score seen between the two groups; At end of study, yoga group had significantly lower heart rate (p=0.024) and systolic (p=0.033) and diastolic blood pressure (p<0.001) compared to the control group	Yoga with light movements and deep breathing might lead to improved QOL, lower blood pressure, and lower heart rate in patients with PAF compared to a control group

[1]Table abbreviations

AF- Atrial fibrillation
PAF- Paroxysmal Atrial Fibrillation
QOL- Quality of Life
VAS- Visual Analogue Scale
SD- Standard deviation
Min- Minute/s

Table 2: Studies Reporting Effects of Yoga on the ANS [1]

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
Telles, S. et al., (2013)	To assess changes in autonomic and respiratory variables in normal healthy volunteers before, during, and after four types of meditation (viz., cancalata, ekagrata, Dharana, and dhyana) on separate days	30 healthy volunteers ranging from 20-45 years (mean age 29.1, SD±5.1 years); Average experience practicing meditation on Sanskrit syllable Om (Mean 20.95 months, SD ± 14.21 months)	Exclusion criteria: chronic illnesses especially psychiatric and neurological disorders; females excluded because autonomic variables tend to vary with phases of the menstrual cycle	Each participant assessed in four sessions on 4 different days at same time of day, including two meditation sessions- *dharana* (meditative focusing) and *dhyana* (meditative defocusing or effortless meditation); two control sessions- *ekagrata* (non-meditative focused thinking) and *cancalata* (random thinking); All four sessions consisted of 3 states: pre (5 min), during (20 min) and post (5 min) on the 4 separate days	Randomized controlled single-group design	Respiratory rate, heart rate, skin resistance, amplitude of digit pulse volume, frequency domain and time domain analysis of HRV	Maximum changes in autonomic variables and the breath rate during *Dhyana,* including decreased heart rate - increase in digit pulse volume (based on the photo-plethysmo-gram amplitude) - increase in skin resistance, reduction in breath rate; - decrease in LF power of HRV, increase in HF power, increase in NN50 and pNN50 in time domain analysis of HRV indicative of parasympathetic	Changes during *dhyana* suggestive of reduced activity in different subdivisions of sympathetic nervous system activity, showing a shift in autonomic balance towards vagal dominance

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
							activity	
Markil, N. et al., (2012)	To compare acute sympatho-vagal changes as measured by HRV responses to yoga nidra relaxation alone compared to yoga nidra relaxation preceded by hatha yoga	15 women and 5 men (mean age 29.15, SD ±6.98, range 18-47 yrs)	Inclusion criteria: Healthy men and women Exclusion criteria: previous history of musculo-skeletal disorders, cardiovascular disease, taking medications that affect heart rate and blood pressure, known cardiac arrhythmias, engaged in regular aerobic exercise or strength training exercise >3 days per week over prior 6 months	Yoga plus relaxation group included 20 min of rest followed by traditional 60-min Hatha yoga session follow-ed by 30 min of yoga nidra relaxation; Relaxation group included 20 min of supine rest followed by 30 min of yoga nidra relaxation	Randomized counter-balanced trial	Baseline heart rate, and indices of HRV, including time and frequency domains	Significant changes in heart rate and HRV indices from baseline in both yoga plus relaxation group and relaxation alone group	Changes in heart rate and HRV reflect a favorable shift in autonomic balance to parasympathe-tic branch of ANS, occurring for both yoga nidra relaxation and yoga nidra relaxation preceded by Hatha yoga
Melville, G. W. et al., (2012)	To compare effect of seated yoga posture and guided meditation practice on physiologi-cal and psychologi-	20 adults (mean Age: 39.6, SD ± 9.5), Sex: 8 men, 12 women; BMI 22.5, range (19.8-44.1) One obese	Inclusion criteria: Adult age ≥ 18 yrs, employed full-time in a sedentary job (i.e., office-based position) Exclusion	5-min baseline assessment followed by engaging in one of three conditions (yoga, meditation, or control group assignment) for	Exploratory study, involving within-subjects crossover design	Perceived stress, blood pressure, heart rate, respiratory rate, indices of HRV	- Significant reduction in perceived stress immediately post-yoga and post-meditation versus control	15 mins of chair-based yoga postures or guided meditation in office work-space can acutely improve several physiological

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
	cal markers of stress	participant with type 2 diabetes mellitus; Other controlled diseases among cohort included asthma (n = 3), chronic fatigue (n = 2), and hypertension (n = 1); No history of tobacco use; None engaged in yoga and/or meditation over previous year	criteria: uncontrolled illness, use of medication known to alter heart rate or blood pressure, and acute or chronic medical condition that would impede assessment of outcome measures	15 min Control group participants instructed to continue with their office work with same movement level and talking restrictions as applied to the baseline recording			- Both systolic and diastolic pressure significantly reduced in meditation versus control - Respiratory rate decreased significantly during yoga and meditation and increased in control group, but regressed toward baseline value during post-intervention period - Yoga significantly increased heart rate compared to control and meditation decreased heart rate compared to control	and psychological markers of stress; These effects are partially mediated by reduced respiratory rate

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
							- Change in heart rate significantly different between yoga and meditation throughout intervention period - Increase in HRV indices of LF, and LF: HF ratio detected during initiation of physical postures; Trend towards increase in SDDN noted in meditation versus control at end of interven-tion and dur-ing beginning of post-inter-vention phase	
Santaella, D.F et. al., (2012).	To test whether a 4-month respiratory training	76 healthy elderly subjects enrolled and 29 completed	Inclusion criteria- Healthy elderly adults with age > 60 (Mean Age 68,	Subjects underwent 30 min of supervised training classes	Randomized controlled design	Pulmonary function: FEV1, FVC, FEF 25-75%, PEmax	Improve-ments in FVC and FEV1 in yoga group did not reach	4 months of respiratory training in *Bhastrika pranayama*

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
	program (*Bhastrika pranayama*) improves respiratory function, cardiac sympatho-vagal balance and QOL in healthy elderly subjects	the study 46 subjects excluded from study	SD ± 6 yrs; 34% males; BMI mean 25 SD± 3 kg/m2) Exclusion criteria- Age <60 years, previous knowledge of and training in yoga respiratory exercises, inability to comply with protocol (not attending >40% of the classes); presence of any cardiovascular diseases or other diseases, and use of medications that could affect autonomic modulation of the heart mainly because of atrial fibrillation, other diseases, use of anti-hypertension, and thyroid hormone replacement	immediately after twice weekly routine yoga class; subjects also instructed to perform specific exercises twice daily for 10 min in morning and afternoon consisting of either stretching (control, *n*=14) or yoga respiratory exercises - *Bhastrika pranayama* (yoga, *n*=15)		and PImax flow rate; Heart rate variability, spontaneous baroreflex, and QOL	statistical significance compared with control group; In contrast, PE max and PI max increased significantly in Yoga group compared with control group; Yoga group showed a significant decrease in LF component of HRV in LF/HF ratio; No significant changes in either group on Spontaneous baroreflex noted; Yoga group had marginal changes in overall QOL, autonomy and interaction between present, past	increased respiratory function and improved cardiac parasympathetic modulation in a group of health elderly subjects.

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
			drugs				and future	
Dabhade, A.M. et al., (2012)	To evaluate potential beneficial effects of pranayama on indices of ventricular repolarize-tion disper-sion by measuring QTd and JTd on a 12 lead surface ECG in patients with arrhythmia	27 enrolled in pranayama sessions with 15 included in final analy-sis (12 males, mean age 68 , SD± 11 years, EF mean 28 SD ± 9%); 12 patients had arrhyth-mia secondary to ischemic cardiomyo-pathy and others had arrhythmia secondary to non-ischemic dilated cardio-myopathy	Inclusion criteria: Presence of diagnosed arrhythmia, echocardio-graphic evi-dence of depressed left ventricular function (EF <40%), absence of active ischemia as revealed by a clinical exam-ination or by exercise testing at time of enrollment, a stable medical regimen for at least 2 weeks prior to starting session and during entire session, absence of recent coronary revasculari-zation proce-dures (≤ 3 months), no history of MI in 8 weeks prior to enrollment	All patients completed 12-week program (36 pranayama sessions with each session consisting of 5 different pranayama practices (*Bhastrika*- 10 mins, *Kapalbhati*- 10 mins, *Anilom-vilom*- 15 mins, *Bhramari*- 5 times/day, and *Udgit*- 5 times/ day) for 45 mins; Before entering sessions, participants underwent symptom-limited exercise testing that usually consisted of a treadmill protocol	Single-group pre-post test design	Ventricular repolarizati on disper-sions (QTd, JTd), meta-bolic para-meters (changes in exercise capacity and anaerobic threshold)	- Exercise capacity increased from 4 ± 1 MET to 5 ± 2 MET (about 25%) after pranayama and peak oxygen consumption increased from 15 ± 4 ml O2/Kg/ min to 16 ± 6 ml; O2/Kg/min after pranayama (did not reach statistical significance); - Statistically significant decreases in all intervals (QTd, QTc-d, JTd, JTc-d) at the comple-tion of the pranayama program	Pranayama significantly reduced the indices of significant ventricular repolarization dispersion in patients with arrhythmia, suggesting that interventions such as yoga, which increases PNS and GABA activity, might be effective in treatment resistant subjects who failed to respond to pharmacologic agents that increase activity in the GABA system

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
			Exclusion criteria: Class IA/ III anti-arrhythmic medications, inability to complete pranayama session, absence of sinus rhythm at entry or completion of session; a complete bundle branch block of any kind					
Wolever, R.Q. et al., (2012)	To evaluate viability and proof-of-concept for two mind-body stress reduction programs (one therapeutic yoga-based and other mindfulness-based) and to evaluate two delivery venues of a mindfulness-based	239 subjects-63 in California and 176 in Connecticut with 205 completing study; 23.4% male; average age 42.9 yrs; Non-Hispanic = 93.7%, White = 78.2%, Asian = 7.9%, African American = 6.3%	Inclusion criteria: Score of ≥16 on 10-item Perceived Stress Scale Exclusion criteria: Arrhythmia requiring medication or pacemaker, pregnancy, tobacco use, medications affecting heart rate; any major medical condition (e.g.,	239 participants randomized to either 12-week viniyoga stress reduction program or 1 of 2 mindfulness-based programs or control group assessment (assessment only) Viniyoga taught by trained teachers with instructional handouts	Randomized controlled trial	Stress, sleep quality, mood, and pain levels; work productivity, mindfulness, blood pressure, HRV, and breathing rate	Compared with control group, mind-body interventions showed significantly greater improvement on perceived stress, sleep quality, and heart rhythm coherence ratio of HRV; The two delivery venues for the	Mindfulness-based and therapeutic yoga programs might provide viable and effective interventions to target high stress level, sleep quality, and autonomic balance in employees

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
	intervention (online vs in-person)		COPD, CHF, Angina, traumatic brain injury and type I Diabetes) or psychological disorder (i.e., post-traumatic stress disorder, major depression, bipolar disorder, psychosis, severe anxiety, panic disorders; practicing yoga several times a week currently or participation in an extended meditation or yoga retreat of ≥2 days in past 5 years	provided for home practice; half the participants received a DVD to support home practice; two mindfulness-at-work programs identical except one was provided 'in-person' in a conventional classroom, other one provided through online virtual classroom allowing for real-time bidirectional communication			mindfulness program basically produced equivalent results	
Bidwell, A.J. et al., (2012)	To assess whether 10 weeks of yoga training might improve QOL and HRV in patients with asthma	19 females, age: 20-65 years old with clinical and functional evidence of mild to moderate asthma as assessed by physician	Inclusion criteria: FEV1/FVC ratio of < 80% predicted, use of a broncho-dilator at least once daily, symptoms of wheezing and/or coughing for a mini-	1-hour supervised yoga sessions/10 weeks led by certified yoga instructor Each class consisted of 10 min of relaxation/ deep breathing exercises fol-	Randomized controlled trial	St. George's Respiratory Questionnaire to assess QOL and an isometric exercise test to assess HRV pre- and post-intervention	Significant improvements in QOL observed with yoga training, although no changes were found in control group; yoga group	Yoga training improved QOL in women with mild-to-moderate asthma and resulted in decreased parasympathetic and increased sympathetic

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
			mum of 2 years that improves either spontaneously or with drug therapy Exclusion criteria: Smoking ≥ 2 cigarettes per day; participated in yoga in the previous 12 months; diagnosis of hypertension and major orthopedic injuries prohibiting performance of various yoga postures; currently taking medications such as beta blockers that would alter autonomic function	lowed by 40 min of Hatha yoga postures; sessions finished with 10 min of meditation to control stress levels; Additionally, participants supposed to perform 30-min session/wkly at home using a written lesson plan; 1-hour sessions 2/wk/10 weeks in group settings and 30 min sessions of 1 time/wk for following 10 weeks in a group setting			demonstrated decreased parasympathetic modulation (HF); increased sympathetic (LF) and sympatho vagal modulation (Log LF/HF) in response to isometric forearm (IFE) exercise with no change in control group	modulation in response to an IFE
Dolgoff-Kaspar, R. et al., (2012)	To evaluate clinical utility of laughter yoga in improving psychologi-	2 women and 4 men, age 51-69 yrs; 3 awaiting heart transplant and 3 awaiting lung	Inclusion criteria: Awaiting organ transplant Exclusion criteria: major	A control period of 1 week during which participants completed controlled interventions at	Non-randomized, controlled, crossover design	Psychological measures, including fluctuations in current mood,	Participants showed improved immediate mood (vigor-activity and friendliness)	The laughter yoga therapy might improve HRV and some aspects of mood.

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
	cal and physiology-ical measures in outpatients awaiting organ transplant	transplant	surgery in prior 3 months, history of hernia or uncontrolled hypertension; NYHA Class IV heart failure; on vasopressors or intravenous ionotropes	beginning and end of week; After control period, participants completed seven laughter yoga sessions over 3 weeks conducted by a certified therapist; Participants completed one additional control inter-vention at study term-ination; Controlled intervention involved group discussions on topics such as the study procedures, personal intro-ductions, par-ticipants med-ical history and experiences with stress, and closing remarks with review of participants' study experiences		anxiety, depression; Physiologi-cal meas-ures of blood pressure, heart rate, and HRV	and increased HRV meas-ures for both SDNN and RMSDD so that scores are within or closer to normal range; Both laughter and controlled interventions appeared to improve long-term anxiety	

Review of Effects of Yoga on the Autonomic Nervous System

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
Muralikrishnan, K. et al., (2012)	To assess effect of Isha yoga, a system of yoga programs offered by Isha Foundation, on cardiovascular autonomic nervous system through short-term HRV	14 healthy Isha yoga practitioners (12 men, 2 women; mean age 31.57 ±5.83 yrs) compared with age- and gender-matched non-yoga practitioners	Inclusion criteria: Between age18-40 yrs; Additionally, for yoga group engaging in Isha yoga practices for 1.5 hours/ day, 5 times/ wk minimum for ≥6 months Exclusion criteria: Medical illness or on medication or exercise regime; obese; smoking; taking recreational drugs or alcohol; For non-Yoga control group previous exposure to yoga or exercise practice	Practice of Isha yoga for ≥ 6 months, including Surya Namaskar, Hatha yoga, Sakthi chalana Kriya, Shambhavi Maha Mudra and Shoonya meditation	Cross-sectional design	Baseline heart rate, BP, pulse pressure, frequency domain analysis of HRV (R-R interval, LF, HF, LF nu, HF nu, LF/HF ratio) and time domain analysis of HRV (SDNN, RMSSD, NN50, pNN50); Frequency and time domain HRV parameters measured in supine rest position and time domain parameters measures obtained for deep breathing	Statistically significant differences between Isha yoga practitioners and controls in both frequency and time domain analyses of HRV indices, with no difference in resting heart rate between groups	Practitioners of Isha Yoga showed well-balanced beneficial activity of vagal efferents; an overall increased HRV, and sympatho-vagal balance compared to non-yoga practitioners during supine rest and deep breathing
Patra, S. & Telles, S. (2010)	To compare effects of practicing day time	30 male volunteers ranging in age from 20 to 30	Inclusion criteria: Healthy with no history of	Sessions conducted 3 days apart with participants to	Non-randomized, single-group,	Heart rate, breath rate, HRV spectrum	During the night following cyclic	Yoga practice of cyclic meditation during daytime

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
	cyclic meditation with effects of supine rest practice on HRV during sleep	yrs (mean 22.3, SD ±4.6 yrs)	smoking or alcohol use (none were on medications and none used any wellness strategies)	practice supervised cyclic meditation (CM) two times a day (i.e., at 06:00 hr and 18:45 hr followed by a full-night sleep recording beginning at 21:00 on same day; as a control for cyclic meditation after 3 days participants practiced unguided supine rest in *Shavasana* twice a day at same time and duration as the CM sessions, with monitoring done by same yoga instructor, although participants received no instructions; Each session lasted for 22.5 mins with participants	crossover design	(LF, HF, LF/HF ratio, NN50, pNN50, TINN)	meditation, a decrease in heart rate, LF power, LF/HF ratio, and an increase in pNN50 were noted; No changes noted on the night following supine position rest	appears to shift sympatho-vagal balance in favor of parasympathetic dominance and a corresponding shift in the sympathovagal balance during sleep on the following night

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
				reporting to sleep lab at 21:00 for whole night polysomno-graphy record-ing				
Satyapriya, M. et al., (2009)	To assess effects of integrated yoga prac-tice and guided yogic relaxation on perceived stress and measured autonomic response in healthy pregnant women	122 healthy women recruited between 18th and 20th wk of pregnancy at prenatal clinics to be followed until 36th wk of pregnancy; 90 completed study	Inclusion criteria: 18th to 20th wk of pregnancy, primigravida or multigravida when partici-pant had at least one living child Exclusion criteria: Multigravida without any living child, multiple pregnancies, maternal physical abnormalities, psychiatric problems, pregnancy-associated diabetes and hypertension, pregnancy from invitro fertili-zation, intra-uterine growth	45 participants randomly assigned to intervention group practicing yoga and deep relaxation for 1- hr/day; 45 participants assigned to control group and practiced standard pre-natal exercise with supine rest for 1-hr/day	Prospective randomized 2-arm study	Perceived stress and HRV (LF, HF and LF:HF) during 18th week, 20th week, and 36th week	Perceived stress decreased by 31.57% in yoga group and increased by 6.6% in control group; During guided relax-ation in yoga group, the high frequency band of HRV increased by 64% in the 20th wk and 150% in the 36th wk; The LF and the LF:HF ratio was reduced significantly; The LF band remained decreased after deep relaxation in	Yoga reduces perceived stress and improves adaptive autonomic response to stress in healthy pregnant women

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
			restriction in a previous pregnancy, fetal abnormality on ultrasound scan, and previous exposure to yoga				the 36th week in yoga group	
Pramanik, T., et al., (2009)	To evaluate immediate effects of slow pace *bhastrika pranayama* for 5 min on heart rate and blood pressure and effect of same breathing exercise for same duration following oral intake of hyoscine-N-butyl-bromide (parasympathetic blockade)	39 volunteers (age 25-40 yrs) practiced bhastrika prana-yama and 10 volunteers practiced bhastrika pranayama 30-min after oral intake of hyoscine-N-butylbromide	Inclusion criteria: Healthy, non-smoker, seden-tary volunteers	One set of slow pace bhastrika pranayama for 5 min (respiratory rate 6/min)	Two-group experimenal design	Heart rate and blood pressure	Following bhastrika pranayamic breathing for 5 min both systolic and diastolic blood pressure decreased significantly, with a slight decrease in heart rate; The group of volunteers whose heart rate and BP were compared before and after breathing exercise following intake of hyoscine-N-butylbromide showed no	Slow pace Bhastrika Pranayama exercise showed a strong tendency to improving the ANS through enhanced activation of the parasympathe-tic system

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
							significant alteration in either of these parameters	
Mourya, M., et al., (2009)	To analyze whether breathing exercises practiced in various forms of meditations such as yoga might influence autonomic functions and serve as basis of therapeutic benefit to hypertensive patients	60 men and women patients 20-60 yrs of age with Stage I essential hypertension	Inclusion criteria: Diagnosis of essential Stage 1 hypertension with systolic BP 140-159 mm Hg and diastolic BP 90-99 mm Hg; (Some not on any medications, while others were receiving diuretics or angiotensin-converting enzyme receptors or both)	Participants randomly assigned into one of 3 groups (20/group); Group 1 had no intervention, Group 2 practiced slow-breathing exercise, and Group 3 practiced fast breathing exercises 15 min twice daily 10-12 hours apart for 3 months	Randomized, prospective, controlled clinical study	Baseline and post-intervention BP, autonomic function tests such as standing-to-lying ratio, immediate heart rate response to standing (30:15), valsalva ratio, heart rate variation with respiration, hand-grip test, and cold pressor response	BP decreased longitudinally over 3-months in both intervention groups; S/L ratio, 30:15 ratio, E/I ratio, and BP response in hand grip and cold pressor test showed significant changes only in patients practicing the slow breathing exercise	Both types of breathing exercises benefit patients with hypertension; However, improvement in both sympathetic and parasympathetic reactivity might be the mechanism that is associated in those practicing the slow-breathing exercise
Raghuraj, P. & Telles, S. (2008)	To study effects of three yoga breathing practices (right nostril yoga breathing (RNYB), left nostril	21 male volunteers 18-45 yrs (mean age 27.5, SD ±6.3)	Inclusion criteria: Healthy volunteers not on any medications and not using any wellness strategy; no history of smoking or	Participants assigned to five sessions as five possible sequences; Sequence 1 = RNYB, LNYB, ANYB, BAW and NB;	Randomized, controlled, crossover design	Heart rate, skin conductance, finger plethysmogram amplitude, breath rate, blood pressure, fre-	RNYB can increase sympathetic tone and cardiac sympathetic activity given it increases BP and HR;	Yoga breathing practices result in physiologic effects on autonomic activity by increasing sympathetic response, which

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
	yoga breathing (LNYB), and alternate nostril yoga breathing (ANYB) compared to breath awareness (BAW) and normal breathing (NB) on autonomic and respiratory variables in normal volunteers		respiratory ailments, including nasopharyngeal abnormalities; all right handed and had experience in practicing 3 yoga breathing techniques ranging between 3-48 months; all completed 3 months of intensive, residential yoga training Exclusion criteria: Women excluded given autonomic and respiratory variables vary with phases of menstrual cycle	Sequence 2 = LNYB, ANYB, BAW, NB, RNYB; Sequence 3 = ANYB, BAW, NB, RNYB, LNYB; Sequence 4 = BAW, NB, RNYB, LNYB, ANYB; Sequence 5 = NB, RNYB, LNYB, ANYB, BAW; For each sequence five sessions of 40 min each conducted on 5 different days; Each 40-min session consisted of 30 min during which subjects practiced any one of the four breathing techniques or did not do any breath manipulation (in the control session); each 30 min period		quency domain analysis of HRV	LNYB resulted in decrease in systolic BP and mean BP; ANYB resulted in decrease in both systolic and diastolic BP, increase in HR, skin conductance level, LF power, LF/HF ratio of the HRV spectrum	could have been related to slower breath rate; ANYB resulted in decrease in both systolic and diastolic blood pressure

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
				preceded and followed by 5-min 'rest periods' without breath manipulation				
Khattab, K. et.al., (2007)	To determine if Iyengar yoga practice significantly increases cardiac parasympathetic nervous modulation among healthy yoga practitioners	11 healthy yoga practitioners (7 women and 4 men, mean age: 43 SD ± 11, age range: 26-58 yrs; experience = 3 years of regular Iyengar yoga practice; 4 certified as teachers of Iyengar yoga) were compared to an age and gender matched group of healthy individuals who had not been practicing any relaxation techniques	Inclusion criteria: Healthy volunteers with 3 yrs of regular practice in Iyengar yoga Exclusion criteria: Presence of any cardiovascular diseases	Each volunteer subjected to training units of 90 min once a week over 5 successive weeks; During 2 sessions, practitioners engaged in an Iyengar yoga program developed for cardiac patients; For 3 sessions each practiced a placebo program of relaxation; ambulatory 24-hr holter monitoring completed with all sessions; yoga practitioner group compared to a matched group of healthy	Non-randomized, experimental, controlled design	Time-domain HRV: rMSSD, SDNN, SDNNi, SDANN	Mean R-R interval found to be significantly higher during time of yoga intervention compared to placebo and control; increase in HRV significantly higher during yoga exercise than during placebo and control activity, especially for parameters associated with vagal tone (i.e., SDNNi, rMSSD)	Relaxation by yoga training is associated with a significant increase of cardiac vagal modulation; Because this method is easy to apply and leads to a deep mental and physical relaxation, it could be a suitable intervention during cardiac rehabilitation to shift ANS balance to an increase in vagal activity and potentially decrease cardiac mortality

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
				individuals not practicing any relaxation techniques				
Shapiro, D. et.al., (2007)	To present data on yoga as a complementary health intervention treatment for depressed patients on anti-depressant medications but who are only in partial remission regarding their depression	27 women and10 men; 17 completed intervention and pre-and post assessments; 33 White, 1 African American, 3 Asian-American; age range 20-71 yrs; 6 were students, 3 retirees, 2 unemployed, 26 employed; hours of exercise per week = 5.4 (range 0-30); alcohol drinks per week = 1.3 (range 0-8)	Inclusion criteria: All participants diagnosed with unipolar major depression with partial remission Exclusion criteria: >3 months of prior yoga practices; Axis I diagnose of bipolar disorders, delirium, dementia, schizophrenia, or other psychotic disorders, including current substance-related or eating disorders and suicidal thoughts or tendencies; any medical illness that would pose	Yoga intervention provided in 3 groups of 12-13 participants for 60-90 mins 3 times/wk/8-weeks (total of 20 sessions per group), with sessions led by 3 highly experienced Iyengar yoga teachers, rotating over the sessions	Single-group outcome design	Psychological measures: 17-item Hamilton-D, Quick Inventory of Depressive Symptoms, Symptom Check List, Spielberger Anger Expression Scale, Speilberger Trait Anxiety Inventory, Cook-Medley Hostility Scale, Pittsburgh Sleep Scale, SF-36 Short Form Health Survey Physiological measures: heart rate,	Significant reductions were shown for depression, anger, anxiety, neurotic symptoms and LF HRV in 17 completers. Eleven out of these completers achieved remission levels post-intervention. Participants who remitted differed from the non-remitters at intake on several traits and on physiological measures indicative of a greater capacity of emotional	Yoga produces many beneficial emotional, psychological and biological effects in patients diagnosed with depression

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
			a safety concern or limit study participation			blood pressure, measures of HRV, baroreflex sensitivity	regulation. Moods improved before and after the yoga classes	
Vempati, R. P. & Telles, S. (2002)	To identify whether the experience of yoga practice showed greater reduction in physiological arousal after 'Guided relaxation' (with instructions) compared to 'Supine rest' without instructions	35 male volunteers, age 20-46 yrs (mean 27.5, SD 4.7); average yoga practice = 30.2 months (SD 25.7);	Inclusion criteria: completed a 5.5-month residential yoga course	Subjects categorized into either guided relaxation (GR) or supine rest (SR) groups using baseline LF/HF ratio of their HRV; separate relaxation sessions held on different days at same time of day; sessions lasted 20 min with 10 min of guided relaxation or supine rest	Two-group crossover design	Oxygen consumption, skin conductance, frequency domain of HRV	Reduction in skin conductance and heart rate noted both after GR or SR; decrease in finger plethysmogram noted after SR suggestive of increased sympathetic tone; Following guided relaxation subjects with baseline LF/HF ratio of >0.5 showed a significant decrease in LF/HF ratio, whereas same subjects showed no change in the ratio after SR;	Both GR and SR reduced physiological arousal, with changes in a larger number of autonomic variables following GR

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
							subjects with baseline LF/HF ratio of ≤0.5 at baseline showed no change after GR	
Sengupta, P. (2012)	To develop a state-of-the-art review of health impacts of yoga and pranayama				Review of Literature			Yoga and pranayama reduce stress and anxiety, improves autonomic by triggering neuro-hormonal mechanisms by the suppression of sympathetic activity, improves physical health of cancer patients
Streeter, C.C. et al., (2012)	Authors hypothesized that stress (1) induces imbalance of the ANS (2) underactivity of the GABA system, (3)increases				Review of Literature			Depression, epilepsy, post-traumatic stress disorder, and chronic pain exemplify medical conditions exacerbated by stress and reveal low HRV (PNS under-

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
	allostatic load; and (3) that yoga-based practices correct under activity of PNS and GABA systems, in part, through stimulation of vagus nerves, the main peripheral pathway of the PNS, and reduces allostatic load							activity), increased cortisol, and low GABA activity
Brown, R. P. et al., (2005)	To propose a neurophysiologic model to clarify mechanisms by which Sudharshan Kriya yogic breathing can be used to balance the autonomic nervous				Grounded theory		A proposed neurophysiologic model that postulates the following: -Strengthening, balancing and stabilizing the autonomic and stress response systems	Sudharshan Kriya yoga may improve autonomic function, neuroendocrine release, emotional processing, and social binding; The authors' model might be of heuristic value in

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
	system and influence psychologic and physiologic parameters						-Decreasing chemoreflex sensitivity - Improved baroreflex response - Shifting to parasympathetic dominance via vagal stimulation - Balancing of cortical areas (synchronization) by thalamic nuclei - Calming effect on the cortical area involved in executive functions such as anticipation, planning, and worry - Activation of limbic systems leading to stimulation of forebrain reward systems and emotional	identifying areas for future clinical research related to yogic breathing

Article/Study	Purpose	Sample	Inclusion-exclusion Criteria	Intervention Description	Research Design	Outcome Measures	Results	Conclusion
							release - Increased release of prolactin and oxytocin enhancing feelings of calmness and social bond-ing	

[1]Table Abbreviations

ANS- Autonomic Nervous System
PNS- Parasympathetic Nervous System
HRV- Heart rate variability
HF- High-frequency
LF- Low- frequency
VLF- Very-low-frequency
ULF- Ultra-low-frequency
SDDN- Standard deviation of normal-to-normal
RMSSD- Root mean square of successive differences
NN50- Number of pairs of successive NN (R-R) intervals that differ by more than 50 milli seconds
pNN50- Proportion of RR intervals >50 msec
FEV1- Forced Expiratory Volume in 1 second
FVC- Forced Vital Capacity
FEF- Forced Expiratory Flow
PEmax- Maximum Peak Expiratory flow rate
PImax- Maximum Inspiratory flow rate
GABA- Gamma Amino-Butyric Acid
QOL- Quality of Life
Min- Minute/s
Yr- Year/s
MET- Metabolic Equivalent of Task

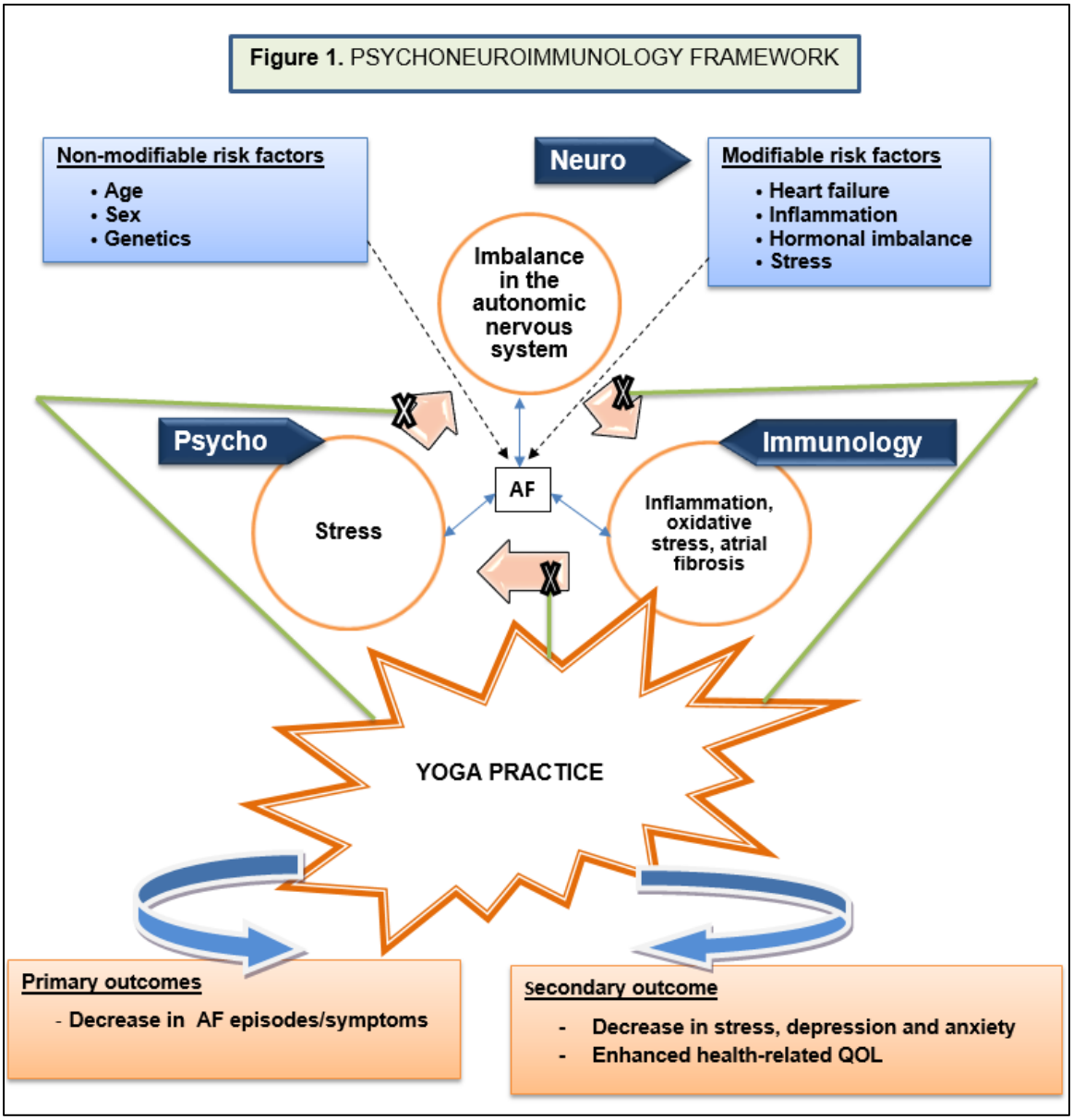

Figure 1 depicts the non-modifiable and modifiable risk factors for development of atrial fibrillation. Psychological stress and the resulting neurological imbalance in the autonomic nervous system trigger inflammation and atrial fibrosis creating the substrate for onset and sustaining persistent atrial fibrillation. The framework indicates that yoga practice can potentially foster the electrical stability of the heart by decreasing stress and re-establishing the autonomic nervous system balance, thereby lessening AF episodes, AF symptoms, stress, depression, and anxiety, thus improving patients' health-related quality of life.

CHAPTER THREE: METHODOLOGY AND PROTOCOL

Manuscript Two

A Feasibility Protocol to Assess Effect of Yoga on Early Recurrence of Atrial Tachyarrhythmia after Atrial Fibrillation Ablation

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Abstract

Objective: The mind-body therapy yoga has been shown to reduce stress, prevent inflammation, and maintain autonomic nervous system balance, which could potentially prevent atrial arrhythmias, including atrial fibrillation (AF). To date, two studies have assessed the impact of yoga on paroxysmal AF, although no studies have investigated the effect of yoga on early recurrence of atrial tachyarrhythmia (ERAT) after AF ablation. Given the many different styles of yoga currently being practiced, rigorous studies are warranted to explore the effect of yoga in individuals with AF. Thus, this article presents the design and protocol for a 6-week Viniyoga intervention aimed at determining the feasibility of selected postures from this gentle style of yoga as an appropriate intervention for persons diagnosed with AF, and also collect preliminary data regarding the effect of yoga on stress, depression, anxiety, prevention of ERAT after AF ablation, and its impact on overall health-related quality of life (HRQOL) in persons undergoing AF ablation.

Method: The proposed study used a sequential mixed methods, prospective, quasi-experimental, two-group design. After Institutional Review Board for Health Sciences Research approval, participants with a diagnosis of paroxysmal and persistent AF who already had an established plan to undergo an AF ablation were recruited for the study. Those participants who were willing to participate in the twice-weekly, 6-week instructor-led Viniyoga intervention were assigned to the yoga intervention plus usual care group (YI) and the remaining were assigned to the usual care alone (UC) group. A psychoneuroimmunology theoretical framework informed the study design. Self-report questionnaires were utilized to assess stress, depression, anxiety, AF symptoms, and

HRQOL. The quantitative findings were compared with qualitative findings from semi-structured interviews during the 6-month post-ablation follow-up clinic visit to capture information about the participants' HRQOL, and for those in the intervention group, the effect of Viniyoga in controlling atrial arrhythmias post-ablation.

Discussion: The study protocol provides a template for designing future randomized controlled trials to evaluate the effect of a gentle style of yoga in individuals diagnosed with atrial arrhythmias, including AF.

KEY WORDS: Atrial fibrillation, Viniyoga, yoga, stress, autonomic nervous system, psychoneuroimmunology, early recurrence of atrial tachyarrhythmia

Introduction

Atrial fibrillation (AF), the most common sustained cardiac arrhythmia, is seen in 1.5% of the U.S. population (Savelieva & Camm, 2004) and results in substantial morbidity and mortality (Kannel et al., 1998). The most common AF symptoms include palpitations, shortness of breath, fatigue, dizziness, and anxiety (Hansson et al., 2004). One of the largest U.S. epidemiological studies, the Framingham Heart Study, predicted that AF prevalence doubles with each advancing decade of age, from 0.5% at age 50-59 years to almost 9% at age 80-89 years, independent of the increasing prevalence of known predisposing conditions (Kannel et al., 1998). AF is a potent risk factor for ischemic stroke, increasing the risk of stroke 5-fold, causing approximately 15% of all strokes nationally (Go et al., 2001). AF contributes to increased morbidity in the elderly by adversely affecting their quality of life (QOL) and by deterioration in myocardial function, increasing susceptibility to heart failure, stroke, hospitalization, and mortality (Mirza et al., 2012).

AF is known to be triggered in many instances by psychological stressors (Hansson et al., 2004). Also, acute life stressors can affect the development and spontaneous conversion of AF, which is thought to be mediated by the sympathetic nervous system (Mattioli et al., 2005), with regulation of the heartbeat being achieved, in large part, by the balance between the sympathetic and parasympathetic nervous systems (Arora, 2012). Lower overall HRV as well as increased sympathetic/parasympathetic tone have been shown to be associated independently with a higher risk of AF (Agarwal et al, 2017).

Medical treatment involving catheter ablation has become a well-accepted management strategy for AF (Kumar & Mounsey, 2012). However, failure of this therapy is common, with only two-thirds or less of the patients treated remaining free of AF on long-term follow-up (Kumar & Mounsey, 2012). Consequently, many of these individuals experience poor health-related QOL. Early recurrence of atrial tachyarrhythmia (ERAT), usually defined as arrhythmia recurrence within the first 3 months following ablation, is frequently associated with late recurrence of atrial tachyarrhythmia (Themistoclakis et al., 2008; Choi et al., 2010) after ablation.

Yoga as a Complementary Health-Enhancing Therapy

The mind-body therapy yoga has been shown to reduce stress and maintain autonomic nervous system balance (Streeter et al., 2012). To date, two studies have assessed the impact of yoga on AF. One, a proof-of-concept study (Lakkireddy et al., 2013), revealed that 60-minute Iyengar yoga sessions at least twice a week for 3 months improved symptoms, arrhythmia burden, heart rate, blood pressure, anxiety and depression scores, and several domains of QOL in adults with paroxysmal AF. A second study (Whalstrom et al., 2017) using Mediyoga as the intervention showed that this style of yoga might potentially lower blood pressure and heart rate in patients with paroxysmal AF and improve QOL compared with a control group. No studies were identified that documented the effect of yoga in preventing ERAT in adults with AF after AF ablation.

Yoga postures (Muralikrishnan et al., 2012), breathing exercises (Mourya et al., 2009), pranayama (Sengupta, 2012), and meditation (Patra & Telles, 2010) have been shown to be related to a significant shift in autonomic balance towards vagal dominance

that can prevent tachycardia, an important goal in the management of AF. In particular, the breath can have a significant influence on physiology, especially the balance between sympathetic and parasympathetic tone in the autonomic nervous system. This is the prime focus in Viniyoga. Varying the respiratory rate, depth, and ratio of inhalation to exhalation can refine this effect. Similarly, the choice and sequence of poses can be used to modulate this balance and influence physical structures affected by stress. Selecting the postures within the practice sequence to accommodate individual limitations of participants is important. Previous work suggests that application of the principles of Viniyoga may extend the known health advantages of other forms of yoga and increase one's potential to manage stress (Wolever et al., 2012).

The investigators hypothesized that Viniyoga will reduce stress, anxiety, and depressed mood, which are triggers and/or symptoms of AF, and also maintain the autonomic nervous system balance, which is essential for regulation of the normal electrical conduction in the heart. Thus, the investigators, using their extensive knowledge of the AF population of patients from which a study sample would be drawn and their understanding of the published literature about yoga in general, designed an intervention using selected gentle postures from Viniyoga for use with patients diagnosed with AF.

Methods

Primary aims

The specific aims of the study were two-fold. The first aim was to examine the feasibility and acceptability of a Viniyoga intervention for individuals with AF by

evaluating (a) descriptions of participants' experiences with the yoga intervention and their perceptions of the efficacy, barriers to, and how they believe that yoga could help them; (b) descriptions of perceptions about yoga and the rationale for control group participants to decline participation in the yoga intervention; and (c) retention rate and adherence to the intervention for those who participate in the yoga intervention. The second specific aim was to test whether or not this 6-week Viniyoga intervention in persons (18 to 65 years old) with paroxysmal or persistent AF prior to ablation would decrease AF symptoms, stress, depression, anxiety, prevent ERAT after AF ablation, and improve overall health-related QOL during the 6-month post-ablation period if these participants continued to practice yoga post-ablation at least twice a week for 50 minutes.

Secondary aim

A secondary aim was to capture all participants' perceptions of health-related QOL given their diagnosis of AF, using semi-structured interviews, and, for the yoga intervention group only, their experiences with yoga as well.

Theoretical Framework

Given that modulating factors such as stress can lead to an imbalance in the ANS, which, in turn, can lead to AF, a psychoneuroimmunology framework guided this study design. Figure 1 (page 107, adapted from McCain et al., 2005) depicts the electrical, mechanical, and structural changes in the heart that lead to a stress-related imbalance in the ANS, resulting in AF (Murugesan & Taylor, 2017). Autonomic nervous system activation can induce significant and heterogeneous changes of atrial electrophysiology and induce atrial tachyarrhythmia, including atrial tachycardia (AT) and AF (Chen et al.,

2014). Beta-adrenergic receptor activation increases L-type calcium current (ICaL), ultra-rapid delayed rectified potassium current (IKur), slow delayed rectified potassium current (IKs), and acetylcholine-dependent potassium current (IKACh) (Schotten et al., 2011). As a net result of sympathetic stimulation, the plateau potential of the action potential is increased (Liang et al., 1985 & Sosunov et al., 2002) while the total action potential duration is unaffected or even decreased (Zipes et al., 1974). Vagal stimulation leads to M2R-mediated activation of atrial IKACh, leading to a potent effective refractory period shortening that promotes atrial arrhythmias (Allessie et al., 2001; Nattel, 2002; Wakili et al., 2011; Schotten et al., 2011; Iwasaki et al., 2011). AF itself causes shortening of atrial refractoriness, thereby contributing to the progression from paroxysmal to more persistent forms of AF (AF begets AF), early AF recurrence after cardioversion, and progressive drug resistance of longer-lasting AF (Allessie et al., 2001; Nattel, 2002, Wakili et al., 2011; Schotten et al., 2011; Iwasaki et al., 2011). Calcium enters atrial cells with each action potential. During rapid atrial rates, increased calcium loading initiates auto protective mechanisms that reduce calcium entry by calcium current inactivation and L-type calcium current down-regulation. This results in decreased calcium loading and a shortening of the action potential duration, leading to a stabilization of re-entry circuits perpetuating AF (electrical remodeling) (Allessie et al., 2001; Nattel, 2002; Wakili et al., 2011; Schotten et al., 2011; Iwasaki et al., 2011). Additionally, the high calcium load in the atrial cardiomyocytes results in an increased spontaneous release of calcium from the sarcoplasmic reticulum, leading to atrial ectopy (trigger loop), potentially initiating and perpetuating AF (Allessie et al., 2001; Nattel, 2002; Wakili et al., 2011; Schotten et al., 2011; Iwasaki et al., 2011). Given that the autonomic nerve activity plays an important

role in the initiation and maintenance of AF and that modulating the autonomic nerve function may contribute to AF control (Chen et al., 2014), we propose that the breath and gentle yoga postures known to have an impact on maintaining autonomic nervous system balance, could potentially prevent AF. Yoga interventions can foster the electrical stability of the heart by maintaining ANS balance and lessening AF episodes, AF symptoms (palpitations, shortness of breath, dizziness, and fatigue), stress, depression, and anxiety, thus improving the participants' health-related QOL.

Mind-body approaches use the concept of body and self-awareness to promote rechanneling of energy within the body, thereby maintaining an internal balance that can further reduce psychological stressors and inhibit inflammatory processes that are important modulating factors in AF. It can also modulate the ANS to parasympathetic dominance maintaining a stable myocardium, thereby preventing arrhythmias.

Study Design

The proposed study used a sequential mixed methods prospective, quasi-experimental, two-group design (Teddlie & Tashakkori, 2009) shown in Figure 2 (page 108). The purpose of using a mixed methods design was for complementarity, triangulation, and expansion of research findings (Teddlie & Tashakkori, 2009). This design involved an initial quantitative data collection phase followed by a qualitative data collection phase, using a semi-structured interview with participants from the quantitative phase of research. Integration of the quantitative and qualitative data were carried out during the data analysis phase. The semi-structured interview of the participants helped the researchers capture data that may have been missed by the structured nature of the quantitative instruments. The qualitative data helped to rationalize further the

interpretation and utilization of the quantitative findings to address specific aim 1 and the secondary study aim.

Subjects and Sampling

After receiving approval for the study from the University's Institutional Review Board for Health Sciences Research, participants between 18 to 65 years of age with an established medical diagnosis of paroxysmal or persistent AF scheduled for AF ablation were recruited from the University's AF Center clinic. Potential participants were pre-screened for participation in the study and their study eligibility confirmed according to the inclusion exclusion criteria shown in Table 1 (page 101). Those eligible were scheduled for a 45-minute visit to explain in detail what participation in the study would involve and informed consent obtained. Participants also completed study-related measures, including a demographic form, medical record review form, Perceived Stress Scale, Beck Depression Inventory II, State-Trait Anxiety Inventory-Y, and the Atrial Fibrillation Effect on Quality-of-Life Questionnaire. A copy of the consent form and the study brochure were provided to participants. After the informed consent process was completed, those participants willing to practice yoga were assigned to the yoga intervention (plus usual care) group, hereinafter referred to as "YI" group. Those enrolled but not willing to practice yoga were assigned to the usual care alone group, hereinafter referred to as "UC" group. Study participant flow is presented in Figure 3 (page 109).

Methods and Procedures

Following the consent process and group assignment, the YI group began the 6-week intervention. Given that no dose and duration of any yoga intervention for AF had been established to date, the intervention was designed for 6 weeks. The YI group

continued with all usual care and engaged in 50-minute yoga sessions twice weekly for 6 weeks, receiving a DVD of the intervention at the end of week 2 to guide their home yoga practice. After 6 weeks, these participants underwent AF ablation. Following a 1-week post-ablation recovery, participants resumed home yoga practice twice a week. They remained on an antiarrhythmic drug for 1-month post-ablation to prevent arrhythmias re-occurring as a result of inflammation secondary to the ablation, with the plan for participants' physicians discontinuing the drug at the 1-month post-ablation follow-up visit.

Data were collected at baseline; weeks 2, 4, and 6 prior to ablation; within 24 hours post-ablation; and at clinic visits 1-, 3-, and 6-months post-ablation as shown in Table 2 (page 102). In both the YI and UC groups, those who did not have an internal monitor such as a pacemaker (PM), implantable cardiac defibrillator (ICD), or subcutaneous electrocardiogram implant (SEM), were provided with a novel technology, the AliveCor™ monitor, to transmit ECG at least once a day and at any other time they believed they were experiencing AF symptoms. At the 6-month post-ablation visit, a semi-structured interview (see Table 3, page 103) was conducted with all participants to capture their perceptions about their health-related QOL, and, in addition for those in the YI group, their experiences with yoga.

Study participant compensation

As compensation for their time and effort in the study, participants in both groups who did not have an internal cardiac monitoring device at the time they were enrolled in the study were provided with an AliveCor™ monitor that they kept upon study

completion. Those participants who did not require the AliveCor™ monitor because they already had an internal monitor received a check for $25 at week 6 prior to ablation and a check for $75 upon completion of the month-6 clinic visit for a total of $100 for study completion.

Treatment fidelity/Training of study staff

The 50-minute YI was detailed in a training manual developed by the researchers in consultation with a Viniyoga consultant. Using this manualized approach to maintain treatment fidelity, two yoga instructors were trained in the intervention to ensure consistency in delivering the intervention if the lead instructor became unavailable because of unexpected life circumstances. They used identical scripts for each yoga session, including the same oral instructions, thus keeping these as close to identical as possible for all yoga sessions. One investigator was physically present during all yoga sessions to observe that there were no deviations from the script or other fidelity concerns with the intervention.

Adverse events prevention and reporting

An adverse event was considered to be any undesirable sign, symptom, or medical condition related to the Viniyoga intervention. Given that participants in the YI group met twice a week for 6 weeks prior to their ablation procedures, during this time the researcher had multiple opportunities to discuss any safety concerns they had, any deterioration in their AF symptoms or any AF episodes they had experienced, as well as to learn about their health-related QOL. During the post-ablation period, the researcher made follow-up telephone calls to all the participants once a week until the end of the

study period to answer questions related to home yoga practice and any other safety concerns that the participants wanted to discuss regarding their arrhythmia symptoms. Heart rate monitoring data from the AliveCor™ or an implantable cardiac defibrillator, pacemaker, or subcutaneous electrocardiogram were reviewed weekly with the electrophysiologist to ensure that there were no significant increases in symptomatic and/or asymptomatic AF episodes. Adverse events, if any occurred, were reported to the Institutional Review Board for Health Sciences Research office based on the severity of the event and in accordance with the Board's guidelines.

The Yoga Intervention

The gentle 50-minute Viniyoga intervention included breath awareness and selected body postures (asanas) with breath work (pranayama) appropriate to cardiac patients. The yoga sequence (Iyengar, 2005; Cole, 2005; Raupach et al., 2008; Woodyard, 2011; Giya & Lee, 2012; Papp et al., 2013) as described in Table 4 (page 104) began with breath awareness to allow the participants to decompress, adjust to the environment, and focus their attention on their breath, which, from a yogic point of view, is the primary catalyst for adjusting one's autonomic nervous system. The yoga sequence was developed to promote the desired outcomes or characteristics, with progression of movement and breath from easy to more demanding forms of asanas and breath patterns (Mohan. A.G & Mohan.I, 2004). Asanas primarily promote strength and flexibility while developing mental focus and drawing attention to the present state of the mind. Breath in combination with an asana supported the movement of the asana and prepared the individual physically and mentally for pranayama practices (Mohan. A.G & Mohan.I, 2004). Pranayama's principle purpose was to focus the mind and regulate breathing

patterns, thereby creating mental steadiness while secondarily providing a means of conscious manipulation of the autonomic nervous system. That is, the slow breathing increases cardiac-vagal baroreflex sensitivity, improves oxygen saturation, lowers blood pressure, and reduces anxiety. Within the yoga tradition, slow breathing is sometimes paired with a contraction of the glottis muscles, leading to resistance breath or "ujjayi," which can be performed at various rates and ratios of inspiration/expiration. Slow breathing also decreases chemoreflex sensitivity, improves baroreflex response, and increases exercise and stress tolerance (Brown & Gerbarg, 2005).

The proposed yoga sequence begins with equal inhale and exhale (without strain) in postures 2, 3, 4, and 5 as described in Table 4 (page 104). There is a break from regulating the breath pattern in posture 6. Posture 7 begins with equal inhale and exhale and then progresses to lengthening of the exhale segment of the breath. The breath length is extended moving the individual from an easy to a more demanding form of breath work, preparing the body and mind for the upcoming pranayama practice. Equal inhale and exhale balances the sympathetic and parasympathetic systems, while extending the exhale enhances parasympathetic engagement and encourages healthy vagal tone.

Participants in the YI group maintained a diary of frequency and duration of home yoga practice, with the researcher making weekly telephone calls to these participants to address any issues or questions related to the home yoga practice. The researcher also made telephone calls to the participants in the UC group to discuss their AF symptoms, thus balancing the attention given to both groups.

Setting for the yoga intervention

All instructor-led yoga intervention classes were held in a room designed for yoga practice at the School of Nursing within the University. Free parking and direct elevator access to the yoga room were available to the participants.

Outcome Measures

Primary outcome measures were defined as (1) participants' experiences with the yoga intervention and their perceptions of the efficacy, barriers to, and how they believed that yoga could help them, and reasons for participants in the control group to decline participation in the yoga group; (2) recruitment, retention, and protocol adherence; (3) decrease in AF symptoms, stress, depression, anxiety, and prevention of ERAT during the 6-month post-ablation period. A secondary outcome measure was participants' health-related QOL.

Participants' experiences with yoga

Participants in both the YI and UC groups participated in a one-on-one semi-structured interview during their 6-month post-ablation clinic visits. The interview (see Table 3, page 103) captured their typical daily activities; physical symptoms of AF; their perceptions, thoughts and feelings related to AF; any triggers for AF; any measures to control AF symptoms; and, in addition for the YI group participants, their experiences with the yoga, including any challenges to participating in the study; and home yoga practice. The reasons for control group participants not participating in the yoga intervention were identified at the time of recruitment. In addition to the semi-structured interview, question and answer sessions at the end of instructor-led yoga sessions, weekly

telephone calls, and YI group participants weekly home practice diaries also identified their experiences with yoga.

Recruitment

Recruitment rate was determined by the number of potential participants screened for study eligibility versus the number of participants who enrolled. Of the two studies identified in the literature (Lakkireddy et al., 2013; Whalstrom et al., 2017) that had used yoga as an intervention with patients diagnosed with AF, only the first reported a recruitment rate of 50.49%. Therefore, a recruitment rate above 51% was considered an acceptable rate to support recruitment feasibility.

Retention

Retention rate was defined as the number of participants who completed the study activities through the 6-month post-ablation period. Attrition rates for the two studies of yoga interventions in adults with AF have ranged from 5.77% (Lakkireddy et al., 2013) to 13.75% (Whalstrom, 2017). Therefore, a retention rate >86% was considered an acceptable retention rate to support feasibility of the intervention.

Protocol adherence

Adherence to the study YI protocol was determined by this group's class attendance rates and their home practice rates as reported in the daily practice logs. Adherence to home practice was encouraged during the weekly telephone calls and follow-up clinic visits. Two studies that have used a yoga intervention in AF reported a class yoga intervention adherence of 83.3% (Whalstrom, 2017) and 100% (Lakkireddy et

al, 2013), with one reporting that the home yoga practice ranged from 1 to 4 sessions a week (Whalstrom et al., 2017), with the other reporting 2 to 7 home yoga practice sessions per week (Lakkireddy et al, 2013). Thus, an adherence rate of >84% for the instructor-led yoga intervention sessions and the twice-weekly home yoga practice was considered indicative of intervention adherence.

Atrial Fibrillation Symptoms

AF symptoms were monitored using the Atrial Fibrillation Effect on QualiTy-of-Life Questionnaire that includes a 4-item symptoms domain. Also, any AF symptoms participants reported during the weekly telephone calls and post-ablation clinic visits were documented.

Early Recurrence of Atrial Tachyarrhythmia (ERAT) after Atrial Fibrillation Ablation

ERAT was defined as any documented ECG evidence of atrial tachyarrhythmia within the first 3 months after ablation, using the AliveCor™ external cardiac monitor or other internal cardiac monitors such as pacemakers (PMs), implantable cardiac defibrillators (ICDs), and SEMs (subcutaneous electrocardiogram monitors).

Study Measures

The primary and secondary outcomes were measured using valid and reliable self-report questionnaires, including the Perceived Stress Scale, Atrial Fibrillation Effect on QualiTy-of-Life Questionnaire, Beck Depression Inventory II, and State-Trait Anxiety Inventory-Y. Additional objective data regarding AF episodes were obtained using

internal and external cardiac monitors. Semi-structured interview data were used to validate further the information collected using the self-report questionnaires and also provided information that might not be captured within the questionnaires.

Demographic Form

The demographic form captured participants' age, sex, education in years, annual income, ethnicity, prior exposure to yoga practice, the days and time that was suitable for the participants to attend yoga sessions twice a week, and the distance between their homes and the study setting.

Medical Record Review Form

After obtaining informed consent from each participant, the researcher used a medical record review form to capture the following: participant's medical history, including whether the participant was on any cardiac rate and/or rhythm control medications for management of AF, with the dosage used in the past and at present; frequency of AF episodes; AF symptoms; prior cardioversion or ablations; and any other complementary health care therapies that the participant had tried in the past.

Perceived Stress Scale (PSS)

The PSS is a well-validated and reliable instrument used to measure perceived stress (Cohen et al., 1983). This 14-item, self-report scale measured the degree to which situations in one's life are appraised as stressful. Participants rate each of these 14 items on a Likert-type scale of 0-4 (0 = never, 1 = almost never, 2 = sometimes, 3 = fairly often, 4 = often). PSS-14 scores were obtained from reversing the score on the seven

positive items 4 through 9, 10, 13 and then summing across all 14 items. Coefficient alpha reliability was 0.84 through 0.86 in the three different samples in which the questionnaire was validated. The total score range is 0-56, with higher scores indicating increased levels of perceived stress. The relationships between the PSS and validity criteria is unaffected by age and sex. The PSS provides a potential tool for examining issues about the role of appraised stress levels in the etiology of disease and behavioral disorders. Cronbach's alpha for the PSS-14 was >0.70.

Atrial Fibrillation Effect on QualiTy-of-Life (AFEQT) Questionnaire

This comprehensive, validated, disease-specific questionnaire measures the spectrum of quality of life domains affected by AF (Spertus et al., 2011). It included 4 conceptual domains (Symptoms, Daily Activities, Treatment Concern, and Treatment Satisfaction) from which individual domain and global scores were calculated. The 20-item instrument provides a 4-item Symptoms score, an 8-item Daily Activities score, a 6-item Treatment Concern score, and a 2-item Treatment Satisfaction scale. Each item was scored from 1 (no difficulty at all) to 7 (extremely limited). Questions 19 and 20 were related to treatment satisfaction and were not included in the health-related QOL score of this questionnaire. Overall scores or subscale scores range from 0-100. A score of 0 corresponds to complete disability while a score of 100 corresponds to no disability. Cronbach's alpha coefficient was >0.88 for the AFEQT overall score and the 4 domains: Symptoms (0.95), Daily Activities (0.94), Treatment Concern (0.90), and Treatment Satisfaction (0.88), supporting the questionnaire's internal consistency. The intra-class correlation coefficients (ICC), used to assess test-retest reliability on 43 patients were all acceptable: Overall (0.8), Daily Activities (0.8), Treatment Concern (0.7), and Treatment

Satisfaction (0.7) except for the symptoms that was at 0.5. This slightly lower ICC was attributable to the nature of patients' AF disease whose symptoms are more variable. The construct validity of the AFEQT questionnaire demonstrated adequate convergent and divergent correlations ($r \geq$ and <0.4 respectively) of the AFEQT domains with other commonly used well-validated questionnaires such as the Short Form Health Survey (SF-36) and the EuroQol. The known group validity was confirmed by comparing the AFEQT global scores with clinicians' assessments of asymptomatic, mild, moderate, and severe AF, which showed significant statistical correlation. If the AFEQT score change is at least 19 points, there was very likely to be a substantial improvement in QOL, and this was achieved in 35% of the entire cohort; this improvement can be termed a meaningful important improvement.

Beck Depression Inventory (BDI-II)

This is a 21-item self-report instrument intended to assess the existence and severity of symptoms of depression as listed in the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders*-Fourth Edition (Beck et al., 1996). There was a 4-point score for each of the 21 items, ranging from 0 to 3. On two items (16 and 18) there are seven options to indicate either an increase or decrease in appetite and sleep. The 21 items are summed to give a single score. A total score of 0-13 is considered minimal range, 14-19 is mild, 20-28 is moderate, and 29-63 is severe depression. Used for 35 years to identify and assess depressive symptoms, the BDI is reported to be highly reliable regardless of the population. It has a high coefficient alpha (0.92 for outpatients and 0.93 for college students), its construct validity has been well established, and it is able to differentiate depressed from non-depressed individuals. The

BDI serves as tool to identify the presence and severity of symptoms consistent with the criteria of the DSM-IV, and should not be used as a sole diagnostic measure, as depressive symptoms can be part of other primary diagnostic disorders.

State-Trait Anxiety Inventory (STAI Form Y)

This instrument is used extensively in research and clinical practice. It comprises separate self-report scales for measuring state and trait anxiety (Spielberger, 1983). The S-Anxiety scale (STAI Form Y-1) consists of 20 statements that evaluated how respondents feel "right now, at this moment." The T-Anxiety scale (STAI FORM Y-2) consists of 20 statements that assess how respondents "generally feel." In the construction and standardization of Form Y, more than 5,000 subjects were tested. The alpha coefficient for the S-Anxiety scale was 0.93 and 0.90 for the T-anxiety scale. Data on the internal consistency and validity of the individual STAI items showed that, in general, the coefficients for each of the 20 items were higher in more stressful conditions than in relaxed conditions.

Subcutaneous Electrocardiogram Monitoring (SEM)

Medtronic Reveal LINQ™ and St. Jude Medical Confirm™ are two currently available SEMs. The Reveal LINQ™ SEM System, a wireless implant, is the smallest implantable cardiac monitoring device to gain FDA approval. It was approximately one-third the size of an AAA battery (about 1 cubic centimeter), making it more than 80% smaller than other SEMs. Despite its size, the device was part of a powerful system that allows physicians to monitor a patient's heart continuously and wirelessly for up to 3 years. Implanted through an incision less than 1 cm in the upper left side of the chest, the

device was safe in patients undergoing magnetic resonance imaging. In addition to its continuous and wireless monitoring capabilities, the system provides remote monitoring through the Carelink Network through which physicians can request notifications of their patients' cardiac events. The Reveal LINQ™ is indicated for patients who experience symptoms such as dizziness, palpitations, syncope, and chest pain, which might suggest a cardiac arrhythmia, and for patients at increased risk for cardiac arrhythmias (www.medtronic.com). The American Heart Association guidelines note that SEMs are cost effective in patients with unexplained symptoms and yield diagnostic information in more than 90% of patients (Arzbaecher et al., 2010). For potential participants who did not wish to have a monitor subcutaneously implanted, we used the AliveCor™ monitor (Hickey et al., 2014).

AliveCor™ Heart Monitor

The AliveCor™ heart monitor is an FDA-approved ECG device compatible with most Apple and Android mobile devices. The monitor easily attached to the back of these devices, after which the free "AliveECG" application can be downloaded from the Apple iTunes store or Android Play store. A picture then appears on the screen, demonstrating how to hold the device while recording the ECG. This could be done either by placing the device on one's fingertips or chest wall. Recording begins automatically when both electrodes make contact with the skin, taking approximately 30 seconds to complete. The electrodes use ultrasound to transmit an ECG recording corresponding to a standard Lead I on a 12-lead ECG. When the ECG is captured, it is automatically transmitted to a secure, online "cloud" via Wi-Fi and/or cellular service. Patients and health care

providers can view previously recorded ECGs within the "AliveECG" application or by logging into the HIPAA-compliant cloud at www.alivecor.com (Hickey et al., 2014).

Pacemakers and Implantable Cardiac Defibrillators

In patients with dual chamber pacemakers (PMs), the accurate detection and quantification of asymptomatic AF episodes is possible (Hohnloser et al., 2006). Most of these asymptomatic episodes are of very short duration, often lasting only a few seconds to minutes, and are called "atrial high rate episodes" to distinguish these from the longer episodes of overt AF (Hohnloser et al., 2006). Using PMs, it is possible to detect every episode of AF and to measure total burden of AF as the percentage of time in AF each day (Hohnloser et al., 2006). Data from 354 patients showed that 50.6% of these patients had supraventricular arrhythmias, 65% of patients remained asymptomatic after 28 days of monitoring (Defaye et al., 1998). Arrhythmia relapses were documented in only 46% of patients with the use of surface ECGs during follow-up visits, whereas device-stored ECGs revealed an arrhythmia recurrence in 88% of patients (Israel et al., 2004).

Participant home yoga practice logs

Participants in the YI group maintained logs of daily home yoga practice to document their feelings before yoga practice, time spent in the yoga practice, as well as their thoughts and feelings after yoga practice. The researcher collected completed logs during the yoga sessions and clinic visits post-ablation, distributing logs for the following weeks at these times.

Telephone calls and log

Each week following a participant's ablation, the researcher called those in the UC and YI groups to gather information related to any AF episode/symptoms, any difficulties using the AliveCor™ heart monitor in transmitting ECGs (for those who had this device), any other concerns a participant might have had. For the YI group, in addition to the foregoing information, the researcher also gathered information related to difficulties with home yoga practice and any problems completing the practice log. The researcher maintained a log of the weekly telephone calls (Table 5, page 106).

Data Analysis

Quantitative data analysis

Screening, recruitment, retention, and intervention adherence rates were calculated using a simple ratio calculation. Quantitative data analyses were conducted using SPSS software version 24, with descriptive statistics calculated for all variables. Chi-square tests was used for categorical variables and Mann-Whitney U for continuous variables. Two-tailed tests were used to determine improbable values in both ends of the sampling distribution (Polit & Beck, 2012). The level of significance (α) was set at 0.05. The researchers were responsible for all aspects of data collection, entry, and analysis, with input from the electrophysiologist regarding the data from the cardiac monitors. To ensure validity and integrity of the data, the research team conducted weekly audits of quantitative data to confirm that it has been entered accurately into the data analysis software (SPSS).

Qualitative data analysis

Thematic content analysis was used for analysis of the semi-structured interview transcripts to categorize the 'recurrent' or common 'themes' (Green & Thorogood, 2011). The audio interviews were transcribed verbatim using a transcription service approved for use by the Institutional Review Board for Health Sciences Research. The researcher verified the transcripts with the audio recordings to ensure accuracy. Coding was achieved both deductively from concepts the researchers brought to the study and inductively through emergence from the data (Miles et al., 2014). The transcripts were coded one after the other and not simultaneously, helping the researcher to remain focused and promote in-depth analysis of each of the transcripts.

The first cycle of coding was done using Dedoose version 7.6.24, qualitative data analysis software for managing, analyzing, and presenting qualitative and mixed-methods research data (www.dedoose.com). Descriptive coding strategy was used; assigning labels to data to summarize in a word or a phrase the basic topic of a passage of qualitative data (Miles et al., 2014). Each transcript was read from beginning to end at least three to four times before starting the coding strategy. Following this, a careful reading of each sentence was done, with the text then divided into individual units of analysis or "meaning units" (Rennie et al., 1988). Meaningful units (MUs) are manageable passages of text that have been partitioned on the basis of what appeared initially to be expressing one main thought or essential concept. Each MU was then examined to see if it would emerge as a code. If the MUs did not match with an existing code, a new code was created. Many such codes was created with constant comparison to

the existing codes. When the analyses of MUs no longer create any new codes, then "data saturation" was reached.

For further validation, second cycle of coding was done following the same methods as the first coding cycle using InVivo coding, which used words or short phrases from the participant's own language in the data record as codes (Miles et al., 2014). Simultaneously, analytic memo was used to draft the thought processes and to maintain notes of other assumptions and biases. Analytic memos was used throughout the coding process to organize the thought process of the researcher. The analytic memo includes expression of thoughts in words, sentences, diagrams, and symbols (Miles et al., 2014) that allowed the researcher to experience free flow of thoughts and organize thoughts and ideas to help in generation of new ideas and stimulate good thinking. The maintenance of analytic memos throughout the data analysis process helped the researcher in identifying the themes that emerged from this analysis. The researcher consulted with two experts in mixed-methods research to confirm validity of the themes that emerged from the qualitative data analysis.

Discussion

To the researchers' knowledge no studies have reported the effect of yoga in prevention of ERAT after ablation. Thus, this study protocol assessed the feasibility of a Viniyoga intervention for adults diagnosed with AF and collected preliminary data on its perceived effects on AF episodes, symptoms, stress, anxiety, depression, ERAT after AF ablation, and overall health-related QOL in patients with AF. Feasibility studies using rigorous research methodologies are needed to help researchers in designing large scale,

randomized, controlled trials to identify the effects of gentle yoga postures on ERAT after AF ablation.

The ANS is involved in the genesis of both AF triggers and the creation of a more established AF substrate needed for the maintenance of AF and is enhanced in the presence of structural heart disease (Arora, 2012). It has been shown that the abnormal electrical conduction within the pulmonary veins could be sustained only in the presence of isoproterenol or acetylcholine, indicating that sympathomimetic or cholinergic stimulation appears to be necessary to promote the development of sustained focal activity in the pulmonary veins (Arora, 2003). Given the potential impact of yoga on the autonomic nervous system and stress, designing a yoga intervention to promote ANS balance may help in preventing recurrent AF. The wide range of yoga styles makes it challenging for patients and health care providers to identify the one appropriate for patients with AF. Hence, it is important that researchers identify through rigorous research safe and effective yoga sequences for patients with AF.

Research has shown that ERAT within the first 3 months after AF ablation is usually associated with late recurrence of atrial tachyarrhythmia. Among patients with recurrent AF, the frequency of recurrence was strongly associated with higher resource use, with each recurrence increasing annual costs by an average of $1600 (Reynolds et al., 2009). Therefore, implementing a cost-effective, complementary health-enhancing mind-body therapy such as yoga before and after ablation may prevent recurrent AF episodes, reduce related-health care costs, and improve overall health-related QOL in patients who undergo AF ablation.

As discussed earlier in this protocol, yoga uses the concept of body awareness as a progression towards greater unity between mind and body, with self-awareness guiding the individual in making decisions related to her/his health, healing, and well-being, thus facilitating understanding of one's self. Health care providers need to be able to assist individuals in identifying appropriate yoga protocols that are safe and effective for their disease conditions. Rigorous research is warranted to identify the impact of yoga on specific patient populations and the protocol described here is an effort to identify a safe yoga intervention to prevent ERAT in patients who undergo AF ablation.

The integration of the quantitative and qualitative data was carried out during the data analysis phase of the study. These data when analyzed separately and compared with the other to assess whether one method offers further explanation for research findings derived from the other, provide a broader and in-depth interpretation of the findings.

Conclusion

This sequential mixed-method, prospective, quasi-experimental, two-group design study provided feasibility and preliminary data for designing future larger, randomized, controlled trials to investigate the effect of yoga in prevention of ERAT after ablation. The selection of a psychoneuroimmunology theoretical framework provided structure for identification of the appropriate outcome variables and identification of valid and reliable instruments to collect research data as well as interpretation of the study findings. Research frameworks aid in replication and validation of research findings and promote clinical application of cost-effective, complementary health-enhancing therapies such as yoga in the management of patients with AF with recurrent atrial arrhythmias. Risks to

subjects were reasonable, with the yoga intervention designed to be gentle and safe for yoga-naïve patients.

Conflict of Interest

The authors declare that no economic interest or any conflict of interest exists.

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Table 1: *Inclusion/Exclusion Criteria and Rationale*

Inclusion Criteria	**Rationale**
Adults (male or female) of any race or ethnic group between 18 to 65 years of age with an established diagnosis of paroxysmal or persistent AF	Incidence of AF below the age of 18 is relatively less. Research has shown that the risk of AF increases with age
Scheduled for an AF ablation that will take place at least 6 weeks from the time of enrollment	The usual wait period for an AF ablation procedure in the academic hospital where participants are recruited is at least 6 weeks, making it possible for participants to complete the proposed 6-week yoga intervention without any delay in care
Able to perform a gentle yoga intervention that consists of breath awareness, postures, and meditation.	Although the postures can be modified to accommodate to each participant's flexibility, to ensure safety of the intervention, participants should be comfortable in practicing the breath awareness and yoga postures that comprise the yoga intervention
English speaking/writing	Proposed protocol did not have resources necessary to accommodate or evaluate non-English speaking/writing participants
Live within 50 miles radius from AF Clinic (participants in YI group only)	To foster attendance to the twice-weekly instructor-led yoga sessions
Exclusion Criteria	**Rationale**
Participants with *permanent* AF	It is very difficult to prevent recurrence of AF in patients with permanent AF and the resulting left atrial enlargement
Very unstable patients with symptoms such as hypotension and/or syncope	These patients may require immediate medical management or ablation. It may not be safe for them to wait the 6 weeks required to participate in the yoga intervention
Participants with any changes made in their medical regimen for management of AF within the month prior to recruitment	Any treatment changes within a month prior to study participation might confound the study findings
Any comorbid condition (such as a chronic spinal problem), recent major surgery, active seizures, terminal illness, or pregnancy	These conditions might restrict participants engaging in safe yoga practice. Regarding pregnancy, radiation exposure during ablation and selected yoga poses would not be safe.

Table 2: *Study Schema of Measures by Time points*

				Pre-Ablation (weeks)				Post-Ablation (months)		
Person/Measure	**Admin Time**	**Screening**	**Baseline**	**2**	**4**	**6**	**Ablation**	**1**	**3**	**6**
Researcher										
Demographic form	10 min	**X**								
Medical record review form	15 min	**X**								
Participant										
Perceived Stress Scale	10 min		**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Beck Depression Inventory	10 min		**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
State-Trait Anxiety Inventory (Y-1 & Y-2)	10 min		**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Atrial Fibrillation Effect on Quality-of Life	5-10 min		**X**			**X**		**X**	**X**	**X**
At-home yoga practice diary to researcher	5 min (wkly)			**X**	**X**	**X**	**X**	**X**	**X**	**X**
Semi-structured interview	30-45 min									**X**

Table 3: *Semi-Structured Interview Questionnaire*

Thank you for agreeing to talk with me for a few minutes about your atrial fibrillation and the study that you have just completed.

- First, please share with me your typical daily activities, thinking generally in terms of 2-hour segments of time within your day, beginning with 8-10 A.M. and then 10 A.M. to 12 noon, 12-2 P.M., 2-4 P.M., 4-6 P.M., 6-8 P.M., 8-10 P.M.
    - Have your typical daily activities changed at all in the last 6 months?

      If Yes, how so?
- Describe for me your typical atrial fibrillation symptoms
    - Physical symptoms that you experience
    - Psychological-related symptoms, including your perceptions, thoughts, and feelings related to your atrial fibrillation
- Tell me about your atrial fibrillation symptoms within the past 3 months
    - How do these symptoms compare to those in the prior 3 months?
- Does anything aggravate your atrial fibrillation symptoms?
    - If Yes, what?
- Have you experienced any life stressors in the past 6 months?
    - If so, can you describe these and the impact of these on your quality of life?
- What do you believe helps in controlling your atrial fibrillation symptoms?
- Describe your experiences with or your thoughts about yoga prior to this study.
- Did you experience any barriers/challenges/difficulties in participating in this study?
- *Describe your experiences with the yoga classes led by the trained instructors.
- *Describe for me your experience with home yoga practice.
- *Would you recommend yoga practice to other atrial fibrillation patients? If so or if not, why?
- Would you like to share with me any other information that has not been discussed so far?

*****Questions for participants in the YI group only

Table 4: *Yoga Sequence and Rationale for Sequence*

Yoga Sequence	Rationale for sequence
Breath awareness	• Begin to develop inner focus • Connect to breath • Initiate process of balancing ANS through equal inhale & exhale
Vajrasana variation (Thunderbolt pose)	• Continue to bring mental focus inward by linking breath & movement • Begin to warm-up muscles including those of the shoulder used to lift the arms overhead in preparation for the next posture • Contract abdominal muscles during the forward bend to strengthen respiratory muscles used in exhale as preparation for pranayama • Introduce progressive lengthening of equal inhale & exhale • Promote calm & relaxation through balancing breath effect on the ANS
Balancing Tadasana (Mountain pose)	• Promote shift from focus on external stimuli to internal stimuli through balancing on toes. • Begin to develop an awareness of internal processes as they relate to breath & movement as first step in conscious control of these processes. • Expand inhale as a result of creating space and negative pressure in the chest during upward stretch with arms overhead
Uttanasana variation (Forward bend pose)	• Progressive lengthening of inhale & exhale to promote calm and relaxation • Forward bend abdominal contraction further strengthen muscles used in exhale • Partial inversion baroreceptor response to modulate ANS
Utthita Trikonasana variation (Standing triangle pose)	• Stretch, strengthen, and mobilize intercostal muscles in preparation for pranayama • Continue the process of progressive increase in the length of inhale and exhale in preparation for pranayama

Yoga Sequence	Rationale for sequence
Cakravakasana (Ruddy goose or modified cat/cow pose)	• Transition from standing to kneeling • Link breath to movement • Strengthen and flatten upper back, stretch front of shoulders, stretch lower back, strengthen abdominal muscles in preparation for sitting during and performing pranayama • Slight inversion promotes parasympathetic enhancement
Jathara Parivritti (Twist pose)	• Preparation for sitting in pranayama (stretching hip muscles) • Lengthening exhale to promote calm through parasympathetic dominance • Increase exhale count over inhale. • Assist in lengthening exhale by compressing abdominal muscles
Apanasana (Knees to chest pose)	• Structural compensation for preceding twist - realigning the spine • Stretch lower back in preparation for sitting • Further increase exhale to inhale ratio enhancing parasympathetic engagement
Savasana (Corpse pose)	• Decrease external stimulation of the sympathetic system by closing the eyes (reticular formation stimulation decreased) • Cessation of movement and contact with floor diminishes sensory input • Transition from asana to pranayama practice
Modified Pratiloma Ujjayi	• Pranayama technique considered a balancing breath • Alternate nostril balancing breath works to bring equilibrium between the sympathetic (right nostril) and parasympathetic (left nostril) nervous systems. Promotes calm and relaxation while mitigating stress response • Alternating breathing with one nostril valved then breathing with both nostrils without valving reduces physiological stress of continuous resistance from valving. • Modified Pratiloma Ujjayi used to reduce stress of yoga naïve study participants

Table 5: *Weekly Telephone Log*

Weekly telephone call questions for the YI group participants	**Weekly telephone call questions for the UC group participants**
1. How are you today? 2. Are you having any difficulties with the home yoga practice? 3. Are you having any problems completing the practice log? If so, tell me about these. 4. Have you had episodes of AF? 5. Are you having any difficulties using your AliveCor Heart Monitor to transmit your ECGs? 6. Do you have any questions or concerns that you would like to discuss with me?	1. How are you today? 2. Have you had any episodes of AF? If so, tell me about these. 3. Are you having any difficulties using your AliveCor Heart Monitor to transmit your ECGs? 4. Do you have any questions or concerns that you would like to discuss with me?

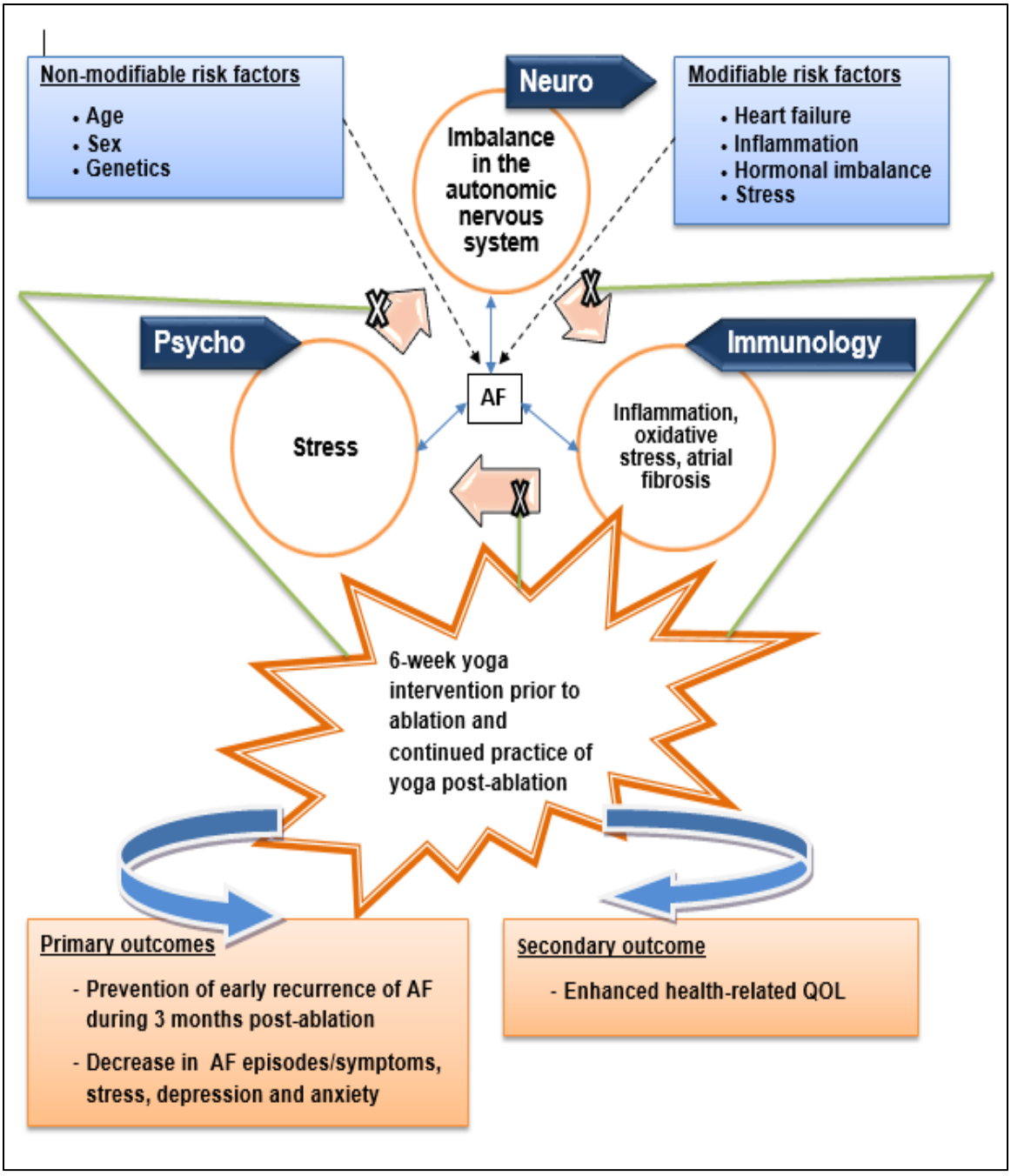

Figure 1. Psychoneuroimmunology Theoretical Framework

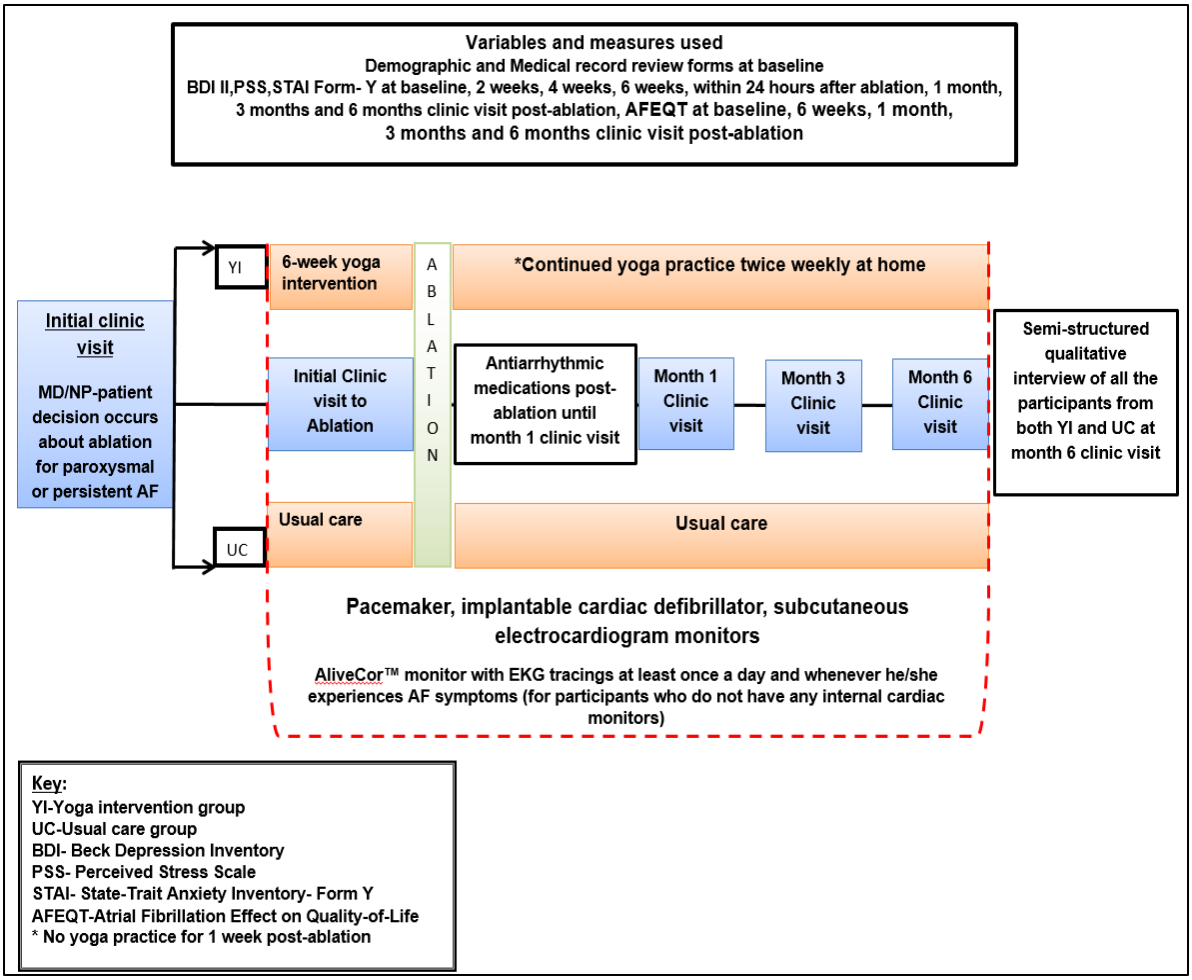

Figure 2. Research Design

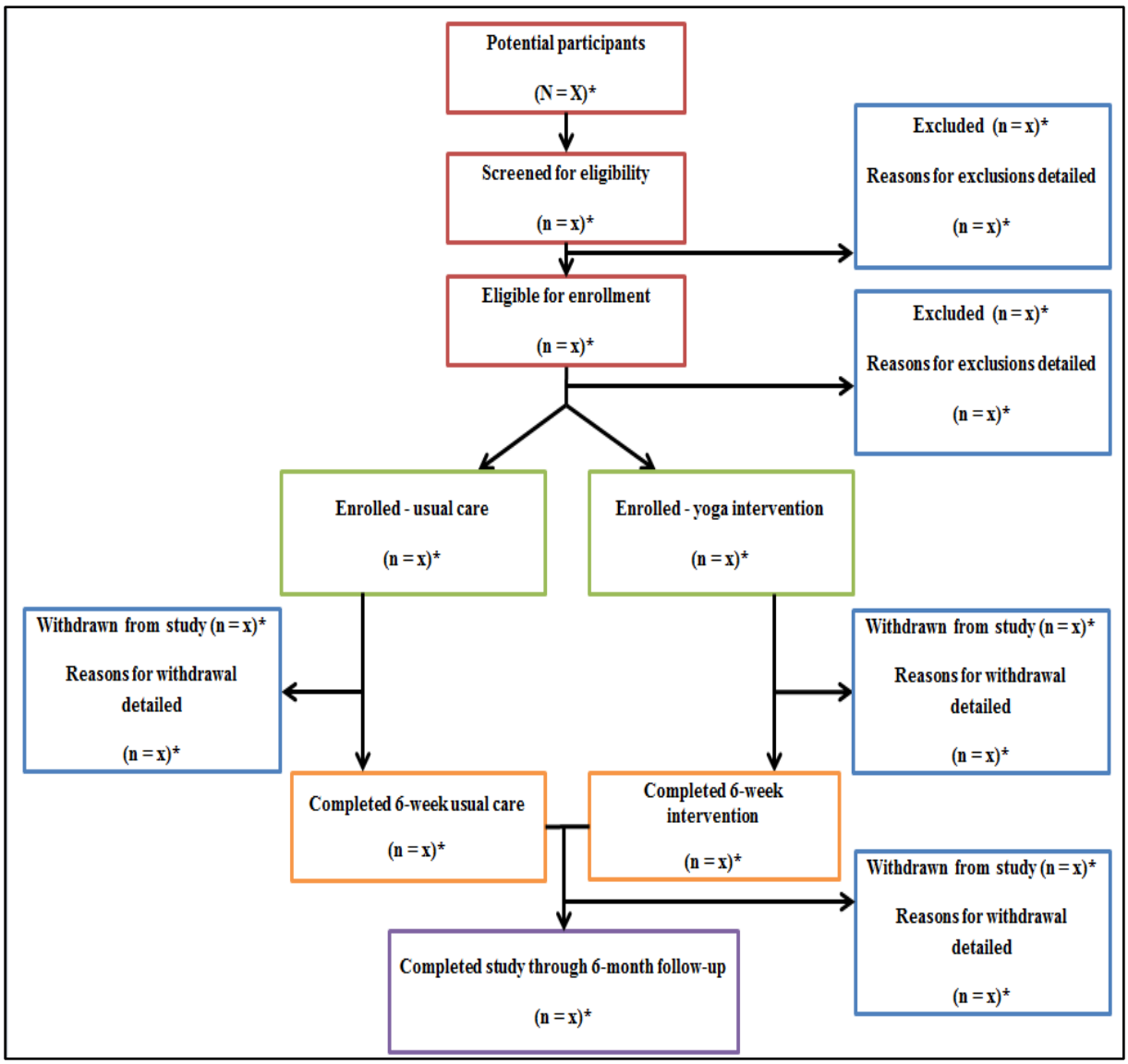

Figure 3. Participant Study Flow According to the Study Design

*****Number of participants will replace 'X' when results are reported*

CHAPTER FOUR: RESULTS

Manuscript Three

Effect of Yoga on Early Recurrence of Atrial Tachyarrhythmia after Atrial Fibrillation Ablation: Results of a 6-week Viniyoga Intervention

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Abstract

Objective: The specific aims for this study were (1) to examine the feasibility and acceptability of a Viniyoga intervention for individuals with AF and (2) to test whether or not a 6-week Viniyoga intervention in persons between the ages of 18 to 65 years old with paroxysmal or persistent AF planning to undergo ablation will decrease AF symptoms, stress, depression, anxiety, prevent early recurrence of atrial tachyarrhythmia (ERAT) after AF ablation, and improve overall health-related quality of life (HRQOL) during the 6-month post-ablation period, if these participants continued to practice yoga at least twice-weekly for 50 minutes compared with a usual care alone group. A secondary aim was to capture the participants' perceptions of HRQOL, using semi-structured interviews with all participants, and for the yoga intervention group, their experiences with yoga.

Design and Methods: A sequential mixed methods, prospective, quasi-experimental, two-group design informed by a psychoneuroimmunology theoretical framework guided the study design to investigate the effect of a twice-weekly, 6-week Viniyoga intervention and continued practice of yoga at home in prevention of ERAT after AF ablation. Self-report questionnaires were completed at 8 different time points, including baseline and at the 6-month post-AF ablation clinic visit. All participants participated in a semi-structured interview during their 6-month post-ablation clinic visit.

Results: The recruitment rate for the yoga intervention plus usual care (YI) group was only 16.67%, whereas it was 50% for the usual care (UC) group with recruitment for the UC group having been stopped because of less recruitment to the YI group. A total of

four UC group participants and two YI group participants completed the study. Two major reasons for participants declining participation were the travel distance and challenges in attending the twice-weekly YI sessions for 6 weeks. Other reasons included current practice of yoga or mindfulness meditation, lack of a smart phone or iPad to download the Alivecor™ app, and questions about the affiliation of yoga with a religion that the participants did not practice. No statistical significance was achieved for any of the study outcome measures given the small sample size, although clinically meaningful improvements were noted in the Atrial Fibrillation Effect on QualiTy-of-Life questionnaire overall score and symptom score for the two YI group participants compared to the scores for the four participants in the UC alone group. The study also showed that ERAT after AF ablation in the YI group was 0% compared with 75% in the UC group. Minimal decreases in stress, depression, and anxiety scores were noted although qualitative data analysis revealed that the participants identified stress, depression, and anxiety as both triggers and manifestations of their AF. The reason for no significant change in the anxiety scores may be related to the fact that a new diagnosis of AF is compounded with much anxiety about the disease course itself and at post-ablation these participants continued to be worried about recurrences of AF.

Conclusion: This study did not show any statistical significance in the outcome measures given the small sample size, although it did show clinically meaningful improvements in a few outcomes as described above. These preliminary findings support the need for future randomized controlled studies to determine the impact of yoga on prevention of recurrent atrial arrhythmias.

KEY WORDS: Atrial fibrillation, Viniyoga, yoga, stress, autonomic nervous system, psychoneuroimmunology, early recurrence of atrial tachyarrhythmia

Introduction

One of the largest U.S. epidemiological studies, the Framingham Heart Study, predicted that atrial fibrillation (AF) prevalence doubles with each advancing decade of age, from 0.5% at age 50-59 years old to almost 9% at age 80-89 years old, independent of the increasing prevalence of known predisposing conditions.[1] It is the most common sustained cardiac arrhythmia occurring in 1.5% of population.[2]

The total annual medical cost for the treatment of AF in inpatient, emergency department, and hospital outpatient settings, which is estimated at $6.65 billion, is likely underestimated as costs for long-term anticoagulation, stroke prevention, inpatient drugs, and hospital-based physician services were not included.[3] Patients with AF enrolled in the Fibrillation Registry Assessing Costs, Therapies, Adverse events, and Lifestyle (FRACTAL) study who were managed with cardioversion and pharmacotherapy incurred AF and other cardiovascular-related health care costs of $4000 to $5000 each year.[3] Among patients with recurrent AF, the frequency of recurrence was strongly associated with higher resource use, with each recurrence increasing annual costs by an average of $1600.[3] Researchers evaluating the cost-effectiveness of AF ablation compared with rhythm control or antiarrhythmic agents have shown that ablation treatment results in improved quality-adjusted life expectancy, although at a higher cost.[3, 4]

Although medical treatment involving catheter ablation has become a well-accepted management strategy for AF,[5] failure of this therapy is common, with only two-thirds or less of the patients treated remaining free of AF on long-term follow-up.[5] Early recurrence of atrial tachyarrhythmia (ERAT), usually defined as arrhythmia recurrence

within the first 3 months following ablation, is frequently associated with late recurrence of atrial tachyarrhythmia.[6, 7, 8]

Yoga has been shown to reduce stress, anxiety, inflammation, and maintain autonomic nervous system balance, which could potentially prevent AF.[9,10,11,12,13,14,15,16,17] To date, two studies have assessed the impact of yoga on AF. One, a proof-of-concept study[18] revealed that 60-minute Iyengar yoga sessions at least twice a week for 3 months improved symptoms, arrhythmia burden, heart rate, blood pressure, anxiety and depression scores, and several domains of quality of life (QOL) in adults with paroxysmal AF. A second study[19] using Mediyoga as the intervention in patients with paroxysmal AF showed that this style of yoga might potentially lower blood pressure, lower heart rate, and improve QOL in these patients compared with a control group. No studies to date have evaluated the impact of yoga on ERAT after ablation.

The investigators hypothesized that selected gentle Viniyoga postures would reduce stress, anxiety, and depressed mood, which are triggers and/or symptoms of AF, and also maintain autonomic nervous system balance essential for regulation of the normal electrical conduction in the heart.

Methods

The Institutional Review Board for Health Sciences Research at a research-intensive academic medical center approved the protocol, procedures, and materials of this sequential, mixed method, prospective, quasi-experimental, two-group research design.[20] A psychoneuroimmunology framework[17, 21] guided the study design and interpretation of study results. The participants could be males and females of any race or

ethnic group between the ages of 18 to 65 years old with an established diagnosis of paroxysmal or persistent AF who made the decision to undergo AF ablation in the AF Center clinic associated with the academic health system. Informed written consent was obtained from all participants prior to participation in any study related activities.

Recruitment and sampling methods

Beginning January 2016 and ending in March 2017, a consecutive sample of 8 adults diagnosed with paroxysmal or persistent AF who made the decision to undergo AF ablation were enrolled in the study. Those participants willing to do the yoga intervention were assigned to the "yoga intervention (YI)" group and those willing to participate in the study, but not interested in doing yoga, were enrolled in the "usual care alone (UC)" group. Participants were recruited by brochures placed in the AF clinic waiting areas and distributed by the physicians to potential participants. The physicians notified the investigators either by pager, email, phone, or through personal conversation, regarding potential participants, and the investigator met them in the clinic, screening each for eligibility according to the study inclusion and exclusion criteria. Inclusion criteria were as follows: (a) adults (male or female) of any race or ethnic group between the ages of 18 to 65 years old with an established diagnosis of paroxysmal or persistent AF; (b) scheduled for an AF ablation within at least 6 weeks from the time of recruitment; and (c) English speaking/writing. Additionally, for participants to be assigned to the YI group, (d) able to perform a gentle yoga intervention that consists of breath awareness, postures, and meditation; and (e) living within a 50-mile radius of the AF clinic. Prospective study participants were excluded from the study for following reasons: (a) diagnosed with permanent AF, (b) noted to have unstable symptoms such as hypotension and/or syncope,

(c) had undergone changes in their medical regimen for management of their AF within the month prior to recruitment, (d) had practiced yoga previously, and (e) had been diagnosed with any comorbid condition (such as a chronic spinal problem), and recent major surgery, active seizures, terminal illness, or pregnancy. The participant study flow is shown in Figure 1 (page 152).

As compensation for time and effort in the study, participants in both groups who did not have an internal monitoring device at the time of their enrollment in the study were provided with an AliveCor™ [22] monitor that they kept upon study completion. Those participants who did not require the AliveCor™ monitor because they already had another internal monitor received a payment of $25 at week 6 prior to ablation and a payment of $75 upon completion of the month 6 clinic visit, for a total of $100 for study completion.

Study Intervention

Participants in the YI group completed a 50-minute, cardiac patient-appropriate Viniyoga session twice a week for 6 weeks that included breath awareness and selected body postures (asanas) followed by pranayama. Using a manualized approach, including the same oral instructions at each session, an expert practitioner in Viniyoga provided the intervention. The investigator was physically present during all yoga sessions to observe that there were no deviations from the script or other fidelity concerns with the intervention.

The yoga sequence [23, 24, 25, 26, 27, 28] shown in Figure 2 (page 153) began with breath awareness to allow the participants to decompress, adjust to the environment, and focus

their attention on their breath, which is the primary catalyst for adjusting one's autonomic nervous systems from a yogic point of view. The yoga sequence was developed to promote the desired outcomes using a progression of movement and breath from easy to more demanding forms of asanas and breath patterns.[29] Breath in combination with asana supports the movement of the asana and prepares the individual physically and mentally for pranayama practices.[29] Pranayama's principle purpose is to focus the mind and regulate breathing patterns thereby creating mental steadiness, and secondarily, providing a means of conscious manipulation of the autonomic nervous system. Resistance with slow breathing (ujjayi) enhances parasympathetic activity and indicators of vagal tone, specifically, respiratory sinus arrhythmia and heart rate variability. It also decreases chemorelfex sensitivity, improves baroreflex response, and increases exercise and stress tolerance.[30]

The instructor-led 50-minute yoga sessions were followed by a 10-minute question and answer period, providing an opportunity for participants to talk about their at-home yoga practice, guided by a DVD with identical video recordings of the yoga intervention. All YI sessions were held in a room designed for yoga practice within the School of Nursing. Free parking and direct elevator access were available to all participants.

Participants maintained a diary of frequency and duration of home yoga practice and the investigator made weekly telephone calls to the participants to address any issues or questions related to their practice. Also, the investigator made weekly telephone calls to the participants in the UC group to discuss their AF symptoms, thus balancing the attention given to both groups.

Safety and confidentiality

No adverse events or breaches of confidentiality were reported during this study. Participants were able to complete successfully the required instructor-led yoga sessions without experiencing untoward study-related physical or psychological events. One participant in the UC group developed a pericardial effusion secondary to pericarditis post-ablation, which is one of the reported complications after AF ablation.[31] Her pericardial effusion resolved with medical management.

Study fidelity

Study fidelity was maintained throughout the study design, training, and intervention. Study logs and checklists were maintained by the research team to document study fidelity. Yoga classes and postures were delivered according to the yoga manual developed by the expert yoga instructor. The instructor used the same script for each yoga session. The investigator was physically present during all sessions to observe that there were no fidelity concerns with the intervention.

Data collection

Baseline demographic and health history data were collected at the beginning of the study. Self-report questionnaires and practice logs were used to collect data at 8 time points during the study. Electrocardiogram recordings were obtained using external and internal cardiac monitors. Participants participated in a semi-structured interview at the completion of the study. The interview was conducted by the researcher for 30-40 minutes to capture their typical daily activities; physical symptoms of AF; their perceptions, thoughts and feelings related to AF; any triggers for AF; any measures to control AF symptoms; and, in addition for the YI group participants, their experiences

with the yoga, including any challenges to participating in the study; and home yoga practice. Paper forms, logs, and questionnaires were used for data collection. Given the characteristics of the YI, blinding of the participants to the intervention was not possible. Also, the investigators and data analysis could not be blinded because of the convenience sampling of the participants; however, all data were de-identified.

Study outcome data

Primary outcome data for the study were defined as (1) participants' experiences with the YI and their perceptions of its efficacy, barriers to engaging in the yoga, and how they believed that yoga could help them, as well as reasons for participants in the UC group declining to participate in the YI; (2) recruitment, retention, and protocol adherence; (3) decrease in reported AF symptoms, stress, depression, and anxiety; and (4) no ERAT during the 6-month post-ablation period. A secondary outcome was participants' reported health-related QOL.

Study measures

The primary and secondary outcomes were measured using valid and reliable self-report questionnaires, including the Perceived Stress Scale (PSS),[32] Atrial Fibrillation Effect on QualiTy-of-Life Questionnaire (AFEQT),[33] Beck Depression Inventory II (BDI),[34] and State-Trait Anxiety Inventory- Form Y (STAI).[35] Objective data regarding AF episodes were obtained using internal and external cardiac monitors, including AliveCor™, [22] subcutaneous electrocardiogram monitoring,[36] pacemakers,[37] and implantable cardiac defibrillators.[38, 39] Study population characteristics were obtained using demographic and health history forms. Semi-structured interview data further

validated the information collected using the self-report questionnaires and also captured information that may have been missed because of the structured nature of the questionnaires. In addition, the YI group participants kept logs of home yoga practice that documented their feelings before yoga practice, time spent in yoga practice, and their thoughts and feelings after yoga practice. The investigator collected completed logs during the YI sessions and at the post-ablation clinic visits, distributing logs for the upcoming weeks at that time. Each week after ablation, the investigator called all participants to gather information related to any AF episode/symptoms, any difficulties using the AliveCor™ heart monitor in transmitting EKGs, and any other health-related concerns they may have at the time. For the YI group, in addition to the above information, the investigator also gathered information related to any difficulties with their home yoga practice and/or any problems completing the practice log.

Statistical analysis

Screening, recruitment, retention, and intervention adherence rates were calculated using a simple ratio calculation. Quantitative data analyses were conducted using SPSS software version 24.0.[40] Descriptive statistics, including mean, standard deviation, and range were calculated for all variables. Given the small sample size, Chi-square test was used for categorical variables and Mann-Whitney U was used for continuous variables. Two-tailed test was used to determine improbable values in both ends of the sampling distribution.[41] The level of significance (α) was set at 0.05. The investigator was responsible for all aspects of data collection, entry, and analysis, with input from the electrophysiologist regarding the data from the cardiac monitors. To ensure validity and

integrity of the data, the research team conducted weekly audits of the quantitative data to confirm that it had been entered accurately into the data analysis software (SPSS).

Qualitative data analysis

The qualitative data collected through tape recorded semi-structured interviews with the participants were transcribed by a commercial service approved by the institution's IRB for Health Sciences Research. The investigator next verified the transcriptions of the interviews with the audio recordings to ensure accuracy in the transcriptions. Thematic content analysis was used for analysis of the interview data to categorize the 'recurrent' or common 'themes'.[42] Coding was achieved both deductively from concepts the investigator brought to the study and inductively through emergence from data.[43] The transcripts were coded one after the other and not simultaneously, thus keeping the investigator focused and promoting in depth analysis of each transcript.

The first cycle of coding was completed using Dedoose version 7.6.24[44] a qualitative data analysis software for managing, analyzing, and presenting qualitative and mixed-methods research data. Descriptive coding strategy was used, assigning labels to data to summarize in a word or a phrase the basic topic of a passage of qualitative data.[43] For further validation, a second cycle of coding was done using InVivo coding, identifying words or short phrases from the participants' own language in the data records as codes.[43] Simultaneously, analytic memo was used to draft the thought processes and also to maintain notes of other assumptions and biases. The analytic memo included expression of thoughts in words, sentences, diagrams, and symbols.[43] The maintenance of analytic memos throughout the data analysis process helped the

investigator in identifying the themes that emerged from this analysis. Similar codes that emerged were grouped together to develop preliminary themes. [43] Finally, the investigator consulted with two experts in mixed-methods research to confirm validity of the themes that emerged. The specific themes that emerged from the analysis were stress, anxiety, and depression as triggers and manifestations of AF, impact of AF on QOL, perceptions regarding practice of yoga and its impact on AF, barriers to yoga practice, sense of self-control with using technology to detect AF, awareness regarding lifestyle modifications, barriers to participation in this study, and fear of the unknown related to disease progression. The themes identified were compared against quantitative findings to explain and expand on feasibility findings and to provide contextual meaning to the YI participants' experiences of participating in a 6-week Viniyoga intervention and their perceptions on quality of life.

Mixed methods approach

The sequential mixed methods design was used as the approach for the study. This approach involved an initial quantitative data collection phase followed by a qualitative data collection phase using a semi-structured interview of the participants from the quantitative phase of the research. Integration of the quantitative and qualitative data was carried out during the data analysis phase and the findings from both the quantitative and qualitative analysis were compared to corroborate, expand, and cross-validate the findings from each method.

Results

The demographic characteristics of the study sample as described in Table 1 (page 147) included 6 adults with a diagnosis of paroxysmal or persistent AF who were

scheduled to undergo AF ablation within 6 weeks. Of the 6 participants, 3 were non-Hispanic White men and 3 non-Hispanic White women. Two participants (1 male and 1 female) who were willing to practice yoga were assigned to the YI group and those not willing to practice yoga were assigned to the UC group. The mean age of the participants in the YI group was 65 and in the UC group 56.75 (±10.436) years. The two participants in the YI group had paroxysmal AF and in the UC group, 3 participants had paroxysmal AF and 1 had persistent AF. The study outcomes are presented in Table 2 (page 149). One of the participants in the YI group did not return for the 3-month clinic visit post-ablation despite multiple reminders, thus no study measures for this assessment time were available.

Recruitment, retention, and protocol adherence

A recruitment rate of 51% and a retention rate of > 86% were considered acceptable to support feasibility of the intervention. The recruitment rate for the study was 16.67% for the YI group and 50% for the UC group. It would have been possible to have achieved 100% recruitment for the UC group but recruitment to this group was stopped because of less recruitment to the YI group. The two major reasons for participants declining participation in the study were travel distance and challenges in attending twice-weekly YI sessions. Other reasons included current practice of yoga or mindfulness meditation, lack of a smart phone or iPad to download the Alivecor™ app, difficulty in committing to a specific time of day for YI group sessions, and questions about the affiliation of yoga with a religion that the participants did not practice. The retention rate for the YI group participants was 100%, although one participant missed his 3-month post-ablation follow-up visit. The retention rate was 66.7% for the UC group, with two participants having been withdrawn from study; one had osteomyelitis

and her primary electrophysiologist made the decision to manage her osteomyelitis, deferring her AF ablation beyond the study criterion; another participant had issues with downloading the Alivecor^{TM} app onto his phone that were beyond those that could be resolved by the investigator.

The mean number of YI group sessions participants attended was 11 (±1.414) out of a total of 12. These participants reported practicing home yoga 1 to 4 times a week. The common reasons for not attending all of the instructor-led yoga sessions and not engaging in twice weekly home yoga sessions were related to work commitments and family care giver responsibilities.

Early Recurrence of Atrial Tachyarrhythmia after AF Ablation

Participants in the YI group did not experience any documented evidence of ERAT after their ablations. One YI group participant was on an anti-arrhythmic drug (Amiodarone) for 1 month post-ablation; however, the other participant did not require any anti-arrhythmic drug post-ablation. Three of the four participants in the UC group experienced ERAT after their ablations. The time of the first post-ablation documented episode of atrial arrhythmias was 16 and 64 days for two participants, although one participant had recurrence of symptomatic paroxysmal AF 5 days after his anti-arrhythmic drug (Multaq) was stopped at his 1-month post-ablation follow-up. One UC participant required cardioversion for ERAT and all three participants in the UC group with recurrent atrial arrhythmias had their anti-arrhythmic medication continued until the 6-months follow-up post-ablation. The trigger for ERAT for one of the participants may have been pericarditis-induced pericardial effusion,[44] which was most likely a post-procedure complication after her AF ablation.

Atrial Fibrillation Symptoms

The AF symptoms score of the AFEQT questionnaire showed that this score improved to 100 for the YI group and 96.88 for the UC group at 6 months post-ablation, increasing from baseline scores of 70.5 and 81.25, respectively. A change in the AF symptom score by 19 points, suggests a clinically meaningful change. The AF symptoms score for the YI group participants increased by 29.5 during the 6-month post-ablation, although no statistical significance was noted because of the small sample size. Some AF symptoms reported by participants were palpitations, chest pressure, shortness of breath, pre-syncope, and fatigue.

Quality of Life

The baseline score of the AFEQT for the YI group was 70.5 (±6.364) and for the UC group it was 81.25 (±17.515). The score increased by 38.89 points for the participants in the YI group and 24.08 points for those in the UC group at the end of 6-month post-ablation. A change in score by 19 points, suggests a clinically meaningful improvement in QOL. Although the change in the AFEQT score was >19 points for participants in both the groups at 6 months post-ablation, the score for participants in the YI group increased by 22.23 points at the time of 1 month-post ablation clinic visit but it took 6 months post-ablation for the UC group to notice a meaningful improvement in QOL, although statistical significance could not be established because of the small sample size. This delay in improvement in the QOL for participants in the UC group is most likely due to the ERAT after AF ablation.

The qualitative interview data are presented using pseudonyms. The data revealed that the participants' QOL was significantly impaired when they were in AF. John who participated in the UC group had pre-syncopal spells with symptomatic AF and described his experience with AF episode as follows:

> …During the first one [pre-syncopal spell] I did not know I had AF. I was in my vehicle trying to find a parking spot [when] everything in front of my eyes went black. …I was conscious but I couldn't see. …I just threw the car into park … and called my wife. The other time [I experienced a spell] I was in my office and [heard] my telephone ring. I [recalled] I looked at the phone, grabbed at it, and at that point [realized that although] I could hear the phone [ringing] I could not see it for about 15 seconds.

Matt from the UC group reported the impact of his AF on his routine activities, noting "a lack of energy [and that] stairs occasionally would be a challenge, depending on the time of day."

At the time of the 6-months post-ablation clinic visit interviews, all participants reported that they were able to perform their routine activities without any AF-related symptoms, suggesting that their QOL improved when they were in normal sinus rhythm. John in the UC group had recurrent AF post-ablation that required management with an anti-arrhythmic drug. Several months passed without any recurrent AF episodes for John, following which he shared how he coped:

> I took it one day at a time and … tried to focus on that day even though I had setbacks in the early part [of my treatment]. Then there was also a time when it [AF] didn't show up again. … I think at that point [I felt] somewhat of a relief….

All participants reported since their diagnosis of AF and their ablation that they had set goals and made some lifestyle modifications, with most of these focusing on exercise and diet. The following quotes from two participants are representative of the perspectives that all participants shared regarding lifestyle modifications. Matt noted, "I think the fact that I'm exercising now is a big part of changes I have made. [Also] my interpretation of what's important in life after this major medical crisis has changed." Regarding changes John had made in his lifestyle, he shared the following:

> ... for me it' s been a different experience having been completely healthy and all of a sudden getting hit with this [AF]. It has definitely changed me and my life, [including] what I used to eat…my diet has changed. Also, being more active and …working on weight reduction, … these are two big goals … that I'm going to work towards.

Stress, Depression, and Anxiety

Participants in both the YI and UC groups had minimal improvement in their scores from baseline to 6 months post-ablation regarding their stress, depression, and anxiety. However, the qualitative interview data provided more insight into the reasons that the anxiety scores did not improve much. Sarah from the UC group reported that she thought her symptoms of palpitations and shortness of breath were related to her feelings of anxiousness and anxiety until the symptoms progressively worsened and a heart

monitor confirmed the diagnosis of AF. She explained, “When I got a heart monitor, I learned that the fluttery feeling in my chest and the shortness of breath that I had been experiencing were not feelings of anxiety, but were symptoms related to AF.”

When asked about any psychological-related symptoms and their perceptions, thoughts, and feelings regarding their AF, all of the participants reported that they felt anxious about the potential for recurrence of AF, its impact on their QOL, and their fear that they may become dependent on others for the remainder of their lives. A few mentioned that their fears surrounding AF often led to feeling depressed or saddened. Julie, a participant in the YI group, reported, “I realize the chances of me going into AF are certainly possible and I never really gave it a second thought before.”

John from the UC group provided a more complex response about how his AF had affected him in the past and at the present time, explaining as follows:

> How it [AF] is affecting me now, it is probably anxiety, probably some feelings of depression, [still] not knowing … what might be happening to me and what might be in my future. At first, it was fear [of the] unknown regarding what I had and, then second, learning that I have AF became an issue for me because the environment in this country today [really does not support] public transportation [and if transportation] isn't readily available to you and you have lost your driver's license and you black out, somebody else has to take care of you… you have to find public transit or have somebody else get you to and from work.

Stress was identified by most of the participants as the trigger for their AF. Julie from the YI group shared her view of the role that she thought stress was playing in her

AF symptoms, declaring, **"**I think stress and lack of sleep tend to trigger my AF." Matt a participant in the UC group reported the following:

> I think that a specific emotional episode shone a light on the fact that I wasn't in a normal sinus rhythm. I think it [the emotional episode] has made me realize that my ability to be stressed has been compromised by being in AF.

Participants' perceptions of yoga and their experiences with study participation

The two participants in the YI group reported that yoga made them feel calm and relaxed, improved their balance, and that they had experienced only limited challenges initially in doing a few of the yoga poses, with the instructor quickly and appropriately modifying the poses to meet their needs. Julie noted the following:

> There was one pose for which I can't remember the name …, where you had to turn your feet out and bend down. She [instructor] had me sort of structure my feet a little bit different. I'm not quite sure why I was having difficulty with the particular pose, but it was the only one I recall being a challenge for me.

Paul also in the YI group acknowledged that he had old pain issues, causing him to experience some discomfort with a few of the postures, although he had not told anyone. Reluctantly, he disclosed the following during his weekly telephone call:

> Because of knee and shoulder pain that I have at times, I started doing water yoga twice a week about two months after my ablation surgery… in addition to my two

> times a week home yoga practice…. I learned that my body is more flexible while in water and I was able to do the yoga poses without difficulty while in the water.

The two YI participants also acknowledged that they were not disciplined enough to do home yoga practice every day because of real life situations that interrupted their practice. Their home practice logs showed that they practiced the poses one to four times most weeks, although there were several weeks that they did not practice yoga at all. Julie shared that she preferred to do yoga in the group setting rather than alone at home. Both YI participants reported that they would definitely recommend yoga for other individuals with AF.

Each of the participants in the UC group reported that they had never thought about practicing yoga themselves but would be willing to consider it after participating in this study. However, Sarah explained that she has severe peripheral neuropathy and balance issues secondary to the neuropathy, leading her to think that she would not be able to practice yoga given her balance issues.

The theme "sense of self-control" emerged from the transcripts of those participants using the novel external cardiac monitor—the AliveCor™. They described how the monitor enabled them to assess reliably their heart rate and rhythm whenever and wherever they wanted to do so within a few seconds rather than worrying about what was happening with their heart until they could see their physicians. Lori from the UC group reported, "I enjoy having the AliveCor™ device because it gives me a great sense of control. If I feel even a little bit different I can always go check my rate and heart rhythm, which actually reassures me."

Barriers noted to yoga practice identified by Julie and Paul from the YI group included challenges associated with travel for the group yoga sessions, adherence to the twice-weekly home yoga practice, and a few physical issues with practicing some of the yoga poses, although they pointed out that these were overcome readily by modifications for each participant's needs. Paul shared that his work commitments prevented him from attending two of the group yoga sessions. Participants using the AliveCor ™ reported that their discipline with recording daily EKGs dwindled as they began to feel better from improved AF symptoms.

Discussion

This is the first study to assess the effect of yoga on ERAT after ablation. Although the recruitment rate was set at 51%, the study yielded only 16.7% of the proposed recruitment to the YI group. Recruitment to the UC group could have been 100%, although the researchers stopped recruitment to this group as they did not identify benefits in continued recruitment to the UC group without having a comparable number of participants in the YI group. The primary barriers to the recruitment were distance to travel and commitment to the specific day and time for the instructor-led yoga intervention sessions. Potential approaches to overcome these barriers for future studies might be the use of an online yoga intervention or establishing multiple yoga studios in different geographical areas where the researchers predict potential recruitment. Literature searches revealed two types of online yoga interventions—an online virtual classroom that allowed for real-time bidirectional communication and online pre-recorded videos of the yoga intervention. A study done to assess the effect of mindfulness-based and yoga-based stress reduction programs during the work day

delivered the mindfulness programs in conventional classrooms and through an online virtual classroom that allowed for real-time bidirectional communications.[45] Higher levels of attrition (27.3%) were reported in the in-person mindfulness group compared with the online mindfulness group (3.8%). Another study used a 12-week online-streamed yoga intervention for women after still birth to identify their satisfaction and perceptions of yoga videos posted on a password protected website, with the progression of videos up to 60 minutes in duration.[46] The women reported that the barriers for practicing the online intervention were noisy home environment, lack of motivation, lack of instructor feedback and help with correct alignment in the yoga poses, and the difficulty of learning and practicing yoga poses simultaneously.[46]

The early recurrence rate of atrial tachyarrhythmia in the YI group was 0%; however, it was 75% in the UC group. The AFEQT overall score and symptom score showed meaningful clinical improvement in the YI group compared with the UC group participants. Although no statistical significance could be established given the small sample size, it is worth considering larger randomized control studies to explore the impact of yoga on ERAT after AF ablation.

Both quantitative and qualitative data in this study revealed that QOL improved among participants when their irregular heart rhythm was restored to sinus rhythm. Given that one of the participants disclosed that he had added twice-weekly water yoga approximately two months post-ablation to his home yoga practice, this additional yoga practice could have enhanced the prevention of ERAT in him.

Changes to the stress, depression, and anxiety scores from baseline to end of study were minimal. The relatively higher anxiety state might be related to the fact that a

new diagnosis of AF is compounded with much anxiety about the disease course and that post-ablation these participants continued to be worried about recurrences, which likely was impacting their QOL.

The AliveCor ™ monitor provided a sense of self-control and reassurance to the participants as it helps immediately to detect any concerning arrhythmias without the patient having to wait to see a provider. This sense of self-control and immediate feedback potentially reduces stress and anxiety, both of which can trigger AF. Likewise, the immediate feedback also prevents clinic and emergency department visits for "false" arrhythmias. All the participants reported that they learned to recognize their symptoms of AF once they had an established diagnosis. It is not uncommon for those with AF to experience brief arrhythmia episodes after ablation, including paroxysmal atrial tachycardia, which can be confused with AF. Portable heart monitors aid providers in detecting and differentiating arrhythmias. Even though such external cardiac monitors are most useful in managing AF, sometimes these monitors capture artifacts that are not true electrical signals of the heart. Thus, teaching patients to use the monitor to differentiate between artifacts and true electrical signals of the heart is important in promoting user satisfaction and unnecessary health care costs related to false arrhythmias.

The theme "life style modifications" emerged from participants' focus on improving their diets and exercising more than they had in the past. The ARREST-AF[47] cohort study showed that modifying risk factors such as weight, hypertension, diabetes mellitus, and hyperlipidemia prior to ablation could lead to a decrease in AF frequency and duration as well as a decrease in symptoms and symptom severity. On multivariate analysis, type of AF and risk factor modification were independent predictors of

arrhythmia-free survival. Yoga has shown to improve blood pressure, improve glycemic control in type II diabetes mellitus, reduce low density lipoprotein and very low-density lipoprotein, and to lead to an increase in high-density lipoprotein levels, and increase exercise tolerance.[48] These added benefits of yoga in modifying risk factors for AF also provide a compelling argument for the potentially positive impact of selected gentle yoga postures in individuals with AF.

Atrial fibrosis is an inflammatory process seen in individuals with AF, with convincing evidence showing that the resulting fibrotic changes seen in the atrial myocardium causes deterioration of atrial conduction and impulse re-entrant activity that sustain AF.[50] Whether or not fibrosis is a result of structural remodeling caused by persistent AF or a manifestation of occult myocardial processes that lead to development of arrhythmia is less clear.[49] Nonetheless, yoga has been shown to improve exercise tolerance and positively affect levels of inflammatory markers in patients with heart failure, leading to a trend toward improvements in QOL.[50] Although the investigators did not measure the effect of yoga on heart rate variability nor on inflammatory markers in this study, further studies are warranted to explore these variables and the impact in prevention of AF.

Conclusion

This study did not show statistical significance in any outcome measures, most likely because of the small sample size, although it did show clinically meaningful improvements in the AFEQT score and AFEQT symptom score in the YI participants. The study also showed that 75% of the study sample in the UC group had documented ERAT post-ablation but none of the participants in the YI group had any recurrence of

AF post-ablation. These preliminary findings support the need for future randomized controlled studies to determine the impact of yoga on prevention of atrial arrhythmias.

Conflict of Interest

The authors declare that no economic interest or any conflict of interest exists.

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Table 1: *Demographic Characteristics of Participants, Classification of AF, Prior AF Management, Risk Factors for AF*

	Yoga intervention group (*n* = 2)		**Usual care group (*n* = 4)**		
DEMOGRAPHIC CHARACTERISTICS	**MEAN**	**SD**	**MEAN**	**SD**	***p* value***
Age	65	0	56.75	10.436	**0.533**
Weight (kg)	102.4	41.154	90.375	33.687	**0.800**
Body Mass Index	31.87	9.829	29.120	6.305	**0.800**
DEMOGRAPHIC CHARACTERISTICS	***n***	**%**	***n***	**%**	***p* value****
Gender					**1.000**
Male	1	50	2	50	
Female	1	50	2	50	
Race					
White	2	100	4	100	
Ethnicity					
Non-Hispanic	2	100	4	100	
Years of Education					
1-6+ (College)	2	100	4	100	
Partner status					**1.000**
Married	2	100	2	50	
Living as married with a significant other	0	0	1	25	
Divorced	0	0	1	25	
Living situation					**1.000**
With someone	2	100	3	75	
Alone	0	0	1	25	
CLASSIFICATION OF AF					
Paroxysmal	2	100	3	75	**1.000**
Persistent	0	0	1	25	
Symptomatic	2	100	4	100	
Asymptomatic	0	0	0	0	
PRIOR AF MANAGEMENT					
AF Medications					**1.000**
Rate control***	1	50	3	75	
Both rate and rhythm control****	1	50	1	25	
AF procedures					**0.067**
Cardioversion	1	50	0	0	
Both cardioversion and ablation	1	50	0	0	
None	0	0	4	100	
RISK FACTORS FOR AF					
Sleep apnea					**1.000**
Yes	1	50	3	75	
No	1	50	1	25	

	Yoga intervention group (*n* = 2)		**Usual care group (*n* = 4)**		
	n	**%**	***n***	**%**	***p* value****
Stress					**1.000**
Yes	1	50	1	25	
No	1	50	3	75	
Hypertension					**1.000**
Yes	1	50	1	25	
No	1	50	3	75	

* Exact Mann-Whitney U test significance

** Exact Person Chi-Square

*** Metoprolol Succinate, Metoprolol Tartrate, Atenolol, Nebivolol, Diltiazem CD

****Amiodarone, Dofetilide, Dronedarone

Table 2: *Study Outcome Measures*

Outcome measures	**Yoga Intervention group (*n* = 2)**		**Usual care group (*n* = 4)**		
	Mean (±SD)	Range	Mean (±SD)	Range	***p* value***
Perceived Stress Scale					
Baseline	32 (4.243)	29-35	16.75 (12.121)	7-33	0.267
2 weeks	29 (8.485)	23-35	17.75 (13.574)	6-36	0.533
4 weeks	33.50 (2.121)	32-35	16.50 (17.137)	5-42	0.533
6 weeks	27.50 (7.778)	22-33	19.00 (14.376)	6-38	0.533
24 hours after ablation	21.00 (9.899)	14-28	16.00 (15.853)	5-39	0.533
1-month post-ablation	21.00 (1.414)	20-22	12.75 (14.245)	0-33	0.533
3-month post-ablation			16 (12.49)	3-31	
6-month post-ablation	17.50 (0.707)	17-18	16.50 (12.450)	2-30	1.000
Mean difference between baseline and 6 weeks	4.5 (3.536)	2-7	-2.25 (2.500)	-5-1	0.133
Mean difference between baseline and 1 month post-ablation	11 (2.828)	9-13	4 (4.082)	0-8	0.133
Mean difference between baseline and 6 months post- ablation	14.5 (3.536)	12-17	0.25 (5.058)	-4-6	0.133
State Trait Anxiety Inventory (S-Anxiety scale)					
Baseline	47.00 (1.414)	46-48	46.50 (8.813)	39-59	0.533
2 weeks	46.50 (2.121)	45-48	44.50 (5.196)	41-52	0.533
4 weeks	49.50 (2.121)	48-51	45.00 (5.099)	38-50	0.267
6 weeks	44.00 (7.071)	39-49	43.75 (5.315)	38-50	1.000
24 hours after ablation	45.50 (4.950)	42-49	44.50 (7.234)	36-51	1.000
1-month post-ablation	42.50 (9.192)	36-49	44.25 (6.131)	38-50	0.533
3-month post-ablation			43.25 (8.057)	34-50	
6-month post-ablation	45.50 (2.121)	44-47	44.50 (7.141)	34-50	1.000
Mean difference between baseline and 6 weeks	3 (5.657)	-1-7	2.75 (10.935)	-8-18	1.000
Mean difference between baseline and 1 month post-ablation	4.5 (7.778)	-1-10	2.25 (11.758)	-8-19	0.800
Mean difference between baseline and 6 months post- ablation	1.5 (0.707)	1-2	2 (8.042)	-5-12	1.000
State Trait Anxiety Inventory (T- Anxiety scale)					
Baseline	47 (1.414)	46-48	45.25 (4.113)	40-50	0.533
2 weeks	45 (1.414)	44-46	43.75 (2.872)	40-46	0.800
4 weeks	45.50 (3.536)	43-48	45.75 (2.986)	42-49	1.000
6 weeks	45.00 (5.657)	41-49	44.25 (4.113)	39-48	0.800
	Mean (±SD)	Range	Mean (±SD)	Range	
24 hours after ablation	45.00 (5.657)	41-49	46.75 (4.193)	41-51	1.000
1-month post-ablation	41.00 (5.657)	37-45	44.50 (4.041)	39-48	0.533

Outcome measures	Yoga Intervention group (*n* = 2)		Usual care group (*n* = 4)		
	Mean (±SD)	Range	Mean (±SD)	Range	***p* value***
3-month post-ablation			44.50 (3.697)	39-47	
6-month post-ablation	44.50 (4.950)	41-48	44.25 (5.560)	36-48	0.800
Mean difference between baseline and 6 weeks	2(4.243)	-1-5	1 (4.243)	-2-7	0.800
Mean difference between baseline and 1 month post-ablation	6 (4.243)	3-9	0.75 (2.062)	-2-3	0.133
Mean difference between baseline and 6 months post- ablation	2.5 (3.536)	0-5	1 (2.582)	-2-4	0.533
Beck Depression Inventory					
Baseline	17.50 (6.364)	13-22	10.75 (7.974)	2-18	0.533
2 weeks	13.50 (0.707)	13-14	7.25 (4.992)	2-14	0.267
4 weeks	14.50 (3.536)	12-17	7.00 (7.348)	3-18	0.533
6 weeks	11.50 (7.778)	6-17	7.00 (4.967)	3-14	0.533
24 hours after ablation	9.00 (2.828)	7-11	4.50 (4.655)	0-11	0.267
1-month post-ablation	3.00 (2.828)	1-5	3.50 (3.873)	0-9	1.000
3-month post-ablation			2.75 (2.986)	0-7	
6-month post-ablation	3.50 (2.121)	2-5	2.75 (3.403)	0-7	0.800
Mean difference between baseline and 6 weeks	6.00 (1.414)	5-7	3.75 (8.302)	-5 - 15	0.533
Mean difference between baseline and 1 month post-ablation	14.5 (3.536)	12-17	7.25 (7.890)	0-18	0.533
Mean difference between baseline and 6 months post- ablation	14 (8.485)	8-20	8 (7.659)	2-18	0.533
Atrial Fibrillation Effect on QualiTy of life					
Baseline	51.85 (10.479)	44.44-59.26	70.83 (17.738)	47.22-89.81	0.267
6weeks	63.89 (19.643)	50.00-77.78	71.07 (23.611)	38.89-95.37	1.000
1-month post-ablation	74.08 (1.308)	73.15-75.00	86.83 (11.94)	70.47-99.07	0.533
3-month post-ablation			90.28 (13.016)	71.30-100	
6-month post-ablation	90.74 (10.479)	83.33-98.15	94.91 (2.205)	92.59-97.22	1.000
Mean difference between baseline and 6 weeks	-12.04 (9.164)	-18.52-5.56	-0.233 (7.500)	-7.41-8.33	0.267
Mean difference between baseline and 1 month post-ablation	-22.23 (9.171)	-28.71- - 15.74	-15.998 (17.462)	-40.74- - 0.10	0.533

Outcome measures	**Yoga Intervention group (*n* = 2)**		**Usual care group (*n* = 4)**		
	Mean (±SD)	Range	Mean (±SD)	Range	***p* value***
Mean difference between baseline and 6 months post- ablation	-38.89 (0.000)	-38.89- -38.89	-24.075 (16.035)	-45.37 - -6.49	0.533
Atrial Fibrillation Effect on QualiTy of life - Symptoms score					
Baseline	70.5 (6.364)	66-75	81.25 (17.515)	58.33-100	0.533
6weeks	72.92 (14.729)	62.5-83.33	77.09 (17.177)	54.17-95.83	1.000
1-month post-ablation	85.42 (20.626)	70.83-100	94.792 (6.250)	87.5-100	1.000
3-month post-ablation			90.625 (18.75)	62.50-100	
6-month post-ablation	100	0	96.88 (3.988)	91.67-100	0.533
Mean difference between baseline and 6 weeks	-2.415 (8.365)	-8.33-3.5	4.165 (3.401)	0-8.33	0.267
Mean difference between baseline and 1 month post-ablation	-14.92 (26.990)	-34-4.17	-13.543 (14.184)	-33.34-0	1.000
Mean difference between baseline and 6 months post- ablation	-29.5 (6.364)	-34- -25	-15.625 (19.054)	-37.5-8.33	0.533
AF burden					
AF burden in days	0	0	3.25 (2.363)	0-5	0.267
Early Recurrence of Atrial Tachyarrhythmia					
	***n* (percentage)**		***n* (percentage)**		***p* value ****
Yes	0 (0%)		3 (75 %)		0.400
No	2 (100%)		1 (25%)		

* *p* value for exact Mann-Whitney U test significance

****** *p* value for Person Chi-Square

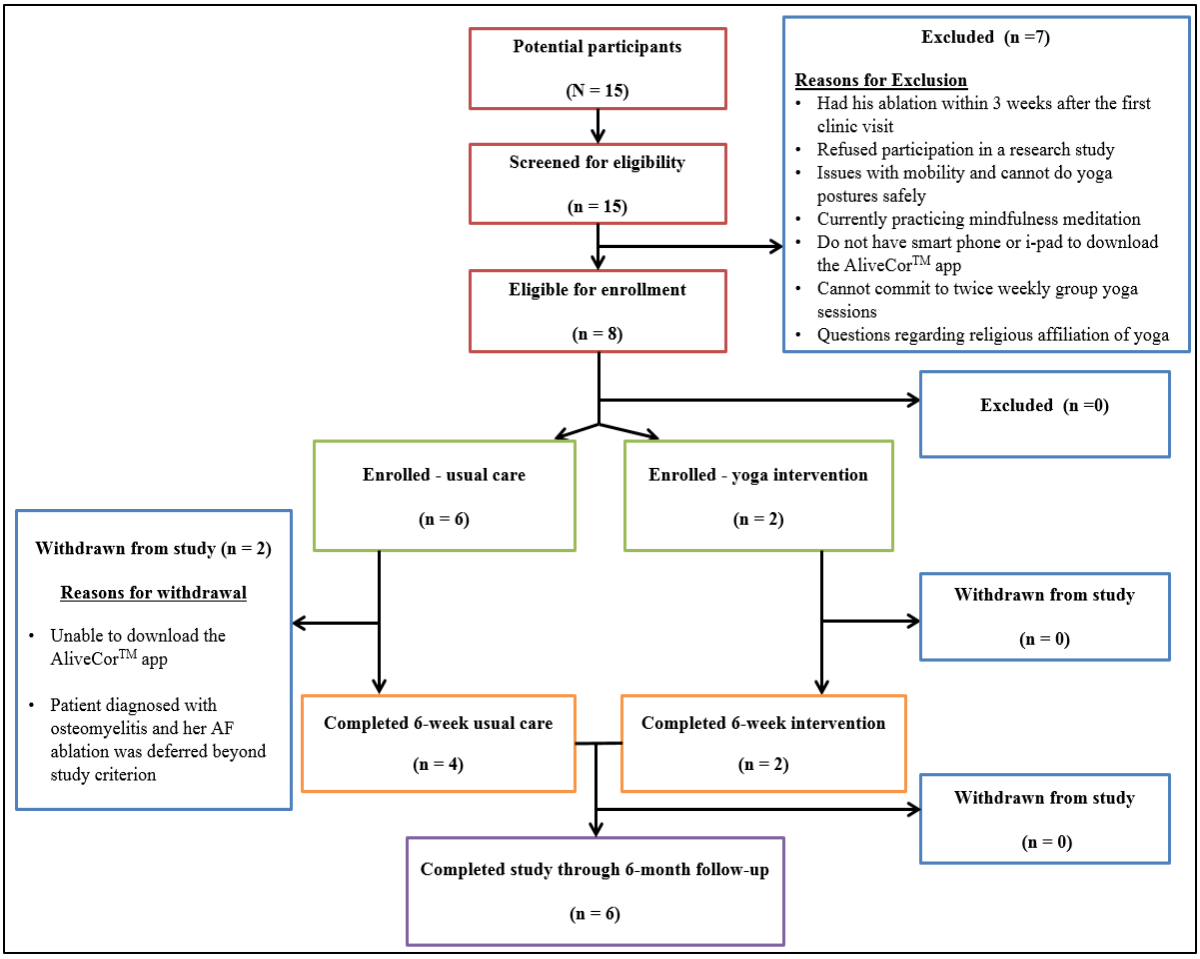

Figure 1. Participant Study Flow

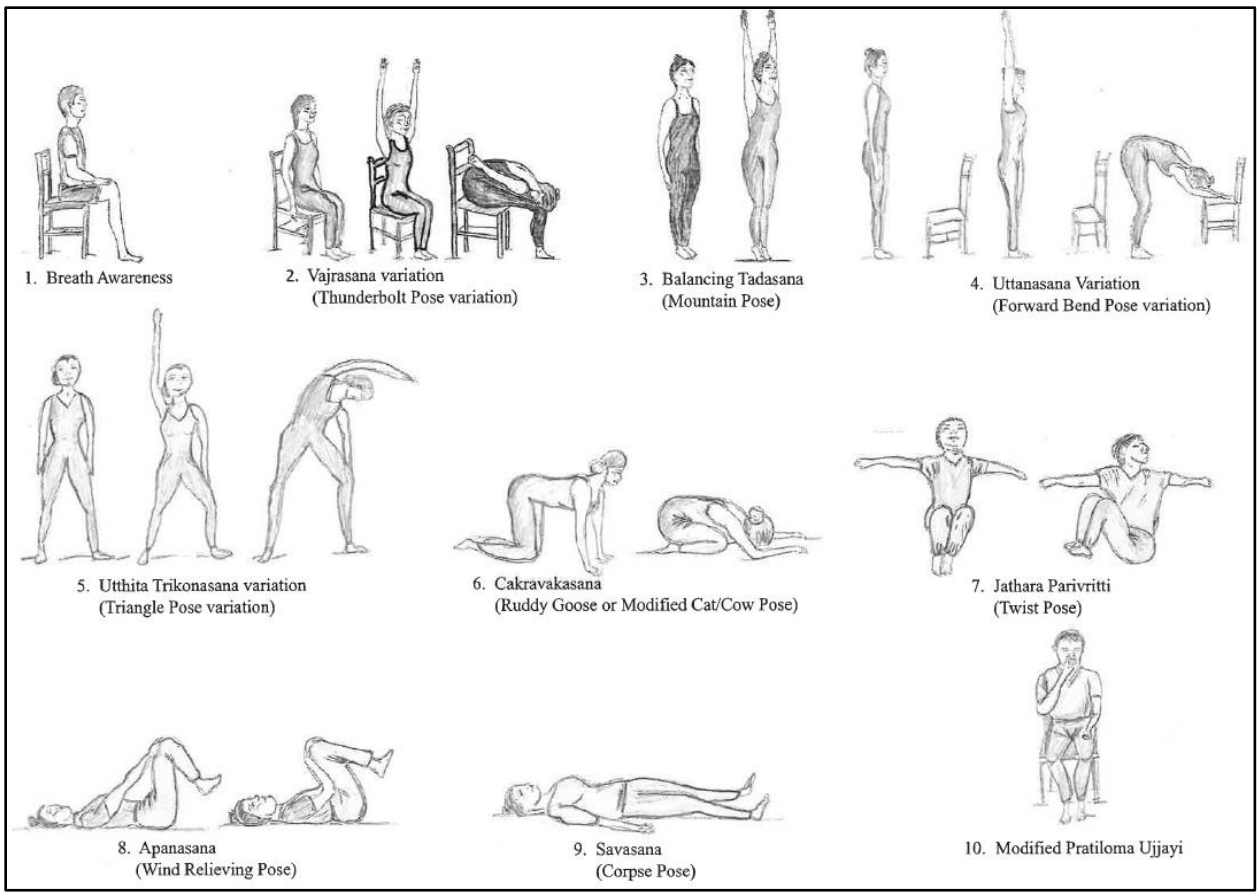

Figure 2. Viniyoga Sequence

CHAPTER FIVE: CONCLUSION

The purpose of the research study conducted to fulfill requirements for this dissertation was to assess the feasibility of a twice-weekly 6-week Viniyoga intervention for prevention of early recurrence of atrial tachyarrhythmia (ERAT) after atrial fibrillation (AF) ablation in participants diagnosed with paroxysmal or persistent atrial fibrillation. The findings describe the intervention group participants' experiences with the yoga intervention, their perceptions of its efficacy, barriers to engaging in the yoga practice, and how they believed that yoga could help them, as well as reasons for participants in the usual care alone (UC) group declining to participate in the yoga intervention. Data were also collected regarding the impact of the yoga intervention on AF symptoms of stress, depression, and anxiety; and all participants' health-related quality of life (QOL).

Recruitment to the study intervention group was challenging. The major reasons for participants declining participation in the yoga intervention were related to the travel distance and challenges in committing to a specific time of a day for instructor-led yoga sessions. Other reasons included current practice of yoga or mindfulness meditation, lack of a smart phone or iPad to download the Alivecor^{TM} app, and questions about the affiliation of yoga with a religion that the participants did not practice.

The instructor-led yoga classes were designed to introduce participants to a twice-weekly 50-minute yoga practice that after the 6-week intervention had concluded, could be done independently at home. The two participants in the yoga intervention plus usual care (YI) group reported that yoga made them feel calm and relaxed and that it improved

their balance. They also reported that they could not do one or two of the yoga poses as demonstrated by the instructor, but that the instructor appropriately modified the poses to meet their needs. The mean number of instructor-led yoga classes participants attended was 11 (±1.414) out of a total of 12 sessions. These participants reported practicing at-home yoga 1 to 4 times a week. The two common reasons for not attending all of the instructor-led sessions and not engaging in twice-weekly at home yoga sessions were related to work commitments and family care giver responsibilities. Participants in the UC group reported that they had never thought about practicing yoga themselves but would be willing to consider it after participating in this study.

Although statistical significance was not possible because of the small sample size, clinically meaningful improvement was noted in AF symptoms and quality of life (QOL) from baseline to 6-month post-AF ablation in participants in the YI group compared with the UC group. Decreases in stress, depression, and anxiety scores were noted although minimal. Thus, Viniyoga home practice warrants further investigation as a means of prevention of ERAT after ablation.

Background information to support the investigation of yoga as an appropriate intervention for prevention of AF episodes and symptoms was presented in Chapter Two, *Effect of Yoga on the Autonomic Nervous System: Clinical Implications in the Management of Atrial Fibrillation.* The literature was reviewed to assess the impact of yoga on stress, anxiety, depression, and autonomic nervous system balance as all these contribute to the initiation and maintenance of AF. Even though the time span of the yoga interventions reported in the studies reviewed ranged from a few minutes to months, all the studies demonstrated some beneficial effect in maintaining autonomic balance and

significant impact on selected physiological and psychological factors, thereby improving the participants' overall QOL. Given its impact on modulating autonomic system balance and reducing psychological stress, selected styles of gentle yoga might be considered as cost-effective, complementary health approaches in managing AF episodes and symptoms. Further rigorous study is warranted to clarify the specific mechanisms involved in the use of yoga in patients diagnosed with AF. To date, two studies have assessed the impact of yoga on paroxysmal AF. No studies have identified the impact of yoga in preventing ERAT after AF ablation in adults with paroxysmal and persistent AF who undergo AF ablation.

Chapter Three, *A Feasibility Protocol to Assess the Effect of Yoga on Early Recurrence of Atrial Tachyarrhythmia after Atrial Fibrillation Ablation* presented the rationale for the choice of selected postures of Viniyoga as an appropriate style of yoga for prevention of ERAT in persons with AF. A psychoneuroimmunology theoretical framework guided the study design, selection of outcome measures, and interpretation of findings. The reason for the sequence of the yoga postures was also detailed in the chapter. The sequential mixed methods design was used for the study. This approach involved an initial quantitative data collection phase followed by a qualitative data collection phase using a semi-structured interview of the participants from the quantitative phase of the research. Thematic content analysis of the qualitative data collected through semi-structured interviews provided further insight into the expansion of the quantitative data analysis results.

Chapter Four, *Effect of Yoga on Early Recurrence of Atrial Tachyarrhythmia after Atrial Fibrillation Ablation: Results of a 6-week Viniyoga Intervention* presented the

results of the feasibility of a Viniyoga intervention and its impact on stress, anxiety, depression, AF episodes and symptoms, ERAT after AF ablation, and health-related QOL in study participants. Feasibility data were collected as recruitment, retention, and adherence rates during the 6-week instructor-led yoga intervention and twice-weekly home yoga practice. Although retention and adherence rates supported the feasibility of the intervention, recruitment to the YI group was challenging. Clinically meaningful improvements were noted in AF symptoms and QOL in participants in the YI group compared with the UC alone group from baseline to 6 months post-AF ablation. Also, reported are changes in anxiety, depression, and stress scores. Data were collected using self-report questionnaires. The YI participants' perceptions of yoga and their experiences with participation in the study were reported from the semi-structured interview data collected at the end of 6-month post-AF ablation clinic visit.

Lessons Learned

As a nurse practitioner (NP) with 6 years of experience in this role, upon launching my clinical study, I expected that I might face a number of variables that would influence the conduct of the study. Although I had this level of awareness from the outset of my research project, I became aware of other challenges that can arise not only from the study population but also from patient providers and the care system itself.

As a consumer of findings from clinical studies, I was already aware that chronic low accrual rates negatively influence study findings and the generalizability of study findings. However, I was somewhat unprepared for the challenges I would face in recruiting study participants, causing me to assess a variety of steps to first address

known challenges, and then subsequently to overcome potential and real recruitment challenges. In this section, I provide an overview of the recruitment challenges encountered, and the procedures and strategies I used to counter these challenges—my lessons learned.

First, a much greater than expected number of potential participants from the medical center's AF clinic from which I was recruiting met one or more of the exclusion criteria—more than I had anticipated. The most common reason for ineligibility, particularly for those who were willing to enroll in the yoga intervention group was the location of the intervention and thus the distance that they would have to travel twice a week to the group yoga sessions over the course of 6 weeks. The second most common reason for ineligibility was that many of the patients with AF were actively trying a few complementary modalities such as yoga and meditation on their own and thus not eligible. Also, a number of patients were in phases of their treatment that did not align with my proposed study, making them ineligible. A few participants' treatment plans changed after they were recruited for the study because of unexpected co-morbid conditions, treatment of which took priority over their AF ablation procedures. In addition, and as somewhat of a surprise, was the number of potential participants' who associated yoga with religions that they did not practice.

Because the study setting was an academic medical center that serves as a referral center, patients often travel several hours or more to clinics to receive their medical care, making potential participants most sensitive to any additional travel that might be associated with study participation. These system-related challenges to recruitment were not readily evident initially to me as a beginning researcher.

I also learned procedural formalities associated with conducting research, including what it takes to obtain approval for studies involving human subjects, and, of course, the effort and detail required for the proposal I submitted to the IRB-HSR for its approval. I learned that obtaining these approvals could be a lengthy process despite planning. Also, I became aware through this process of the importance of advertisements for the research study and the expense that this can pose, especially in small studies that are supported by a limited and fixed budget. However, I learned of several awards for which I applied and obtained a small amount of funds to cover the cost of preparing brochures for distribution in the AF Clinic and to create the DVDs to guide home yoga practice.

Regarding potential provider-related issues, I was aware that patients' health care providers are seen as the gatekeepers to the pools of participants for clinical research, and that gaining support from the providers was critical from the outset. Just making all physicians and NPs in the AF Clinic aware that I was developing a protocol involving patients with AF, led me to consult with the AF Clinic director and other physicians and NPs regarding the study plan and design. Also, I included the AF Clinic director as a research team member in my IRB proposal and also invited him to serve as an external dissertation committee member. Additionally, meetings were held with the clinic NPs to identify potential participants and to obtain their feedback and support. I knew it was important to have access to the clinic appointment list, which permitted the screening of potential participants to occur outside of the small clinic space. Once a potential participant was identified, I was able to speak with the clinic team members to alert them that one of their patients could be a potential participant for the study. When the clinic

team agreed that the patient could be approached based on the patient's ablation date, I was able to see the patient as a potential study participant in a private room to introduce the study, answer questions, and obtain the informed consent.

Competition for study participants is often experienced in research-intensive settings, which was the situation I encountered. At the time I launched my study, I learned that there were at least three physician-sponsored clinical trials within the medical center open concurrent with my study, all competing for potential participants from the same population of patients diagnosed with AF. Upon learning this, I simply had to acknowledge this situation as a reality of conducting research in an academic medical center.

I found few suggestions and guidelines on methods and strategies in the literature to overcome common challenges encountered and to enhance recruitment in my study population. Thus, I worked to achieve full support of all of physicians and NPs in the AF Clinic and was able to see study participants within the context of their usual clinic visits. However, even with full support of the entire AF Clinic providers, the recruitment challenges remained difficult. Although compensation to study participants to offset their time and effort in research sometimes aides in recruitment, the fact that I was using a novel heart rate monitoring device that participants would keep or a small monetary payment as compensation for time and effort devoted to the study, these were less than promotional for recruitment into the intervention arm of the study.

In summary, I learned that conducting clinical research is time consuming and that recruitment of study participants is challenging. I also experienced firsthand that 'attention to detail' is important throughout the research process and pays off in the end.

My goal in sharing my 'lessons learned' and the challenges experienced in my research with others is that these may prove helpful to them in conducting similar research in the future and gives emphasis to the importance of clinical research, which provides reliable and valid findings to drive improvements in patient care.

Implications for Practice

Given that AF symptoms can affect QOL significantly and that none of the current medical management guarantees arrhythmia free survival, identifying cost-effective complementary health-enhancing therapies such as yoga might help in promoting QOL in individuals with AF and decrease health care costs. However, the challenge for providers in recommending yoga for patients with AF is to guide them in selecting safe yoga postures from the existing varieties of yoga styles currently in the public domain. To make that possible, it is important to create yoga sequence such as the one designed in the current study and offer it through cardiac rehabilitation programs. This might be one of the best ways to ensure that patients have access to a trained yoga instructor and a safe yoga sequence that they can then practice safely at home.

Hypertension, diabetes, hyperlipidemia, and obesity have been identified as risk factors for AF. Given that research has revealed yoga can decrease blood pressure and maintain blood sugar and cholesterol levels, those having these identified risk factors might find that practicing yoga may prevent them from developing AF.

Using technology such as AliveCor ™ external monitors will help patients identify their AF episodes as soon as they start noticing arrhythmia-related symptoms and seek immediate medical attention as appropriate. Prolonged AF may result in inflammatory changes in the atria creating a substrate for maintenance of AF leading to

persistent AF. Hence, early diagnosis and treatment of AF decreases recurrence rate and prevent structural changes in the heart.

Many of the participants in this research study identified that stress is a trigger for their AF. Those in the yoga intervention group acknowledged that yoga helped them to remain more relaxed and to gain insight into their individual balance and flexibility. Yoga is an effective intervention that providers can recommend for patients with high levels of stress.

Future Research

The findings of this feasibility study will inform future research and study design for prevention of ERAT in patients with AF undergoing ablation, including those older than 65, which was the maximum age criterion for this study. This study provides insight into barriers for study recruitment, provides extensive detail on a safe yoga intervention for patients with AF, and identifies validated study measures that can be used in data collection in future studies. It also reveals the importance of mixed methods design in identifying the efficacy of a yoga intervention that is currently not well-established in patients with AF and the use of easy-to-use reliable technology that currently exists to detect AF.

One of the major barriers for recruitment to this study was the difficulty that potential participants experienced in attending instructor-led yoga sessions at designated times and on specific days. Future research could be designed to include multiple yoga studios with flexibility of the days and times when participants can participate in the yoga intervention. There are researchers who use online yoga interventions, yet its safety is not established in patients with arrhythmias. Although the researchers in this study used the

same yoga posture sequence with same oral instructions for treatment fidelity purposes, it is important that we design minor modifications in the yoga poses to make these more individualized and safe for all participants. These individualized changes can be made only in instructor-led yoga sessions and may not be possible with online yoga interventions.

This study did not measure heart rate variability nor detect inflammatory markers. Future large-scale studies should be designed to assess the impact of yoga on heart rate variability and inflammatory markers in individuals with AF, which will aid providers and researchers in understanding more fully the mechanisms through which yoga prevents AF.

There are other atrial arrhythmias, including inappropriate sinus tachycardia that are triggered by stress and anxiety. Yoga could be a potential intervention in reducing these arrhythmia symptoms and in maintaining autonomic nervous system balance, thereby preventing these arrhythmias. Thus, future studies are warranted to evaluate the efficacy of yoga in preventing other atrial arrhythmias.

This study did not show any statistical significance in the outcome measures, most likely because of the small sample size. It did show, however, clinically meaningful improvements in the Atrial Fibrillation Effect on QualiTy-of-Life questionnaire's overall score and its symptom score in those practicing the yoga intervention. The study also showed that 75% of the study sample in the UC group had documented ERAT but none of the participants in the YI group had any recurrence of atrial tachyarrhythmia post-ablation. These preliminary findings support the need for future randomized controlled

studies to determine the impact of yoga on prevention of atrial arrhythmias after AF ablation.