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Meditation for Improved Clinical Outcomes in Patients with Implantable Defibrillators for Heart Failure- Pilot Study

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Abstract

Background: Sympathetic activation is associated with congestive heart failure (CHF) and leads to adverse clinical events.We hypothesized that meditation by reducing emotional reactivity would have beneficial effect in reducing arrhythmias compared to control patients.

Methods: Patients known to have CHF and implantable cardioverter defibrillators (ICD) were randomized to Vipassana meditation or usual care control group. Meditation group underwent classes three times during the first week, thereafter once every two weeks. They were encouraged to practice meditation at least once everyday. The ICD was followed by clinic/ remote visits. Atrial (AA) and ventricular arrhythmias (VA) as well cardiac events were assessed in follow up. Chi square test was used to compare nominal variables and t test for continuous variables.

Results: Patients (n=25, 65% male, mean LVEF 25%, HTN 38%, Diabetes 12%, coronary artery disease 38%, NYHA class 2.2) were followed for 79 ± 36 months. Comparing meditation vs control, survival was higher (88%vs 67%); there was less cumulative sustained AF episodes (mean 0.9, IQR 0-1 vs 2.5, IQR 2-4, p=0.045), sustained VT occurred (25% vs 55%, amiodarone use (none vs 44%), and VT ablation in 6.6% vs 33% in the meditation group.

Conclusions: In this first pilot study of meditation in CHF patients with ICD, during long term follow up, there is a trend for improved survival and reduced arrhythmias in patients randomized to meditation.

Introduction

Congestive heart failure (CHF) is associated with significant mortality and a poor median survival.[1] Mortality correlates with functional class and is attributed to sudden cardiac death due to ventricular arrhythmias (VA) or pump failure. These patients are also at higher risk of atrial fibrillation (AF), leading increased morbidity including recurrent hospitalization and stroke.[2]

Sympathetic activation measured by nor-epinephrine levels is correlated with increased mortality, worsening symptoms and increased hospitalization in patients with CHF.[3, 4] Higher resting heart rate is indicative of higher sympathetic tone and a multitude of beta-blocker trials have shown reduction in mortality in patients with congestive heart failure suggesting that sympathetic activation has a significant role in the incidence of sudden cardiac death from ventricular arrhythmias.[5] Studies have shown that implantable cardioverter defibrillator (ICD) and cardiac resynchronization therapy defibrillator (CRTD) improve survival by treating ventricular arrhythmias and by resynchronization of the ventricles respectively.[6] However, unless the left ventricular ejection (LVEF) improves, these modalities do not reduce incident arrhythmias.

Meditation is a restful alert state of mind and has been associated with decreased sympathetic and heightened vagal tones.[7] Physiological markers of norepinephrine levels, vasomotor tone, heart rate and blood pressure have been shown to be lower in meditators.[8-10] These effects likely can counter the heightened sympathetic activation in heart failure patients.

We hypothesized that meditation reduces atrial and ventricular arrhythmias in patients with congestive heart failure during long term follow up.

Key Words

Meditation, Heart Failure, Arrhythmias.

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Methods

Study subjects

After Institutional review board approval, patients were recruited from the Device clinic at our institution and consented for the study. Patients were randomized to two groups: Meditation group were taught Vipassana meditation by a dedicated professional, while the control group was offered usual care consistent with community

standards and health education.

Patients were included if they were ≥ 18 yrs, had an implanted ICD or CRTD for CHF indication according to ACC/AHA/ HRS guidelines.[6] Patients were excluded if life expectancy was < than 6 months due to non-cardiac causes, pregnant, major psychiatry illness, end stage liver, renal or pulmonary diseases, active alcohol or drug abuse and those who were meditators at baseline. Their baseline demographics, co- morbidities, medications, New York Heart Association (NYHA) class, LVEF, 6-min walk duration, BNP levels were assessed. After randomization, the study group was enrolled in meditation classes, three times in the first week after enrollment. Thereafter they attended classes once every two weeks until six months. They were encouraged to meditate at home every day for as long as they can sustain. At the end of six months, BNP levels and 6- min walk test was repeated. All these patients underwent routine device follow up at 3- month intervals per recommendation by guidelines. Arrhythmia log were evaluated and documented during every clinic visit.

Meditation

Subjects were seated in a quiet room on a cushion on the floor or in a straight-backed chair. Those sitting on the floor cross their legs in a comfortable position and those sitting on a chair were requested to place their feet flat on the floor. All adopted the head-and-shoulders posture of meditation -- back straight, hands resting gently on the thighs, head and spine aligned and shoulders relaxed. The eyes were partially open with the gaze directed downward about four feet in front.

Subjects were given instructions by an experienced teacher on the basic technique of concentration-meditation focusing on the breath, leading to the entry stage of Vipassana mediation. While the subjects focus on their breath, they were asked to be aware and follow any random thoughts, feelings, sounds, sights, smells, that arise but knowingly bring the mind gently back to breath. Similarly if one felt a sense of discomfort anywhere in the body, they were asked to adjust their position mindfully, and return to the breath. However, once the subject mastered the breath alone concentration

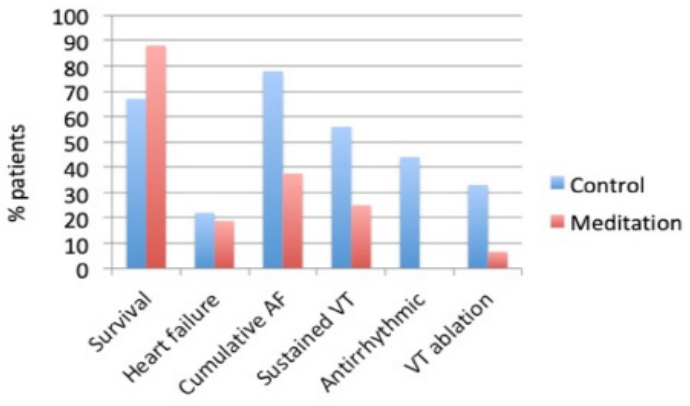

Figure 1: Comparison of clinical outcomes: Blue bars and red bars represent controls and meditators respectively. AF- atrial fibrillation; VT- ventricular tachycardia.

Table 1: Baseline characteristics.

	Control	Meditation	P value
Age	64 + 13	49.7 + 9	0.005
Gender	67	63	ns
NYHA class	2.2 + 8	2.3 + 4	ns
6 min walk	379 + 89	425 + 93	0.03
BNP (IQR)	299 (133-277)	117 (47-97)	ns
Baseline NSVT	11%	35%	ns
Baseline AF	22%	21%	ns
LVEF	24 + 5	26 + 7	ns
Beta blockers	100%	100%	ns
ACEI/ARB	89%	94%	ns
Antiarrhythmic therapy	22%	none	ns
Hypertension	44%	31%	ns
Diabetes	11%	13%	ns
Coronary artery disease	33%	44%	ns

NYHA- New York Heart Association; BNP- B- natriuretic peptide; IQR- interquartile range; NSVT- Non-sustained ventricular tachycardia; AF- Atrial fibrillation; LVEF- left ventricular ejection fraction; ACEI/ ARB- angiotensin converting enzyme inhibitor/

(one-pointedness) there is expected to be less interruptions by other sensations, thoughts, feelings etc. The subjects were then expected to eventually become capable of knowing the breath sensation while focusing on bodily sensations, feelings, thoughts and mental qualities. Concentration leading to Vipassana is a self-investigation process towards perfection which is achieved through practice. The point of this technique is not to stop thinking or achieve a state of bliss, but to become aware of mental activity.

Primary clinical endpoint was cumulative occurrence of AF; secondary end points were mortality, heart failure hospitalization and ventricular arrhythmias. If patients had VA requiring therapy by the device, it was considered sustained VA. Any AF > 7 days duration was considered persistent AF; episodes of AF were tracked, if AF occurred during any visit, the mean episodes were considered cumulative AF. Antiarrhythmic therapy use, ablation, heart failure and survival were also tracked.

Statistics

STATA 13.1 was used for all statistical analyses. Continuous variables are expressed as mean + SD or IQR; categorical variables are presented as percentages, comparisons were performed with t-test and X^2 test respectively. Paired t-test was performed to compare baseline vs follow up BNP and 6- min walk distances among the groups. Adjustment of comorbidities for the clinical outcomes were performed using logistic regression; p-value < 0.05 was considered significant.

Results

Baseline characteristics

Twenty-five patients were enrolled (65% male, mean LVEF 25%, hypertension 38%, Diabetes 12%, coronary artery disease 38%, NYHAclass 2.2) were followed for 84±32 months. Majority of them were implanted for primary prevention (84%). Nine patients were in

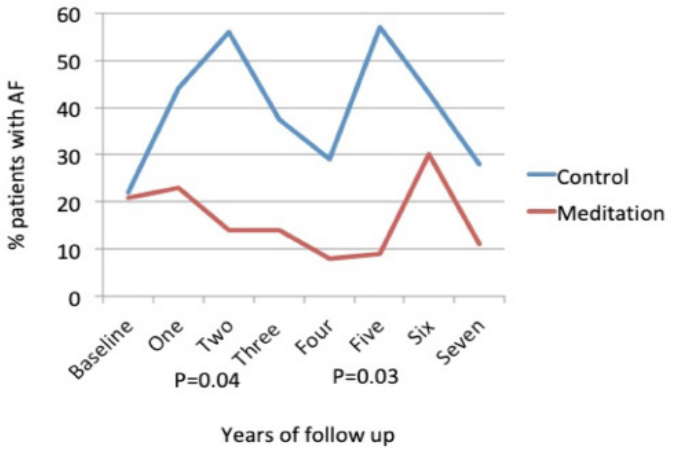

Figure 2: X axis represents years of follow up; Y axis- percent of patients with atrial fibrillation. Blue line and red lines represent control and meditators respectively.

the control arm and 16 in meditation arm. Patients attended 5.9±4.7 classes, with a mean attendance of 55±35 %. The average duration from device implant was 33.6±31.8 months. At baseline (table 1), the meditation group was younger and had longer 6-min walk duration. There was no difference in mean LVEF, beta-blocker or antiarrhythmic drug use.

Atrial fibrillation

During the initial interrogation at enrollment, three patients in control (mean 1.44 min, 0.48 min/month) and two patients in meditation (mean 0.67 min, 0.21 min/month) has documented episodes of paroxysmal AF.

One patient who had persistent AF in meditation group died after cardiac surgery before first three month follow up, therefore was not considered for outcome.

The cumulative AF episodes at six months increased to 127/month in control group vs 0.67 episodes/month in the meditation group. One patient in control group developed persistent AF at six months. Cumulative AF episodes at the end of follow up occurred in 78% of controls vs 37.5% among meditators with mean 0.9, (IQR 0-1) vs 2.5, (IQR 2-4), p=0.045 episodes per visit (fig 1).

The cumulative AF duration increased to 4311 (IQR0-4.3) min/month in controls and 2.7 (IQR 0-0.01) min in meditation group. The duration was driven by three patients in control (11%) who developed persistent AF vs none in mediation group. The patients who had documented AF episodes remained lower in meditation group compared to controls. (Fig 2).

Table 2: Results

(%)	Control (n=9)	Meditation (n=16)	
Survival	67	88	ns
HF hospitalization	22	19	ns
Cumulative AF	78	37.5	0.05
Persistent AF	11	none	ns
Sustained VT	56	25	ns
Ablation for VT	33	6.7	0.09
Antiarrhythmic use	44	none	0.004

Ventricular tachycardia

At baseline, one patient in the control group had 43 episodes of NSVT and five patients in meditation group had NSVT (mean episodes 2.8, IQR 0,1), at six months, 22% of control and 28% (ns) of meditation groups had VT; mean duration of VT increased from baseline to six months in both arms: 0.9 to 8.9 sec in controls (ns) and 3.1 to 8.7 sec (ns) in meditation groups respectively. In the control arm, the number of patients with VT increased from 11% to 22%, while in the meditation arm less patients had VT (38.4 % to 31%) after six months. At the end of long term follow up, although both groups had increase in VT burden, the increase was more significant in the control group-11% to 78%, p=0.003 vs 38% to 64%, p=0.04 in the meditation group. There was no sustained VA at baseline after implantation of the tachy arrhythmia device; during follow up, the control group had higher proportion of sustained VT (56% in control vs 25% in meditation, ns) (table 2, fig-3) as well as need for antiarrhythmic therapy and ablation.

Baseline BNP was non -significantly higher in control group (table 1); there was no significant change between baseline BNP to 6 -month BNP in either groups [mean (IQR)- control: 304 (136-166); meditation: 113 (33-88)]. Six- minute walk was longer in meditation group compared to control at baseline (table 1). Neither group had any significant change in 6- min walk at 6 months (control: 370±152 vs 454±101, ns).

At the end of follow up, 67% in control group vs 87.5% in meditation group were alive (ns) (table 2, fig-1). One patient in meditation group died at 1.4 months after enrollment in the perioperative period after cardiac surgery. Heart failure hospitalization occurred in 22% of control vs 18.8% of meditators.

Discussion

Our principal findings are improved cardiac end points of all parameters investigated in the meditation group. The survival,

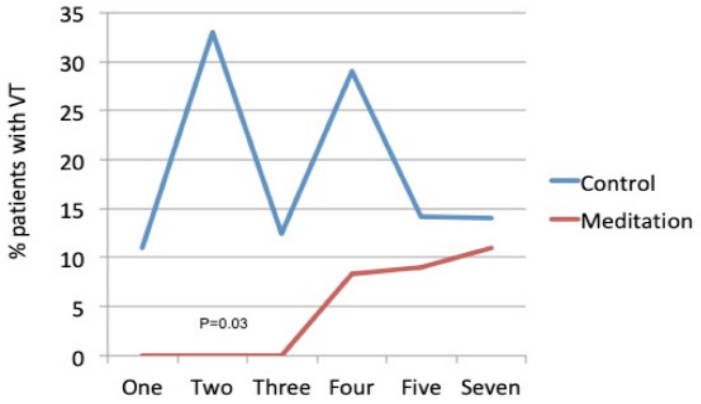

Figure 3: X-axis represents years of follow up; Y axis- percent of patients with sustained ventricular tachycardia requiring therapy. Blue line and red lines represent control and meditators respectively.

heart failure hospitalizations, AF and sustained VT were lower in meditation group. Cumulative AF episodes per visit and need for antiarrhythmic therapy were significantly lower in the meditation group. Though both groups had an increase in VT burden, the episodes were higher in the control group. Although the patients in the meditation group had lower BNP levels and longer 6-min walk distance, they had higher baseline NSVT. This difference could partially explain the difference in outcomes.

Atrial fibrillation is widely accepted as triggered by foci located in thoracic veins; the triggers have been linked to autonomic nervous system via cardiac ganglionic plexi [11] prompting an interest in modulation by ablation.[12] The well acknowledged paradigms of sympathetic stimulation induced ventricular arrhythmias are in congenital conditions including long QT syndrome and catecholaminergic polymorphic ventricular tachycardia. Beta-blockers have been the main stay of therapy in these conditions; refractory arrhythmias have been treated by sympathetic denervation. [13,14] In patients with recurrent shocks from ICD, cardiac sympathetic denervation of thoracic ganglia with or without renal denervation has been shown to reduce arrhythmic events.[15, 16] These efforts cumulatively reiterate the beneficial effects of reversing sympathetic effects on the electrical stimulation of myocardium.

Meditation in scientific terms refers to concentration of mind in order to bring about certain physiologic alterations. Meditation has been used to alleviate stress and anxiety including work place burn outs.[17-19] Since many of these emotions have physiological effects leading to adverse cardiac outcomes, these have been evaluated in clinical settings. Some physiological studies of meditation have shown reduced respiratory rates, decreased skin conductance, total peripheral resistance, cortisol and norepinephrine (NE) levels in healthy populations.[8, 20-22] Improved autonomic balance with reduced sympathetic and enhanced vagal effects have been noted with practice of meditation.[23] Improved Blood pressure in normal and hypertensive individuals have been demonstrated even with short-term meditation.[10, 24] In elderly patients with congestive heart failure, meditation has been shown to reduce NE levels and improve quality of life.[25]

Although different spiritual and non-spiritual techniques have been employed, the basic concept is to focus the mind on a repetitive thought, sound or image. Focusing on the breath has an advantage of something very accessible to everyone. Therefore, one becomes increasingly sensitive to the changes in the body and becomes psychologically tuned to the body rhythms. Concentration on breath as the object of meditation has been shown to improve well-being.[26]

Yoga is a form of meditation in association with structured physical exercises known as “asanas”. Yoga therapy has reduced symptomatic and asymptomatic episodes of AF during short term follow up in patients known to have AF.[27] Since yoga practice requires physical activity that may not be embraced by many of the older patients with heart failure, we chose simple Vipassana meditation to focus only on the mind body effects of meditation. In contrast to the Yoga My heart study where patients acted as their own control, we used a randomized control design in this pilot study. The average number of classes attended was 5.9±4.7 classes, with a mean attendance of 55± 35 %, though we had hoped for 100% attendance. The limitations were the distance for travel and majority of them chose to meditate at home. We had to trust that they were performing meditation based on their verbal report. Our goal was to have larger randomized study groups, however the enrollment was slow. Two patients from meditation group dropped out after the initial class, however we included them in the analysis. Due to limited funding, we could not extend the study for further enrollment. However, we followed these patients for longer period of time to assess their clinical outcomes. We did not identify any adverse effects from meditation.

After focusing two decades on the invasive management of AF by ablation, the electrophysiology world has refocused on lifestyle changes after the results of ARREST-AF and LEGACY studies, which have shown improved control of AF with risk factor modification.[28, 29] One of the key risk factors addressed was weight reduction; mindfulness based approach has been shown to improve eating behaviors and reduction in BMI. [30, 31] Similarly, revisiting arrhythmia control with the old world approach of mindfulness meditation may have positive clinical effects in conjunction with advanced technology.

The effect of meditation on physiological parameters is by reducing emotional reactivity. These have been associated with structural changes in the prefrontal cortex, cingulate cortex, insula and hippocampus in MRI studies.[32] Although these changes are seen even after short-term training, the inertness to negative images seem to require long term practice of meditation [33] as noted in the Buddhist monks.[34] In our investigation, our training period was short, however patients were expected to meditate long term. We did not find any change in heart failure parameters such as BNP or 6 min walk test, however the arrhythmic events were reduced. A larger sustained web or smart phone based meditation study acceptable by many would make it easier for patients and might provide more insight into the clinical benefits.

Limitations

We acknowledge that this is a small pilot study to investigate the effects of meditation in the high-risk heart failure patients with implantable tachyarrhythmia devices. The ability and willingness to attend regular meditation classes and follow through every day is an important factor to assess the clinical effects. Our strength is the study design of randomization and a long term follow up. To our best knowledge, ours is the first study to investigate the clinical effects of meditation in heart failure patients.

Conclusion

In our pilot randomized control trial, meditation seems to have positive effects on cardiac arrhythmia events; we need larger multicenter investigation to evaluate the beneficial effects.

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