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The Effect of Biofeedback on Function in Patients with Heart Failure

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Abstract Decreased HRV has been consistently associated with increased cardiac mortality and morbidity in HF patients. The aim of this study is to determine if a 6-week course of heart rate variability (HRV) biofeedback and breathing retraining could increase exercise tolerance, HRV, and quality of life in patients with New York Heart Association Class I-III heart failure (HF). Participants ($N = 29$) were randomly assigned to either the treatment group consisting of six sessions of breathing retraining, HRV biofeedback and daily practice, or the comparison group consisting of six sessions of quasi-false alpha-theta biofeedback and daily practice. Exercise tolerance, measured by the 6-min walk test (6MWT), HRV, measured by the standard deviation of normal of normal beats (SDNN), and quality of life, measured by the Minnesota Living with Congestive Heart Failure Questionnaire, were measured baseline (week 0), post (week 6), and follow-up (week 18). Cardiorespiratory biofeedback significantly increased exercise tolerance ($p = .05$) for the treatment group in the high ($\geq$31%) left ventricular ejection fraction (LVEF) category between baseline and follow-up. Neither a significant difference in SDNN ($p = .09$) nor quality of life ($p = .08$), was found between baseline and follow-up. A combination of HRV biofeedback and breathing retraining may improve exercise tolerance in patients with HF with an LVEF of 31% or higher. Because exercise tolerance is considered a strong prognostic indicator, cardiorespiratory biofeedback has the potential to improve cardiac mortality and morbidity in HF patients.

Keywords Heart rate variability · Biofeedback · Heart Failure · Exercise tolerance · Functional status · Quality of life · Breathing retraining

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Background

Heart Failure

Heart failure (HF) is a complex syndrome that often results from any cardiac or chronic metabolic disorder, for example, ischemic heart disease, hypertension, diabetes mellitus, cardiomyopathy, or hyperthyroidism, that impairs the ability of the heart's ventricles to effectively eject blood (Carelock and Clark 2001). HF is a significant problem in cardiovascular medicine. Between 1979 and 2000, there has been a 149% increase in the incidence of HF, and in 2003, there were 550,000 new cases. In 2004, the estimated direct and indirect costs for HF in the United States are $28.8 billion. In 2001, the reported mortalities were 52,828 and the death rate from this condition rose 135% between 1979 and 1998. The median survival rate after onset of symptoms

is 1.7 years (American Heart Association 2003). Thus despite advances in treatment, prognosis remains grave. New treatment options are needed.

Heart Failure and the Autonomic Dysfunction

A hallmark of the onset and progression of HF is autonomic imbalance with increased sympathetic activity (Accurso et al. 2001). Initially, the increase in sympathetic activity serves to preserve cardiac function; however, over time the enhanced sustained adrenergic drive contributes to the onset and severity of symptoms, functional impairment, progressive ventricular dysfunction and remodeling (Carelock and Clark 2001; Cesario and Fonarow 2002; Sabbah 1999). As a result, the cardiovascular system is less reflexive in maintaining long-term homeostasis via responding to "rapid dynamic responses to physiologic needs and environmental changes" (Accurso et al. 2001, p. 41). The heart's decreased versatility, or heart rate variability (HRV), in meeting its environmental demands is associated with morbidity, sudden death, all cause mortality, and several poor health outcomes (Liao et al. 1997).

HRV and Heart Failure

HRV is defined as the fluctuations in heart rate (HR) from beat-to-beat as measured in milliseconds. The standard deviation of normal-to-normal beats (SDNN) is significantly related to cardiac function (Task Force of the European Society of Cardiology and North American Society of Pacing and Electrophysiology 1996). Depressed HRV is consistently observed in HF patients (Appel et al. 1989; Casolo et al. 1989; Kamath and Fallen 1993; Kienzle et al. 1992; Nolan et al. 1992; Tsuji et al. 1996). It is related to severity of left ventricular dysfunction, and time domain measures parallel the severity of the disease (Nolan et al. 1992). Furthermore, most patients in very advanced stages of HF have a drastic reduction in HRV where the low frequency (LF) component was undetectable despite evident signs of sympathetic activation (Kienzle et al. 1992). Additionally, HF patients with low HRV ($\leq$50 ms) as compared with those with high HRV ($\geq$100 ms) have a higher risk for death. Importantly, low HRV was a better predictor than other conventional methods. Conventional methods included cardiothoracic ratio, left ventricular and end-systolic diameter and serum sodium levels (Nolan et al. 1992).

Treatment Considerations in Heart Failure

Pharmacological

Several studies have investigated medicinal therapy to alter autonomic function and improve cardiac function. Substantial evidence demonstrates Beta-adrenoreceptor antagonist, or beta-blockers, as an agent that increases HRV (Aronson and Burger 2001; Cesario and Fonarow 2002; Choudhury et al. 1996; Cleland 2000; Cohn 2003; Copie et al. 1996; Pritchett and Redfield 2002). However, lifetime costs, side-effects contribute to non-compliance and improper use (Butler et al. 2003; Evangelista et al. 2003). Also, recent research found although medication approaches do improve survival and morbidity they do not have a beneficial impact on the quality of life of individuals who have HF (Dobre et al. 2006).

Behavioral

There is considerable evidence that behavioral treatments reduce the risk of cardiac events and death in individuals who have heart disease (Aldana et al. 2003; Billings 2000; Koertge et al. 2003) as well as improve psychological well-being (van Dixhoorn et al. 1990). Exercise, stress management and relaxation, cognitive behavioral therapy, and smoking cessation have been found to increase HRV (Stein et al. 1999; van Dixhoorn et al. 1990; van Dixhoorn and White 2005). Despite the above mentioned positive impact of behavioral interventions compliance is a significant problem in HF patients (Evangelista et al. 2003).

Biofeedback and Heart Failure

HRV biofeedback is intended to specifically target autonomic function. It has demonstrated clinical efficacy in asthma, hypertension, as well as cardiac disorders other than HF (Cowan et al. 1990; Del Pozo et al. 2004; Lehrer et al. 1986, 2000; however, few studies using biofeedback to improve HRV in HF patients have been conducted.

Increased HRV is synonymous with parasympathetic tone or vagal tone (Bernardi et al. 2002; Gevirtz and Lehrer 2005; Porges 1995). Several studies have investigated slow breathing near 6 breaths per min and found parasympathetic outflow appears to be controlled by breathing patterns, there is an increase in RSA amplitude and baroreceptor sensitivity, biological body systems are synchronized (Reyes del Paso et al. 1992), increased homeostatic reflexes, lower blood pressure, improved lung function (Lehrer et al. 2000), and improved oxygen saturation and exercise tolerance (Bernardi et al. 2002). These results also suggest balance between the sympathetic and parasympathetic nervous systems, which should also increase HRV.

Luskin et al. (2002), conducted a controlled pilot study investigating stress management in 33 elderly patients with documented NYHA class I-III HF. Participants attended eight training sessions over a course of 10 weeks. HRV, depression, anxiety, stress management, optimism,

emotional distress, and functional capacity/6-min walk test (6MWT) were the primary outcome measures. Significant improvements ($p \leq .05$) were observed in perceived stress, emotional distress, distance walked on the 6MWT, anxiety and depression. The authors noted that there were nominal improvements in HRV in SDNN in the treatment group that did not differ statistically from the control group. This finding may have been due to a lack of power considering only 14 participants of the 33 that were randomized completed the study. A noteworthy limitation of this study is that is the investigators used partial randomization.

Of all the cardiac disorders, HF is the only cardiac disease increasing in incidence and prevalence (American Heart Association 2003; Senni et al. 1999; Szlachcic et al. 1985); however, compared to coronary artery disease and myocardial infarction where cardiorespiratory biofeedback and breathing retraining have shown promising results in improving HRV (Cowan et al. 1990; Del Pozo et al. 2004; Lehrer et al. 2000), quality of life and exercise tolerance (Luskin et al. 2002) there has been a paucity of research in biofeedback methods in HF patients. Although the underlying physiological mechanism is not fully understood, the literature supports biofeedback and breathing retraining as a treatment to reverse decreased HRV (Cowan et al. 1990; Reyes del Paso et al. 1992).

The Present Investigation

The aim of this research is to examine if a 6 week course of cardiorespiratory biofeedback with patients with known NYHA Class I-III HF could increase exercise tolerance and HRV, and improve quality of life.

Main Hypotheses

Hypothesis 1: Exercise Tolerance Exercise tolerance, as measured by the distance walked in meters on the 6-min walk test (6MWT), will significantly increase from week 0 (Visit 1), to week 6 (Visit 7) and week 18 (Visit 8) in the treatment group (Biofeedback Training Group I), and that the improvement in the treatment group will be larger that improvement in the comparison group (Biofeedback Training Group II).

Hypothesis 2: HRV HRV, as measured by Standard Deviation of Normal to SDNN, will significantly increase from week 0 (Visit 1), to week 6 (Visit 7) and week 18 (Visit 8) in the treatment group (Biofeedback Training Group I), and that the improvement in the treatment group will be larger that improvement in the comparison group (Biofeedback Training Group II).

Exploratory Hypothesis

Hypothesis 1: Quality of Life Quality of life as measured by the Minnesota Living with Congestive Heart Failure Questionnaire (LHFQ) will significantly increase from week 0 (Visit 1), to week 6 (Visit 7) and week 18 (Visit 8) in the treatment group (Biofeedback Training Group I) more than for the comparison group (Biofeedback Training Group II).

Methods

Study Design

This study was a 2 (treatment vs. control) × 3 (pre, post, and follow-up) randomized, single-blind, controlled, factorial design with repeated measures. Participants who agreed to participate and met the criteria were randomly assigned to the treatment group (Biofeedback Training Group I) or the attention placebo comparison group (Biofeedback Training Group II). Randomization was stratified by pre-treatment left ventricular ejection fraction (LVEF) values and gender. LVEF values were stratified into high (50 to 35%), medium (34 to 19%), and low (18 to 3%) categories for each gender. The investigators were blind to the randomization order.

Participants

Patients were recruited from the International Heart Institute in the Heart Failure Clinic at Loma Linda University Medical Center (LLUMC) in Loma Linda, California. Inclusion criteria included documented Heart Failure NYHA Class I, II, or III, a left ventricular ejection fraction (LVEF) of 50% or lower, stable condition as evidenced by an absence of medication changes within the 2 prior weeks to their initial study treatment visit, and every participant provided written consent for participation. Exclusion criteria were: (1) concurrent participation in another research study or participation in another research study within the past 30 days; (2) acute coronary syndrome such as unstable angina, or acute myocardial infarction within the past 6-weeks; (3) non-bypassed left main coronary artery with a luminal stenosis of 50% or more, except on patients where bypass was not feasible or refused; (4) Coronary Artery Bypass Grafting (CABG) or Percutaneous Coronary Intervention (PCI) within the past 3-months; (5) clinically significant valvular heart disease; (6) acute myocarditis; (7) presence of a permanent continuous pacemaker; (8) presence of a cardiac arrhythmia, for example atrial fibrillation,

making HRV uninterpretable; (9) uncontrolled hypertension, defined as a systolic blood pressure of 180 mmHg or more and/or a diastolic blood pressure of 110 mmHg, measured as the average of at least two readings, each obtained on different occasions; (10) any medical, psychological, cognitive, social, or legal condition that would have interfered with the ability to give and Informed Consent and/or his or her capacity to comply with all study requirements, including the necessary time commitment; (11) a diagnosis of cardiomyopathy where a beta-blocker was being titrated to the optimal dose; (12) any etiology of heart failure that was treated with dobutamine or any injectable inotropic agent. All patients provided written consent. Approval from the institutional review boards at Loma Linda University Medical Center and Alliant International University was obtained. Refer to Fig. 1 for a flow chart of experimental design and study participation.

Pretreatment Measures

Demographics Health Questionnaire

Participants asked to report their education, race, socioeconomic status, alcohol consumption, tobacco use and current medications (Del Pozo et al. 2004).

Outcome Measures

The following outcome measures were given during weeks 1, 6, and 18.

6 Minute Walk Test

The 6MWT is a self-paced, submaximal corridor walk during which duration of time, distance walked, and perceived exercion are measured (Adams and Bennett 2000).

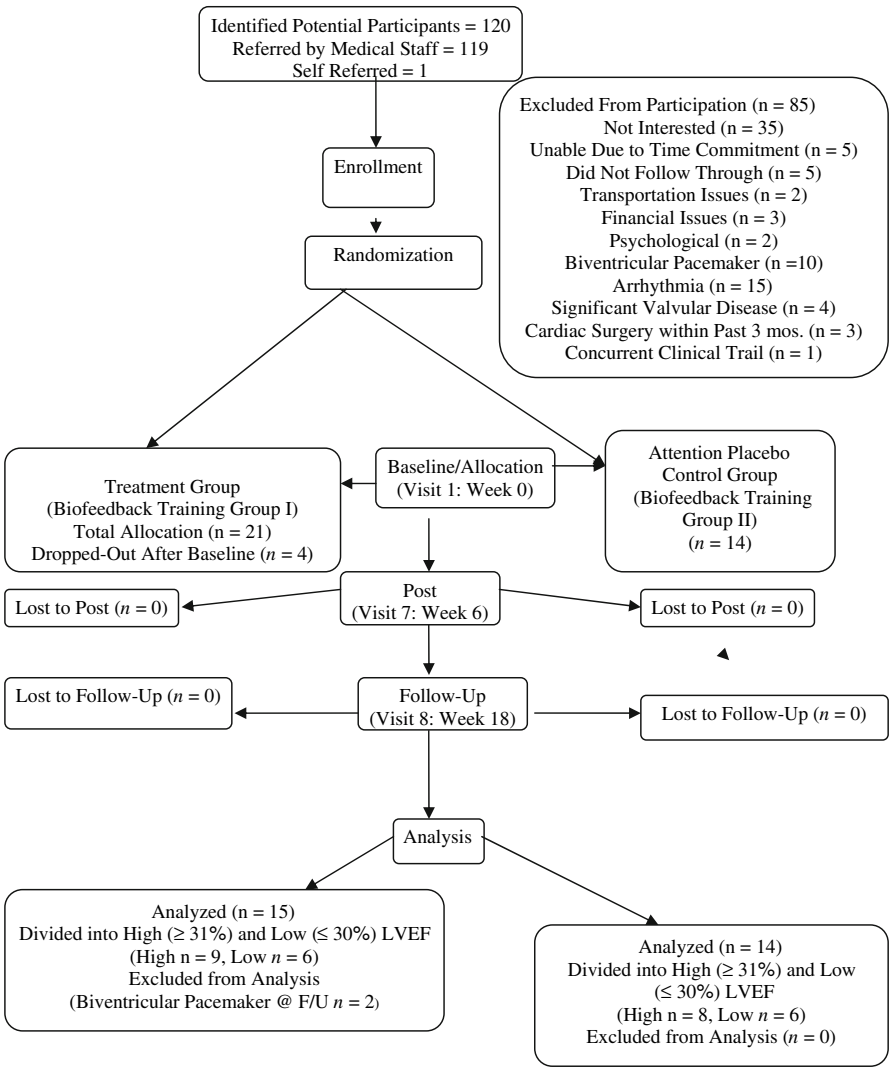

Fig. 1 Experimental design and flow chart of study participation

The American Thoracic Society (2002) standardized guidelines as well as their published manual for administration and safety procedures were followed. The 6MWT is an indicator of functional capacity with regard to activities of daily living, and a predictor of morbidity and mortality (Adams and Bennett 2000; American Thoracic Society 2002). It is tolerated well by HF patients (Guyatt et al. 1985; Lipkin et al. 1986), and has high interclass correlations ($r \geq .98$) between daily sessions (Kervio et al. 2004). The 6MWT was administered in the hallway. The hallway was flat and free from obstacles, was low in human traffic, and was marked in feet to record distance walked. The total distance walked was converted into meters after completion of test. The participant was given instructions regarding the test and was instructed to stop walking immediately if he/she experienced chest pain, unbearable shortness of breath, leg cramps, or became unstable on their feet (American Thoracic Society 2002).

Borg Scale

The Borg Scale quantifies of symptoms of dyspnea and fatigue. These are the two most common symptoms that are thought to limit exercise capacity in HF patients (Lipkin and Poole-Wilson 1986). Each participant was asked to verbally grade their perceived level of severity of dysnpea and fatigue on a 10-point scale pre and post 6MWT per standard protocol (American Thoracic Society 2002). A zero rating on this scale indicates no symptomology and a 10 indicates maximal symptomology (Borg 1982).

Physiological Monitoring and Instrumentation

HRV measurements were recorded using one J&J Engineering I-330-C-2 + 12 Channel Physiologic Monitoring System (J&J Engineering, Inc., Poulsbo, WA) connected to a laptop personal computer (PC) with a one gigaHertz (GHz) Pentium processor and a 17-in. monitor. HRV analysis was conducted using HRV Analysis Software for Windows (Biosignal Analysis and Medical Imaging Group, University of Kuopio, Kuopio, Finland). These procedures met the instrumentation requirements for recording of HRV and HRV analysis outlined by the Task Force of the European Society of Cardiology and North American Society of Pacing and Electrophysiology (1996). Electrocardiograph (ECG) data was recorded using an ECG electrode cable, disposable electrodes, and conductive cream placed on the right and left wrist. Abdominal respiratory deviations were measured using a pneumograph magnetic strain gauge secured around the upper abdomen. Breathing pacing and HRV feedback stimuli were displayed on a 17-inch monitor using Physiolab software. All participants listened to a neutral travel story on a compact disc, ("Inside the Hidden Kingdom" by Jessica Maxwell from *The Best American Travel Writing*, 2000) during HRV measurement.

The Task Force of the European Society of Cardiology and North American Society of Pacing and Electrophysiology (1996), recommends short term measurements of HRV should be 5 min and long term measures should be 24 h for standardization purposes. In this study, HRV measurements were 5 min using similar conditions for each participant of a resting baseline with spontaneous breathing. A long term measurement was not feasible for this study.

HRV is generally measured using the normal-to-normal RR interval (NN), which is the interval between each QRS complex. In order to quantify HRV, the standard deviation of the NN interval (SDNN) was calculated. SDNN is considered the most complete measure of HRV as is "reflects all the cyclic components responsible for variability in the recording period" (Task Force of the European Society of Cardiology and North American Society of Pacing and Electrophysiology 1996, p. 1045). Another HRV measure, pNN50, was also examined because it strongly reflects vagal modulation and is not dependent on homeostatic changes or length of recording period. Recommendations regarding signal-to-noise ratio, common mode rejection, and bandwidth were followed (Task Force of the European Society of Cardiology and North American Society of Pacing and Electrophysiology 1996). Vital signs were taken with a stethascope and sphygmomanometer.

Minnesota Living with Heart Failure Questionnaire

The LHFQ is a disease specific, paper and pencil, questionnaire that measures the patient's perceptions of the influence of HF on their physical, socioeconomic, and psychological aspects of their life (Middel et al. 2001). Patients were asked to respond to 21 items using a 6-point Likert scale (0–5). The total summary score can range from 0 to 105 and a lower score reflects better health related quality of life. Two subscale scores reflect physical and emotional impairment (Riegel et al. 2002). Psychometric properties have been assessed are are adequate (Rector and Cohn 1992; Rector et al. 1987).

Positive and Negative Affect Scale (PANAS)

The PANAS was given at the beginning and end of each measurement session to measure current self-reported positive and negative affective states. Participants rated 20 emotion adjectives on Likert scales based on how much they experienced the affect at that moment. This was done to explore mood changes as a mediator of treatment effects.

This test has high factorial validity, internal consistency, test-retest reliability, and external validity with the Beck Depression Inventory, the State-Trait Anxiety Scale, and the Hopkins Symptom Checklist (Watson et al. 1988).

Center for Epidemiological Studies-Depression Scale

The Center for Epidemiological Studies-Depression Scale (CES-D) is a 20-item self-report questionnaire of depression. It measures affective symptomology and current symptoms within the past week. This test was given to explore and control for depression as a confounding variable. A score of 22 or higher indicates probable Major Depression, a score of 16–21 indicates mild to moderate depression, and a score of 15 or less is not indicative of depression. Psychometric properties are adequate for this measure (Hann et al. 1999; Radloff 1977).

Other Measures

Credibility/Expectancy Questionnaire

The CEQ is a brief factor-analytically derived self-report questionnaire. It measures two domains concerning the treatment received: credibility of treatement, expectancy for improvement based on treatment. This was given during week 1, 6, and 18 for exploratory purposes and to control for credibility as a confounding variable. Participants were asked to respond to a series of ten questions. The psychometric properties of this intrument have been assessed. Internal consistency was high within each factor. Test-retest reliability was also high. (Devilly and Borkevec 2000).

Stress Management and Exercise Practices Questionnaire

Participants were asked to complete a questionnaire assessing their baseline daily stress management and exercise practices, Stress Management Practices and Exercise Questionnaire to explore and control for confounding variables. and monitor the client's exercise and stress management practices in between sessions.

Medication Record

Each participant was asked to complete a log monitoring medication changes over the course of the study to explore and control for medication changes as a confounding variable.

Practice Logs

Each participant was given a log to complete each week. Each participant was instructed to fill out the form immediately after completing their daily practice. Participants were asked to turn them in during their next scheduled session. They were called and asked to complete the logs 1 week preceding their follow-up visit at week 18 and instructed to turn them in during their scheduled follow-up visit.

Daily Stress Management and Exercise Record

Each participant was given a log each week to assess their daily stress management and exercise practices to control for these as potential confounding variables. Participants were instructed to fill the form out immediately after they completed either their exercise or stress management practice, and to not include the study intervention they were learning. Participants were asked to turn the log in during each scheduled session.

Vital Signs

Vital signs were taken each session to insure patient safety. Vital signs included blood presure, heart rate, respirations, and weight. Standard blood pressure, heart rate, and respirations measures were taken with the participant in the supine position. Also, weight was taken each using a standard weight scale.

Data Collection Sessions

Outcome measures were administered at weeks 1, 6, and 18. These sessions included questionnaire completion and recording of physiological data. Participants were asked to refrain from caffeine, alcohol, and vigorous exercise for 4 h before each study appointment. Participants were instructed to take all medications as prescribed, and to report all medication changes at the beginning of each study visit.

Participants sat in a comfortable chair, in a treatment room in the Cardiomyopathy Clinic, and each measurement was taken at the same time of day.

HRV was measured for 20-min; however, only the first 5 min were analyzed. A resting baseline measure with spontaneous breathing was taken for 5 min (Epoch 1) while the participant listened to the CD of the previously mentioned travel story, and the investigator waited outside of the room. The investigator re-entered the room after the baseline measurement was complete and assessment of the psychophysiological stressor began. The psychophysiological stressor was assessed using serial sevens, which is a standard stressor assessment, where the participant was asked to subtract seven from 1,000 until they reach zero as quickly as they can. The participants were instructed if they made a mistake they would be required to begin the task

again at 1,000. The CD of the travel story was turned off during the psychophysiological stressor. This took 2 min and then there was a 3 min recovery period to measure physiological response after a stressor (Epoch 2). The remaining 10 min (Epoch 3 and 4) were similar to the 5-min the baseline measurement, the travel CD was turned back on, and the investigator waited outside the room. The 6MWT was then administered in the hallway.

Treatment Protocol

In order to reduce experimenter bias, all of the sessions were scripted. Scripts for the 6MWT were used from the published manual (American Thoracic Society 2002) and scripts for biofeedback group I were used from the published manual (Lehrer et al. 2000). Scripts used for biofeedback training group II were adapted from previously published and empirically established protocols (Birbaumer et al. 1981; Egner et al. 2002; Lehrer et al. 2004). All particpants listened to music and sounds of nature compact disc (Atmospheres, Guitar Reverie, St. Clair Entertainment Group, Inc.) during training sessions.

The treatment group (Biofeedback Training Group I) received biofeedback training once per week for 45 min at weeks 1–6. At weeks 1 and 2 the training occurred after the 20-min HRV measurement. Biofeedback sessions consisted of breath retraining with an emphasis on abdominal breathing as well as cardiac and respiratory feedback. Physiological feedback was monitored visually on a the computer monitor. Participants were trained to practice breathing at their peak respiratory sinus arrythmia (RSA) in an attempt to maximize the peak/valley amplitude of the HR signal. Various color screens were displayed, reflecting depth and frequency of respiration, HR, and HRV. A 3-D screen showed HR frequencies and grouped them into high, low, and very low. Prior to leaving the session, participants received written material that explained the procedures and benefits of home practice of abdominal breathing (Davis et al. 2000; Gevirtz and Lehrer 2005; Gevirtz and Schwartz 2005). Participants with a home computer were provided a Freeze-Framer (Institute of HeartMath, LLC, Boulder Creek, CA) home training unit to enhance their daily breathing practice. The software supplied an interactive physiologic monitoring program that provided visual displays and auditory cues of their heart rhythms on their home computer screen. Heart rhythms were captured via a fintertip pulse sensor that plugs into either the serial port or Universal Serial Bus (USB) port of their computer. The auditory cues differed between heart rhythms to provide auditory reinforcement.

The attention placebo comparison group (Biofeedback Training Group II) received quasi-false alpha-theta EEG biofeedback training once per week for 45 min at weeks 2–5. Weeks 1 and 6 were used for training after the 20-min HRV measurement. This biofeedback placebo method has not produced cardiovascular effects and has been empirically established as an effective placebo (Lehrer et al. 2004). Participants were asked to alternately increase and decrease alpha and theta brainwave activity. EEG was recorded using O1 in the 10–20 system and right ear placements with a bandpass of 10–30 Hz. Participants were instructed to close their eyes, but not fall asleep. They were also instructed that alpha brainwave activity was associated with an a state of relaxation where they are alert and aware of their surroundings, but not ruminating in their thoughts or daydreaming, and theta brainwave activity was associated with a deeper state of relaxation. Data was recorded for a total of 20 min and divided into four sections: (1) increased alpha and decreased theta; (2). increased theta and decreased alpha; (3) increased alpha and decreased theta; (4). increased theta and decreased alpha. Different auditory cues for reinforcement for alpha and theta were used to indicate when the participant was achieving the desired brainwave activity. Specifically, "harp tinker bell chords" played when he or she had achieved the desired alpha brainwave activity and a "ding" played when he or she had achieved the desired theta brainwave activity For the sections of training (sections 1 and 3) where increased alpha and decreased theta activity was desired, the alpha band was set for auditory reinforcement 30% above threshold and the theta band was set for auditory reinforcement 30% below threshold. For the sections of training (sections 2 and 4) where decreased alpha and increased theta activity was desired, the alpha band was set for auditory reinforcement 30% below threshold and the theta band was set for 30% above threshold. Prior to leaving the session, participants received written material that explained the procedures and benefits of home practice.

Both groups were instructed to practice a minimum of 20 min per day, were given weekly practice logs, and Medication Change Logs, Daily Home Stress Management and Exercise Logs, and were instructed of the importance of completing the logs immediately upon completion of practice.

Statistical Analysis

Two-way and three-way analyses of variance (ANOVA) with repeated measures were conducted to examine the SDNN, LHFQ, 6MWT, and exploratory variables. Time functioned as the repeated measure. A p-value of .05 was considered significant. Sphericity, an assumption of repeated measures ANOVA, is generally violated in designs with more than two experimental conditions increasing the probability of creating Type I error; therefore, the

Huynh-Feldt correction was used to correct this violation. Thus, all p values reported were Huynh-Feldt corrected. Additionally, when assessing multiple dependent variables, due to multiple testing, there is an inflated Type I error rate; therefore, more stringent alpha levels are required and a Bonferroni correction was made. All data were analyzed using SPSS 14.0 (SPSS Incorporated, Chicago, IL).

Data Editing

Data editing followed procedures outlined in Del Pozo et al. (2004) and the Task Force of the European Society of Cardiology and North American Society of Pacing and Electrophysiology (1996).

Results

Sample Characteristics

Approximately 120 patients were identified as potential candidates for participation. Refer to Table 1 for characteristics of the study sample. Of the 120 patients recommended, 45 expressed interest and were screened over the telephone. With verbal consent of the patient, a review of the medical charts before a face-to-face appointment was arranged. Of the 45 patients, 35 met the necessary criteria and were randomized. Four participants did not complete the study (11%): two participants listed financial reasons; one participant listed transportation issues; one participant consistently did not take their hypertension medication as prescribed. Thus, their systolic and diastolic blood pressures were clinically elevated rendering it unsafe to perform the 6MWT. Of the 31 who completed the study, two participants received biventricular continuous pacemakers before their follow-up visits. This rendered their follow-up data unusable. The total number of participants included in the analyses was 29. Refer to Table 1 for descriptive statistics for the study sample.

Patients with HF are heterogeneous with regard to symptom presentation and treatment outcomes based on disease severity (Perez de Isla et al. 2008). Therefore, based on previously cited research by Kienzle et al. (1992) discussing drastic reductions the LF component of HRV in patients in advanced stages of HF, the investigators hypothesized differential treatment effects based on LVEF levels. This was because the treatment intervention required the participants to breathe within the LF bandpass and patients in the advanced stages of HF lack this

Table 1 Characteristics of study sample

Measure	Treatment	Control	t/χ^2	df	p
Age (years, *M*/SD)	54 ± 11	56.4 ± 13.5	−.54	27	.59
Sex (%, Male/Female)	80/20	79/21	.01	1	.92
Annual income (US, %)			1.93	4	.75
< $20,000	40	29			
$21,000–$79,999	58	57			
> $80,000	2	14			
% Married	74	50	6.53	3	.09
Race (%)			4.37	3	.22
Caucasian	67	50			
Black	6	36			
Hispanic	20	14			
Other	7	0			
Education (%)			1.1	4	.89
Some high school	13	14			
High school grad	20	36			
Some college	47	36			
College graduate	13	7			
Graduate level	7	7			
Weight (lbs, *M*/SD)	216 ± 62	248 ± 68	−1.3	27	.20
LVEF (%, *M*/SD)	30 ± 13	28.57 ± 13	.29	27	.77
NYHA (*M*/SD)	2.3 ± .72	2.1 ± .83	.91	27	.37
SBP (mmHg, *M*/SD)	114 ± 18	124 ± 15.5	−1.6	27	.13
DBP (mmHg, *M*/SD)	67 ± 8.8	69.7 ± 12.2	−.69	27	.50
LVEF (% *M*/SD)	30 ± 13	28.57 ± 13	.29	27	.77
Etiology			1.3	4	.86
Ischemic (%)	46	36			
Idiopathic (%)	40	43			
HTN (%)	7	7			
Other (%)	7	14			
AICD (%)	20	36	.28	1	.60
Comorbidities					
Arrhythmia (%)	27	50	.83	1	.36
CAD (%)	27	43	.28	1	.59
Hyperlipidimia (%)	27	14	.13	1	.72
NIDDM (%)	20	21	.00	1	1.0
Impaired mobility (%)	20	7	.22	1	.64
Obesity (%)	13	29	.31	1	.58
MDD (%)	20	7	.22	1	.64
Sleep apnea (%)	20	29	.01	1	.92
Medications					
Beta blockers (%)	100	100	N/A		
Diuretics (%)	40	57	.30	1	.58
Anticoagulants (%)	60	29	1.7	1	.19

LVEF: Left ventricular ejection fraction; *NYHA*: New York heart association; *SBP*: Systolic blood pressure; *DBP*: Diastolic blood pressure; *AICD*: Automatic implantable cardioverter-defibrillator; *CAD*: Coronary artery disease; *NIDDM*: Non-insulin dependent diabetes mellitus; *MDD*: Major depressive disorder

biological mechanism. Therefore, the 29 participants were further divided into high and low categories based on LVEF. LVEF was divided based on the median LVEF value which was 30%.[1] The LVEF division was arbitrary in an attempt to obtain the most balanced division between the treatment and control groups as well as the LVEF categories. Individuals with a low LVEF were categorized as 30% or lower and individuals with a high LVEF were categorized as 31% or higher. The investigators hypothesized that individuals with an LVEF of 31% or higher were more likely to benefit from cardiorespiratory biofeedback because this technique requires breathing in the LF bandwidth. Although the gold standard of heart function in heart failure patients is improved LVEF, this study, due to financial constraints, was not able to examine post or follow-up LVEF values.

Group Equivalence

There were no significant baseline differences between the treatment and control groups on demographic or clinical variables; however, dyspnea, t (27) = − 2.0, $p = .056$, approached significance. There were also no significant differences between the treatment and control groups divided into high (≥31%) and low (≤30%) LVEF categories groups on demographic or clinical variables; however, between the treatment and control group in the low (≤30%) LVEF category dyspnea, t (15) = −2.422, $p = .03$ and SDNN, t (15) = 2.304, $p = .036$, and between the treatment and control group in the high (≥31%) LVEF category fatigue, t (10) = 2.301, $p = .044$ approached significance ($p \leq 025$ to control for multiple comparisons between high (≥31%) vs. low (≤30%) LVEF category in the treatment group. There was one significant difference in the high (≥31%) vs. low (≤30%) LVEF in the control group, fatigue, t (12) = 3.06, $p = .01$, while dyspnea, t (12) = 2.068, $p = .061$, approached significance. Additionally, individuals who elected to drop out of the study experienced a greater degree of negative mood (PANAS negative mood subscale, t (18) = 3.43, $p = .003$) depressive symptoms (CES-D, t (18) = 3.208, $p = .005$), and reduced heart rate variability (lower SDNN, t (17) = 3.425, $p = .003$). Therefore, although the total number of the participants who discontinued the study was small, the results may be only generalizable to those who do not have these characteristics.

Manipulation Check

The biofeedback technique in the treatment group stressed producing heart rate frequencies with a specific LF bandpass (0.05–0.14 Hz). To assess treatment effectiveness and the participants' ability to learn the technique between sessions, all participants in the treatment group were evaluated for a manipulation check. LF was measured during training sessions 1, 2, 3, 4, and 5. LF was measured in normalized units (NLF). Normalization values are important in biofeedback studies because it shows that all oscillatory variance occurs in the LF range, recruiting from other frequencies (Vaschillo et al. 2002). NLF was calculated in accordance to the Task Force of the European Society of Cardiology and North American Society of Pacing and Electrophysiology (1996). A paired sample t-test was conducted comparing NLF between sessions 1 and 5 training sessions. There was not a significant difference, but there was a large effect size ($d = 1.79$) between biofeedback training session 1 and session 5 indicating over the course of the training the treatment group increased their NLF in congruence with the protocol (Cohen 1988).[2]

The biofeedback technique in the attention placebo comparison group stressed alternately increasing and decreasing alpha and theta brainwave activity. To assess treatment effectiveness and the participants' ability to learn the technique, all participants in the control group were evaluated for a manipulation check. Alpha and theta brainwave activity was measured during treatment sessions 1, 2, 3, 4 and 5. To assess the ability to learn the alpha and theta brainwave techniques each treatment session was divided into three intervals to determine of participants were able to successfully alternately increase and decrease alpha and theta brainwave activity in accordance with the protocol Paired sample t-tests were conducted among session 1 interval 3 and session 5 interval 3 for alpha and theta brainwave activity, In other words at the end of the first training session and at the end of the last training session. Cohen's d was calculated for all nonsignificant results and revealed a large effect size for increase in alpha brainwave activity ($d = +0.36$) and for increase in theta brainwave activity ($d = -0.35$) between the end of the first training session and the end of the last training session (Cohen 1988) indicating the participants were able to change their brainwave activity in congruence with the protocol.

The non-significant interaction, regardless of LVEF level, in CEQ credibility ratings also suggests that the training

[1] No statistical analyses were conducted when determining the LVEF category split. The investigators had no knowledge of the statistical outcomes based on the LVEF divisions prior to conducting the statistical analyses outlined below.

[2] For Cohen's d an effect size of 0.2–0.3 is considered a small effect size, 0.5 is considered a medium effect size, and 0.8 to 1.0 a large effect size (Cohen 1988).

provided to the comparison group was an effective placebo, F (2, 50) = 1.888, p = .162. However, there was a significant main effect for time, F (2, 50) = 4.743, p = .013, ω^2 = .159.[3] In the low (≤30%) LVEF category, both the treatment and the control group had a decreasing slope between the baseline and post measure; however, the control group had and increasing slope at the follow-up measure. In the high (≥31%) LVEF category, the control group showed an increasing slope between the baseline and follow-up measures. Refer to Table 3 for the descriptive statistics.

Treatment Compliance

All participants were asked to practice the techniques learned during their respective biofeedback training sessions for a minimum of 20 min per day. Participants in both groups were required to turn in a total of seven logs and compliance of 100% was considered a total of 980 min of practice. To insure accuracy of information reported on the logs, participants were instructed to completed the logs immediately after completing their daily practice rather than waiting to fill them out just prior to their next scheduled study visit. Home practice varied greatly: 31% fulfilled 90% or more of the required practice, 6% fulfilled between 50 and 89% of the required practice, 29% fulfilled between 16 and 49, and 17% fulfilled between 0 and 15% of the required practice. The median reported practice time for all participants was 610 min (SD = 793 min) over the 18 weeks. The median reported practice for all participants in the treatment group (N = 15) was 640 min (SD = 398 min). The median reported practice for participants who elected to use the Freeze-Framer for home practice in the treatment group and completed the study (N = 5) was Mdn = 600 min (SD = 157 min) versus those in the treatment group who did not (N = 10), Mdn = 326 min, (SD = 477 min). The median reported practice for participants in the control group (N = 14) was Mdn = 545 min (SD = 1,049 min).

Experimental Findings

Refer to Table 2 for descriptive statistics and p-values for the main outcome analyses.

Hypothesis 1: Exercise Tolerance Data The 6MWT data were first analyzed using a 2 × 3 (group × time) two-way ANOVA. The probability of Type I error was maintained at .05 for this analysis. Neither main effects nor interactions were found. The data were further analyzed using a

[3] Cohen (1973) considers .01–.05 a small magnitude of effect, .06–.14 a medium magnitude of effect, and ≥.15 as a large magnitude of effect.

Table 2 Descriptive statistics for the three-way interactions with LVEF divided into high and low categories for main and exploratory outcome variables

Measure	Group	LVEF (%)	Time	n	M	SD	α	df	p
6MWT	Treatment	≤30	Baseline	9	394	73	.05	2	.05*
			Post	9	391	70			
			Follow-up	9	395	87			
	Treatment	≥31	Baseline	6	432	77			
			Post	6	460	113			
			Follow-up	6	485	109			
	Control	≤30	Baseline	8	318	113			
			Post	8	346	128			
			Follow-up	8	325	115			
	Control	≥31	Baseline	6	416	166			
			Post	6	400	167			
			Follow-up	6	383	160			
SDNN	Treatment	≤30	Baseline	9	.03	.02	.025[a]	2	.09
			Post	9	.04	.02			
			Follow-up	9	.04	.02			
	Treatment	≥31	Baseline	6	.03	.02			
			Post	6	.03	.03			
			Follow-up	9	.04	.02			
	Control	≤30	Baseline	8	.02	.01			
			Post	8	.02	.01			
			Follow-up	8	.06	.07			
	Control	≥31	Baseline	6	.04	.04			
			Post	6	.03	.03			
			Follow-up	6	.02	.01			
pNN50	Treatment	≤30	Baseline	9	7.3	11	.025	2	.04
			Post	9	12	17			
			Follow-up	9	8.5	12			
	Treatment	≥31	Baseline	6	7	8.7			
			Post	6	8	11			
			Follow-up	6	11	19			
	Control	≤30	Baseline	8	2.6	5			
			Post	8	2.6	3.6			
			Follow-up	8	8.4	11			
	Control	≥31	Baseline	6	6.8	13			
			Post	6	5.8	11			
			Follow-up	6	1.4	1.3			
LHFQ	Treatment	≤30	Baseline	9	35.8	26.1	.05	2	.66
			Post	9	33.1	19.9			
			Follow-up	9	27.1	26.8			
	Treatment	≥31	Baseline	6	33.0	23.2			
			Post	6	32.8	18.9			
			Follow-up	6	38.0	19.5			
	Control	≤30	Baseline	8	39.8	30.6			
			Post	8	27.6	24.4			
			Follow-up	8	39.1	28.4			

Table 2 continued

Measure	Group	LVEF (%)	Time	*n*	*M*	SD	α	*df*	*p*
Control	≥31	Baseline	6	33.7	15.9				
		Post	6	22.2	23.3				

* Because the assumption of normality was violated for SDNN and pNN50, Keppel and Wickens (2004) recommend establishing a *p* value of .025, thus this is not a significant finding

2 × 2 × 3 (group × LVEF category × time) three-way ANOVA. LVEF was divided into high (31% and higher) and low (30% and lower) categories. The probability was maintained at .05 for this analysis, and family wise error rate was tolerated due to the importance of this result. This analysis revealed a significant three-way interaction, F (2, 50) = 3.189, $p = 0.05$, $\omega^2 = .113$. The treatment group had a higher increase in meters walked than did the control group, and the difference was higher among the participants in the high (≥31%) LVEF category.

A simple effects analysis, using the original error term (MS = 1,299.893) from the original significant three-way interaction was conducted. Again family wise error was tolerated for these analyses, and the probability of Type I error was maintained at .05. This analysis revealed a significant time effect for the treatment group in the high LVEF category (31% or higher), F (2, 50) = 3.1687, $p = .05$, $\omega^2 = .036$. However, there was not a significant time effect using the original error term for the treatment group in the low LVEF category (30% or lower), for the control group in the high LVEF category, or for the control group in the low LVEF category.

Subsequent paired sample *t*-tests were conducted across the groups with LVEF divided into high (31% or higher) and low (30% or lower) categories within the time periods. Due to the multiple comparisons, to control for family-wise error, the probability of Type I error was maintained at .025. The only significant finding was between the baseline and post measure, t (7) = − 2.881, $p = .024$, for participants in the control group with an LVEF of 30% or lower. Small sample sizes within the respective LVEF categories resulted in a lack of power most likely accounting for the nonsignificant findings in the other time periods.

Hypothesis 2: HRV Data Because the assumption of normality was violated, the probability of Type I error was maintained at .025 for all statistical analysis related to HRV data. The HRV data were first analyzed using a 2 × 3 (group × time) MANOVA for SDNN and the percentage of interval differences of successive NN intervals greater than 50 milliseconds (ms) (pNN50). Neither a significant interaction nor a significant main effect for time was found.

A subsequent analysis was conducted using a 2 × 2 × 3 (group × LVEF category × time) MANOVA with LVEF divided into high (≥31%) and low (≤30%) categories. The probability of Type I error was maintained at $p = .016$ to control for family wise error. This analysis revealed a significant three-way interaction F (2, 50) = 4.816, $p = .012$, $\omega^2 = .162$. For SDNN in the low (≤30%) LVEF category, SDNN increased more for the control group than the treatment group. For SDNN in the high (≥31%) LVEF category, SDNN increased more in the treatment group than in the control group. Similarly, for pNN50 in the low LVEF category, pNN50 increased more for the control group than the treatment group. For pNN50 in the high LVEF category, pNN50 increased more for the treatment group as compared to the control group.

A 2 × 2 × 3 (group × LVEF category × time) three-way ANOVA was analyzed for both SDNN and pNN50. The probability of Type I error was maintained at 0.01 to control for family-wise error. There was not a three-way interaction for pNN50 F (2, 50) = 3.459, $p = .036$, $\omega^2 = .122$, or for SDNN, F (2, 50) = 2.771, $p = .090$, was not found. Consistent with the above findings, pNN50 increased more for the control group than the treatment group in the low LVEF category, while pNN50 increased more for the treatment group as compared to the control group in the high LVEF category.

Exploratory Data

Refer to Table 2 for descriptive statistics for the exploratory analyses.

Hypothesis 1: Quality of Life The LHFQ was analyzed using a 2 × 3 (group × time) ANOVA, first for the entire group, Type I error was maintained at .05 for this analysis, and subsequently dividing LVEF into high vs. low categories in a 2 × 2 × 3 (group × LVEF category × time), Type I error was maintained at .025 for this analysis to control for family wise error. There were no findings for main effects or interactions for the total scale score or for the physical or emotional subscales.

Additional Findings

Refer to Table 3 for the descriptive statistics for the analyses for the additional findings. Because the following analyses were exploratory to control for confounding variables, family wise error rate was tolerated and the probably of Type I error was maintained at .05.

CES-D Data

The CES-D was initially analyzed using a 2 × 3 (group × time) two-way ANOVA. Neither a significant interaction nor main effects were found.

A successive analysis was conducted using a 2 × 2 × 3 (group × LVEF category × time) three-way ANOVA with one repeated measure. Neither a three-way interaction nor main effects were found.

PANAS Data

The positive affect PANAS data were first analyzed using a 2 × 6 (group × time) ANOVA. Neither an interaction nor main effects were found. The positive affect PANAS data were further analyzed using a 2 × 2 × 6 (group × LVEF category × time) three-way ANOVA with time as the repeated measure. No significant interaction or main effect was found.

The negative affect PANAS data were then analyzed using a 2 × 6 (group × time) two-way ANOVA. No significant interaction was found; however, there was a main effect for time, F (5, 135) = 3.449, $p = .006$, $\omega^2 = .113$. Both the treatment and the control groups had a decreasing slope, with the treatment group having lower scores, indicating less negative affect over time. The negative affect PANAS data were additionally analyzed using a 2 × 2 × 6 (group × LVEF category × time) three-way ANOVA. No significant interaction was found; however, there was a main effect for time, F (5, 125) = 3.067, $p = .046$, $\omega^2 = .109$. In the low (≤30%) LVEF category, both the treatment and control groups had a decreasing slope, however, the treatment group showed less negative affect over time compared to controls. In the high (≥31%) LVEF category, overall, only the control group showed a decreasing slope.

Borg Scale Data

The Borg Scale data were first analyzed for the self-report of dyspnea using a 2 × 6 (group × time) two-way ANOVA. There was not a significant two-way interaction; however, there was a significant main effect for time, F (5, 135) = 9.4, $p = .0001$, $\omega^2 = .258$. Overall, the control group had higher scores for perceived dyspnea over time. The dyspnea data were further analyzed using a 2 × 2 × 6 (group × LVEF category × time) three-way ANOVA. A significant interaction was not found: however, there was a significant main effect for time, F (5, 125) = 8.976, $p = .0001$, $\omega^2 = .264$. In the low (≤30%) LVEF category, the control group had relatively higher scores indicating higher levels of perceived dyspnea than the treatment group. In the high (≥31%) LVEF category, the treatment group had relatively higher scores indicating higher levels of perceived dyspnea.

The Borg Scale data were further analyzed for the self-report of fatigue using a 2 × 6 (group × time) two-way ANOVA. No significant interaction was found; however, there was a significant main effect for time, F (5, 135) = 2.609, $p = .05$, $\omega^2 = .08$. The treatment group showed less fatigue over time while control group showed a consistent increasing slope between the post-post measurement and the post-follow-up measurement indicating higher scores for perceived fatigue.

The Borg Scale fatigue data were further analyzed using a 2 × 2 × 6 (group × LVEF category × time) three-way ANOVA. A significant interaction was not found; however, there was a significant main effect for time, F (5, 125) = 2.668, $p = .038$, $\omega^2 = .096$. In the low (≤30%) LVEF category, the control group overall had higher scores for perceived dyspnea. In the high (≥31%) LVEF category, the treatment group had higher scores for perceived fatigue.

Discussion

This study investigated cardiorespiratory biofeedback and breathing retraining with patients with known New York Heart Association class I-III HF who were medically stable and under optimal drug treatment to improve exercise tolerance, HRV, and quality of life. One specific important finding was that HRV biofeedback does not appear to be helpful for people with more severe disease, although it may help people with milder disease. Perhaps baroreflex mechanisms or mechanics of the heart are too impaired to produce therapeutic effects, particularly in this time frame. Additionally, the results do not appear to be related to depression, mood, amount of time practiced, level of dyspnea or fatigue, perception of credibility of treatment received, and there were relatively few medication changes throughout the study. However, the results of this study should be interpreted with caution due to the low sample size.

Clinical Implications

The American Thoracic Society (2002) has established guidelines that an increase of 50 m or more distance walked on the 6MWT is clinically significant. In this study, 20.6% of the study population demonstrated a clinically significant increase in distance walked between baseline and follow-up measures. In the treatment group, 33% of the participants exhibited a clinically significant increase in distance walked, while only 12.5% of the participants in the control group demonstrated clinical significance in distance walked between baseline and follow-up measures. Furthermore, 50% of the participants in the high LVEF and 22% in the low LVEF category in the treatment group were able to demonstrate the aforesaid clinically significant distance while the percentage for the control group remained at 12.5% for both LVEF categories between

Table 3 Descriptive statistics for the three-way interactions with LVEF divided into high and low categories for additional findings

Measure	Group	LVEF (%)	Time	*n*	*M*	SD	α	*df*	*p*
CES-D	Treatment	≤30	Baseline	9	10.4	6.6	.05	2	.097
			Post	9	14.1	10.4			
			Follow-up	9	11.3	11.1			
	Treatment	≥31	Baseline	6	13.3	5.8			
			Post	6	20.2	13.5			
			Follow-up	6	20.7	15.5			
	Control	≤30	Baseline	8	15.8	6.5			
			Post	8	13.1	9.3			
			Follow-up	8	21.4	9.1			
	Control	≥31	Baseline	6	11.3	7.6			
			Post	6	11.7	11.5			
			Follow-up	6	8.3	6.2			
PANAS positive	Treatment	≤30	Pre baseline	9	33.2	8.9	.05	5	.63
			Post baseline	9	33.1	10.8			
			Pre post	9	32.6	10.4			
			Post post	9	34.9	12.1			
			Pre follow-up	9	31.8	13.3			
			Post follow-up	9	31.2	14.8			
	Treatment	≥31	Pre baseline	6	29.2	10.6			
			Post baseline	6	33.2	2.1			
			Pre post	6	26.7	7.8			
			Post post	6	28.8	8.2			
			Pre follow-up	6	27.2	6.4			
			Post follow-up	6	26.2	9.1			
	Control	≤30	Pre baseline	8	32.6	8.3	.05	2	.66
			Post baseline	8	28.9	7.7			
			Pre post	8	32.0	14.5			
			Post post	8	31.1	16.8			
			Pre follow-up	8	28.8	11.6			
			Post follow-up	8	29.3	12.9			
	Control	≥31	Pre baseline	6	32.8	2.14			
			Post baseline	6	32.7	7.20			
			Pre post	6	30.0	9.30			
			Post post	6	30.3	9.71			
			Pre follow-up	6	35.3	3.39			
PANAS negative	Treatment	≤30	Pre baseline	9	10.8	.97	.05	5	.40
			Post baseline	9	10.8	1.4			
			Pre post	9	17.0	9.5			
			Post post	9	15.3	9.7			
			Pre follow-up	9	13.0	5.0			
			Post follow-up	9	10.9	1.4			
	Treatment	≥31	Pre baseline	6	12.2	5.3			
			Post baseline	6	12.0	4.9			
			Pre post	6	15.3	8.7			
			Post post	6	13.2	9.4			
			Pre follow-up	6	14.3	6.1			
			Post follow-up	6	14.3	7.0			

Table 3 continued

Measure	Group	LVEF (%)	Time	*n*	*M*	SD	α	*df*	*p*
	Control	≤30	Pre baseline	8	14.1	9.3			
			Post baseline	8	13.3	6.1			
			Pre post	8	15.4	5.9			
			Post post	8	16.1	7.3			
			Pre follow-up	8	16.6	6.6			
			Post follow-up	8	15.8	7.6			
	Control	≥31	Pre baseline	6	10.3	.52			
			Post baseline	6	10.5	1.2			
			Pre post	6	14.8	6.4			
			Post post	6	13.2	5.4			
			Pre follow-up	6	12.3	3.5			
			Post follow-up	6	10.5	.53			
Borg dyspnea	Treatment	≤30	Pre baseline	9	.44	.68	.05	5	.61
			Post baseline	9	1.8	1.3			
			Pre post	9	.89	1.1			
			Post post	9	2.7	2.5			
			Pre follow-up	9	.22	.67			
			Post follow-up	9	1.7	2.0			
	Treatment	≥31	Pre baseline	6	.42	.80			
			Post baseline	6	1.3	1.2			
			Pre post	6	.75	.76			
			Post post	6	2.4	1.0			
			Pre follow-up	6	1.4	1.1			
			Post follow-up	6	2.4	1.7			
	Control	≤30	Pre baseline	8	2.1	2.0			
			Post baseline	8	2.7	2.5			
			Pre post	8	1.1	1.4			
			Post post	8	2.1	1.3			
			Pre follow-up	8	1.6	1.4			
			Post follow-up	8	2.4	2.6			
	Control	≥31	Pre baseline	6	.42	.49			
			Post baseline	6	1.4	.92			
			Pre post	6	.58	.80			
			Post post	6	1.5	1.4			
			Pre follow-up	6	.83	.98			
			Post follow-up	6	1.7	1.4			
Borg fatigue	Treatment	≤30	Pre baseline	9	2.06	1.5	.05	5	.24
			Post baseline	9	2.28	1.4			
			Pre post	9	1.56	1.5			
			Post post	9	2.56	2.5			
			Pre follow-up	9	1.56	1.3			
			Post follow-up	9	2.11	2.2			
	Treatment	≥31	Pre baseline	6	1.75	1.5			
			Post baseline	6	2.00	1.3			
			Pre post	6	1.92	2.6			
			Post post	6	3.00	1.6			
			Pre follow-up	6	2.17	1.2			
			Post follow-up	6	2.75	1.5			

Table 3 continued

Measure	Group	LVEF (%)	Time	*n*	*M*	SD	α	*df*	*p*
	Control	≤30	Pre baseline	8	2.81	2.0			
			Post baseline	8	4.19	1.6			
			Pre post	8	1.50	1.3			
			Post post	8	2.31	1.8			
			Pre follow-up	8	3.50	2.1			
			Post follow-up	8	4.25	3.0			
	Control	≥31	Pre baseline	6	.25	.4			
			Post baseline	6	1.33	1.2			
			Pre post	6	2.00	2.0			
			Post post	6	2.58	2.2			
			Pre follow-up	6	1.42	1.9			
			Post follow-up	6	2.17	2.1			
CEQ credibility	Treatment	≤30	Baseline	9	46	7.6	.05	2	.162
			Post	9	41	10.1			
			Follow-up	9	42	12.3			
	Treatment	≥31	Baseline	6	46	9.9			
			Post	6	37	8.4			
			Follow-up	6	42	10			
	Control	≤30	Baseline	8	48	8.0			
			Post	8	41	11.7			
			Follow-up	8	46	8.2			
	Control	≥31	Baseline	6	43	8.4			
			Post	6	45	9.0			
			Follow-up	6	47	18.8			

baseline and follow-up. This finding is of particular clinical importance considering prognosis is highly related to exercise capacity in HF patients. The treatment group in the high LVEF category improved distance walked despite increases in perceived fatigue and dyspnea between baseline and follow-up (Pilote et al. 1989; Szlachcic et al. 1985). This finding replicates Luskin et al. (2002) research demonstrating the Freeze-Framer stress management program significantly increased exercise capacity. Additional research is needed to strengthen this result.

Research has been limited regarding behavioral interventions to increase HRV, improve exercise tolerance, and improve quality of life such as biofeedback in HF patients. The present findings may be strengthened by measuring other outcomes such as future cardiac events, mortality rates, hospitalization rates due to cardiac events, and other objective cardiac test.

Past research has determined that patients in the advanced stages of HF with high levels of sympathetic activity show a complete absence of LF variability (Kienzle et al. 1992; van de Borne et al. 1997). The absence of LF variability has remained even after heart transplantation (van de Borne et al. 1997). Although the cause of reduced or absent LF variability it is not known it is suggested that high adrenergic drive saturates the sino-atrial node. potentially rendering it less capable of maintaining rhythmic modulation or beta-adrenoreceptor downregulation (Kienzle et al. 1992; Malik and Camm 1993; van de Borne et al. 1997). Furthermore, the absence of LF variability may not an exclusive consequence of peripheral changes in that central autonomic regulatory functions may be also be compromised (Kienzle et al. 1992; Kjaer and Hesse 2001; La Rovere et al. 2003; Lucreziotti et al. 2000; Sandercock and Brodie 2006; van de Borne et al. 1997). This has important prognostic and clinical implications. Because autonomic derailment appears more profound in patients in the advanced stages of HF several possibilities exist. First, longer and more intensive interventions may be necessary. Second, longer follow-up periods may be required to allow more time for autonomic re-regulation. Last, behavioral interventions, such as biofeedback, may be a fruitless endeavor in HF patients in the advanced stages of the disease to increase HRV. More research is needed to determine the best course of treatment.

Although there is currently no normative data for HRV, correlations between HRV measures and health have lead to commonly used end points of 50 and 100 ms for SDNN.

Over 100 ms is considered "healthy", between 50 and 100 ms is considered "compromised health", while under 50 ms is considered "unhealthy"(Kleiger et al. 1987). Using the above mentioned criteria to classify participants in this study, at completion of the study, 83% of the entire study sample had an SDNN in the "unhealthy" category, 14% had an SDNN in the "compromised health" category, 3% had an SDNN in the "healthy" category, and only two participants (7% of the sample) had improved SDNN values placing them in higher health category (both participants were in the control group and in the low LVEF category). Although overall there was not a change in health category for participants in the high LVEF category in the treatment group, they all demonstrated improvement in SDNN between baseline and follow-up. More research is needed with perhaps longer follow-up periods to determine long-term trends in HRV.

Another important demarcation for SDNN in HF patients is 44 ms (Kleiger et al. 1987). This value is similar to the best predictive risk value of <50 ms in myocardial infarction patients as an independent predictor of death (Kleiger et al. 1987). Using this criterion, at baseline in the treatment group in the low LVEF category, six out of nine participants had an SDNN value less than 44 ms which they did not exceed at follow-up. At baseline in the treatment group in the high LVEF category, four out of six participants in had an SDNN value of less than 44 ms which again did not change at follow-up. At baseline for the control group in the low LVEF category at baseline all participants (8) had an SDNN value less than 44 ms; however, at follow-up five participants had an SDNN value less than 44 ms. At baseline in the control group in the high LVEF category four out of six participants had an SDNN value less than 44 ms, and at follow-up all of them had an SDNN value less than 44 ms. More research is needed to examine long-term morbidity and mortality rates to determine if the increase in SDNN is clinically predictive in the reduction of cardiac related risk.

Future Research

Several studies have investigated distanced walked during the 6MWT as a prognostic marker in HF patients. Exercise capacity values <300 m are predictive of mortality and morbidity as evidenced by increased hospitalizations due to exacerbation of HF symptoms (Bittner et al. 2003; Zugck et al. 2000; Roul et al. 1998). In the SOLVD study, total mortality was 10.23% in participants with a 6MWT < 300 m, and 2.99% for participants who walked ≥450 m (Bittner et al. 2003). Further research is needed to establish HRV biofeedback with breathing retraining as a viable treatment in a HF population to improve exercise tolerance.

Previous research (Luskin et al. 2002) has also demonstrated an increasing trend of SDNN after a short-term intervention that was somewhat similar to this study. Consistent with the recommendations in Luskin et al. (2002), perhaps a longer follow-up period is needed due to the pathophysiology of HF. Future research is needed to determine if SDNN will continue to increase over time.

Kleiger et al. (1987) reported a comparative risk of mortality to be 5.3 times higher for individuals with an SDNN less than 50 ms as compared to those with an SDNN over 100 ms, and 1.6 times higher for individuals with an SDNN between 50 and 100 ms as compared to those with an SDNN over 100 ms. More research is needed to examine long-term morbidity and mortality rates to determine if the increase in SDNN is clinically predictive in the reduction of cardiac related risk.

Additionally, it was discovered to be an active treatment worthy of future examination. This condition was carried out in a way that would maximize relaxation effects by insuring that the EEG skills were learned. Perhaps a stress management intervention, like the Luskin et al. (2002) study, would be beneficial for the HF population.

Study Limitations

This study has several limitations. First, there was a small sample size that was ex post facto divided into an even smaller sample size based on Kienzle et al. (1992) research. The small sample resulted in a lack of power; therefore, there was not a clear understanding of the true impact of the intervention over the time periods. Thus, significant results should be interpreted with caution.

There are many sources of variability for the 6MWT. Many sources of variability were controlled by following the published American Thoracic Society Guidelines for administration of the test (American Thoracic Society 2002); however, some variables were beyond control. The following factors have been found to decrease distance walked on the 6MWT: (1) shorter height; (2) older age; (3) higher body weight; (4) female sex; (5) pulmonary disease; (6) cardiovascular disease; (7) musculoskeletal disorders; (8) low motivation. Additionally, the following factors have been found to increase distance walked on the 6MWT: (1) taller height; (2) male gender; (3) high motivation; (4) a patient who has previously performed the test; (5) medication for a disabling disease taken right before the test (Olsson et al. 2005). Even though repeated testing has produced practice effects, it is thought that the training effect does not persist after a few weeks. Furthermore, the correct way to express changes in the 6MWT, for example absolute value, percentage change from baseline, or percentage change from predicted value, is not yet known (American Thoracic Society 2002).

The actual mechanism of the change in HRV is not fully understood. Porges (1995) conveyed that the nucleus ambiguous innervates the sino-atrial node by the vagus nerve. The vagus nerve in responsible for regulating cardiac output. The amplitude of RSA in the LF range is believed to be an index of vagal tone. Vagal tone appears to respond to stress, moods, and illness (Carels et al. 2003; Carney et al. 2000; Cohen et al. 2000; Dekker et al. 2000; Edner et al. 2000; Fleisher 1996; Guck et al. 2003; Porges 1995, 1997; Porges et al. 1994). When vagal tone withdraws, HRV decreases. Lehrer et al. (2003) found RSA biofeedback trainingincreased the variability in the RR inter-beat-interval which in turn trains the baroreflexes resulting in more effective functioning of the baroreceptors. The researchers hypothesized that RSA training re-regulates the autonomic nervous system and restores balance between the sympathetic and parasympathetic branches. Del Pozo et al. (2004) findings supported the above mentioned hypothesis.

To date, there is no standardized method of measurement of HRV. This currently includes duration of long-term and short-term measurements, and commercial equipment sampling rates. However, the Task Force of the European Society of Cardiology and North American Society of Pacing and Electrophysiology (1996), have established some measurement guidelines. There is also debate regarding the interpretation of autonomic mediation of the components of the spectral analysis. Additionally, frequency domain variables are strongly correlated with each other. Furthermore, because total variance increases with measurement duration, differing durations of SDNN cannot be compared (Berntson et al. 1997, Task Force of the European Society of Cardiology and North American Society of Pacing and Electrophysiology 1996).

Although depressed HRV is a strong independent predictor of mortality, morbidity, and arrhythmic complications in patients with HF, and there is a growing consensus that increased vagal activity can be beneficial, it is yet to be established how much vagal activity would have to be increased for it to be clinically protective (Task Force of the European Society of Cardiology and North American Society of Pacing and Electrophysiology 1996). Furthermore, this study conducted standardized short-term 5-min measurements of HRV; however, 24-h measurements are considered more predictive (Task Force of the European Society of Cardiology and North American Society of Pacing and Electrophysiology 1996).

Currently, commercial equipment is not standardized and has sampling rates between 212 and 1,024 Hz, or samples per second. The ideal range for sampling rate is between 250–500 Hz or higher to "avoid a jitter of the *R*-wave point" (Task Force of the European Society of Cardiology and North American Society of Pacing and Electrophysiology 1996, p. 1047). The I-330-C2 + 12 Channel Physiologic Monitoring System (J&J Engineering, Inc., Poulsbo, WA) currently meets the suggested sampling rates.

HRV outcome measures are generally altered by ectopic heart beats. Ectopic beats are often generated from various arrhythmias, and noise from movement. Editing the data by adding, dividing or averaging ectopic heart beats prevents selection bias that may arise from deleting data or using commercial equipment to "clean" the heart rate data (Task Force of the European Society of Cardiology and North American Society of Pacing and Electrophysiology 1996). Editing of heart rate data in this study was conducted manually, and heart rate editing was done in a consistent, previously agreed-upon method (refer to "Methods"). The number of edited heart beats was below 10% in each case.

Also length of diagnosis was not measured. Length of diagnosis has been found to be an important factor influencing compliance behaviors. Specifically, patients who have been diagnosed longer demonstrate less compliance (Dobre et al. 2006; Evangelista et al. 2003; Juenger et al. 2002).

Although this study included a comparison treatment, it was a single blind design. All sessions were scripted to control for experimenter bias; however, this is best controlled by double blind designs to eliminate the possibility of all experimenter bias in influencing the results. Furthermore, in some cases, the comparison condition had stronger effects then the active treatment condition. It is difficult to find control conditions in biofeedback studies that are completely neutral.

Another limitation was generalizability. Although the total number of participants who elected to discontinue study participation was small, they were experiencing higher levels of dysphoria and lower HRV, thus the results of this study may only generalizable to individuals who are not experiencing these characteristics. Also, there may have been a selection bias as evidenced by approximately 50% of the individuals who were approached and eligible for participation did not elect to participate. However, the study population represented a realistic clinical population. Thus, the results may not be generalizable to the general population, but are to a clinical population.

Conclusions

To conclude, the present findings have several indications. First, cardiorespiratory biofeedback with breathing retraining can increase exercise capacity in patients with known NYHA Class I-III HF with an LVEF of 31% or higher. Additionally, 50% of participants in the high LVEF category were able to demonstrate clinically significant

changes in distanced walked on the 6MWT (≥50m). Second, there appears to be a difference in treatment response based on disease severity and LVEF values. Third, although SDNN was trending toward improvement for treatment group participants in the high LVEF category, potentially due to the pathophysiology of HF and the autonomic derailment, there may be a need for either more intensive behavioral interventions, longer follow-up periods to increase SDNN, or biofeedback may be a fruitless endeavor in patients in the advanced stages of HF.

The aforesaid improvement in exercise capacity can help to improve prognosis and potentially reduce risk of morbidity and mortality because it is an independent prognostic indicator than traditional cardiac risk factors. Cardiorespiratory biofeedback appears to be another treatment than can be used to improve cardiovascular risk in HF patients. It is a non-invasive and relatively inexpensive intervention.

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