A MINDFULNESS BASED INTERVENTION FOR TREATMENT OF ANXIETY IN ICD PATIENTS: FEASIBILITY AND BASELINE FINDINGS

A Dissertation Presented

By

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To Carla,

May your memory be for blessing

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ABSTRACT

Background. Primary and secondary prevention trials have shown that implantable cardioverter-defibrillators (ICD) reduce the risk of cardiac death, but concerns have been raised regarding the psychological well-being of ICD patients. Anxiety can affect a significant proportion of these patients, but there is limited information about prevalence and determinants of anxiety after the implementation of the more recent guidelines for ICD implantation. Several behavioral interventions have been effective in improving anxiety in these patients, however the efficacy of mindfulness-based interventions (MBI) has not been investigated in ICD patients, and there is limited information regarding the characteristics of pre-intervention, "dispositional" mindfulness in patients with cardiovascular disease never exposed to mindfulness training. The aims of this dissertation project were: 1) To determine the feasibility of a randomized clinical trial of a phone-administered, mindfulness-based training program, as measured by recruitment and retention rates, treatment adherence and fidelity; 2) To evaluate the current baseline prevalence and determinants of anxiety in the study population and 3) To describe the correlates of dispositional mindfulness in the study population.

Methods. The study was conducted at the Electrophysiology Service at the UMass Memorial Medical Center. All consecutive patients who recently underwent an ICD procedure or received ICD shocks were screened for eligibility to participate in a pilot randomized controlled trial in which an eight session, phone-delivered, weekly MBI was compared to a usual care condition. Assessments were performed at baseline and post-intervention. A cross-sectional design was used for aims 2 and 3. Anxiety was assessed

using the Hospital Anxiety and Depression Scale; a shortened version of the Five Facets of Mindfulness questionnaire was used to evaluate mindfulness.

Results. Thirty patients (21 M, 9 F; mean age 63.1 ±10.3 years) were enrolled in the study. The methods ultimately adopted to screen, recruit, and retain study participants were feasible to conduct and satisfactory to ICD outpatients, and the study intervention was safe. Phone delivery resulted in excellent retention rates and limited costs. Assessments of treatment fidelity showed that the content of the intervention was delivered as intended in almost 100% of cases.

The study findings do not show a decrease in the overall prevalence of anxiety in ICD patients compared with earlier cohorts; anxiety was associated with young age, low socio-economic status and previous psychological morbidity, but not with ICD-related factors including prior shock delivery.

Finally, baseline mindfulness was most strongly associated with previous psychological morbidity (in particular, depression), and current anxiety symptoms.

Conclusion. Psychological morbidity appears to be the major determinant of anxiety in the patients currently enrolled in the study. Dispositional mindfulness is inversely associated with current anxiety and depression and with prior psychological morbidity, supporting the hypothesis of a modulating role of mindfulness on the processing of negative emotions. A phone-delivered, individual MBI is feasible, acceptable to patients and can be adequately delivered by trained instructors. The findings from this dissertation work support the need for larger clinical trials of MBI in ICD patients.

Table of Contents

Page

LIST OF TABLES

LIST OF FIGURES

Figure *Page*

CHAPTER I

Introduction

Psychological Complications of Implantable Cardioverter Defibrillators

Implantable cardioverter-defibrillators (ICD) have been demonstrated to reduce the risk of cardiac death in both primary and secondary prevention trials,[1-5] but concerns have been raised regarding the quality of life[6-10] and psychological well-being[11-13] of ICD patients. Although many patients adapt to the device over time, a significant proportion experience symptoms compatible with a diagnosis of anxiety disorder.[14, 15] However, indications for ICD implantations[16] have changed over the past twenty years, and a large percentage of patients determined to be at high risk for sudden cardiac death now receive an ICD as a primary prevention procedure. As a result, the current prevalence of symptoms of psychological discomfort may also have changed, but they have been largely unexplored.

In the past twenty years, several behavioral interventions aimed at improving psychological well-being in these patients have been developed, and preliminary evidence of a positive effect has been shown in small studies published in the past ten years.[17] Many studies employed relaxation techniques as an adjunct to cognitive behavioral therapy (CBT), exercise programs, or educational programs, but the possible effect of relaxation and meditation techniques and specifically of mindfulness-based interventions have not been investigated. However, most studies investigating the possible effects of mindfulness training have been only exploratory, often using convenience samples, non-randomized designs, and short follow-up periods.[18] Also, there

is very limited information regarding the characteristics of pre-intervention (or "dispositional") mindfulness and its possible association with specific demographic and psychological characteristics.

This study explored the baseline prevalence of anxiety and the predictors of anxiety and mindfulness in ICD patients and pilot tested the feasibility a mindfulness-based intervention intended to improve mindfulness and anxiety levels in these patients. A randomized controlled study design was used in which an eight session phone-delivered mindfulness intervention was compared to a usual care condition among consecutive candidates for ICD procedures. The study was conducted at the Electrophysiology Service at the UMass Memorial Medical Center. Assessments were performed at baseline and at the end of the intervention (9 weeks after enrollment). The following specific aims and associated hypotheses were proposed for this dissertation project:

1) To determine the feasibility of a randomized clinical trial of a phone-administered, mindfulness-based training program, as measured by recruitment and retention rates, treatment adherence and fidelity.

Hypothesis: A phone-delivered mindfulness based intervention will be feasible and result in higher retention rates compared to traditional mindfulness training programs.

2) To evaluate the current baseline prevalence of anxiety in the study population, and evaluate its association(s) with disease and ICD characteristics.

Hypothesis: The prevalence of anxiety will be lower than that previously reported in the literature; anxiety with be associated with young age, female gender, and prior ICD shocks.

3) To describe the baseline distribution and correlates of mindfulness in patients with cardiovascular disease who were never exposed to formal mindfulness training, and whether mindfulness is associated with baseline demographic and psychological characteristics

Hypothesis: Baseline mindfulness levels will be inversely associated with anxiety and depression.

Considering the widening of the indications for ICD treatment, the number of patients undergoing this procedure will continue to increase, and the number of patients in need of psychological support may increase accordingly. The long-term objective of this study, should an effect be demonstrated, is to offer an inexpensive, easily delivered intervention to decrease psychological distress in ICD patients.

Indications to ICD implantation

ICDs[19] are electronic devices used to treat severe ventricular arrhythmias and to prevent sudden cardiac death. The ICD was first developed in the late 60s by Dr Michel Mirowski and his colleagues after the death of a close friend and mentor who had been affected by recurrent episodes of ventricular arrhythmia. The limited availability of effective medical treatments for patients at risk of sudden death motivated the authors to design a device that would monitor the cardiac rhythm and deliver defibrillating shocks

upon the occurrence of a severe cardiac arrhythmia. The first ICD was implanted in 1980 in a patient who had a history of multiple cardiac arrests.[20]

ICDs are composed by electronic circuitry, a power source, and a memory, with a microprocessor coordinating the various parts of the system.[21] High-voltage capacitors transform the battery-provided voltage into discharges ranging from less than 1V for pacing to 750V for defibrillation. ICDs can terminate ventricular arrhythmias in three ways: by anti-tachycardia pacing (ATP), by cardioversion (synchronized shock), or by defibrillation (non-synchronized shocks). The therapy is delivered based on the rhythm detected by the device. Tachyarrhythmias in the ventricular fibrillation range (typically hemodynamically unstable) are treated by immediate defibrillation, whereas ventricular tachycardias, particularly the slower ones that are more hemodynamically stable, are usually treated by ATP.[19] Modern ICDs store all information relative to ICD activity, such as number of shocks and type of arrhythmia; all the information can be retrieved non-invasively.

Shock delivery and electrical storms (i.e., malignant ventricular arrhythmias resulting in device intervention $\geq$ 3 times during 24 hours) are not rare occurrences: the incidence of electrical storms is between 10% to 28% over a one to three year follow-up period when ICDs are implanted for secondary prevention,[22, 23] and 4% in patients receiving an ICD for primary prevention.[24]

Primary and secondary prevention trials[1-5] have consistently shown that ICDs reduce the risk of cardiac death. Consequently, ICDs have become the first choice treatment for patients at risk of sudden cardiac death. In fact, according to weighted

national estimates from the Healthcare Cost and Utilization Project [25] in 2007 insertion, revision, replacement, removal of cardiac pacemaker or cardioverter/defibrillator procedures ranked 20 among all hospital procedures with a total of 329,904 procedures, and four for total costs, with a national bill reaching almost 25 million dollars.

Coronary heart disease and its consequences account for at least 80% of sudden cardiac deaths in Western countries[21] thus constituting the most common diagnosis in ICD recipients, while non-ischemic cardiomyopathies cause another 10 to 15%. More rare cardiac pathologies are usually the underlying cardiac disease in younger ICD candidates, among whom the prevalence of coronary atherosclerosis is lower.

ICD-related concerns: anxiety and quality of life

Despite the proven efficacy of the ICD, concerns have been raised regarding the quality of life [7-12] and psychological well-being of ICD patients. [11, 12] Although many patients adapt to the device over time, some degree of psychological distress is experienced by up to 87% of patients,[26] and a significant proportion (from 13% to 38%) experience symptoms compatible with a diagnosis of anxiety disorder,[27] while the prevalence of depression is similar to the general population.

Generally, patients experiencing shocks are at higher risk of psychological distress.[8-10, 28] ICD shocks are often perceived as very painful by patients. Patients can be frightened and anxious after experiencing a shock, anticipating that the next movement or activity might trigger another shock. Some patients may experience inappropriate shocks (typically the result of atrial fibrillation with a rapid ventricular response) as occurred in

11.5% of the 719 patients enrolled in the Multicentre Automatic Defibrillator Implant Trial (MADIT) II study.[29]

Sears and colleagues[30] suggested that young age (<50 years), female gender, poor device understanding, and electric storms are important risk factors for the development of psychological problems, while a limited number of studies have examined the role of pre-implantation psychological characteristics and co-morbidities. [31, 32]

Finally, there are several reasons to hypothesize that the prevalence of anxiety in ICD patients may be decreasing.[31] Most data regarding the prevalence of psychological disturbances in ICD patients were generated from studies conducted well before the publication of the MADIT II and the Sudden Cardiac Death in Heart Failure Trail (SCD-HeFT) studies[4, 5] and before the implementation of the American Heart Association/American College of Cardiology guidelines[16] recommending ICD implantation for the primary prevention of sudden cardiac death. Thus, most patients now receiving an ICD never experienced a cardiac arrest or severe ventricular arrhythmia. As a result, the there have been preliminary reports[33] that the current prevalence of symptoms of psychological discomfort may be lower compared to earlier reports referring to patients receiving an ICD for secondary prevention only.[14]

Patients' perspective on ICD implantation

In order to understand the experience of living with an ICD during the first six months after implantation, in 1993 Burke[34] interviewed a group of twenty-four subjects who underwent ICD implantation in one of two mid-western medical centers. Patients' descriptions of spontaneous ICD discharges included:[34] "Getting kicked by a horse in the

chest", "Like you've been hit by a cement truck", "Like being hit with a Mack truck", "Like running into a cement wall", "Like touching an electric fence with a weed eater". A further source of concern is the possible failure of the ICD, including concern that the system will not be able to control the dysrhythmia or concern about depending upon an electronic device for survival.[34] Patients are sometimes afraid that the ICD battery might fail without warning, thus endangering their lives; they also worry about the need to replace the battery in the future.[35]

Another important cause of anxiety in ICD patients arises from the confrontation with death. Burke et al. concluded:

On a day-to-day basis, every person lives as though invulnerable to death. That is, we all know we will die someday, but we usually do not think, believe, and act as though today is the day. All of the (ICD) patients in this study experienced life-threatening ventricular dysrhythmias or significant events that led them to think, believe, and act as though each day might be the day.[34]

Although this daily confrontation with death may lead to a better appreciation of life in some patients, many patients feel they lost control over their lives.

Anxiety and mortality in cardiac and ICD patients

Strong emotions triggered by earthquakes, war and terroristic attacks can precipitate cardiac events.[36-39] Emotional[40,41] and mental stress[42] have a detrimental effect on both cardiac perfusion and function, suggesting that at least in some settings negative emotions may play a causal role in cardiac events, as opposed to being secondary phenomena. Similarly, anxiety can significantly contribute to the overall cardiovascular

mortality and morbidity in patients with coronary heart disease [43-48] and to the high one-year mortality rate[1] observed in ICD patients despite the effectiveness of the device in treating dangerous arrhythmias and in preventing sudden cardiac death. A decrease in heart rate variability[49-51] and baro-reflex control, [52-54] and alterations in the coagulation system[55] are among the different mechanism by which anxiety may worsen cardiac outcomes.

Review of psychosocial interventions in ICD patients

Prior research has demonstrated that conditions promoting psychological well-being such as social support or pet ownership [56, 57] improve heart rate variability and survival in patients affected by coronary heart disease. During the past ten years, different psychosocial interventions have been designed with the aim of promoting psychological well-being in ICD patients.[58] From the introduction of the ICD in clinical practice up to 2009, 12 experimental studies of non-pharmacological interventions have been published. Such studies evaluated the effect of educational interventions, support groups and cardiac rehabilitation, sometimes delivered as mixed interventions (i.e. a psychological intervention or a support group combined with an exercise program). Of the 12 studies reviewed, ten adopted a randomized controlled trial (RCT) design;[59-69] in particular, one study used a cluster RCT design,[70] and two adopted a cross-over RCT design.[64, 65] Recruiting centers were teaching hospitals,[59, 60, 63, 66, 68, 69, 71] or tertiary referral centers.[61, 64, 65, 67, 72] Sample sizes were generally small (range 12-192): in seven studies, the intervention or the control arm had less than 20 participants.

The effect of the intervention on anxiety [60-68, 72] and depression[60-68] was assessed in all but three[69, 71 59] studies by means of self-administered questionnaires. For anxiety, the most frequently used instruments were the Hospital Anxiety and Depression Scale (HADS),[64, 65, 67] and the State-Trait Anxiety Inventory (STAI);[61, 66, 68, 72] for depression, the Beck Depression Inventory (BDI),[60, 66] the Center for Epidemiological Studies Depression Scale (CES-D),[61, 68] and the HADS.[64, 65, 67] The same instrument was sometimes used across studies; however, different outcomes were often evaluated. Mean scores pre/post intervention within groups were compared in some studies, [61, 64, 72] while others compared mean pre/post intervention changes in HADS anxiety scores between groups,[65] mean STAI anxiety scores between groups,[66] or change in the proportions of patients with HADS scores indicating significant anxiety.[67] Kohn[66] evaluated both STAI trait anxiety and state anxiety scores, while others [61, 68, 72] focused on state anxiety only.

Some studies used multi-component interventions,[64, 65, 67-69] while others employed single-component interventions such as support groups,[71, 72] phone support,[61] CBT therapy, [60, 66] or educational interventions.[59, 63] CBT was generally a core component of interventions using multiple components.[60, 64, 65, 67, 68] In three studies [64, 65, 67] patients were also involved in an aerobic exercise program. The duration of the intervention was different across studies, ranging from two [63] to 20 weeks.[66] The control condition was represented by "usual care" in nine studies; in one study it was not reported,[72] and it was described as "no therapy" in another.[66] Sears reported delivering a shorter version of the intervention (one-day workshop) in addition to usual care for ethical reasons.[68] Only eight studies reported what a "usual care" assignment would

entail; [48,50,52-54,56-58] patients receiving usual care were exposed to very different "usual care" procedures.

Overall, out of nine studies evaluating the impact of the intervention on anxiety, six [60, 64-68] showed a significant positive effect, while three [62, 63, 72] showed no improvement. In the remaining two studies that measured psychological outcomes other than anxiety, Badger[71] showed no improvement in psychological adjustment, and Sneed[69] reported no differences in the mood state profile at four months; both used a support-group intervention. All the studies showing a positive effect included CBT either as the only intervention,[66] or as an element of a multi-component intervention.[60, 64, 65, 67, 68] The three studies showing no effect were either purely educational programs,[63] or support interventions.[61, 72]

One study [68] included biological markers of stress (salivary cortisol) and inflammatory markers (TNFα and IL-6) in the outcome measures reporting a significant reduction of cortisol level over time in both groups. Overall, studies showed a positive effect on anxiety. CBT was the most effective intervention for anxiety, either as the only intervention,[66] or as an element of a multi-component intervention.[60, 64, 65, 67, 68]

Of the eight studies including depression as an outcome, only four [64-67] showed an effect. Fitchet[64] found a reduction in mean HADS depression scores from pre- to post-rehabilitation in the intervention group (9.9 to 6.7), while scores increased in the control group. In the study by Frizelle[65] HADS depression scores decreased significantly post vs. pre-treatment. Kohn[66] reported a decrease in mean BDI depression scores in the intervention group (6.9 vs. 15.0, but baseline depression scores were not reported).

Lewin[67] found a reduction in the proportion of patients with HADS scores > 8 (clinically significant anxiety) in the intervention vs. the control group (-13% vs. -2.1%). Interestingly, three of the studies showing a positive effect included an exercise component.[64, 65, 67]

Fifty percent of the studies included cardiac outcomes: shocks in six studies;[60, 61, 64-67] sustained ventricular tachycardia requiring pacing for termination in two,[64, 65] and number of ICD storms in one study.[67] Two studies[62, 67] also evaluated the effect of the intervention on the number of hospitalizations and visits, and three[64, 65, 67] included exercise capacity as well. The only study including heart rate variability among the study outcomes [60] found an improvement in two indicators of autonomic tone, and concluded that the intervention improved adrenergic/vagal balance. None of the studies showed a significant effect on shocks. At one year of follow-up, Chevalier[60] showed a non significant reduction in the number of patients receiving a shock (three in intervention vs. six in control group) and a reduction in shock rate and in the use of beta-blockers and other anti-arrhythmic drugs in the intervention group (post-hoc analysis). Lewin[67] showed a non-significant difference in the proportion of patients receiving shocks (9.5% vs. 13%) and ICD storms (1.6 vs. 4.8) at six months of follow-up. The mean number of shocks was similar in both groups.

Three additional studies were recently published. The first[73] was a randomized clinical trial of a six-month individual phone counseling intervention compared to usual care in 119 ICD patients with anxiety symptoms. The improvement in anxiety (HADS-Anxiety), psychological distress (SCL-K-9), and somatic quality of life (SF-36-PCS) was

limited to patients aged less than 65 years old but was not observed in older patients. The second randomized controlled study[74] compared the effect of a psycho-educational intervention (group or telephone counseling including ICD education, symptom management, and coping skill training) on anxiety, depressive symptoms, functional status, and health resource use vs. usual care during the first year after ICD implantation in 246 ICD patients. Anxiety (State-Trait Anxiety Inventory) and depressive symptoms (Beck Depression Inventory II) decreased in all groups over the 12 months follow-up and early after ICD implant; the probability of depressive symptoms was lower in the intervention group at one year, as well as disability days/calls to providers.[74] A third study evaluated the effectiveness of a female-specific intervention including ICD education, CBT strategies, and group social support in 29 female ICD recipients versus a wait-list control group, and showed that pre-post measures of shock anxiety decreased significantly in the intervention group, with women under the age of 50 experiencing greater reduction in shock anxiety.[75]

Overall, psychosocial interventions demonstrated a positive effect on anxiety. CBT was the most effective intervention, either as the only intervention,[66] or as an element of a multi-component intervention.[60, 64, 65, 67, 68] However, they generally demonstrated no effect on the number of shocks and arrhythmic events, likely because most studies were not sufficiently powered and were of too short a duration of follow-up to detect this infrequent outcome. Many studies suffered from additional methodological limitations, such as inadequate randomization, heterogeneity of the study population, and different timing of intervention delivery. Likewise, lack of information about cardiac

conditions during follow-up made it impossible to conclude whether the improvement in anxiety scores was due to the intervention or to an improvement in the underlying cardiac condition. In conclusion, the initial evidence of a beneficial effect of psychosocial interventions in ICD patients needs to be confirmed by further research. Future studies should be designed as large scale RCTs. The recruitment of a large number of patients, together with an adequate duration of follow-up (at least one year), would allow the determination of the effect of the intervention on shocks and arrhythmias. Considering the non-pharmacological nature of the treatments, an adequate description of the interventions, (standardization procedures, implementation and treatment fidelity assessments) is required. An "attention control" comparison group would probably be ethically and methodologically superior to a "usual care" condition. Finally, although many studies supplemented the intervention with relaxation techniques taught during sessions or self-taught with the use of tapes,[60, 64, 65, 67, 69] no study evaluated if relaxation or meditation alone may have a favorable effect on anxiety.

Physiological effects of meditation

Wallace and Benson[76] described for the first time the characteristics of the "relaxation response", i.e., the physiological response associated with meditative practices. In this study the relaxation response consisted of a generalized decrease in sympathetic nervous system (SNS) activity, decreased oxygen consumption, respiratory rate, and minute ventilation; a slight decrease in arterial blood pH and base excess; and a decrease in blood lactate levels (an indicator of stress). In another experiment, the effect of meditation on SNS activity was assessed in experimental and control subjects exposed

to graded orthostatic and isometric stress.[77] Plasma norepinephrine concentrations, an index of SNS activity, increased disproportionately over heart rate and blood pressure in the experimental group, suggesting that in subjects eliciting the relaxation response more norepinephrine is required to produce the normal compensatory increases in heart rate and blood pressure. There is also evidence of reduced end-organ sensitivity to catecholamines in subjects practicing meditation, possibly mediated by a lower percentage of functional lymphocyte beta-adrenergic receptors compared to non-practitioners.[78] These changes, which are different from those occurring during sleep or quiet sitting, led the authors to describe meditation as a "wakeful hypo-metabolic state" or "relaxed alertness". In summary, previous research has shown that meditative practices are usually associated with a reduction in the activity of the SNS.

Meditation-based interventions in patients affected by coronary heart disease

The decreases in SNS activity and in oxygen consumption that accompany meditation states may be beneficial in patients affected by coronary heart disease. Nevertheless, only a few studies have evaluated the effect of meditation training in these patients, and they mostly adopted a meditation technique called transcendental meditation. Transcendental meditation is a meditation technique introduced in the sixties by Maharishi Mahesh Yogi, based on concentration practices such as the repetition of a sound called a "mantra". Cunningham and colleagues observed that the practice of transcendental meditation for three months significantly improved exercise tolerance, angina episodes, and quality of life in nine women affected by syndrome X, [79] a syndrome characterized by anginal chest pain, positive response to exercise stress testing,

and normal coronary angiograms. In an eight month transcendental meditation program, Zamarra and colleagues observed increased exercise tolerance, maximal workload, and delayed onset of ST-segment depression at exercise tolerance testing in a group of patients with documented coronary artery disease compared to a wait-list control group.[80] Benson and colleagues found that a non-cultic meditation technique reduced the number of premature ventricular contractions in patients affected by coronary heart disease.[81] A recent randomized study of transcendental meditation compared to an educational program in twenty-three African American patients aged 55 or older with New York Heart Association class II or III chronic heart failure showed a significant improvement in functional capacity, quality of life and re-hospitalizations during the six months of follow-up.[82]

Mindfulness-based interventions

Definition of mindfulness-based intervention

Mindfulness is the English translation of the word "Sati" in Pali, an ancient language from northern India. Sati means memory, recognition, consciousness, intentness of mind, wakefulness of mind, mindfulness, alertness, lucidity of mind, self-possession, conscience, self-consciousness.[83] The construct of mindfulness is rooted in ancient Buddhist treatises, which present an elaborate psychological theory of the mind, based on the practice of a particular technique called mindfulness meditation ("vipassana"). Mindfulness can be defined as a non-judgmental, sustained moment-to-moment awareness of mental states, physical sensations, perceptions, affective states, and thoughts.[18] The basic mechanism[84] behind mindfulness-based training is that an enhanced

awareness of the experiences of the present moment helps reduce or modulate negative emotions such as anxiety and depression and improves coping with stress and negative emotions.

Mindfulness-based programs are behavioral interventions aimed at developing mindfulness.[85] Mindfulness-based interventions have been shown to reduce anxiety, depression, sleep disturbance and a variety of physical symptoms in different medical conditions[18] such as cancer,[86-89]chronic pain,[90, 91] anxiety disorders,[92] rheumatoid arthritis,[93] and fibromyalgia.[94] When associated with CBT, mindfulness training has been shown to reduce the rate of relapse/recurrence in major depression.[95] Mindfulness meditation decreased anxiety and increased influenza antibody titers in response to vaccinations in healthy volunteers.[96] Despite the increase in the quantity and quality of research in this field, studies of mindfulness-based interventions still suffer from several limitations. Many studies have been only exploratory, often using convenience samples, non-experimental or quasi-experimental designs, and short follow-up periods. Adherence to mindfulness programs was rarely assessed, and most studies did not include an active control group.[97] As has been emphasized by Grossman and colleagues,[18] only large scale, appropriately designed studies would fill the gap between the promising results of mindfulness-based training and these important methodological limitations. In addition, there is very limited information regarding the characteristics of baseline, or "dispositional" mindfulness and its possible association with specific demographic and psychological characteristics.

Studies of mindfulness-based intervention in patients with cardiac diseases

Only a few studies have explored the possible effect of mindfulness-based interventions in cardiac patients.[98-100] A randomized, controlled pilot study by Tacon and colleagues in 2003[98] evaluated the effect of an eight week mindfulness-based stress reduction program on anxiety in 18 women affected by different cardiac pathologies. Pre/post intervention state anxiety scores improved in the mindfulness group compared to a wait-list control group. The effects of an eight-week mindfulness-based stress-reduction program on the resting levels of stress hormones, physical functioning, and sub-maximal exercise responses in women with heart disease was evaluated in a study reported by the same group of researchers in 2004, and probably refers to the same study sample.[99] The study did not show pre/post intervention changes in cortisol levels, physical functioning, or sub-maximal exercise responses. The Support, Education, and Research in Chronic Heart Failure (SEARCH)[100] study was a quasi-experimental study evaluating the impact of a mindfulness-based intervention on clinical outcomes, depression, and quality of life in of 208 adults with chronic heart failure. Treatment resulted in lower anxiety and depression, and in improved symptoms and clinical scores over time, while there were no effects on death or number of re-hospitalization at one year.

Due to different flaws in study design, such as the lack of randomization, the evidence of a therapeutic effects of meditation on cardiovascular and other diseases is weak;[101] further studies with a rigorous design are needed.

Conceptual framework

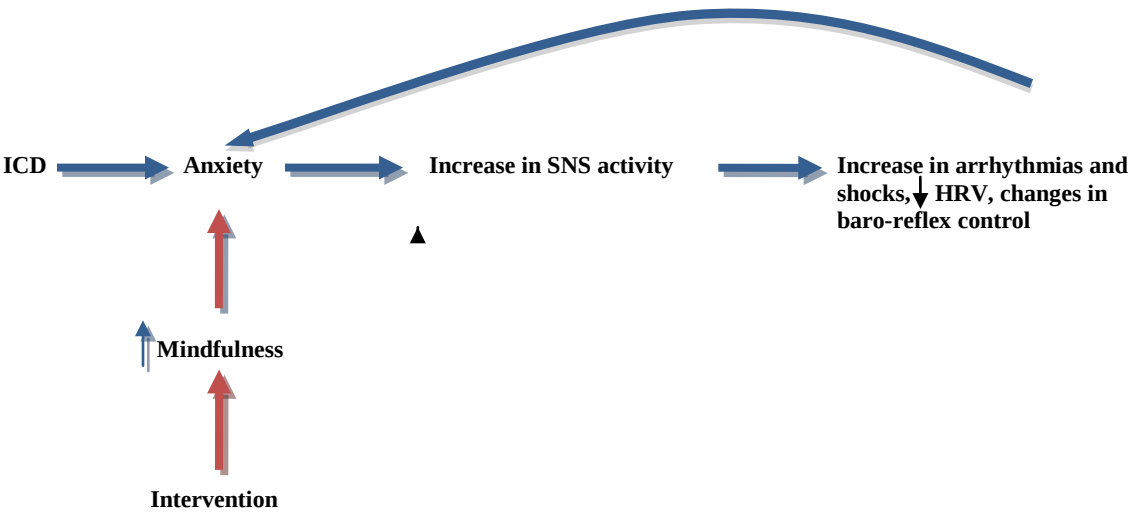
The overall framework for this pilot study is based on the association between

ICD and anxiety. Increased anxiety leads to an activation of the SNS, and an activation of the SNS may in turn trigger more arrhythmic episodes and more shocks. The hypothesized mechanism by which the proposed intervention may affect anxiety levels in ICD patients is through an increase in participants' mindfulness levels, which will in turn reduce anxiety. This may then result in a reduction of the activity of the SNS, and to a reduction in the number of arrhythmic/cardiac events. ICD patients provide a unique and ideal model to test this hypothesis because the device allows the recording of many parameters including the number of delivered shocks and the frequency of serious arrhythmias (e.g., ventricular tachycardia) even when a shock does not result. (Figure 1.1.)

Theoretical model

A number of possible psychological mechanisms have been suggested to explain the effects of mindfulness. The basic mechanism of mindfulness-based training[84] is that an enhanced awareness of the experiences of the present moment leads to a decrease in negative emotions such as anxiety and depression and improves coping with these negative emotions. This is achieved through a change in the patient's relationship to his/her thoughts and emotions. The trainee is encouraged to view thoughts and emotions as events/products of the mind rather than as reality. In fact, mindfulness training has been shown to reduce both distractive and ruminative thoughts/behaviors[102] when compared with relaxation techniques, and this may be a unique mechanism by which mindfulness meditation reduces stress. Consequently, mindfulness training results in improved *regulation* of emotions. Regulation of emotions is different from control of

Figure 1.1. Conceptual framework of the study



SNS=Sympathetic nervous system
HRV=heart rate variability

emotions. In fact, mindfulness may temporarily increase emotional discomfort because the patient is no longer avoiding his/her feelings. Nevertheless, the component of nonjudgmental acceptance accompanying mindfulness training is expected to help the patient recover more quickly from strong emotional reactions associated with a specific stressful event - in this case, the experience of living with an ICD (Figure 1.2).

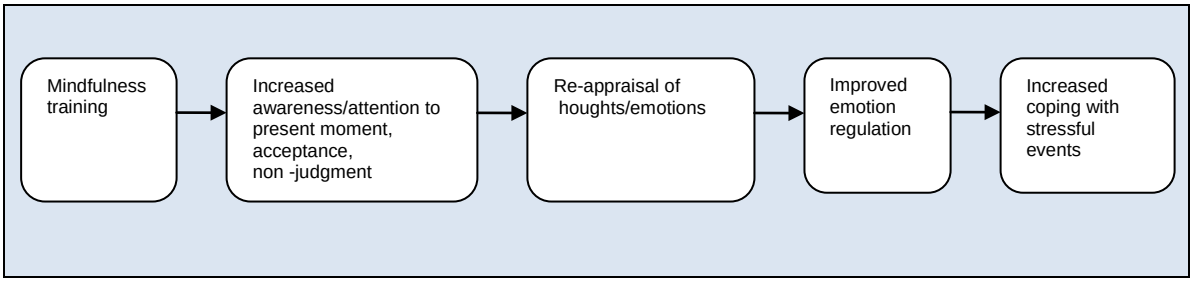
Human subjects

The study protocol and all the study materials to be used in this project have been approved with an expedited review by the Committee for the Protection of Human Subjects at the University of Massachusetts Medical School (Docket H-13078). The study has been re-approved for each following year of study.

Summary and significance of the proposed study

The significance of this project is potentially great because the number of candidates for ICD implantation is rising due to a broadening of indications to include primary prevention of sudden death, and because the prevalence of anxiety in this population reaches up to 40%. To date, there have been no published studies of mindfulness-based interventions in ICD patients. A mindfulness-based intervention, adapted to this group of patients, is relatively inexpensive, and, once learned, can easily be self-administered by the patient. If proven effective, it could positively impact the quality of life, and, possibly, the incidence of arrhythmias and delivered shocks in these patients.

Figure 1.2. Mindfulness theoretical model



CHAPTER II

Design and Feasibility of a Mindfulness-Based Intervention for Treatment of Anxiety in Patients with an Implantable Cardioverter Defibrillator (ICD)

Introduction

According to a large population-based survey study,[103] up to 36% of patients affected by cardiovascular disease in the United States report to have used complementary/alternative therapies during the previous year, and up to 17% report the utilization of different "mind-body" techniques such as meditation, guided imagery, progressive muscle relaxation, or deep breathing exercises. Among the recipients of mind-body treatments, 93% defined them as at least somewhat important, and 33% rated them as "very important".[103] Despite the popularity of mind-body therapies, there are a limited number of studies evaluating the efficacy of such approaches in patients with coronary heart disease.

There is sound theoretical evidence supporting the possible usefulness of meditation-based approaches in patients with cardiovascular disease. Wallace and Benson[76] described for the first time the characteristics of the "relaxation response", i.e. the physiological response associated with meditative practices. The relaxation response consists of a generalized decrease in sympathetic nervous system (SNS) activity, decreased oxygen consumption, respiratory rate, and minute ventilation, with no change in respiratory quotient; slight decrease in arterial blood pH and base excess; and a decrease in blood lactate levels (an indicator of stress). In another experiment, the effect

of meditation on SNS activity was assessed in experimental and control subjects exposed to graded orthostatic and isometric stress.[77] Plasma norepinephrine concentrations, an index of SNS activity, increased disproportionately over heart rate and blood pressure in the experimental group, suggesting that in subjects eliciting the relaxation response more norepinephrine is required to produce the normal compensatory increases in heart rate and blood pressure. There is also evidence of reduced end-organ sensitivity to catecholamines in subjects practicing meditation, possibly mediated by a lower percentage of functional lymphocyte beta-adrenergic receptors compared to non-practitioners.[78] These changes, which are different from those occurring during sleep or quiet sitting, led the authors to describe meditation as a "wakeful hypo-metabolic state" or "relaxed alertness".

Overall, research has shown that meditative practices are usually associated with a reduction in the activity of the SNS and in oxygen consumption that may be beneficial in patients affected by coronary artery disease. However, despite this preliminary evidence, there is limited information regarding the effect of meditation training in cardiovascular patients. Previous investigations principally studied a meditation technique called transcendental meditation, [79-81] while fewer have explored the possible effect of mindfulness-based interventions in this population. Mindfulness interventions generally utilize a non-cultic form of the so-called "vipassana" technique, a meditation practice rooted in ancient Buddhist tradition. The most popular and well known mindfulness-based program is the Mindfulness-Based Stress Reduction (MBSR)[90] program. Since its founding by Dr. Jon Kabat-Zinn three decades ago over 13,000 medical patients with

various chronic diseases have completed the program, which has shown promising results in a wide range of medical and psychological conditions.[18]

A limited number of studies examined the possible effect of mindfulness-based approaches in patients with cardiovascular disease. A randomized, controlled pilot study by Tacon and colleagues [98] evaluated whether an eight-week MBSR program would improve anxiety in 18 women affected by different cardiac pathologies. Pre/post intervention state anxiety scores improved in the mindfulness group compared to a wait-list control group. The effect of the same intervention on resting levels of stress hormones, physical functioning, and sub-maximal exercise responses in women with heart disease was studied by the same group of researchers in 2004, and probably refers to the same study sample.[99] The study did not show pre/post intervention changes in cortisol levels, physical functioning, or sub-maximal exercise responses. Finally, the Support, Education, and Research in Chronic Heart Failure (SEARCH)[3] study was a quasi experimental, non-randomized study of 208 adults designed to assess the impact of a mindfulness-based intervention on clinical outcomes, depression, and quality of life in patients with chronic heart failure. Treatment resulted in lower levels of anxiety and depression, and in improved symptoms and clinical scores over time, while there were no effects on death or number of re-hospitalization at 1 year.

Most studies of mindfulness-based interventions in cardiac patients suffer from several limitations. First, they have rarely been conducted in clinical settings. Second, they did not provide a description of the flow of patients through the study (i.e., they did not include a CONSORT[104] diagram). Consequently, no information is available about

the number of patients that needed to be screened in order to recruit the final study sample, refusal rates, and other indicators of interest in a mindfulness-based intervention, and it is thus problematic to estimate the feasibility of such interventions in a "real life" clinical setting. Another common limitation of studies of mindfulness in this population is the lack of treatment fidelity evaluations. According to Resnig and colleagues,[105] the demonstration of treatment fidelity is a fundamental methodological requirement of any trial testing the efficacy of behavioral interventions. According to these authors, a behavioral intervention satisfies treatment fidelity requirements if the treatment provided is delivered consistently to all participants randomized to a specific intervention, if there is no evidence of non-treatment related effects, and if the intervention is consistent with the theoretical models and goals of the study. In studies of mindfulness-based interventions, treatment fidelity is usually ignored and this constitutes one of the major limitations of this kind of research.

The present study was a randomized clinical trial designed to pilot-test the feasibility and the efficacy of a phone-administered, mindfulness-based training program intended to improve mindfulness and anxiety levels in patients undergoing an ICD procedure. The study intervention was modeled on the curriculum of the renowned MBSR[106] program offered at the Center for Mindfulness at the University of Massachusetts, adapted to the needs of ICD patients. Since the study intervention was based on an innovative MBSR format (i.e., phone administered) in a completely new population, it was extremely important to pilot-test the intervention curriculum for acceptability, usefulness of phone delivery in improving retention and adherence, and

logistics. This chapter describes the feasibility of the study recruiting, screening, and enrolling procedures as well as the intervention's content and fidelity. Baseline demographic and clinical characteristics of the study sample are also presented.

Methods

Setting

The study was conducted at the university campus of the UMass Memorial Medical Center, a high technology, state-of-the-art tertiary care medical center located in Worcester, MA, which is a clinical partner of the University of Massachusetts Medical School. The Electrophysiology Service in the Division of Cardiovascular Medicine admits more than 300 patients every year for ICD procedures.

Population and recruitment

Patients who had an ICD related event (shock) or who were scheduled for an ICD-related procedure at the catheterization lab were screened for study eligibility within a month of the procedure/event. All potentially eligible patients were mailed an interest survey and a letter inviting them to participate in the study. Patients were invited to return the survey at the occasion of their next visit or to call a dedicated phone number to communicate that they were not planning to participate; if they did not call, the PhD candidate would follow-up by phone. Since recruitment was based on mailings to eligible patients, a HIPAA waiver was obtained in order to access the medical record for a preliminary evaluation of eligibility and to obtain patients' addresses and phone numbers. In order to ensure a consistent and unbiased presentation of the study, a script of the first

phone contact call was developed. Once the patient expressed interest, a screening visit was scheduled. Since many ICD patients lived far from the hospital, they were offered the option to schedule the screening appointment at the same time of their scheduled visit to the outpatients' clinic.

Patients were considered to be eligible if they met the following criteria: age ≥ 21; ICD related procedure or recent ICD shocks*;* ability to understand and speak English; and access to a telephone. Patients were excluded from the study under the following conditions: inability/unwillingness to give informed consent, cognitive impairment, New York Heart Association (NYHA) functional class >III or an angina Canadian Cardiovascular Society class III and IV or otherwise clinically unstable, pending coronary by-pass or heart transplantation, co-morbid life threatening conditions, and ongoing severe depression or psychosis. The Blessed Orientation Memory and Concentration test[107] was used to screen patients for cognitive impairment. This questionnaire is an extremely condensed form (consisting of only six simple verbal questions) of a larger 26-question instrument, the Information-Memory-Concentration Mental Status Test devised by Blessed and colleagues. Patients scoring ≥ 10 were excluded from the study. Cognitive impairment would limit the ability of the subjects to adequately participate in the intervention, since mindfulness training requires a normal cognitive function and ability to focus the attention. Screening for ongoing depression and psychosis was based on DSM criteria of major depressive disorder or psychosis as documented by the physician in the charts of the most recent medical evaluation. Patients with a previous history of severe depression, post-traumatic stress disorder or psychosis

were not excluded from the study if during the study period they were under close supervision of their therapist or psychiatrist who needed to provide written approval of their participation in the study. Once eligibility was confirmed, full informed consent was obtained in person after a thorough explanation of the randomization process, of the study intervention, and of the risks and benefits involved. Since the study required access to protected health information, a HIPAA authorization was signed by each study subject in order to access his or her medical records. Participants received a copy of the consent and HIPAA document for their records. After baseline data collection, participants were assigned to the intervention arm or to the control group.

Randomization

Randomization was performed using a computer generated randomization scheme. The randomization sequence was generated using STATA[108] "ralloc" command, which produces a sequence of group assignments randomly permuted in blocks of several sizes. Block sizes of four and six were used in this study. A programmer generated the random allocation sequence and uploaded the table containing the random sequence of group assignments to an Access database. Based on this table, the participant was automatically assigned to a group by clicking the "Randomize" button.

Follow-up

In order to maximize retention, patients in both study arms received a weekly phone call inquiring about possible questions and concerns regarding their participation in the study. In case a participant missed an intervention session without giving notice to the instructor, he/she was immediately contacted by the instructor to inquire about possible

problems. After three missed contacts, a letter was sent to non-responding participants encouraging them to call to discuss their status. Study patients were not expected to stop any of their usual support services while at home or in the hospital, e.g., professional counseling, support groups, complementary or alternative therapies, or any anti-anxiety or antidepressant treatment.

The study protocol and the study materials were approved by the Committee for the Protection of Human Subjects at the University of Massachusetts Medical School (Docket H-13078).

Data management

The PhD candidate coordinated the initial eligibility screening; the mailing of the invitation letters; the interest follow-up calls; and the scheduling of the intervention sessions. She was also responsible for scheduling and facilitating the instructors' meetings and for conducting the weekly follow-up phone calls to study participants.

Daily management of study activities was facilitated by the use of Access ® Microsoft 2007 tracking system software. Scores from study questionnaires were immediately calculated, copied into abstraction forms together with other relevant study variables, and then entered into Stata software.[108] The study databases were kept on a server at UMMS, with multiple levels of password protection ensuring data security. All study materials were kept in a locked file cabinet.

Mindfulness-based intervention (MBI)

Rationale and format

The study intervention was modeled on the Mindfulness Based Stress Reduction (MBSR)[106] program offered at the Center for Mindfulness at the University of Massachusetts Medical School. This program, created by Jon Kabat-Zinn in the early eighties with the purpose of integrating mindfulness into everyday life[106] as a support in dealing with illness and stressful life events, offers training in traditional mindfulness meditation adapted to a non-Buddhist, clinical context. The MBSR program has been shown to be effective in the treatment of a variety of physical and psychological disorders. [18] Its curriculum includes participation in a weekly two and a half hour class for a total of eight classes; an all-day retreat; and the practice of mindfulness and yoga exercises at home. The following conditions suggested the need for a partial modification of the standard MBSR program for ICD patients:

1) Since up to 8% of patients may experience a shock while driving,[109] this activity may be discouraged in ICD patients in the six months following the ICD surgery. [110] Consequently, driving to regular MBSR classes would become problematic, limiting recruitment and adherence.

2) Anxiety levels are higher soon after ICD implantation,[111] and starting the intervention as close as possible to the ICD procedure may be important in these patients and help alleviate their symptoms when they are more intense. Since the regular MBSR program is offered four times a year, it was impossible for many ICD patients to receive the intervention when it was most needed.

3) Physical activity may trigger arrhythmias and shocks[112] and it is usually avoided by patients at this early stage for fear of ICD discharges. Consequently, the yoga exercises

included in the standard MBSR curriculum were excluded from the intervention. This modification also limited the confounding effect that physical activity per se may have on the psychological benefit derived from mindfulness training.

4) Similarly, the group format offered by the standard MBSR program may affect psychological outcomes just because of the social support and sense of belonging derived from the interaction with classmates over an extended period.

5) The individual home practice was shortened (to about 20 minutes daily) compared to the traditional 45 minutes recommended in the MBSR program. The rationale for this modification was to facilitate the adherence to the recommended individual practice in a population with severe health problems.

Since the proposed intervention involved several changes from the traditional MBSR program, the question arose of whether such changes were legitimate and if they might affect its efficacy. Since its inception in the early eighties the MBSR program has been successfully modified either to meet the needs of hospitalized patients[113] or to minimize the time commitment required.[114] Carmody et al.[115] found no association between the number of class hours employed in published trials of MBSR and the effect sizes for measures of psychological distress, leading the authors to conclude that the traditional eight-week program with 26 hours of class contact time may not be necessary for all participants to obtain significant reductions in psychological distress. Furthermore, different psychological interventions, including CBT,[116-125] have been successfully delivered over the phone, with a positive impact on retention. Consequently, it seemed

reasonable to hypothesize that mindfulness training could be successfully delivered over the phone.

The approach proposed for this study included eight phone delivered individual mindfulness training sessions (Table 2.1). Each training session lasted 30 minutes (20 minutes for intervention plus an additional ten minutes for questions, answers, and for scheduling the next intervention). At the beginning of the study, patients received an audio CD consisting of two different mindfulness practices, each lasting 15-17 minutes, consistent with the techniques learned during each session with the instructor: track one - sitting practice; track two - body scan practice). The script of the study CD is provided in the Appendix, page. The CD could be played using a regular CD player or a computer. A portable CD player was given to participants when needed. Participants were encouraged to listen to the audio CD every day, at least once a day, starting after the delivery of the first intervention, and then throughout the study. Patients had to track their mindfulness practice in a diary to be kept daily, and mailed to the study coordinator (the PhD candidate) once completed using pre-stamped envelopes. Family members were allowed to attend the intervention sessions, if they wished to do so.

Instructors

Instructors (five total) were healthcare professionals and graduates of the Center for Mindfulness professional training program with at least five years experience in mindfulness training and with a well developed mindfulness practice. In order to ensure continuity of delivery, each patient was trained by the same instructor throughout the duration of the intervention. Prior to the beginning of the study, the instructors received

Table 2.1. Characteristics of the study intervention

Component	Duration	Objectives/Content	Strategies/materials
Screening visit	10 minutes	• Patient receives general instructions about the intervention by the PhD candidate • Patient receives study CD player if needed, intervention CD, mindfulness diary	Study CD player Intervention CD Mindfulness diary
Phone sessions (8)	30 minutes	• Instructor checks on patient ability to practice specific mindfulness technique(s) taught during previous session(s) • Instructor inquires about symptoms/side effects • Instructor guides patient in mindfulness exercise and receives feedback from patient • Instructor and patient develop goals for next session • Instructor encourages participant to practice mindfulness technique with help of study CD (specifies track, 20'every day) • Instructor arranges next phone session • Instructor completes intervention checklist • Instructor reports problems to study manager (PhD Candidate)	Intervention checklist Digital recorder for session recording by the instructor

three hours of training. The training included a detailed review and discussion of the intervention script (see Appendix, page112), and of treatment fidelity procedures including completion of the intervention checklist at the end of the intervention (see Appendix, page 116 for a copy of the intervention checklist).

Instructors were also trained to use a digital recorder in order to tape-record each intervention session. Every week the instructors sent an electronic copy of the attendance form, the checklist, and the MP3 file of the recorded session to the PhD candidate. Recording were used for treatment fidelity assessments, and not to provide individual feedback to instructors. Bi-monthly meetings with the instructors were held under the supervision of Dr. James Carmody and of the PhD candidate. Meetings were aimed at discussing any difficulties that might be arising during training sessions. Although obviously not blinded to group assignment, instructors were blinded to the study outcomes.

MBI content

The study intervention maintained the basic components of the MBSR curriculum, while simplifying as much as possible their delivery. The theoretical background informing the intervention was inspired by the "parsimonious" model recently proposed by Carmody,[126] in which the capacity for attention control may explain the positive psychological outcomes associated with mindfulness programs. According to this model, mindfulness training can be described as an attention-redirecting training in which the trainee first learns to notice where his/her attention is drawn to, and then to shift the focus of attention from distressing objects of experience to

a “neutral object”. In the untrained individual, the presentation of a frightening thought usually generates an associational cycle in which the worrying thought leads to an unpleasant feeling, and the feeling in turn triggers an unpleasant physical sensation and so on (figure 2.1.A). This negative cycle can begin with a thought, a feeling, or a sensation, and self-maintain as long as the subject’s attention remains engaged with the content of any of its components.

During mindfulness training, the trainee learns two basic processes: 1) to notice where the attention is directed in a determined moment and 2) to choose to keep the attention where it is or to redirect it to another object, usually an emotionally “neutral” object such as the sensations of breathing. In the example presented in Figure 2.1.B, the negative cycle of associations is interrupted by redirecting the attention to the neutral sensations of the breath. With time and practice, participants become increasingly able to recognize where their attention is drawn to and to deliberately redirect it to the sensations of breathing, thus interrupting the habitual, conditioned cycle of negative associations. The study intervention involved two basic components: 1) the body scan, a technique based on the cultivation of attention to bodily sensations that would normally go unnoticed, and 2) awareness of breath, a technique in which trainees learn to attend to the sensations associated with breathing. In addition, participants were gradually taught to direct their attention to simple activities of daily life (through exercises involving mindful eating and drinking), and to direct their attention to thoughts and emotions. Only at the final session they did practice an “open awareness” technique by which they were invited to direct their attention to every event arising in their field of experience, whatever it may

be - physical sensation, sound, visual object, emotion or thought. Other components usually included in the MBSR program curriculum, such as the practice of “metta” (a technique based on deliberately directing feelings of compassion, benevolence and acceptance towards self and others), were excluded because there is insufficient evidence for a benefit of such a practice on anxiety in patients with cardiovascular disease and because it would imply a different study hypothesis that deserves to be tested in a separate investigation.

In order to ensure that the delivery of the intervention was similar across instructors a script of each intervention session was developed (see Appendix, page). Although instructors did not have to follow the script verbatim for each session, they were invited to follow the sequence indicated in the script. Table 2.3 presents the different components of the intervention, each shown in a different color, and the session at which each component was introduced. By looking at each row in Table 2.3 is possible to identify the content of the individual session.

Control group: usual care (UC)

Prior to hospital admission for their ICD procedure, patients in both study conditions met a nurse and at least one physician and received a number of printed education materials. In the hospital, patients were followed daily by physicians and staff nurses. Finally, patients in both groups were invited to attend the ICD support meetings organized by the Electrophysiology Service, usually including a discussion/conference regarding topics such as ICD side effects, indications, concerns about life with an ICD,

Figure 2.1.Study intervention's theoretical model

2.1.A. Self-maintaining cycle of associations when the attention is undirected during a stressful experience.

2.1.B. The negative cycle of associations is interrupted by redirecting the attention to the neutral sensations of the breath.
Adapted from Carmody, 2009 – with permission from the author.[126]

Figure 2.1.Study intervention's theoretical model

Figure 2.1.A

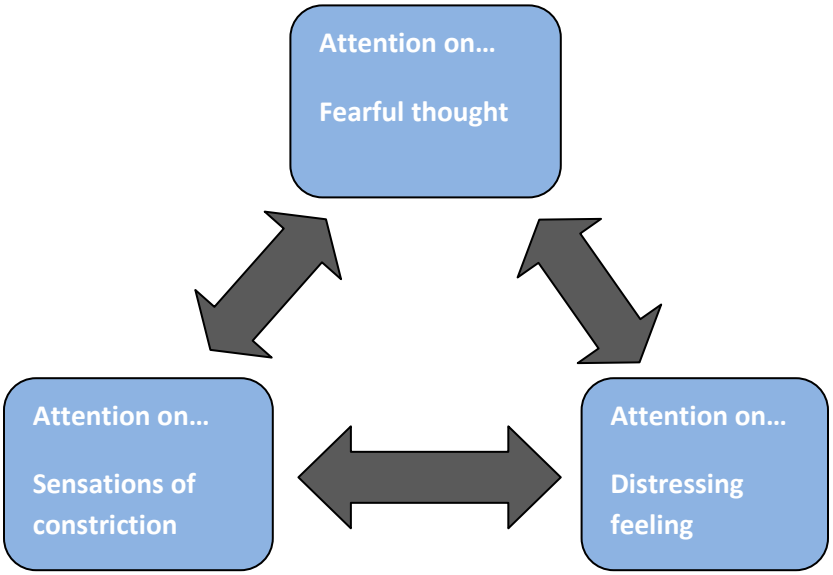


Figure 2.1.B

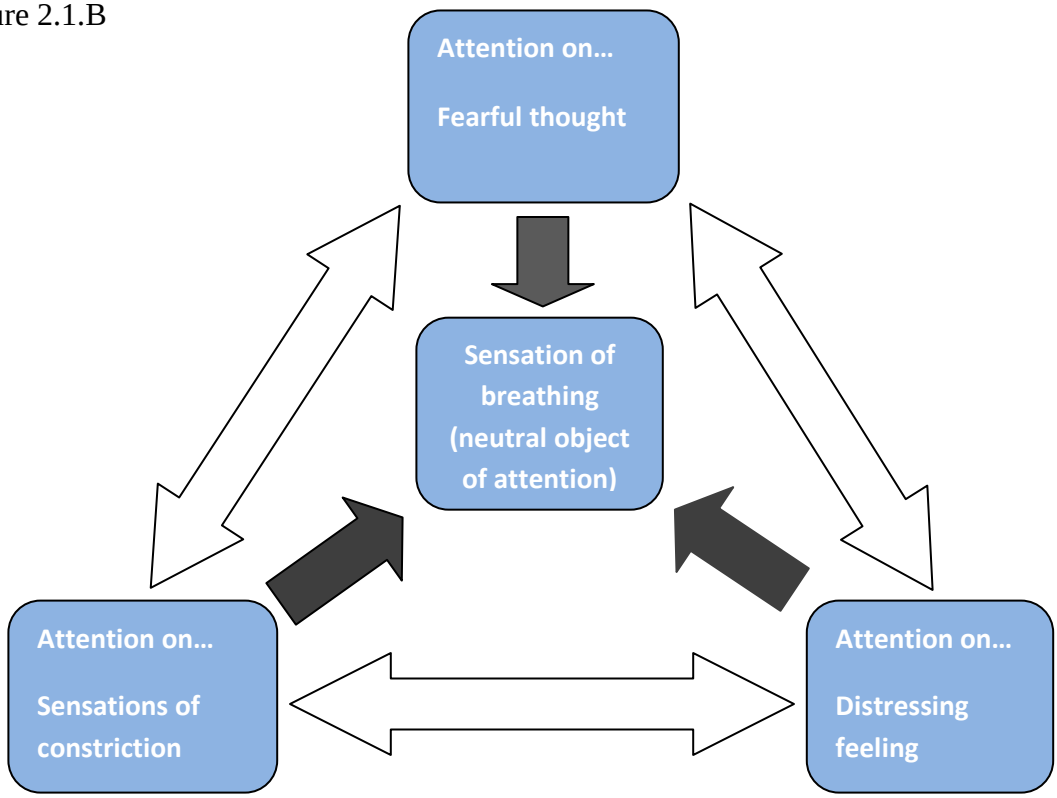


Table 2.2. Overview of the study intervention component by session number. Each color indicates a different component of the intervention.

Sessions	Intervention components							
	Awareness of Breath	Mindful eating exercise	Body scan	Mindful drinking exercise	Awareness of Sounds	Awareness of emotions	Awareness of thoughts	Open awareness
1								
2								
3								
4								
5								
6								
7								
8								

and sharing the experience of other patients. Due to budgetary constraints, it was not possible to use an active control arm. In order to offset this limitation at least partially, patients in the usual care arm received a weekly phone call that, although not designed to offer a specific intervention, was aimed at addressing patients' possible concerns regarding his health or the ICD. If such concerns presented, the patient was advised to contact his/her physician or nurse at the electrophysiology clinic.

Assessments

The outcomes of this study were process evaluation measures that allowed the determination of pilot study feasibility. Assessed metrics included eligibility and recruitment rates, retention rates, intervention adherence rates, treatment fidelity, and intervention participant experiences (Table 2.3).

Recruitment: number of screened and eligible patients, number of eligible patients who refused to participate and reasons for refusal.

Retention: number of dropouts (i.e. participants who leave the study before its completion), number of subjects lost to follow-up (i.e. participants who dropped out and did not provide follow-up information) and reason(s) for dropping out. Retention rates were calculated and compared between the two study arms.

Participant adherence to the intervention: adherence was defined by two indicators: the total number of sessions attended and the total time spent in mindfulness practice (hours) over the intervention period. In addition, the time spent engaging in each separate technique was recorded, such as the body scan (cultivation of attention to bodily sensations) and the awareness of breath (cultivation of attention to sensations associated

Table 2.3. Feasibility study questions

Recruitment process • Is recruitment in the clinic feasible? • Is it acceptable to patients?
Retention • Does phone delivery facilitate/improve retention rates compared to retention rates of traditional MBSR programs?
Adherence to the intervention • Will patients attend session regularly? • Will patients practice mindfulness techniques as instructed?
Treatment fidelity • Is the intervention consistently delivered across instructors? • Are the objectives of the intervention achieved?
Acceptability • Is the intervention acceptable to patients?

with breathing. Mindfulness practice was recorded by means of a daily diary. A similar diary was successfully used in a previously mentioned study[127] of the effect of mindfulness training on hot flashes in menopausal women. Patients received the diary forms at the consenting visit, and were instructed to mail them back using pre-stamped envelopes. When a daily diary was missing or not completed the corresponding daily practice was imputed as zero. Patient's engagement was evaluated immediately after each session and scored on a scale of one (completely unengaged) to 10 (extremely engaged).

Treatment fidelity: at the end of each session, the instructors completed a checklist in which duration and delivery of the intervention as specified in the intervention script, as well as their perception of the patient's level of engagement during the session were evaluated. Instructors' fidelity was defined as the average of the ratio between the numbers of objectives achieved vs. the number of objectives planned for each session, multiplied by 100, calculated from the checklist form. In order to monitor the provider's adherence to the protocol and the consistency of the delivery of the intervention across providers, each session was tape-recorded by the provider using a digital recorder. A random sample (10%) of all recorded sessions was reviewed by the PhD candidate and scored using the method described above for the instructors' self-determination of treatment fidelity.

Participant feedback and experience in the intervention: this outcome was evaluated through a semi-structured qualitative phone interview conducted at the end of the study. Data were collected on a range of factors including satisfaction/ enjoyment, and facilitators/barriers to participation. In addition, information was collected at baseline

regarding demographics (age, gender, ethnicity, education, marital status, and financial status), type, indication and time from the ICD procedure, and relevant clinical data such as medical history, ejection fraction and functional status, and ongoing medications.

Statistical analysis

Descriptive statistics (e.g. mean, median, confidence interval) were used to describe retention, adherence, and treatment fidelity indexes; a graphical examination of the distribution of the continuous variables was used to assess the need for transformation and to show patterns (for example, whether the amount of self-reported daily mindfulness practice shows preferential 'patterns' of practice). Correlates of adherence, defined as the total time spent in mindfulness practice in hours over the intervention period, such as age, gender, severity of cardiac illness, and indication for ICD (i.e. after a cardiac arrest or only as a preventive measure) were evaluated using Spearman's correlation.

Results

Recruitment started on May 15, 2009 and was completed on June 30, 2010. Three hundred and twenty-one patients were screened for study eligibility: 113 (35.3%) were excluded from the study because they did not meet eligibility criteria. Reasons for ineligibility included: not speaking English (11), NYHA class>III (19), current depression or psychosis (25), clinically unstable (26), co-morbidities (32*).* Of the 208 eligible patients, 118 (56.7%) declined to participate. Reasons for refusal were no interest (43), no anxiety (52), no time (11) and other (12). Thirty-one patients were enrolled, of which 15 were assigned to MBI, and 16 to UC. One participant was found to be ineligible

after randomization (serious memory problems) and was not included in the analysis. The flow of patients through the study (Consort diagram) is presented in Figure 2.2.

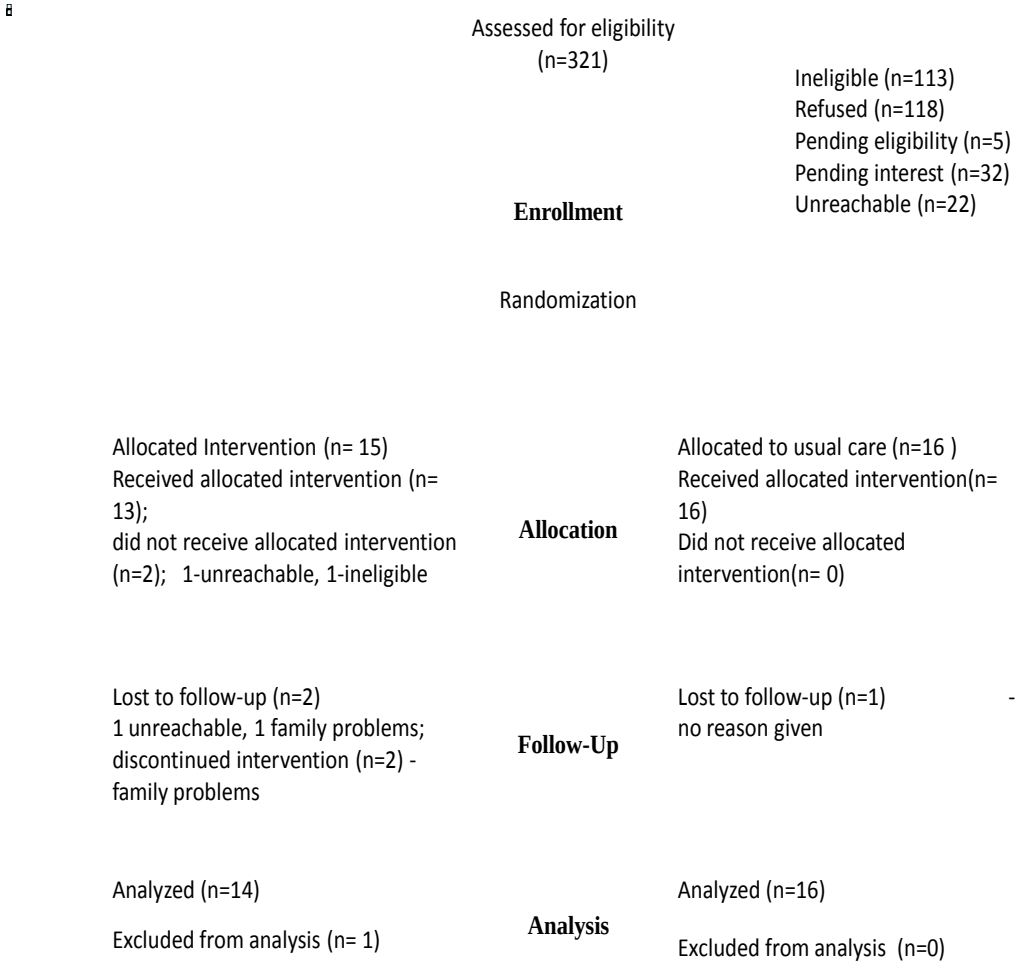
Characteristics of the study population

The average age at enrollment was 63.1 (range: 46 -78). Study participants were mostly males (70%), White-non Hispanic (90.0%), and married or in a committed relationship (70%). Regarding socio-economic status, the study sample included a significant proportion of less educated (60% with less than college degree) and less affluent (30%) participants. The most common diagnosis was coronary heart disease; mean ejection fraction was 0.31 (normal value: > 0.50), and 80% of participants were in NYHA class II or III. The most common reason for ICD implantation (76.7%) was primary prevention of sudden cardiac death. Patients most commonly had a bi-ventricular ICD (70%). The median time from the first ICD implantation to enrollment in the study was 1.4 months, with 70% of participants being enrolled within 2.5 months of the ICD procedure. Seventy-three percent of study patients received a new ICD or upgraded from a pacemaker to an ICD and 20% had recent multiple ICD shocks. Four patients (13.3%) reported to have used other integrative/alternative treatments such as expressive writing (one), reflexology (one), or meditation (two) during the previous month. The baseline demographic and clinical characteristics of the study population are shown in Table 2.4.

Recruitment

Feasibility of recruitment

Figure 2.2. Consort diagram describing the flow of participants through the study.



The eligibility and refusal rates during the first four months of recruitment were 60% and 46%, both better than the rates anticipated in the dissertation proposal (50%). However, the number of consecutive candidates to the implantation of a new ICD turned out to be smaller than expected, with an average of one patient per week vs. the six planned. In fact, only 43 out of the 101 patients screened had received a new ICD, while others had ICD related procedures such as generator change, ICD update or lead revisions. In order to boost recruitment, a series of measures were taken. First, the initial study population was modified to include, besides recipients of a new ICD (initial population), all patients undergoing an ICD-related procedure and/or reporting recent events such as ICD discharges or storms. Second, patients were recruited from another clinic affiliated with the University of Massachusetts Memorial Medical Center (Cardiology Consultants of Central Massachusetts in Worcester, MA). Planned inclusion criteria also required potential study candidates to have a HADS anxiety score ≥8 at the screening visit (i.e. clinically significant anxiety). Four patients had to be excluded from the study during the first three months of recruitment because the anxiety score recorded at the consenting visit were less than eight. Eligibility criteria were then modified to include patients with sub-clinical anxiety and a minimal HADS score was no longer needed to be enrolled in the study.

All changes were submitted and subsequently approved by the IRB at UMass Medical School.

Table 2.4 - Baseline characteristics of the study population

N		30 (100)
Age (mean, SD)		63.1 (10.3)
Gender		
	Males	21(70)
	Females	9 (30)
Race/ethnicity		
	White-non Hispanic	27 (90.0)
	Hispanic	2 (6.7)
	Asian	1 (3.3)
Education		
	High School	7 (23.3)
	Some college	11 (36.7)
	College graduate	4 (13.3)
	Post graduate	8 (26.7)
Marital status		
	Married or in committed relationship	21 (70.0)
	Separated/divorced/single	9 (30.0)
How hard to pay for basics [b)]		
	Not at all hard	21 (70.0)
	Somewhat hard	4 (13.3)
	Very hard	5 (16.7)
Cardiac diagnosis		
	Coronary heart disease	16 (53.3)
	Idiopathic dilated cardiomyopathy	6 (20.0)
	Other	8 (26.7)
Previous CABG		6 (20.0)
Previous PCI		9 (30.0)
Indication for ICD		
	Primary prevention	23 (76.7)
	Secondary prevention	7 (23.3)
ICD procedure		
	New ICD	19(63.3)
	ICD upgrade	3 (10.0)
	Battery change/lead revision	2 (6.7)
	ICD shocks/storms	6 (20.0)
ICD type		
	Bi-ventricular	21 (70.0)
	Single chamber	9 (30.0)
Time from ICD procedure [c)] (months)		1.43 (0.3, 14.2)
Smoking	Never	16 (53.3)
	Ex-smoker	12 (40.0)
	Current smoker	2 (6.7)
Therapy at discharge	Beta-blockers	26 (86.7)
	Anti-arrhythmics	6 (20.0)
	Anxiolytics	7 (23.3)
	Anti-depressants	8 (26.7)

Table 2.4. Baseline characteristics of the study population (cont.)

Ejection fraction (%)		0.31 (0.12)
New York Heart Association class		
	I	7 (23.3)
	II	16 (53.4)
	III	7 (23.3)
Use of integrative medicine treatments during previous month [d)]		4 (13.3)

[(a)]Values are means (SD) or n (%) unless otherwise indicated
[b)] Food, housing, medical care and heating
[c)] Median (25^{th}-75^{th} percentile)
[d)] Expressive writing, reflexology, or meditation

Recruitment strategies

The initial recruitment strategies planned in the dissertation proposal turned out to be time consuming and not very effective. For example, according to the recruitment plan described in the dissertation proposal, potential study participants were individuated first by obtaining from administrative personnel the list of *all* patients (ICD and non-ICD) scheduled for a visit at the Electrophysiology clinic; possible eligible patients were then retrieved using Meditech software system. Eligible patients were then to receive the study invitation letter from the attending nurse or physician at the end of their visit in the clinic, and the PhD candidate would contact each patient after his/her visit was completed. This procedure results to be very time consuming. In addition, some ICD candidates were admitted to the Cath lab directly from other centers, or from the emergency room, and thus missed since their names would not appear in the clinic schedule. Also, the clinical personnel often would not have the time to give the patients the study survey and invitation letter. Consequently, recruitment strategies had to be modified. First, in order to capture all (or most) candidates to an ICD procedure, the Cath lab schedule was used instead of the clinic schedule. Every week, the PhD candidate would obtain a printed list of ICD procedure candidates from the person responsible for the scheduling of appointments at the Cath Lab. Next, the study invitation letter and interest survey were mailed to patients about two weeks before the procedure with an “opt-out” option, meaning that if the patient did not call back after receiving the invitation letter, the PhD candidate would follow-up on the patient’s interest by phone. This “opt-out” option was preferred to an “opt-in” option (in which only interested patients are invited to call)

because some patients would not call after receiving the invitation letter even if they were interested, thus resulting in the loss of potential participants. Recruitment strategies included also presentations of the study at ICD meetings organized by the Electrophysiology Unit.

Overall, the most successful recruitment technique was mailings followed by phone calls from the PhD candidate. Presentations at ICD meetings were not successful (only one patient enrolled). Recruitment was facilitated when the provider (attending physician or nurse practitioner) reinforced the information provided during the mail/phone contacts by presenting/recommending the study to a specific patient.

Acceptability of recruitment in the clinic

Since many ICD patients lived far from the hospital, they were offered the option to schedule the screening appointment at the same time of their scheduled visit to the outpatients' clinic. If the patient preferred to schedule a specific appointment for the consent visit, or if he/she needed additional time to think about his/her participation, he/she was given the possibility to do so. However, before ICD surgery patients were too busy and overwhelmed to consider their participation in the study, and refused to participate or tended to postpone their decision until after the ICD procedure. It became thus impossible to maintain the planned recruitment window of one week after the ICD procedure. In order to give patients more time to decide, the recruitment window was widened to one month after the ICD procedure. For the outcomes analysis (to be conducted once recruitment is completed), time from the procedure will be included among study covariates in order to adjust for between-groups differences. The follow-up

visit (usually involving a check of the ICD insertion site) planned about seven-10 days after the procedure turned out to be a very favorable recruiting environment because patients were not anticipating the procedure and therefore were less distracted.

Recruitment in a clinical setting presented additional challenges. Some participants did not grasp the "experimental" nature of the study intervention and instead thought that the intervention was a "treatment" offered to everybody, and were then disappointed when told about the randomization procedures, even though this point was clearly explained in the invitation letter and in the consent form. In order to avoid confusion, patients were specifically and repeatedly told that they were volunteering for a research study, and that the study intervention was not part of their regular treatment.

Retention

The overall retention rate was 90%. Three patients (10%) dropped out of the study: one (0.6%) in the UC arm, and two (14%) in the MBI arm. Of the participants enrolled in the MBI arm, one never received the allocated intervention (reason unknown, patient unreachable after randomization), and one dropped out after three sessions; both were lost at follow-up, but we were able to retrieve clinical information from their attending nurses and neither had major cardiac events. Reasons for dropping out were loss of employment (one), and unknown (two).

Adherence

Sessions attendance

Patients assigned to the MBI intervention attended a mean of 6.9± 2.5 sessions. The attendance rate was 86.6% (intention to treat). If the two patients who dropped out

and attended respectively zero and three session are excluded, attendance was 97.9% with 11 out of 12 patients attending 100% of sessions (Figure 2.3). As reported in the intervention checklist, the mean engagement score during sessions (on a scale from zero to 10) was 8.74 ±1.27.

Mindfulness home practice

Overall, 10 out of the 12 patients who received the intervention completed the set of eight mindfulness logs. The total amount of time spent in the individual practice of the study techniques (sum of awareness of breath, body scan, and informal practice) varied considerably across individuals (median: 15.92 hours; range: 6.35, 75.68 hours). Awareness of breath was the technique practiced most frequently (median: 8.17 hours; interquartile range: 2.52, 10.04), followed by the body scan (median: 4.17 hours; interquartile range: 2.16, 7.0). Since by definition informal practice involved practicing without the aid of the CD, it was likely to be the least reliable self-reported information. Features such as the lack of within-patients variance in the data suggest that this section of the log was not reliably completed. Despite these limitations, exploratory analyses were conducted to identify possible factors associated with poorer practice. Table 2.5 shows the correlations between different variables and the duration of individual practice. Although most correlations were not significant because of the small sample size, participants who spent a longer time engaging in individual mindfulness practice had lower Hospital Anxiety and Depression (HADS) anxiety scores at baseline (r=-0.55, p=0.063), higher NYHA class (0.65, p=0.022), had a more recent ICD procedure (- 0.37) and were more educated (0.44). The duration of daily practice did not differ by gender,

Figure 2.3. Graph of sessions' attendance (intention to treat)

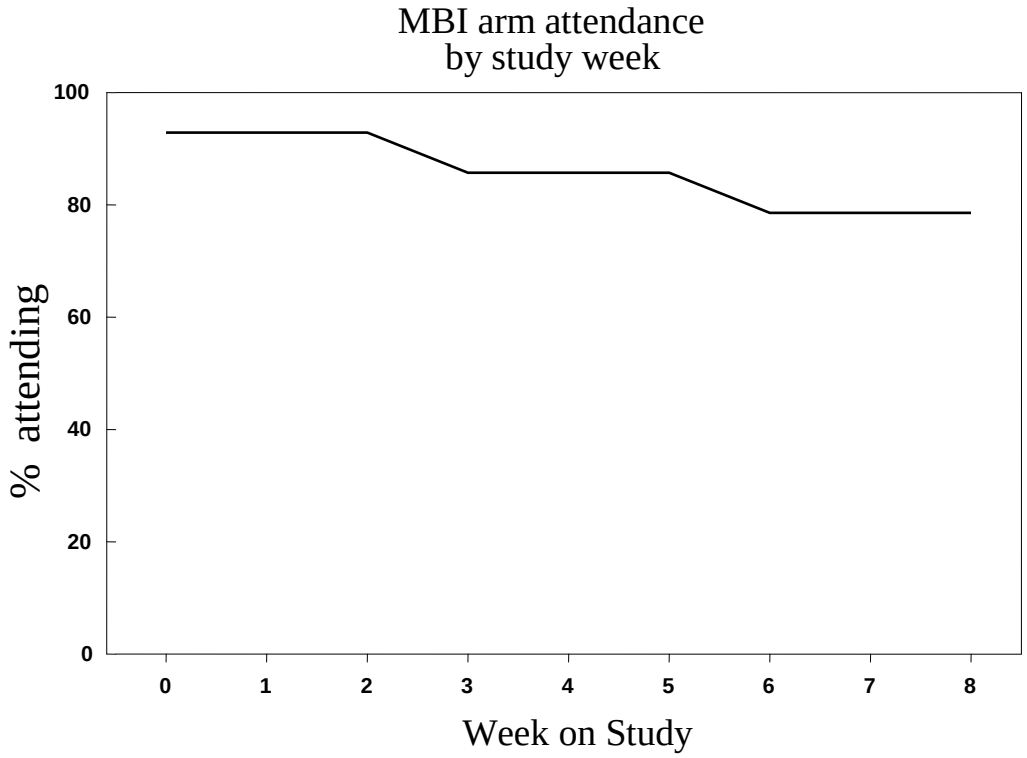


Table 2.5. Correlations[a] between duration of individual mindfulness practice and baseline characteristics

Variable	**rho[b]**	**p value**
NYHA class	0.65	0.022
Time from implantation	-0.37	0.230
Baseline HADS score	-0.55	0.063
Baseline FFM score	0.04	0.91
Age	0.34	0.279
Education [c]	0.44	0.154
Engagement	0.29	0.363

[a] Correlations with other baseline variables not shown because r<0.20
[b] rho= Spearman correlation coefficient
[c] High School, Some College, College Graduate, Post-graduate
NYHA= New York Heart Association; HADS= Hospital Anxiety and Depression Scale; FFM=Five Facets of Mindfulness

Table 2.6 – Intervention adherence - study instructors [a]

% total available objectives met	714/793 (90.03%)
% objectives met per session[b]	97.5

[a] n =13 (patients assigned to MBI who received the intervention)
[b] Average of objectives met/objectives available for each session

history of depression or anxiety, marital status, use of anxiolytics and antidepressants (Wilcoxon rank-sum test).

Treatment fidelity

Table 2.6 summarizes data regarding instructors' adherence to the intervention. Overall, based on instructors' self-reported checklist, participants received for the most part, what was planned in the intervention. For each patient 61 objectives were to be achieved. Instructors covered on average 97.5 % of objectives per session.

A random sample of 10% of all recordings was reviewed to evaluate consistency of delivery with the intervention script. Results from this treatment fidelity assessment protocol indicate that for the 10% of all session tapes reviewed the instructors delivered the MBI content with fidelity to the intervention checklist 95.5% of the time.

Initially, some instructors reported to be uncomfortable with phone delivery of the intervention; however, these difficulties improved over time as they became more familiar with the intervention and with the new modality of delivery and they did not report further difficulties.

Acceptability of intervention to patients

A semi-structured qualitative phone interview was conducted at the end of the study to gather preliminary participant feedback about the intervention and other hypothesis-generating information. Overall, 10/12 (83.3%) of participants reported that the study intervention was "somewhat" to "extremely" helpful in coping with the ICD procedure [possible answers: not at all (n=1), a little (n=1), somewhat (n=3), very much (n=4), extremely (n=3)], with 58.3% rating the intervention as "very much" or

"extremely" helpful. Nine out of twelve (75%) reported that the intervention had moderate to great impact on their well-being. Participants were also asked to rate the different intervention components as to whether they find them helpful in coping with the ICD procedure/event (not at all helpful, a little, somewhat, very much, extremely). The most helpful aspects of the intervention were, in decreasing order of importance: interaction with the instructor (rated by 91.7% of patients as "very much" to "extremely" helpful); awareness of breath exercise (83.0%), body scan (58.3%). About 83% of participants reported that they often or always used one of the study techniques in their daily life, with 91.7% using the awareness of breath exercises and 8.3% using the body scan. Finally, 66.7% reported other positive life changes associated with his/her participation in the program, such as a general feeling of wellbeing, improved emotions control, and better sleep quality; some reported that the intervention had helped them face challenging times in their life (i.e. serious illness of a close relative). All patients considered the intervention acceptable in its present format, with two patients suggesting that it would have been useful to meet the instructor in person before the intervention started. However, no participant mentioned that the phone contact was inadequate, reported to dislike the phone delivery or left the study because he/she disliked the intervention. Interestingly, some patients in the UC group reported that they greatly appreciated the "support" received during the weekly phone call by the PhD candidate. This may raise the possibility of a (probably minor) intervention effect in the control group.

Side effects

No participant had to discontinue the intervention because of side effects such as increasing anxiety or psychological discomfort. During the study period two serious adverse events (SAE) were recorded, one in the MBI group and one in the UC group. SAEs were readmission to the hospital because of worsening of heart failure (1) and pneumonia (1). Neither was considered related to the intervention.

Costs

The cost of the intervention (instructor only) for each patient was $ 225. It was not possible to estimate costs associated with other study components (i.e. instructors' training) because they were conducted by the PhD candidate.

Discussion

The purpose of this study was to evaluate whether a pilot randomized clinical trial of a mindfulness-based behavioral intervention based on the traditional MBSR program, adapted to the needs of ICD patients, would be feasible and acceptable to these individuals. Overall, the methods ultimately adopted to screen, recruit, and retain study participants were feasible to conduct and satisfactory to ICD outpatients, and the study intervention was safe and acceptable to patients. The initial screening and recruitment methods planned in the dissertation proposal had to be adapted based on the challenges encountered upon trying to conduct a research study in a "real life" clinical setting. In this respect, having conducted this pilot project has been extremely valuable since it

permitted the identification of barriers and obstacles to recruitment and to experiment with different solutions that will be extremely helpful in the design of a future larger trial.

In order to reach this specific population, which has different needs from the usual patients attending regular MBSR classes due to the underlying cardiac disease and to the inability to drive following shock therapy or ICD implantation several modifications were made to the traditional MBSR program. First, the intervention was delivered individually over the phone instead of the traditional class format; second, sessions lasted 30 minutes each vs. the traditional two and a half hours; third, the recommended individual daily mindfulness practice was shortened to about 20 minutes instead of 45 minutes. Data from this feasibility study indicate that such adaptations were well received by the study patients.

Similarly to previous studies of behavioral interventions in ICD patients[61, 66, 68, 70] the study population included a majority of males (70%) and was mostly white (90%). In contrast with these studies, however, the PhD candidate was able to recruit a sample including less educated patients (60% with less than college degree) and a significant proportion of women (30%). A unique feature of this study was the documentation of the cardiac diagnosis underlying the indication for an ICD procedure, which is rarely reported in the literature. In this study, 56% of participants had a diagnosis of coronary heart disease, as in Dougherty[61] and Chevalier who did report diagnoses.[60] The patients' clinical condition was more severe than in other studies, as 76.6% of patients were in NYHA class II or III (75% of Lewin's [70] study population was in class I or II) with a low mean ejection fraction.

The study eligibility rate (64.7%) was lower than the one reported in the only study providing this detail, the multicenter cluster randomized trial of Lewin and colleagues (80%);[67] the refusal rate was 56.7%, while in the three other studies reporting this information, the proportion of patients who refused was 15%,[67] 65%,[60] and 46%.[65]

There were a number of strengths in the present study. The retention achieved in this study of two months duration was 90%. The only two studies with a relatively short duration (three months) had retention rates of 69%[64] and 95%,[128] respectively. Retention in the intervention arm (86%) was superior to that reported by Carmody in a study of MBSR in healthy post-menopausal women (75% - article submitted for publication). It was also significantly better than the completion reported for the regular MBSR program (76%).[129] The attrition rate (7.6%) in a meta-analysis of studies evaluating the effect of telephone-administered sychotherapy on symptoms of depression was similar to the one reported in this study (10%). In addition to the strengths noted above, adherence in the patients who completed the study (12/14) was excellent with a 98% session attendance and high engagement scores during sessions. Finally, this study provided an assessment of treatment fidelity, showing that on average the content of the intervention was delivered as intended in 95.5% of cases. To date, the majority of behavioral interventions for ICD patients[58] and of mindfulness-based interventions have not focused on treatment fidelity issues and this constitutes an absolute novelty of this study.

The intervention was safe, acceptable and enjoyed by participants. As suggested by some of the study participants, the first session could be delivered in person (at home or in the clinic). With the collaboration of providers, it may be possible to begin

delivering the intervention during the pre-ICD implantation period, when anxiety levels are higher.[111]

Some limitations of this study should be considered. First, the PhD candidate was unable to recruit an ethnically representative sample because she did not have the resources to recruit from additional clinical centers a more ethnically diverse population. The study findings thus may not apply to minorities, as 90% of participants were white. Second, the enrollment rate was low, as only about 10% of screened patients were ultimately enrolled. Thus, the study participants may not be representative of the general outpatient ICD population. Another important limitation is the relatively high refusal rate (56.7%). One possible reason for this finding is the lack of anxiety symptoms in 25% of eligible individuals. A possible future strategy could be to target exclusively patients with a previous history of psychological distress and/or to screen the ICD outpatients' population for psychological discomfort in order to identify subjects with mild/moderate levels of distress. Third, individual mindfulness practice was self-reported and consequently logs might have been retrospectively (and imprecisely) completed. With adequate funding it would be possible to develop techniques to track the amount of time spent in listening to the study CD, such as the device used by Bauer-Wu[113] ("Tracware", a mechanical sensor using micro switch technology, Thriving Today, Inc.), or by posting each recorded session on a dedicated intervention website and then tracking the time that each participant is logged onto the website. Fourth, the study involved only pre- and post-intervention assessments; since participants were not followed up once the intervention

was completed, we do not know whether patients would keep practicing the study techniques over time.

In conclusion, phone delivery of mindfulness training appears to be a feasible alternative to traditional MBSR classes for patients with severe cardiovascular disease who are unable to attend regular MBSR classes, with a low attrition rate, high adherence and limited costs. The intervention is safe and acceptable among ICD outpatients and can be successfully delivered by experienced instructors.

CHAPTER III

Baseline Prevalence and Determinants of Anxiety in ICD Outpatients

Introduction

Among cardiac devices, the implantable cardioverter defibrillator (ICD) has probably achieved the most impressive successes. Since its conception and development by Dr Mirowski[130] and colleagues following the death of his mentor for cardiac arrest, the progress in the utilization of ICDs in cardiac care has been substantial. Primary and secondary prevention trials [1, 3, 131, 132] have consistently shown its efficacy in preventing sudden cardiac death and life-threatening arrhythmias compared to anti-arrhythmic agents alone. Recent studies [4] have shown that ICD therapy achieved a 23% reduction in mortality when used as primary prophylaxis against sudden cardiac death in patients with a ventricular ejection fraction of 35% or less and New York Heart Association (NYHA) class II or III compared to medications alone. Combination of an ICD with the clinical benefits of biventricular pacing (cardiac resynchronization) has also been shown to improve symptoms, quality of life, and survival in selected patients with NYHA functional Class III or ambulatory Class IV heart failure symptoms with an EF less or equal to 35%, a QRS duration greater than or equal to 0.12 seconds, and sinus rhythm.[133] According to the American Heart Association/American College of Cardiology guidelines published in 2008,[16] the ICD alone or with resynchronization therapy is now the treatment of choice for patients with life-threatening arrhythmias, and also for patients with congestive heart failure regardless of previous arrhythmic episodes.

Impressive technological advances have contributed to the successful use of ICD in clinical care. Current defibrillators are much smaller than early devices and have advanced algorithms to distinguish between non-life threatening supra ventricular arrhythmias and life threatening ventricular arrhythmias. Devices are capable of storing events, transmitting information over the internet, and doing automatic internal device checks. Early ICDs were implanted in the abdomen, required an open chest procedure and the use of general anesthesia, and were associated with significant morbidity and mortality. Currently, ICD procedures are performed using local anesthesia and mild sedation, and patients are usually discharged home within 24 hours.

The number of ICD implantations and ICD related procedures has increased accordingly, although there have been recent indications that these figures may be reaching a plateau.[134] From 1990 to 2005 the estimated number of hospitalizations for ICDs implantation increased from 5,600 to more than 108,000 for the total United States population, and the estimated annual rate of hospitalizations for the implantation of ICDs increased 10-fold.[135]

However, there have been trade-offs. As more patients have received implanted devices, other device related problems have surfaced.[136, 137] Over time most patients adapt fairly well to living with an ICD; however, a significant proportion of psychological disturbances has been reported, with figures reaching of up to 38% for clinically significant anxiety, [27, 111] while the prevalence of depressive symptoms (24–33%) is similar to other cardiac populations.[27] There are a number of ICD-related stressors that can cause significant psychological distress,[35] thus impacting the quality of life of an ICD

recipient. A substantial amount of psychological discomfort is related to device therapies, i.e., shocks: patients are afraid of the pain caused by a shock[138] and of the circumstances related to the unpredictability of its occurrence, such as the possibility of receiving a shock while out of the house, or the reaction of bystanders not familiar with the patient or the ICD.[34, 139] During the past ten years a significant number of studies has examined possible determinants of psychopathology and quality of life after ICD implantation.[31] Prior research[30] has suggested that young age (<50 years), female gender, poor device understanding, and electric shocks/storms are important risk factors for the development of psychological problems. However, more recent data somehow seem to contradict these findings suggesting that pre-implantation psychological and personality characteristics may give a higher contribution to post-implantation distress than what previously thought. [31, 32]

Anxiety can significantly contribute to the overall cardiovascular mortality and morbidity in patients with coronary heart disease[43-48] and a role of anxiety and stress in inducing ventricular arrhythmias has been hypothesized since the late 1970s.[140-142] Emotional[40 41] and mental[42] stress were shown to have a detrimental effect on both cardiac perfusion and function. Multiple mechanisms have been hypothesized in order to explain the negative effect of anxiety on cardiac outcomes, such as reduced heart rate variability [49-51] and baro-reflex control, [52-54] and alterations in the coagulation system.[55] Paradoxically, ICD patients are at higher risk of having arrhythmias and therefore of receiving shocks because of their fear of receiving shocks.

However, there are several reasons leading to hypothesize that the prevalence of anxiety in successive cohorts of ICD patients may be decreasing.[14, 15] First, following the implementations of the American Heart Association/American College of Cardiology recommendations,[16] the ICD population is changing, with most patients now receiving an ICD as a preventive measure and consequently not having experienced a prior cardiac arrest or severe ventricular arrhythmia. Furthermore, the device is now smaller than in the past and as a result the implantation procedure has become easier and faster. As a result there have been preliminary reports[33] that the current prevalence of symptoms of psychological discomfort may also have changed compare to earlier reports referring to patients receiving an ICD for secondary prevention only.[14]

The aim of this study was to evaluate the baseline prevalence of anxiety and its association(s) with disease, demographic and ICD characteristics, and previous history of anxiety and depression in a group of patients enrolled in a pilot randomized clinical trial of a mindfulness-based behavioral intervention designed to reduce anxiety in ICD patients.

Methods

Extensive details about the study design and the study intervention are provided in chapter 2. Briefly, the study was conducted at the University Campus of the UMass Memorial Medical Center in Worcester, MA. All consecutive patients scheduled for an ICD related procedure at the catheterization lab were screened for study eligibility within a month since the ICD procedure. Patients were considered to be eligible if they met the

following criteria: age ≥ 21, ability to understand and speak English, and access to a telephone. Patients were excluded from the study under the following conditions: inability/unwillingness to give informed consent, signs of cognitive impairment, New York Heart Association (NYHA) functional class >III or angina Canadian Cardiovascular Society class III and IV or otherwise clinically unstable, pending coronary by-pass or heart transplantation, co-morbid life threatening conditions, and ongoing severe depression or psychosis. The Blessed Orientation Memory and Concentration test[107] was used to screen patients for cognitive impairment. Screening for ongoing depression and psychosis was based on DSM criteria of major depressive disorder or psychosis as documented by the physician in the charts of the most recent medical evaluation.

Potentially eligible patients received an interest survey and a letter inviting them to participate in the study. Patients were invited to return the survey at the occasion of their next visit or to call a dedicated phone number to communicate that they were not planning to participate. If the patients did not call, the graduate student followed up by phone. Once the patient expressed interest, a screening visit was scheduled. After confirmation of study eligibility, patients signed an informed consent form and a HIPAA authorization, and baseline data collection was performed. Patients were then assigned to the intervention (Mindfulness Based Intervention, MBI) or to the control group (usual care, UC) through a computer-generated randomization scheme.

Baseline and outcome measures

Baseline demographic and clinical characteristics

Information was collected at baseline from the Medical Record on patient demographic characteristics, history of anxiety and depression and related prescriptions, and disease/ICD related characteristics/prescriptions. Demographic characteristics included age, gender, income, education and racial/ethnic background. Disease/ICD characteristics of interest included underlying cardiac diagnosis, current use of β-blockers, anti-arrhythmic drugs and anxiolytics, indication for ICD implantation (primary vs. secondary prevention), type of ICD procedure, NYHA class, and ejection fraction (EF: End diastolic volume - End systolic volume/End diastolic volume, collected from an echocardiogram or a ventriculogram whichever was more recent). Since the screening visit was performed at different times since the ICD related procedure, time since ICD procedure was included among the study covariates.

Outcome measure: Anxiety

Baseline anxiety, consistently measured after the ICD procedure, was assessed using the Hospital Anxiety And Depression Scale, or HADS,[143] a 14-items, self-administered questionnaire with two sub-scales measuring anxiety and depression, with higher scores indicating greater psychological morbidity. Many studies conducted throughout the world have confirmed its validity not only in hospital settings, but also when used in primary care medical practice.[144-146] A cut-off point of 8 is usually recommended to screen patients for clinically significant depression and anxiety.[147, 148] The use of the HADS questionnaire has been validated in cardiac patients[149, 150] and three of the four most recently (2003-2008) published studies on psychological interventions in ICD patients[67, 128, 151, 152] have used the HADS to assess anxiety and depression. A

correlation between 0.6-0.8 has been reported between the HADS and other commonly used questionnaires for anxiety and depression such as the Beck Depression Inventory and the State-Trait Anxiety Inventory.[153] Furthermore, the HADS offers the advantage of focusing on cognitive symptoms of anxiety instead of physical symptoms; this is particularly useful in cardiac patients where symptoms of the underlying cardiac disease maybe similar or identical to those resulting from somatic manifestations of anxiety.

Statistical analysis

Descriptive statistics were used to evaluate the prevalence of anxiety at baseline in the study population [mean HADS score and its distribution; proportion of patients with a clinically significant HADS score (≥8)]. Age, ejection fraction, and HADS scores were treated as continuous variables; sex, race, financial status, education, use of antidepressant and anxiolytics, previous history of anxiety and depression, use of psychotropic and anti-arrhythmic therapy were treated as categorical variables. Loess curves were used to test linear vs. non-linear associations of predictors with continuous HADS scores. The association between anxiety scores and different possible predictors [previous history of anxiety/depression; previous use of anxiolytics/antidepressant, cardiac function, cardiac diagnosis, ICD indication, demographic characteristics, time from ICD procedure (dichotomized with a cut-point at 2.5 months because of lack of linear association with anxiety scores), and use of complementary/alternative medicine therapies (other than the study intervention)] was estimated in univariate linear regression models. Variables that showed an association with anxiety ($p \leq 0.10$) were then included in a multivariate linear regression model. Two-tailed T-test was used to compare means; the

Wilcoxon test was used if the assumption of normal distribution was not met. The two-tailed Fisher exact test was used to compare proportions with HADS<8 vs. HADS ≥8. Results are presented as beta coefficient (with confidence intervals), where the null hypothesis was that $\beta_1=0$. P values <0.05 were considered significant. All analyses were performed using STATA statistical software.[108]

Results

Three-hundred and twenty-one patients were screened for study eligibility. A full Consort diagram reporting the flow of patients through the study and including detailed information on the number of randomized participants, the number of patients receiving the intended treatment, the number of subjects completing the study protocol, and analyzed for the primary outcome is shown in Chapter 2, Figure 2.3. Of 208 eligible patients, 118 (56.7%) declined to participate; 52/118 (44.0%) refused because they reported no anxiety. Thirty-one patients (9 females, 22 males) consented to participate and were randomized to the study intervention or the control arm; one participant was deemed ineligible after randomization because of cognitive impairment and was not included in the final analysis. The baseline demographic and clinical characteristics of the study sample are presented in Table 3.1.

Baseline anxiety scores

At baseline, mean anxiety scores were 6.4 ±4.3, with 11/30 (36.7%) participants having clinically meaningful anxiety and 2/30 (6%) with scores equal of above 14 (moderate anxiety). None reported scores >21 (severe anxiety). Table 3.2 shows the baseline sample characteristics by presence or absence of clinically meaningful anxiety

Table 3.1 – Baseline demographic and clinical characteristics of the study sample [a]

n	30
Age (mean, SD)	63.1 (10.3)
Males	21(70)
Females	9 (30)
White-non Hispanic	27 (90.0)
Hispanic	2 (6.7)
Asian	1 (3.3)
High School	7 (23.3)
Some college	11 (36.7)
College graduate	4 (13.3)
Post graduate	8 (26.7)
Married or in committed relationship	21 (70.0)
Separated/divorced/single	9 (30.0)
How hard to pay for basics [b]	
Not at all hard	21 (70.0)
Somewhat hard	4 (13.3)
Very hard	5 (16.7)
Coronary heart disease	16 (53.3)
Idiopathic dilated cardiomyopathy	6 (20.0)
Other	8 (26.7)
Prior cardiac arrest	7 (23.3)
New ICD	19(63.3)
ICD upgrade	3 (10.0)
Battery change/lead revision	2 (6.7)
ICD shocks/storms	6 (20.0)
Time from ICD procedure (median (25^{th}-75^{th} percentile))	1.43 (0.3, 14.2)
Beta-blockers	26 (86.7)
Anti-arrhythmics	6 (20.0)
Anxiolytics	7 (23.3)
Anti-depressants	8 (26.7)
Ejection fraction (mean (SD))	0.31 (0.12)
New York Heart Association class	
I	7 (23.3)
II	16 (53.4)
III	7 (23.3)
HADS scores anxiety (mean, (SD))	6.4 (4.3)
Clinically significant anxiety (HADS≥8)	11(36.6)

[a] Values are n (%) unless otherwise indicated
[b] Food, housing, medical care and heating
ICD= Implantable cardioverter Defibrillator; HADS= Hospital Anxiety and Depression Scale

Table 3.2 - Baseline sample characteristics by anxiety status [a]

	Anxiety (HADS≥8)	No anxiety (HADS<8)	P value [b]
N	11	19	
Age (mean, SD)	59.1 (9.93)	65.4 (9.97)	0.05 [c]
Females	45.5	21.1	0.22
College or post-graduate education	45.5	36.8	0.71
Married or in committed relationship	54.6	79.0	0.22
Not at all hard to pay for basics [d]	54.6	79.0	0.09
Somewhat hard	9.1	15.8	
Very hard	36.4	5.3	
Coronary heart disease	54.6	52.6	0.46
Primary prevention	27.3	21.1	0.51
Secondary prevention	72.7	78.9	
New ICD	54.6	68.4	0.51
ICD shocks/storms	18.2	21.0	
Months from ICD procedure (mean, SD)	24.5 (41.8)	9.7 (17.3)	0.97
History of depression	63.4	5.26	0.001
History of anxiety	36.4	10.5	0.11
Current smoker	9.1	5.26	0.51
Beta-blockers	81.8	89.5	0.6
Anti-arrhythmics	18.2	21.1	1.0
Anxiolytics	45.5	10.5	0.07
Anti-depressants	54.6	10.5	0.03
Ejection fraction (mean, SD)	0.29 (0.16)	0.32 (0.09)	0.33
New York Heart Association class III	27.3	21.0	0.37
Baseline HADS score anxiety (mean, SD)	11.1 (2.21)	3.63 (2.24)	0.001

[a] Values are % unless otherwise indicated
[b] 2-tailed Fisher exact or Wilcoxon
[c] T-test
[d] Basics: Heating, groceries, and health insurance
ICD=implantable cardioverter defibrillator; HADS=Hospital Anxiety and Depression Scale

(no anxiety: HADS scores <8; mild/moderate anxiety: HADS scores ≥8). Although most differences were not statistically significant due to the small sample size, patients meeting HADS criteria for anxiety were younger, female, single or divorced, currently smoking, had lower socio-economic status, had a history of anxiety and depression, and were receiving antidepressants or anxiolytics. There were no statistically significant differences between the two groups in cardiac diagnosis, use of beta-blockers or anti-arrhythmics, type of ICD or ICD procedure, history of prior cardiac arrest, NYHA class or ejection fraction, previous ICD shocks, and time from ICD procedure.

Univariate models

The following variables were associated with anxiety scores in univariate models with $p \leq 0.10$: age, history of anxiety and depression, past use of antidepressants and anxiolytics, financial status, and marital status (Table 3.3). Anxiety scores were inversely related to age, while there was a positive association between anxiety scores and history of anxiety or depression, use of anxiolytics and antidepressants, being single or divorced, and lower socioeconomic status. Anxiety scores were not associated with smoking, underlying cardiac diagnosis, history of cardiac arrest/arrhythmia vs. no history), ICD procedure or type of ICD implanted, previous CABG or PCI, use of beta-blockers and anti-arrhythmics, race, education, previous use of complementary/alternative therapies, NYHA class and ejection fraction at baseline.

Multivariate analysis

Due to the high correlations between previous use of anxiolytics and history of anxiety ($r=0.70$) and antidepressants and history of depression ($r=0.65$), only history of

depression and use of anxiolytics were entered in the final model because in univariate models the association of each covariate with the outcome was stronger. In the multivariate model (Table 3.3) associations became non-significant (age: p=0.0625; previous depression: p=0.067), with further widening of the confidence intervals due to the small sample size. Post regression testing indicated no heteroskedasticity and collinearity, and residuals were normally distributed.

Discussion

As described above, anxiety has been associated with increased cardiovascular mortality in patients with coronary heart disease.[43, 44, 154] Several studies reported that anxiety can be a relevant problem in ICD patients, with figures reaching up to 38%.[155] Previous research has determined that ICD-related concerns and delivery of shocks were the most important causes of psychological morbidity in these patients.[8, 27, 156] One of the hypotheses of this cross-sectional analysis was that the prevalence of anxiety and anxiety correlates might be lower than in previous patients cohorts due to changes in ICD implantation guidelines to include patient who never experienced severe arrhythmic events or sudden death, and to technological improvements at both the device and the ICD procedure level. Within the limitations of this analysis, which evaluated the prevalence of baseline anxiety in a group of patients enrolled in a pilot randomized clinical trials of the effect of a behavioral intervention for anxiety in ICD patients, the findings of this study do not show that the overall prevalence of anxiety in ICD patients is decreasing. In fact, the prevalence of anxiety in this population as measured by the

Table 3.3. Univariate and multivariate associations with HADS scores

	Unadjusted Coefficient (95% CI)	p	Adjusted Coefficient (95% CI)	p
Covariate				
Age	-0.19 (-0.33, -0.05)	0.01	-0.16 (-0.33, 0.01)	0.0625
Previous depression (yes vs. no)	5.47 (2.47, 8.46)	0.001	3.05 (-0.24, 6.34)	0.067
Use of anxiolytics (yes vs. no)	4.18 (0.70, 7.66)	0.02	2.27 (-0.92, 5.45)	0.155
Marital status (married vs. single)	-3.13 (-6.45, 0.20)	0.064	0.85 (-2.83, 4.54)	0.63
How hard to pay for basics :				
Not at all	Reference		Reference	
Somewhat hard	1.67 (-2.80, 6.13)	0.45	0.06 (-3.87, 3.50)	0.97
Very hard	4.87 (0.80, 8.94)	0.02	2.84 (-0.91, 6.61)	0.13

F (6, 23) = 4.31; Prob > F = 0.0047; R-squared = 0.5290

HADS was 36.6%, similar to the overall prevalence of 38% reported in earlier literature[27, 111]referring mostly to patients who underwent an ICD implantation for secondary prevention of sudden cardiac death. Second, demographic characteristics such as young age, low socio-economic status and previous psychological morbidity appear to be associated with increased anxiety in ICD patients, while anxiety seems to be unrelated to cardiac diagnosis, ICD indication, cardiac functional status, and ICD-related factors including shock delivery Recent reports[33] have suggested that anxiety prevalence may be decreasing in ICD populations due to changes in indications and better technical equipment. In this analysis of a sample of patients enrolled in a pilot randomized trial of a mindfulness-based intervention for anxiety treatment, the baseline prevalence of clinically significant anxiety as assessed by the HADS was 36.6%. Although selection bias cannot be excluded, since this is a secondary analysis of baseline data of a pilot study designed to pilot test a behavioral intervention for anxiety, this figure agrees with recent studies of anxiety prevalence in larger ICD outpatients' populations that used the HADS questionnaire for anxiety screening. In a recent publication, Kapa[32] reports a similar prevalence of anxiety (35%) evaluated within 2 months of ICD surgery using HADS similar cut-off points, and a mean baseline HADS scores in the whole population of 5.95± 3.43 (similar to the mean scores in this study, 6.4 ±4.3). In a prospective study of changes in neuropsychological functioning after ICD surgery, Hallas[157] found a prevalence of anxiety of 23% (HADS score 8-10) and 26.6% (HADS score 11-21) at 6 weeks after implantation, while anxiety scores decreased over time; however, different HADS cutoff scores were used. Pedersen[158] reported a prevalence of clinical anxiety of

21% (state anxiety) and 39% (trait anxiety) using the State-Trait Anxiety Inventory (STAI).

Our findings of an association of greater anxiety with younger age (i.e. defined as < 50 years of age) are consistent with what has been reported in the literature,[159, 160] as well as the association with female gender.[161] Forty-five percent of women met criteria for clinically significant anxiety compared to 21.1% of men in this study, although this difference was not statistically significant due to the small sample size.

Anxiety was not associated with disease-specific or ICD specific characteristic, including cardiac diagnosis, NYHA functional class or EF, type of ICD, ICD indication, time from ICD procedure, and history of ICD shocks. A previous meta-analysis published in 2003[162] suggested that poor psychosocial outcomes in ICD patients may be a consequence of the underlying ventricular arrhythmia, rather than of ICD implantation/ICD therapy "per se". A recent study by Kapa and colleagues [32] has confirmed that psychological discomfort improves over time and is not associated with ICD events (i.e. shocks). In a recent study examining the course of anxiety over a one-year period, social support and type D personality[163](i.e., a personality with high levels of negative affectivity and social inhibition) were predictors of state anxiety trajectories over time, while ICD indication, shocks, severity of heart failure had no effect.[158] Furthermore, a recent literature review reports a lack of evidence for an impact of ICD indication (primary vs. secondary prevention) on quality of life and psychological well-being.[164]

The strongest univariate predictors of anxiety in this population were history of co-morbid depression, past use of antidepressants and anxiolytics, younger age, and low socioeconomic status. Younger age and previous psychological morbidity were not independently associated with anxiety scores in the multivariate model (p=0.06); however, it is possible that the lack of significance is due to the small sample size and consequent lack of power do determine this association. A limited number of studies have assessed the impact of a history of anxiety /depression on anxiety scores in ICD patients, with recent studies suggesting that the pre-implantation psychological profile of ICD patients may contribute to poorer psychological outcomes and worse quality of life more than underlying cardiac or ICD related conditions.[14] Sears and colleagues[165] observed that psychological variables were as strong as, or stronger than, age, ejection fraction, and ICD shocks in predicting quality of life outcomes in ICD patients. Van Den Broek[166] and colleagues found that particular personality characteristics (type D personality)[163] and anxiety sensitivity, but not shocks, were independent predictors of interviewer-rated anxiety. Finally, Hallas et al.,[167] employing an interview-based qualitative grounded theory methodology to explore the impact of medical history heterogeneity and illness beliefs on quality of life, found that perceived control, illness beliefs, and coping had an impact on adjustment after ICD implantation.

There were a number of limitations to this study. First, this was a secondary cross-sectional analysis and it was not powered to detect independent association(s) between different covariates and anxiety. Second, since the results are based on baseline data collected for a pilot randomized trial evaluating the effect of a behavioral intervention on

anxiety, results are not generalizable to the entire ICD population, even if no minimal anxiety score was required to be enrolled in the study. We cannot exclude the possibility that patients enrolled in the study were more anxious than the general ICD outpatients' population. In fact, 25 % of eligible patients refused to participate because they reported no anxiety. Third, anxiety was self-reported. This may result in information bias and misclassification of exposure if anxious patients were classified as non-anxious and vice versa. However, HADS performed well in both assessing symptom severity and detecting cases of anxiety disorders and depression in somatic, psychiatric and primary care patients and in the general population with a sensitivity and specificity of 80%.[153, 168]

In conclusion, this study confirms that despite changes in ICD indications that have led to the treatment of patients with better clinical condition and who never experienced disastrous cardiac arrhythmia, the prevalence of anxiety in proximity of an ICD related procedure is still elevated. Contrary to earlier reports, cardiac condition and ICD related characteristics, including a history of shock therapy, are not associated with anxiety, which appears to be associated with younger age at implantation, previous psychiatric morbidity, and lower socio-economic status. The results of this study have important clinical implication. First, there is still a sizable proportion of patients with ICD that have significant anxiety. Even though anxiety does not appear to be related to the ICD/ ICD therapies "per se", or to the underlying cardiac diagnosis, it is important to identify and treat this condition due to its impact on long-term prognosis and quality of life. In particular, younger patients, women, patients with no or limited support from significant others and patients with previous co-morbid depression seem to be at higher

risk of anxiety. Patients with co-morbid depression are at higher risk of shocks, and both depression and depression severity have been associated with shortened time to first shock. [160] These sub-groups may benefit from early screening and support therapies.

CHAPTER IV

Predictors of Self-Reported Dispositional Mindfulness in Patients with Implantable Cardioverter Defibrillators (ICD)

Introduction

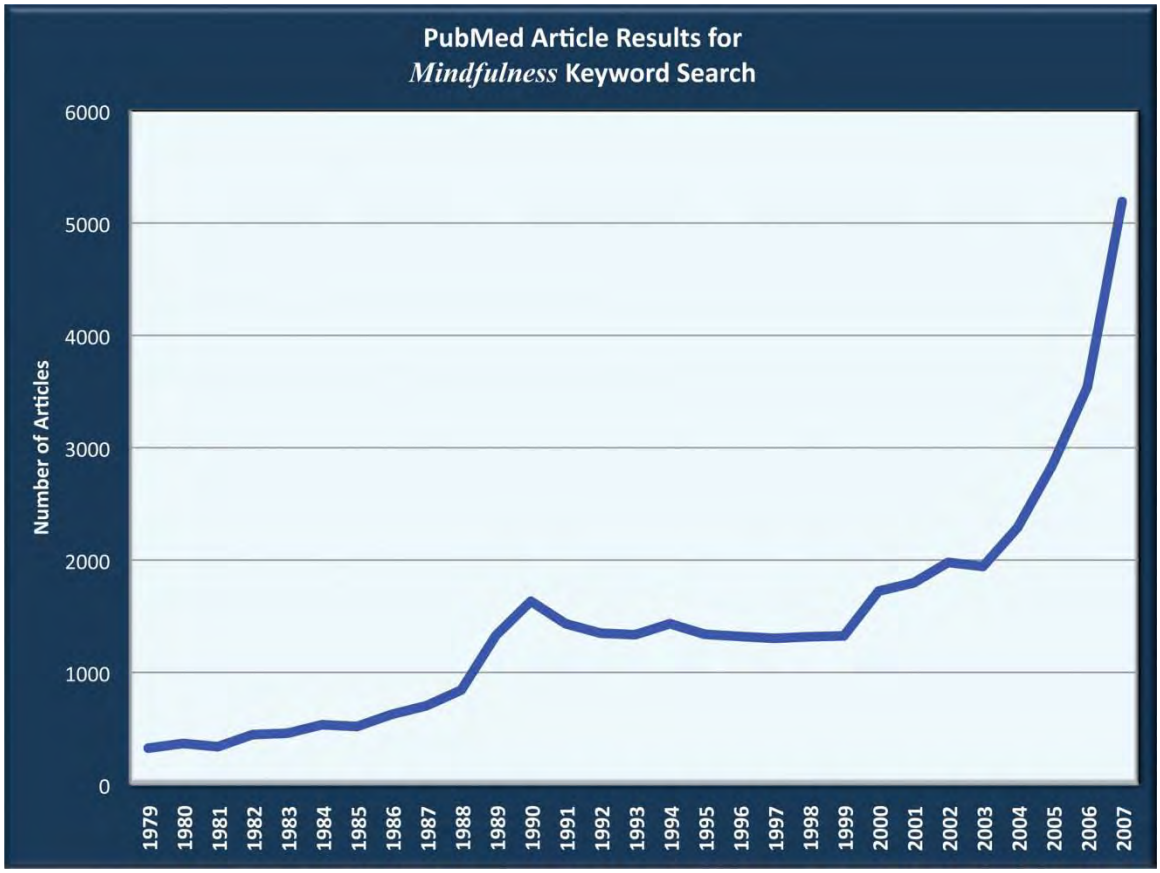
The practice of mindfulness has been the mainstay of Eastern religions and philosophies for centuries. According to these traditions, the cultivation of mindfulness is conducive to a reduction of suffering and an increase in qualities such as compassion, equanimity, and wisdom; expressed in Western words, a reduction in negative mood states and better well-being.

Mindfulness-based interventions have been shown to reduce anxiety, depression, sleep disturbance and a variety of physical symptoms in different medical conditions[18] such as cancer,[86-89]chronic pain,[90, 91] anxiety disorders,[92] rheumatoid arthritis[93] and fibromyalgia,[94] with an estimated effect size around 0.5.[18, 169] When associated with cognitive behavioral therapy, mindfulness training has been shown to reduce the rate of relapse/recurrence in major depression.[95]

There is a growing interest in mindfulness research within the scientific world, clearly manifested by the increasing number of papers (over a thousand) published on this topic over the past twenty years. Figure 4.1 shows the number of articles retrieved from a PubMed search using "mindfulness" as a keyword.

The skeptical view of the British Medical Journal in 2003[101] which concluded for

Figure 4.1. Papers (1979-2007) retrieved based on a PubMed search using “mindfulness” as keyword.
(Courtesy of Dr. Saki Santorelli - Center for Mindfulness, University of Massachusetts Medical School).



a weak evidence of any therapeutic effect of meditation-based interventions has been replaced by a more open one emphasizing the role of mindfulness in preventing and treating disease, in increasing coping with stress and chronic diseases, and in reducing stress both in patients and health providers.[170]

However, the current evidence for a beneficial role of mindfulness on physical and psychological health is based almost exclusively on studies of mindfulness training. Very limited work has been done to investigate the role of dispositional mindfulness (DM) in promoting well-being [171] and to evaluate whether an increased tendency to be mindful is associated with better psychological and physical well-being in individuals who were never exposed to any formal training.

"Natural", "dispositional", or "trait" mindfulness refers to the ability to be mindful in everyday life,[171, 172] and although it can be purposely cultivated and enhanced through training and practice,[173] it is not necessarily related to previous training. In fact, mindfulness traits are present also in individuals who were never exposed to meditation and individuals may differ as to their predisposition to be mindful in everyday life.[171, 172] Although usually assessed through different instruments and across diverse populations, DM has been linked with several personality and mood characteristics. Significant negative correlations have been observed between DM measured with the Mindful Attention Awareness Scale [171] and personality characteristics such as neuroticism (particularly with the facets of depression, self-consciousness, and angry hostility)[171, 174, 175] and with self-reported aggressiveness and hostile attribution bias.[176] Moreover, DM has shown an inverse relationship with depression and anxiety. [171] Similar associations

have been documented by Baer and colleagues[177, 178] and in a recent cross-sectional, population based study[179] using a different instrument (the Five Facets of Mindfulness questionnaire).[180]

Recent research has examined the neural correlates of the association between DM and depressive symptoms using neuroimaging techniques. Way and colleagues[181] have shown a linear inverse association between dispositional mindfulness and baseline neural activity in the amygdala (an area of the brain that shows increased resting activity in individuals with depression), concluding that changes in amygdala activity could be a potential mechanism by which interventions such as mindfulness-based cognitive therapy (interventions combining mindfulness training with cognitive therapy)[95] improve depression symptoms. Creswell and colleagues have shown that dispositional mindfulness was associated with greater widespread prefrontal cortical activation, and reduced bilateral amygdala activity during affect labeling tasks.[182] Finally, another study evaluating whether dispositional mindfulness may modulate brain activity triggered during instructed re-appraisal of negative emotions concluded that individual differences in dispositional mindfulness may modulate the activity of neural systems involved in the cognitive control of negative emotions.[183]

Most studies of dispositional mindfulness, however, have been conducted in healthy individuals. Possible predictors of DM have rarely been explored in populations with chronic diseases. In patients with cancer, higher levels of baseline mindfulness (i.e., before the delivery of mindfulness interventions) were associated with lower levels of mood disturbance and stress.[171] The authors noted that the baseline average mindfulness

score in this group was higher than in other populations, and hypothesized that the experience of cancer may lead patients to reconsider their view of life, and to focus more intensely on the present and on present-moment experiences. Patients receiving an implantable cardioverter defibrillator (ICD) present characteristics similar to those of cancer patients. Likewise, ICD patients are facing a severe chronic disease; they are, by definition, facing death, either because they are at risk of dying suddenly or because they survived a prior cardiac arrest. Finally, they are usually symptomatic, often reporting severe shortness of breath, fatigue, chest pain and palpitations. Thus, the purpose of this study was to describe the characteristics of DM in a group of patients with severe cardiovascular disease who were largely naïve to mindfulness practices, and specifically whether mindfulness is associated with indicators of disease severity and with psychological morbidity and well-being.

Methods

The present study was a pilot randomized controlled trial designed to evaluate the feasibility and the preliminary efficacy of a mindfulness-based intervention in patients undergoing an ICD procedure and/or who had ICD related events (shocks). Extensive details about the study are reported in chapter 2. Briefly, the study was conducted at the university campus of the UMass Memorial Medical Center, a high technology, state-of-the-art tertiary care medical center located in Worcester, MA, which is a clinical partner of the University of Massachusetts Medical School. All consecutive patients scheduled for an ICD related procedure at the catheterization lab were screened for study eligibility within a month of the procedure. Eligible patients received an interest survey and a letter

inviting them to participate in the study. Patients were invited to return the survey at the occasion of their next visit or to call a dedicated phone number to communicate that they were not planning to participate. If the patients did not call, the graduate student followed up by phone. Once the patient expressed interest, a screening visit was scheduled. Patients were considered eligible if they met the following criteria: age ≥ 21, ability to understand and speak English, and access to a telephone. Patients were excluded from the study under the following conditions: inability/unwillingness to give informed consent, signs of cognitive impairment, New York Heart Association (NYHA) functional class >III or an angina Canadian Cardiovascular Society class III and IV or otherwise clinically unstable, pending coronary by-pass or heart transplantation, co-morbid life threatening conditions, and ongoing severe depression or psychosis. After confirmation of study eligibility, full informed consent was obtained in person by the PhD candidate after a thorough explanation of the study design and of the study conditions, usual care and intervention, including the risks and benefits involved. Following baseline data collection, patients were assigned to the experimental or to the control group using a computer generated randomization scheme.

Assessments

Mindfulness scores

Baseline and post-intervention mindfulness scores were measured using the Five Facets of Mindfulness (FFM) questionnaire,[177,180] a self reported measure of mindfulness derived from a factor analysis of questionnaires measuring mindfulness in daily life. A shortened version was used to reduce paper burden in this particular population,

consisting of 15 items exploring different aspects of mindfulness: observing, describing, acting with awareness, non-judging of inner experience, and non-reactivity to inner experience. Each item is rated on a Likert scale ranging from one (never or very rarely true) to five (very often or always true). Total scores range from zero to 75.

Study covariates

Information was collected on demographic characteristics (age, gender, income, marital status, education and ethnicity) and on variables that could affect DM (the outcome variable) such as previous history of anxiety and depression and related prescriptions; baseline anxiety and depression scores; disease-related characteristics such as ejection fraction, NYHA functional class and history of cardiac arrest; use of other complementary and alternative therapies; and physical activity. Demographic information, NYHA class, ejection fraction (obtained from the most recent echocardiogram or ventriculogram) and other clinical information were collected from the electronic version of the medical record. Anxiety and depression scores were measured using the Hospital Anxiety and Depression Scale (HADS),[143] a 14-items self-administered questionnaire with two sub-scales measuring anxiety and depression, with higher scores indicating greater psychological morbidity. Many studies conducted throughout the world have confirmed its validity not only in hospital settings, but also when used in primary care.[144-146] A correlation between 0.6-0.8 has been reported between the HADS and other commonly used questionnaires for anxiety and depression such as the Beck Depression Inventory and the State-Trait Anxiety Inventory.[153]Furthermore, the HADS offers the advantage of focusing on cognitive

symptoms instead of physical symptoms; this is particularly useful in cardiac patients where symptoms of the underlying cardiac disease maybe similar or identical to those resulting from somatic manifestations of anxiety and depression. Information about the use of other complementary/alternative therapies and physical exercise was collected by means of self-administered questionnaires.

The study protocol and all the study materials were approved by the Committee for the Protection of Human Subjects at the University of Massachusetts Medical School (Docket H-13078).

Statistical analysis

A preliminary analysis was conducted to determine the variability and distribution of mindfulness scores (i.e., to identify a bi-modal distribution vs. a normal distribution), to evaluate the appropriateness of the model's assumptions, and to assess correlations between covariates to avoid collinearity in the multivariate model. Variables were checked for missing data and distribution, if continuous; for counts, if categorical. Loess curves were used to examine and test linear vs. non-linear associations. Age, ejection fraction, time from ICD implantation, HADS and FFM scores were treated as continuous variables. Sex, race, financial status, marital status, education, use of antidepressant and anxiolytics, previous history of anxiety and depression, psychotropic and anti-arrhythmic therapy, type of ICD implanted (bi-ventricular vs. ventricular), prior ICD shocks, history of cardiac arrest or severe cardiac arrhythmia, NYHA class, physical exercise and use of complementary therapies during prior month were treated as categorical variables. Spearman's rho was to evaluate correlations between FFM scores and continuous

variables. Mean baseline FFM scores were compared across categories of non-continuous variables using T test; Kruskall-Wallis was used when the assumption of constant variance was not met. The association between mindfulness scores and the different variables was estimated in univariate linear regression models. Variables that showed an association with the outcome ($p \leq 0.10$) were then included in a multivariate linear regression model according to the following equation:

$$y\ (FFM\ scores) = \beta_0 + \beta_1\ HADS + \beta_2\ age + \beta_3\ gender\ (0,1) + \beta_4\ marital\ status(0,1) \ldots + \varepsilon$$

Results are presented as beta coefficient (with confidence intervals), where the null hypothesis was that $\beta_1 = 0$. P values <0.05 were considered significant. All statistical analyses were performed using STATA 10 statistical software.[108]

Results

A diagram reporting the flow of patients through the study and including detailed information on the number of randomized participants, the number of patients receiving the intended treatment, the number of subjects completing the study and being analyzed for the primary outcome is shown in Chapter II, Figure 2.3. One participant was ineligible after randomization because of cognitive impairment and was excluded from the study. Thus, data from 30 patients were available for this analysis.

The baseline demographic and clinical characteristics of the study sample are presented in Table 4.1. The average age at enrollment was 63.1 (range: 46-78). Study participants were mostly males (70%), white-non Hispanic (90.0%) and married or in a committed relationship (70%). Sixty percent had less than a college degree and 30% reported that it was somewhat hard to very hard to provide for basics such as heating,

Table 4.1. Baseline characteristics of the study sample

n	30 (100)
Age (mean, SD)	63.1 (10.3)
Males	21(70)
Females	9 (30)
White-non Hispanic	27 (90.0)
High School	7 (23.3)
Some college	11 (36.7)
College graduate	4 (13.3)
Post graduate	8 (26.7)
Married or in committed relationship	21 (70.0)
Separated/divorced/single	9 (30.0)
Not at all hard to pay for basics [(b)]	21 (70.0)
Somewhat hard	4 (13.3)
Very hard	5 (16.7)
Coronary heart disease	16 (53.3)
Idiopathic dilated cardiomyopathy	6 (20.0)
Other	8 (26.7)
Previous cardiac arrest or severe cardiac arrhythmia	7 (23.3)
Previous ICD shocks/storms	6 (20.0)
Months from ICD procedure median (25^{th}-75^{th} percentile)	1.43 (0.3, 14.2)
Bi-ventricular ICD	21 (70)
Ejection fraction (mean, SD)	0.31 (0.12)
New York Heart Association class	
I	7 (23.3)
II	16 (53.4)
III	7 (23.3)
Beta-blockers	26 (86.7)
Anti-arrhythmics	6 (20.0)
Anxiolytics	7 (23.3)
Anti-depressants	8 (26.7)
Exercise at least 30' once a week during past month	6 (20)
Used integrative medicine treatments during previous month	4 (13.3)
FFM[d)] scores (mean, SD)	57.3 (8.2)
History of anxiety	6 (20.0)
History of depression	8(26.7)

[a)] Values are n (%) unless otherwise indicated
[b)] Food, housing, medical care and heating
[c)] Expressive writing, reflexology, or meditation
[d)] FFM= Five Facets of Mindfulness

food or health insurance. The most common diagnosis was coronary heart disease; cardiac function was usually compromised with a mean ejection fraction of 0.31 (normal value: >0.50), and with 80% of participants in NYHA class II or III. Twenty-three percent of patients had experienced a previous severe arrhythmia or cardiac arrest, and 20% had experienced a recent ICD shock. Twenty-three percent were currently receiving anxiolytics and 26.7 % were on anti-depressants, while 20% and 26.7% had a prior history of anxiety and depression, respectively. Four patients (13.3%) reported to have used other integrative/alternative treatments such as expressive writing (2), reflexology (1), or meditation (1) during the previous month. The mean FFM score was 57.3 (SD 8.2, range: 38-75). The distribution of FFM scores was normal.

Table 4.2 shows the mean baseline mindfulness scores by different clinical characteristics. Due to the small study sample, most comparisons were not statistically significant. Mindfulness scores did not differ by demographic characteristics, prior shocks or history of cardiac arrest, and cardiac diagnosis. Mindfulness scores were higher in patients with a bi-ventricular ICD (p=0.057), and increased with increasing NYHA class. Likewise, patients with no history of depression (p=0.016) or anxiety had higher mindfulness scores, as well as those not taking antidepressants or anxiolytics. Finally, FFM scores were higher in patients reporting to exercise at least once a week during the previous month vs. those not exercising. Mindfulness scores were significantly and inversely correlated with baseline HADS anxiety (Spearman rho: - 0.57, p=0.0005) and depression scores (Spearman rho: -0.37, p=0.04), while there was no association with other continuous variables such as age, ejection fraction and time since ICD procedure.

Table 4.2. Mean values of FFM scores by baseline characteristic [a)]

	Variables	FFM score	P value [b)]
Sex	Male	58.2 (6.7)	0.365
	Female	55.2 (10.7)	
Education	High School	56.4 (6.9)	0.920 [c)]
	Some college	57.1 (8.5)	
	College graduate	60.0 (10.9)	
	Post graduate	57.1 (8.9)	
Marital status	Married or in committed relationship	57.6 (7.9)	0.776
	Separated/divorced/single	56.6 (9.4)	
Financial status	Not at all hard to pay for basics [(b)]	57.1 (8.7)	0.837[c)]
	Somewhat hard	59.5 (7.0)	
	Very hard	56.2 (8.4)	
Diagnosis	Coronary heart disease	59.3 (6.55)	0.390[c)]
	Idiopathic dilated cardiomyopathy	55.8 (11.0)	
	Other	54.6 (9.1)	
Previous cardiac arrest	yes	58.0 (10.5)	0.810
	no	57.1 (7.7)	
Previous ICD shocks/storms	yes	58.6 (7.7)	0.664
	no	57.0 (8.5)	
Type of ICD	Bi-ventricular	59.2 (7.1)	0.057
	Single chamber	53.0 (9.4)	
NYHA class	I	53.6 (9.4)	0.360[c)]
	II	58.0 (7.0)	
	III	59.6 (9.6)	
History of depression	Yes	51.5 (8.3)	0.016
	No	59.5 (7.2)	
History of anxiety	Yes	52.8 (10.5)	0.136
	no	58.5 (7.4)	
Antidepressants	yes	54.3 (10.2)	0.221
	no	58.5 (7.3)	
Anxiolytics	yes	53.9 (7.9)	0.206
	no	58.4 (8.2)	
Exercise at least 30' once a week during past month	yes	62.5 (5.5)	0.084
	no	56.0 (8.3)	
Used integrative medicine treatments during previous month	yes	53.5 (6.8)	0.338
	no	57.9 (8.5)	

[a)] Values are means (SD)

[b)] T-test unless otherwise indicated

[c)] ANOVA

ICD=Implantable cardioverter defibrillators

Table 4.3 shows the variables that were associated with baseline mindfulness scores in univariate models with $p<0.10$. Baseline FFM scores were significantly and inversely associated with baseline HADS anxiety scores ($p=0.001$), with a previous diagnosis of depression ($p=0.016$); and positively associated with type of ICD implanted (bi-ventricular vs. single chamber, $p=0.057$). Baseline mindfulness scores were not associated with age, gender, race/ethnicity, marital status, education, financial status, smoking, EF, previous cardiovascular procedures, previous cardiac arrest or severe arrhythmia, cardiac diagnosis, time from ICD procedure, previous ICD shocks, current use of anti-arrhythmics or beta-blockers, and use of other complementary/alternative therapies during the past month. There was a positive, non-significant, association between FFM scores and exercise (30 minutes at least once a week during the previous month), and with NYHA class, and an inverse relationship between FFM scores and history of anxiety and HADS depression scores. Next, a multivariate model was generated including all the variables that were associated with the outcome with $p\leq0.10$ in univariate models (Table 4.3). Most psychological variables were highly correlated; in order to avoid collinearity, only covariates showing the strongest associations with the outcome in univariate models were included. In the multivariate model, no variable appeared to be independently associated with FFM scores ($p=0.054$ for the association between anxiety and mindfulness scores).

Table 4.3. Univariate and multivariate associations with FFM scores

	Unadjusted Coefficient (95% CI)	P value	Adjusted Coefficient (95% CI)	P value
Covariate				
Baseline HADS anxiety scores	- 1.10 (-1.71, -0.49)	0.001	- 0.77 (-1.55, 0.02)	0.054
Previous depression (yes vs. no)	- 7.95 (-14.31, -1.6)	0.016	- 3.14 (-10.21, 3.93)	0.369
Bi-ventricular vs. single chamber ICD	6.19 (-0.19, 12.57)	0.057	4.03 (-1.87, 9.92)	0.172
Exercise[a)] 30 minutes once a week (yes vs. no)	5.51 (-1.22, 12.24)	0.10	1.96 (-5.08, 9.0)	0.571
F (4, 25) = 4.44	Prob > F = 0.0076		R-squared = 0.4152	

[a)] Walking or golfing

FFM= Five Facets of Mindfulness; HADS=Hospital Anxiety and Depression Scale; ICD=implantable cardioverter defibrillator

Discussion

In this sample of patients with severe cardiovascular disease and depressed heart function who underwent ICD implantation for sudden cardiac death prevention or received recent ICD shocks, DM was associated with psychological characteristics. The most relevant associations were observed with previous depression and current anxiety symptoms as measured by HADS anxiety scores. These associations, however, became non-significant after adjustment for other covariates. Associations with other psychological variables (i.e. use of antidepressants and anxiolytics, previous anxiety, current depression scores), although not reaching statistical significance, were in the expected direction, i.e. they were inversely associated with DM, supporting the hypothesis of an inverse association between DM and negative mind states. These findings are in agreement with other studies of DM. [171, 175, 178-180]

DM appears to be inversely associated not only with self-reported current anxiety and depression (as measured by HADS scores and consequently referring to the past month only) that could be dependent on current circumstances such as the ICD procedure and the recent hospitalization, but also with a prior diagnosis of anxiety and depression. The inverse association between DM and previous psychological morbidity is a specific contribution of this study to the current literature on this topic, since this information has been never or rarely collected.

In univariate models, patients with more severe cardiovascular symptoms tended to show higher DM, as indicated by the increased FFM scores in patients with higher NYHA class and in those receiving a biventricular ICD. In fact, biventricular ICDs are

usually implanted in patients with more severe heart failure symptoms (i.e. patients having an EF less than or equal to 35%, a QRS duration greater than or equal to 0.12 seconds, sinus rhythm and NYHA functional class III or IV).[16, 133, 184]

Two hypotheses can be made to explain this finding. First, since ICD patients are usually educated by their providers to pay attention to physical symptoms (such as chest pain, palpitations or shortness of breath) that may signal a worsening of their conditions, they may learn to be more conscious of physical sensations and, in general, to pay more attention to what unfolds in the present. Alternatively, since cardiac conditions are usually worse in severely symptomatic patients, they may have become more aware of the value of their lives and learned to appreciate the present similarly to what was reported in a study of cancer patients.[171] To the knowledge of the PhD candidate, most studies of DM have been conducted in healthy individuals, and hence there is limited available information in patients with chronic diseases. Higher psychological and interpersonal growth has been reported in survivors of stem cells-transplantation compared to healthy volunteers;[185] but mindfulness scores in cancer patients have also been reported to be lower than in healthy individuals.[175]

DM was not associated with a history of previous shocks and cardiac arrest; namely, in this group of patients exposure to conditions close to a “near-death” experience did not result in increased DM. However, this study was not powered to detect this association and the number of patients with a history of shocks (6/30) or who received an ICD following a cardiac arrest (7/30) was low.

Finally, one interesting preliminary finding is worth mentioning. Mindfulness scores were higher in patients who exercised at least once a week (Figure 4.2 and Table 4.2) compared to patients who did not. Physical exercise in the form of light yoga exercises is in fact a component of Mindfulness Based Stress Reduction[90, 106] (MBSR), the most popular and world renowned mindfulness-based intervention. Self reported yoga practice has been associated with positive changes in mindfulness during MBSR training.[186] If physical activity is positively associated with mindfulness levels, it might contribute to the increase in mindfulness observed at the end of such training, which in turn may mediate its beneficial effects on psychological and physical well-being.[173, 187, 188]Although differences did not reach statistical significance, this finding deserves further investigation in larger populations.

The most notable strength of this preliminary study is that this is the first study describing the characteristics of DM in patients with severe cardiovascular disease. Second, the study sample was selected from a "real life" diverse population of consecutive candidates to ICD procedures and/or with ICD shocks, thus very different from the highly educated, high socio-economic status, and mostly female population usually accessing mind-body programs.[103] However, there are also several limitations. First, because of the small sample size, this study was not powered to detect associations with less frequent events such as previous cardiac arrest or shocks, and to examine associations with specific facets of mindfulness measured by the FFM questionnaire. Second, a highly selected population was studied, thus limiting the possibility to generalize the study findings to patients with different diseases. Third, although the study

was proposed to all consecutive ICD candidates, it cannot be excluded that only highly motivated participants joined the study and that due to social desirability or other factors they may be more prone to report higher or different levels of mindfulness compared to patients that did not participate. Fourth, DM was self-reported. This is a common limitation of studies assessing the effect of mindfulness training. In fact, despite recent evidence that mindfulness is an important mediator of the effect of mindfulness interventions on anxiety and other psychological outcomes, [173, 187, 188] adequate definitions of mindfulness are often not provided, and when provided, they are either inconsistent or overlapping across studies.[189] Objective criteria for the measurement of mindfulness are currently unavailable and although several self-report instruments were developed to measure this construct,[171, 177, 178, 190, 191] correlations across different scales are modest,[192] further complicating the comparison of results across studies. It is likely that the meaning of some items in mindfulness inventories (including the one used for this study) may have a quite different meaning in mindfulness-trained subjects and in patients such as the ones enrolled in this study, who were naïve of mindfulness training.[189] Finally, this is a cross-sectional analysis, and consequently the direction of the association cannot be established; namely, whether enhanced DM leads to an improved emotional well-being or if the mind's absorption in the powerful struggles and emotions accompanying anxiety and depression is limiting its natural capacity of attending to the present.

In conclusion, current psychological well-being and prior psychological morbidity, and not indicators of disease severity such as prior cardiac arrest or shocks,

appear to be more strongly associated with DM in patients with ICDs who did not receive previous mindfulness training. Further research in larger populations is needed to confirm these finding, which may help shed further light on the mechanism of the beneficial effects of mindfulness on health outcomes.

CHAPTER V

Summary and Conclusions

In this section, a summary of the primary findings of this dissertation will be presented, followed by a discussion of the study limitations, and by questions that need to be addressed in future research based on the preliminary results of this dissertation work. Implications for patients' care and the health care system will also be discussed.

Summary of research findings

Aim 1 - to determine the feasibility of a randomized clinical trial of a phone-administered, mindfulness-based training program, as measured by recruitment and retention rates, treatment adherence and fidelity.

The initial screening and recruitment methods planned in the dissertation proposal had to be adapted based on the challenges encountered upon trying to conduct a research study in a "real life" clinical setting. In this respect, having conducted this pilot project has been extremely valuable since it permitted the identification of barriers and obstacles to recruitment and to experiment with different solutions that will be extremely helpful in the design of a future larger trial. Overall, the methods ultimately adopted to screen, recruit, and retain study participants were feasible to conduct and satisfactory to ICD outpatients, and the study intervention was safe and acceptable to patients. Phone delivery resulted in excellent retention rates and limited costs. Finally, assessments of treatment fidelity showed that instructors delivered the content of the intervention as intended in almost 100% of cases.

Aim 2 - to evaluate the current baseline prevalence of anxiety in the study population, and evaluate its association(s) with disease and ICD characteristics.

The hypothesis of this cross-sectional analysis was that, due to changes in ICD implantation guidelines, and to technological improvements at both the device and the ICD procedure level, the prevalence of anxiety and anxiety correlates might have changed in this population. The study findings do not show a decrease in the overall prevalence of anxiety in ICD patients compared with estimates from earlier cohorts. Young age, low socio-economic status and previous psychological morbidity appear to be associated with anxiety in ICD patients, while anxiety seems to be unrelated to cardiac diagnosis, indication for ICD implantation, cardiac functional status, and ICD-related factors including prior shock delivery.

Aim 3 – To describe the baseline correlates of mindfulness in patients with cardiovascular disease, and whether mindfulness is associated with baseline demographic and psychological characteristics.

In this sample of patients with severe cardiovascular disease who underwent ICD procedures or received recent ICD shocks, baseline ("dispositional") mindfulness was most strongly associated with psychological characteristics, namely, previous psychological morbidity (in particular, depression), and current anxiety symptoms as measured by HADS anxiety scores. Associations with other psychological variables (i.e. use of antidepressants and anxiolytics, previous anxiety, and depression scores), although not reaching statistical significance, were in the expected direction, i.e., they were

inversely associated with DM, supporting the hypothesis of an inverse association between DM and negative mind states.

Strengths and limitations

This dissertation work contributed to this field of research at several levels. First, this is the first study testing a mindfulness-based intervention in patients with severe cardiac arrhythmias. Second, it utilized a novel delivery technique (i.e., phone) in order to reach severely ill patients. Third, it included assessments of treatment fidelity, which have never been performed in studies of mindfulness training. However, some limitations should be noted. Since this was a feasibility study, conclusions regarding efficacy cannot be drawn based on this information. Preliminary data about the efficacy of such a program in the treatment of anxiety in ICD patients will be available once the outcomes analysis is concluded, i.e. in about one year pending accrual completion. Second, participants were recruited from a single site, and the study sample was relatively small and not ethnically representative. This resulted in lack of generalizability and limited power, particularly for the detection of associations of anxiety and DM with relatively rare events such as previous ICD shocks. A third limitation was the cross-sectional design adopted for aims 2 and 3. Such a design does not allow for a causal interpretation of the observed associations between the different variables and anxiety or mindfulness, respectively. Fourth, individual mindfulness practice was self-reported. This is a common limitation of studies of mindfulness-based interventions; however, with adequate funding, it would be possible to utilize devices tracking the amount of time that each participant listens to the study CD, or to post each recorded session on a dedicated intervention

website and then track the time that each participant is logged onto the website. Fifth, since participants were not followed up once the intervention was completed, we do not know whether patients kept practicing the study techniques over time, and a longer duration of follow-up is needed. Finally, the prevalence of anxiety in this study might be overestimated since the results refer to the prevalence of anxiety in patients enrolled in the study, and not in candidates to ICD procedures.

Future work

This is an exciting time for mindfulness research, as the number of ongoing studies and published articles keeps increasing. Further research will involve different strategies to overcome barriers identified in the current study. The main challenge was the recruitment of an adequate number of patients in order to achieve sufficient power to detect the impact of the intervention on less prevalent outcomes (i.e., shocks). This could be resolved by involving multiple recruitment centers. An adequate sample size will result in sufficient power to detect associations of interest that were non-significant in this pilot study, such as the positive relationship of DM with exercise, or the association between anxiety and various demographic variables. A second challenge was the timing of the intervention delivery. Some participants suggested that the intervention should start in the hospital, when they felt they were more anxious. However, it was very difficult to contact, screen and obtain informed consent for the study before patients underwent the ICD procedure. With adequate funding, it would be possible to permanently involve a clinical staff member (i.e. a research nurse), who would propose the study to patients when the ICD implantation is still being contemplated or planned. Budgetary constraints

were also a reason for choosing a "usual care" comparison arm instead of an active control arm. The ideal design would entail a nurse-delivered ICD education intervention similar in format and duration to the mindfulness arm, in order to account for the attention that patients enrolled in the MBI arm received from the instructors.

Furthermore, it will be important to identify patients who may most benefit from the intervention. In agreement with previous literature[30, 31] this work shows that young age, low socio-economic status and previous psychological morbidity appear to be associated with anxiety in ICD patients. A possible approach is to promote screening for anxiety and depression as part of the routine assessments for these patients. This would help identify candidates with higher anxiety levels who may benefit from the intervention.

Finally, future studies should include an evaluation of the effect of the intervention on biomarkers of anxiety such as catecholamines, cortisol levels, and heart rate variability. Neuroimaging techniques could be used in a sub-sample of patients to explore the neural equivalents of the associations of DM and negative emotions.

Implications for patients' care and the health system

There have been recent indications that ICD procedures may be reaching a plateau;[134] however, a significant number of implantations is still performed every year. [25] Despite changes in ICD implantation guidelines, resulting in a different population now receiving ICDs compared to twenty years ago, anxiety and other psychological disturbances are still affecting a significant proportion of patients. Due to the negative impact on cardiac outcomes, patients with psychological distress need assistance. This

can be best accomplished by adequate screening for anxiety and depression in order to identify patients who may benefit from psychological support. Mindfulness interventions have shown benefit for depression[95] and there are data supporting an effect on anxiety, although with different effect sizes.[18, 92, 169] If proven effective, phone delivered, mindfulness-based interventions in ICD patients are feasible with very limited costs.

In conclusion, anxiety is still a significant problem in ICD patients. Psychological morbidity appears to be the major determinant of anxiety in these patients. Dispositional mindfulness is inversely associated with current anxiety and depression and with prior psychological morbidity, supporting the hypothesis of a modulating role of mindfulness on the processing of negative emotions. Finally, phone-delivered, individual mindfulness training is feasible, acceptable to patients and can be adequately delivered by trained instructors with limited costs. The findings from this dissertation work support the need for larger clinical trials of mindfulness-based interventions in ICD patients.

Appendix

STUDY CD - BODY SCAN SCRIPT

In this recording you are beginning the practice of the body scan. The body scan is the beginning step in a method that has been shown to help patients deal with stress and to enter and dwell in states of deep mental and physical relaxation. This initial practice is to develop the ability to pay deliberate careful attention and to become more aware of your body. So remember that each time you take the few minutes to practice this you are taking a powerful and active role in improving your health and well-being.

Do the body scan either lying or your bed or sitting in an easy chair. Dress in loose, comfortable clothes and try to arrange not to be interrupted by friends, family, or phone calls. It's most helpful to see this as a time for self care - a time to give yourself unconditional attention and to hold yourself with kindheartedness. Try to stay awake and alert - If you find yourself repeatedly falling asleep, experiment with changing your position to one in which you can remain awake.

We will be bringing awareness to areas of the body in a systematic way. As we go along use the instructions for guidance, simply doing what it says to do - that is simply being aware of each area with an open curiosity and using your attention to notice the sensations in your body and the activity of the mind. There is no right or wrong way to feel while you do this exercise. Just allow yourself to be exactly as you are, accepting whatever you notice is happening in yourself.

And now bringing your attention to the breath - becoming aware of the flow of the breath into and out of the body. You may feel it at the chest or the abdomen, or the flow of air at the nostrils. Not trying to change it in any way - just letting your attention rest lightly upon the sensations of your breathing however that's happening for you. [**PAUSE 5 SECONDS]**

And now making the attention on the breath even more specific by bringing your awareness to the abdomen and following the movement of your abdomen with the in-breath and the out-breath [**PAUSE 5 SECONDS]** On the in-breath the belly expands as the diaphragm muscle presses down, creating more space for the air and lungs. Noticing the flow of this movement with the breath – the belly expanding and then lowering with the out-breath **[Pause 2 seconds]** The abdomen may be moving a lot, or a little – just let it be as it is - simply noticing how it is happening. Sensing the rising and falling of the abdomen with each in-breath, with each out-breath [**PAUSE 5 SECONDS**]. If at any time during the exercise you feel uncomfortable or concerned you can simply return your attention to the sensations of your breathing in this area **[PAUSE 3 SECONDS]**.

Now letting the breath fade into the background as you take your attention and direct it through other areas of the body. So for now, take your attention to both feet and narrowing your focus to sense all of the toes, perhaps being aware of the skin of the toes - perhaps aware of the pads of the toes - perhaps aware of the spaces between the toes **[PAUSE 7 SECONDS]**.

Moving attention now from the toes to the rest of the feet - aware of any sensations here **[PAUSE 2 SECONDS]**. The soles and the tops of the feet, the heels - using your attention to explore deeply, noticing what's there for you right now. Perhaps there is a sensation of

temperature - coolness or warmth - or lightness, or heaviness, moisture. Exploring the skin perhaps, or maybe exploring very deeply into the feet, aware of the bones, the muscles. Whatever sensations happen to be present in the feet. If you have no sensation there, being simply aware of that fact **[PAUSE 12 SECONDS]**.

Bringing attention now up to the ankles and the lower legs - to the bones and tendons passing through the ankles. Aware of the large calf muscles and the shinbones - exploring the density or thickness of the lower legs, and whatever sensations are present in the knees **[PAUSE 12 SECONDS]**.

Remembering that there is no right or wrong way to go about this - Sensations may feel pleasant or unpleasant it doesn't matter - it's rather a process of investigation and exploration, deepening your awareness of your body - noticing the difference between the sensation, and the feeling that may be associated with it. Simply accepting whatever sensations you find, giving yourself permission to feel whatever it is without struggling to change it.

Moving now to the thighs and the hamstrings and the hips - perhaps noticing the large muscles of this area - feeling the support on which you're lying, feeling the contact that the thighs and hamstrings are making here - perhaps aware of the touch of clothing, pulsation of circulation. Perhaps sensing no feeling at all, and just aware of that **[PAUSE 10 SECONDS]**.

Now, bringing attention to the buttocks and the pelvis. Perhaps aware of the muscles here - the contact with the supporting surface. Perhaps sensing any feelings in the intestines, the lower abdomen. Then bringing the attention to the upper abdomen and stomach area - aware of any sensations in that area including no sensations if that is the case **[PAUSE 10 SECONDS]**.

Now bringing your attention around to the lower back. Many of us hold tension in the lower back, so allowing this area to ease with deep attention. Noticing the muscles, the contact that the back makes with the surface you're lying or sitting on - noticing being held by that support **[PAUSE 2 SECONDS]**. Then bringing attention to the upper back - aware of the spine - aware of the all of the nerves encased in the spine and branching out to all parts of the body **[PAUSE 2 SECONDS]**. Aware of the muscles of the back - muscles which hold us upright **[PAUSE 5 SECONDS]**.

Now bringing your attention back to the sensations of the breathing - aware of the abdomen rising and falling with each breath - bringing in freshness with the in-breath and releasing any congestion, constriction or heaviness with the out-breath. Just following the breath in that way for the next few breaths [**PAUSE 15 SECONDS].**

Aware now of the very bottom of the rib cage and in back, the ribs attaching to the spinal column and moving awareness into the area of the chest - deeply exploring here, bringing a very gentle attention **[PAUSE 2 SECONDS]**. You may be aware of the diaphragm gently moving with the in- and out-breath - feeling the movement of the back with each in-breath and each out-breath. Aware of the muscles of the chest region and the skin - sensing the movement of the ribcage opening to the volume of fresh air being brought into the body, and what is no longer needed flowing out on the out breath **[PAUSE 2 SECONDS]**. Aware of the area of the heart and the lungs - the lungs filling with fresh oxygen with each in breath, delivering vitality to the blood - perhaps feeling the beating of the heart as it delivers fresh blood around the body **[PAUSE 5 SECONDS]**.

Remember, if any sensation or area is too uncomfortable at any time, you can always override the instructions and come back to the sensations of the abdomen moving with the breath. Simply paying attention to the breathing until the mind settles again **[PAUSE 10 SECONDS]**.

Now bringing the attention down both arms to the hands and fingers - aware of any sensations here - perhaps noticing moisture, or coolness, or warmth - aware of the skin of the palms, the back of the hands **[PAUSE 10 SECONDS]**.

And moving attention now to the wrists and forearms - the delicate skin on the underside of the wrist, and the bones and muscles in the lower arms, the elbows **[PAUSE 5 SECONDS]**. Exploring the upper arms, perhaps aware of the triceps and biceps muscles, aware of the bones inside the arms - the arm bones resting in the shoulder sockets - the arm pits. Aware of any sensations at all in this area, including no sensation if that is the case **[PAUSE 5 SECONDS]**.

And now coming to the shoulders and the tops of the shoulders. Here is another area that many of us hold tensions - exploring in detail all parts of the shoulders. Allowing our attention to be like a light fingertip massage, releasing any tightness as it moves. Breathing deeply in, and on the out-breath letting any tightness and congestion simply flow away **[PAUSE 10 SECONDS]**.

Aware now of the neck and the throat - aware of the ability to speak and to swallow, perhaps feeling the breath moving in the trachea. Noticing the muscles of the neck, the strong muscles that hold up the head, and the place where the spinal column meets the skull bones **[PAUSE 8 SECONDS]**.

And moving attention up to the head, aware of the skull, or any sensations of the head being supported **[PAUSE 2 SECONDS]** And bringing attention now to the forehead - aware of any sensations in this area - moving attention from one temple across the forehead to the other, allowing the forehead to smooth with your attention **[PAUSE 10 SECONDS]**.

Aware of the eyelids and the eyeballs resting in their sockets **[PAUSE 5 SECONDS]** - the area of the nose. Perhaps feeling the coolness of the incoming breath in the nostrils, and noticing slight warmth on the outgoing breath **[PAUSE 10 SECONDS]**. Bringing your attention now to the cheeks and the muscles of the face that give expression to our many emotions. Aware of the jaw and the muscles of the jaw **[PAUSE 5 SECONDS] -** allowing the jaw to be completely slack and at ease **[PAUSE 5 SECONDS]**. Aware of the ears - the ability to hear at this moment **[PAUSE 5 SECONDS]**. Aware now of the mouth and the lips, the inside of the mouth, the tongue **[PAUSE 5 SECONDS]**. Breathing deeply, bringing the freshness of this breath to all parts of the head - and breathing out, releasing any tightness, any tensions - letting go of all congestion **[PAUSE 10 SECONDS]**.

Now bringing the attention back to the sensations of the breath and allowing the breath to bring fresh energy through every part of the body, right down to the feet. Feeling the freshness in lower legs, the upper legs, the torso, the hands, arms, shoulders and head - and releasing any tension or congestion on the out-breath **[PAUSE 2 SECONDS]**. With each in-breath drawing in vitality and allowing the newness of it to fill every cell of the body with vital energy. Breathing fully though the body in this way - filling the body with vital energy on the in breath, and releasing on the out breath any tightness or congestion. Like waves of the ocean, moving in and out and out of the body. **[PAUSE 10 SECONDS]**

And now gently beginning to move the toes and fingers, the hands and feet - beginning to move and stretch. Moving in any way that feels comfortable for you right now - giving yourself

plenty of time to do this. Knowing that by allowing yourself to be as you are you are inviting a sense of openness and presence to whatever is happening in your daily life and in this way you are supporting your health and wellbeing. Perhaps bringing a sense of calmness and relaxation into your daily activities.

CD - AWARENESS OF BREATH SCRIPT

In this exercise we are building upon the attentional skills you have been developing in the body scan. In that exercise you are learning to take time just to be with yourself and increasing your awareness of sensations throughout the body - without having to change anything or make anything different - allowing yourself to be exactly as you are in this moment. We will be learning to further use that attention to bring increased awareness to the other realms of everyday experience - experiences that may have become so familiar we are perhaps no longer even consciously aware of them. Studies have shown that doing these exercises reduces patients' reported symptoms and also enhances their daily well-being.

So sitting in a straight-backed comfortable chair just allow the body to become still - feeling the support of the floor and the chair and settling in to this stable seat. The back is straight without being stiff - the posture is relaxed yet awake and dignified.

And now just becoming aware of your breathing - aware of the movement of the breath as it flows in and out of the body. Not controlling it in any way. Just allowing it to be as it is. Simply aware of the sensations - how it feels. You may notice the sensations at the belly - sensing the belly expanding as you breathe in and flattening as you breathe out - just allowing your attention to ride gently on the sensations of each breath. This is not thinking about breathing, but feeling it directly - the best you can. [**PAUSE 15 SECONDS]**

Just allowing the breath to breathe itself – giving it your full care and attention. Being there for the entire cycle of the breath - noticing the very beginning of the in-breath and following that breath as it enters the body, filling the lungs and expanding the abdomen, then as it comes to a tiny moment of stillness before it turns around and makes its journey out of the body. Just noticing this process - letting your attention rest lightly on the sensations. [**PAUSE 25 SECONDS]**

You may notice that from time to time that the attention will wander off – perhaps to memories, fantasies, judgments, worries or regrets. Or it may move to anticipation of the future - planning, wishing or concerns. As soon as you become aware that the attention has moved off to other things gently bring it back to the sensations of the breath - escorting it with a gentle firmness. If you find it wanders off the breath quite quickly, simply noticing that fact - no need to give yourself a hard time about it, it's the habit of the mind to wander. This is simply about bringing your attention back to the breath each time you notice it has wandered - once again aligning the attention with "this" breath in "this" moment. One breath following the next - noticing the movement in your body with each breath [**PAUSE 25 SECONDS]**

Bringing your attention to the breath in this way can be a powerful anchor to this present moment. This is a place you can return to whenever you become distracted, preoccupied or anxious – simply returning your awareness to the breath in this way and returning to this state of awake stillness [**PAUSE 25 SECONDS**].

You may find as you observe the breath that other sensations or feelings in your body come into your field of awareness - perhaps discomfort or perhaps restlessness or distress. These feelings may be more focused and intense from time to time. If you choose to, you can broaden your field of awareness from just the breath to include the entire body, exploring all sensations from the top of your head to your toes and fingertips - aware of the wholeness and completeness of the body - feeling the body making contact with the chair, noticing the touch of the hands, the

legs and the feet. Just aware of the body sitting - being present to whatever sensations or feelings may emerge, perhaps lingering, changing in intensity and passing away. Simply being here as you are in this moment - aware of the flow of the breath and whatever feelings happen to present themselves [**PAUSE 25 SECONDS]**.

At times, strong sensations or feelings may dominate the attention making it more difficult to focus. If a strong feeling emerges you may choose to investigate the feeling, noticing its exact qualities. What are the sensations associated with the feeling? Perhaps it is associated with sensations of tightness, throbbing, pulsing, nausea? Whatever it may be, just noticing which area of the body you experience it in most and imagining the energy of the breath going into and out of that part of the body - going right into it. Noticing also any reactions to the sensation or the feeling - perhaps trying to push it away if it is unpleasant. For now not trying to change it or struggle with it, just noticing it with gentleness, kindness and patience. As these feelings subside, returning the attention again to the whole body, sitting, breathing - breath moving in and out of the body [**PAUSE 25 SECONDS**]

Now for the next couple of minutes, experimenting with expanding the field of your attention to include any sounds that may be present. Not stretching to reach out for the sounds but just allowing them to reach the ear - aware also of the silence between the sounds. Notice any tendency to judge the sounds - to like them or dislike them - just noticing this if it is present without trying to change it, and returning to simply being with hearing - embracing sounds as they occur moment to moment. You might notice the difference between the sound sensation reaching the ear, and the mind's naming and identifying the sound [**PAUSE 10 SECONDS]** If the attention wanders off, simply coming back to whatever sounds are occurring now - alert, alive, receiving sounds in stillness. [**PAUSE 25 SECONDS**]

And now for the next few minutes we will be focusing attention on becoming aware of any thoughts that may be present in the mind. There may be big attention-getting thoughts, or quite subtle barely noticeable thoughts. Or there may be anxious thoughts – thoughts of memories, pressures, concerns or obligations. Or there may be fantasy thoughts - desires, likes, dislikes, plans. For now just allowing whatever thoughts happen to be present without trying to change them. Just noticing them as thoughts, without engaging with whatever it is they are about. Allowing the thoughts to be like clouds, drifting through a vast, spacious sky – you are just being witness to the thoughts **[PAUSE 20 SECONDS]**

You may be finding your mind is quite busy and there are many thoughts, or perhaps it happens to be relatively quiet and there are few thoughts. It doesn't matter - just let it be as it is. It doesn't have to be a problem if it is busy – that's just the way it happens to be right now - just notice that it is busy **[PAUSE 20 SECONDS]**

If you find yourself carried away by a stream of thoughts or if the thoughts are too distressing or unsettling - there is no need to struggle with the thougths. As soon as you recognize if they are too unsettling you can re-anchor your attention in the awareness of the breath - coming now to "this" breath. When you feel steady again, if you choose to you can return to witnessing the thoughts arising in the mind or simply stay with the breath [**PAUSE 15 SECONDS**].

Perhaps you will also become aware of feelings - fear, sadness, joy, peace. Allowing it all to emerge as it will - just witnessing and observing. Thoughts and feelings coming and going – not pursuing them just now – not getting drawn into analysis of them - not rejecting them either,

just seeing them as clouds in the vast, still sky of the mind. If a thought or a feeling is too strong you can always come back to the sensations of the breath at any time [**PAUSE 30 SECONDS**].

And now for the time remaining, letting go of any particular focus of attention and allowing yourself to simply be here, fully present. Aware of the breath moving - sensations in the body - sounds - thoughts and feelings coming and going - allowing it all to be as it is. Just witnessing and present with it all as it unfolds. Complete, as you are right now. **PAUSE 25 SECONDS**.

And now as the recording comes to an end, once again narrowing your attention to the breath - this breath - your attention riding on the flow of the breath - fully present with each in-breath and with each out-breath. Nothing you need to do - just being fully present with the breath flowing into and out of the body [**PAUSE 15 SECONDS**] Recognizing that you have spent this time intentionally nourishing yourself by dwelling in this state of being - allowing yourself to be exactly as you are. Recognizing and honoring your wholeness and completeness. Studies have shown that doing these exercises regularly, reduces patients' reported symptoms and enhances their well-being. You might want to congratulate yourself for taking the time and the energy to do this and perhaps form an intention to make the time to do this on a regular basis. Deepening your ability to be fully present and allowing the benefits of this practice to flow into the entire experience of your daily life.

MINDFULNESS-BASED INTERVENTION OUTLINE

Session 1: (AOB)

- Instructor introduces herself; introduction to intervention (what we will be doing over next 8 weeks) (5 minutes)
- Exercise: direct the attention to the bodily sensations associated with breathing (5)
- Feedback from participant (5)
- Instruct patient to use awareness of sensations of breathing as anchor when they feel anxious or worried (5)
- Instructions: patient encouraged to practice this technique during the following days with the help of CD - track 1 (sitting practice); 15' every day, at least once a day (more if they wish so) (5)
- The instructor double-checks time for the second meeting; instructor gives patient his/her phone number, greetings (5)

Session 2: AOB/Rediscovering daily experience

- Questions and answers related to practice in previous week (5)
  What have we learned? Get small raisin box
- Learning to direct the attention to the bodily sensations associated with breathing ("awareness of breathing" exercise) (5)
- Feedback from patient – anything different from last time, and what (5)
- Experiential exercise of paying attention to an everyday activity/raisin exercise (5)
- Feedback from patient (5)
- Conclusion and greetings, confirm next meeting, practice with CD= track 1 (sitting practice) (5)
- Remind him/her of returning attention to the sensation of breathing and their reactions to them as anchor when anxious/afraid.

Session 3: AOB/sensations

- Questions and answers related to practice in previous week
  What have we learned this week? (5)

- Body scan exercise: Invite patient to sit in comfortable chair. Participant (15)
  is instructed to move his/her awareness to different parts of the body in a systematic way, beginning with the toes and progressing to the top of the head, noticing whatever sensations happen to be present in that part of the body at that moment. Do both sides of the body at once – and do not focus on individual digits. End with awareness of breathing.
- Feedback from patient (5)

- Instructions: start using CD- track 2; body scan; schedule next meeting. (5)
  Remind him/her of using sensation of breathing and reactions to them
  as anchor when they feel anxious/afraid

Session 4: AOB/sensations/informal practice

- Questions and answers related to practice in previous week (5)
  What have we learned this week? Ask relative to get a glass of water or other non-alcoholic drink that patient likes

- Short body scan exercise: Invite patient to sit in comfortable chair. (5)
  Participant is instructed to move his/her awareness to different
  parts of the body in a systematic way, beginning with the toes and progressing to the top of the head, noticing whatever sensations happen to be present in that part of the body at that moment. End with awareness of breathing.

- Feedback from patient – anything different from last week? (5)

- Introduce informal practice: drinking exercise. (5)
  (A DRINK HAS BEEN CHOSEN BECAUSE GOOD EXAMPLE OF A COMMON, EVERY DAY ACTION)
- Feedback from patient. (5)

- Instruct participant to practice this mindful way of relating to their experience (5)
  throughout the day, and to bring this resource to their experience of <u>sensations</u> (pleasant and unpleasant ones). Instructions: Use CD- track 2 (body scan); schedule next meeting. Use the awareness of the sensations of breathing and the reactions to them as a focus of attention that he/she can return to at any time, especially in stressful situations.

Session 5: AOB/sensations/sounds

- Questions and answers related to practice in previous week (5)

What have we learned this week?

- Start with AOB, then body scan, and sounds (15)
  (*explain what experiencing means: the sound, the reactions to the sound, memories, associations with the sound).*

- Feedback from patient (5)

- Participants asked to practice this mindful way of relating to their experience throughout the day, and to bring this resource to their experience of sounds (5)

- Instructions: use CD track 1 – sitting practice; schedule next meeting (5)
  Use the awareness of the sensations of breathing and the reactions to them as a focus of attention that you can return to at any time, especially in stressful situations.

Session 6: AOB/sensations/Emotions

- Questions and answers related to practice in previous week (5)
  What have we learned?
- Awareness of breathing exercise, body scan, and feelings/emotions (15)

- Feedback from patient (5)

- Participants asked to practice this mindful way of relating to their experience throughout the day, and to bring this resource to their experience of emotions/feelings (5)
  (and sensations associated with the emotion).
  Use the awareness of the sensations of breathing as a focus of attention that the patient can return to at any time, especially in stressful situations. Instructions: use CD (either track). Schedule next meeting

Session 7: AOB/sensations/thoughts

- Questions and answers related to practice in previous week (5)
  What have we learned?
- Awareness of breathing exercise, body scan, and thoughts (15)

- Feedback from patient (5)

- Participants asked to practice this mindful way of relating to their experience during the day, and to bring this resource to noticing their experience of thoughts (pleasant and unpleasant ones). Use the awareness of the sensations of breathing (5)

and the reactions to them as a focus of attention that you can return to at any time, especially with difficult thoughts or in stressful situations. Listen to CD- either track/ or practice without CD. Schedule next meeting.

Session 8: **AOB, sensations, sounds, emotions, thoughts, open awareness**

- Questions and answers related to practice in previous week (5)
  What have we learned?
- Awareness of breathing exercise, body scan, sounds, emotions/feelings, (15)
  thoughts, open awareness. Instruct patient to notice where the attention goes when it's not directed, noticing where it went with open awareness.

- Feedback from patient (5)

- Participants asked to practice this mindful way of relating to their experience (5)
  during the day, and to bring this resource to all their experiences
  (pleasant and unpleasant ones). Use the awareness of the sensations of breathing
  as a focus of attention that they can return to at any time, especially in stressful situations.
  Keep practicing with or without CD for at least 15' a day.
  Thank participant.

Mindfulness-Based Intervention Checklist Session 1

Time intervention started _____Time intervention ended_____

Patient ID_____ Date_____ Instructor _____

		Procedures
Yes	No	Instructor introduced herself/himself
Yes	No	Aim of intervention explained
Yes	No	Intervention procedures explained, including number and duration of sessions with instructor, and practice at home
Yes	No	5 minutes AOB exercise
Yes	No	Feedback from participant
Yes	No	Instruct patient to use awareness of sensations of breathing as anchor when they feel anxious or worried
Yes	No	Told patient to listen to CD sitting practice, at least once a day (more if they wish so)
Yes	No	Phone number given to participant
Yes	No	Next meeting scheduled
_____		Of 9 objectives met

On a scale of 0-10, how engaged was the patients during the session? _____

0----------5----------10

Completely unengaged Moderately engaged Extremely engaged

Yes	No	No contact (three attempts)
Yes	No	Session terminated prematurely: specify reason (patient tired, had commitments, did not like intervention…)
Yes	No	Session rescheduled

Mindfulness-Based Intervention Checklist Session 2

Time intervention started _____Time intervention ended_____

Patient ID_____Date_____ Instructor _____

		Procedures
Yes	No	Questions and answers related to practice in previous week
Yes	No	5 minutes AOB exercise
Yes	No	Feedback from patient
Yes	No	Experiential exercise of paying attention to an everyday activity (raisin exercise)
Yes	No	Feedback from patient
Yes	No	Remind participant of using sensation of breathing and reactions to them as anchor when they feel anxious/afraid
Yes	No	Told patient to listen to study CD sitting practice, at least once a day (more if they wish so)
Yes	No	Next meeting scheduled
_____		Of 8 objectives met

On a scale of 0-10, how engaged was the patients during the session? _____

0----------5----------10
Completely unengaged Moderately engaged Extremely engaged

Yes	No	No contact (three attempts)
Yes	No	Session terminated prematurely: specify reason (patient tired, had commitments, did not like intervention…)
Yes	No	Session rescheduled

Mindfulness-Based Intervention Checklist Session 3

Time intervention started _____ Time intervention ended_____

Patient ID_____Date_____ Instructor _____

		Procedures
Yes	No	Questions and answers related to practice in previous week
Yes	No	15 minutes body scan exercise ending with AOB
Yes	No	Feedback from patient
Yes	No	Remind participant of using sensation of breathing and reactions to them as anchor when they feel anxious/afraid
Yes	No	Told patient to listen to study CD body scan, at least once a day (more if they wish so)
Yes	No	Next meeting scheduled
_____		Of 6 objectives met

On a scale of 0-10, how engaged was the patients during the session? _____

0----------5----------10
Completely unengaged Moderately engaged Extremely engaged

Yes	No	No contact (three attempts)
Yes	No	Session terminated prematurely: specify reason (patient tired, had commitments, did not like intervention…)
Yes	No	Session rescheduled

Mindfulness-Based Intervention Checklist Session 4

Time intervention started _____ Time intervention ended_____

Patient ID_____ Date_____ Instructor _____

		Procedures
Yes	No	Questions and answers related to practice in previous week
Yes	No	5 minutes body scan exercise ending with AOB
Yes	No	Feedback from patient
Yes	No	Introduce informal practice (drinking exercise)
Yes	No	Feedback from patient
Yes	No	Instruct participant to practice this way of relating to their experience throughout the day, and to bring this resource to their experience of sensations (pleasant and unpleasant ones).
Yes	No	Remind participant of using sensation of breathing and reactions to them as anchor when they feel anxious/afraid
Yes	No	Told patient to listen to study CD body scan, at least once a day (more if they wish so)
Yes	No	Next meeting scheduled
_____		Of 9 objectives met

On a scale of 0-10, how engaged was the patients during the session? _____

0----------5----------10

Completely unengaged Moderately engaged Extremely engaged

Yes	No	No contact (three attempts)
Yes	No	Session terminated prematurely: specify reason (patient tired, had commitments, did not like intervention…)
Yes	No	Session rescheduled

Mindfulness-Based Intervention Checklist Session 5

Time intervention started _____Time intervention ended_____

Patient ID_____ Date_____ Instructor _____

		Procedures
Yes	No	Questions and answers related to practice in previous week
Yes	No	15' exercise starting with AOB, then body scan, and sounds
Yes	No	Feedback from patient
Yes	No	Instruct participant to practice this way of relating to their experience throughout the day, and to bring this resource to their experience of sounds (pleasant and unpleasant ones).
Yes	No	Remind participant of using sensation of breathing and reactions to them as anchor when they feel anxious/afraid
Yes	No	Told patient to listen to study CD sitting practice, at least once a day (more if they wish so)
Yes	No	Next meeting scheduled
_____		Of 7 objectives met

On a scale of 0-10, how engaged was the patients during the session? _____

0----------5----------10
Completely unengaged Moderately engaged Extremely engaged

Yes	No	No contact (three attempts)
Yes	No	Session terminated prematurely: specify reason (patient tired, had commitments, did not like intervention…)
Yes	No	Session rescheduled

Mindfulness-Based Intervention Checklist Session 6

Time intervention started _____Time intervention ended_____

Patient ID_____ Date_____ Instructor _____

		Procedures
Yes	No	Questions and answers related to practice in previous week
Yes	No	15' exercise: AOB, body scan, and feelings/emotions
Yes	No	Feedback from patient
Yes	No	Participant asked to practice this mindful way of relating to their experience throughout the day, and to bring this resource to their experience of emotions/feelings(and sensations associated with the emotion)
Yes	No	Remind participant of using sensation of breathing and reactions to them as anchor when they feel anxious/afraid
Yes	No	Told patient to listen to study CD (either track), at least once a day (more if they wish so)
Yes	No	Next meeting scheduled
_____		Of 7 objectives met

On a scale of 0-10, how engaged was the patients during the session? _____

0----------5----------10
Completely unengaged Moderately engaged Extremely engaged

Yes	No	No contact (three attempts)
Yes	No	Session terminated prematurely: specify reason (patient tired, had commitments, did not like intervention…)
Yes	No	Session rescheduled

Mindfulness-Based Intervention Checklist Session 7

Time intervention started _____Time intervention ended_____

Patient ID_____ Date_____ Instructor _____

		Procedures
Yes	No	Questions and answers related to practice in previous week
Yes	No	15' exercise: AOB, body scan, and thoughts
Yes	No	Feedback from patient
Yes	No	Participant asked to practice this mindful way of relating to their experience throughout the day, and to bring this resource to their experience of thoughts(and sensations associated with the thoughts)
Yes	No	Remind participant of using sensation of breathing and reactions to them as anchor when they feel anxious/afraid
Yes	No	Told patient to listen to study CD either track/ or without CD, at least once a day (more if they wish so)
Yes	No	Next meeting scheduled
_____		Of 7 objectives met

On a scale of 0-10, how engaged was the patients during the session? _____

0----------5----------10
Completely unengaged Moderately engaged Extremely engaged

Yes	No	No contact (three attempts)
Yes	No	Session terminated prematurely: specify reason (patient tired, had commitments, did not like intervention…)
Yes	No	Session rescheduled

Mindfulness-Based Intervention Checklist Session 8

Time intervention started _____ Time intervention ended_____

Patient ID_____ Date_____ Instructor _____

		Procedures
Yes	No	Questions and answers related to practice in previous week
Yes	No	15' exercise: AOB, body scan, sounds, emotions/feelings, thoughts, open awareness.
Yes	No	Instruct patient to notice where the attention goes when it's not directed, noticing where it went with open awareness
Yes	No	Feedback from patient
Yes	No	Participants asked to practice this mindful way of relating to their experience during the day, and to bring this resource to all their experiences (pleasant and unpleasant ones)
Yes	No	Remind participant of using sensation of breathing and reactions to them as anchor when they feel anxious/afraid
Yes	No	Told patient to keep practicing with or without CD for at least 15' a day (more if they wish so)
Yes	No	Next meeting scheduled
_____		Of 8 objectives met

On a scale of 0-10, how engaged was the patients during the session? _____

0----------5----------10
Completely unengaged Moderately engaged Extremely engaged

Yes	No	No contact (three attempts)
Yes	No	Session terminated prematurely: specify reason (patient tired, had commitments, did not like intervention…)
Yes	No	Session rescheduled

MEASUREMENTS

HADS

INSTRUCTIONS: Please read each item and mark with an X in the box that indicates the reply that comes closest to how you have been feeling *in the past week*. Do not take too long over your replies. Your immediate reaction to each item will probably be more accurate than a long, thought-out response.

1. I feel tense or "wound up":

- ❑ Most of the time
- ❑ A lot of the time
- ❑ From time to time, occasionally
- ❑ Not at all

2. I still enjoy the things I used to enjoy:

- ❑ Definitely as much
- ❑ Not quite so much
- ❑ Only a little
- ❑ Hardly at all

3. I get a sort of frightened feeling as if something awful is about to happen:

- ❑ Very definitely and quite badly
- ❑ Yes, but not too badly
- ❑ A little, but it doesn't worry me
- ❑ Not at all

4. I can laugh and see the funny side of things:

- ❑ As much as I always could
- ❑ Not quite so much now

- ❑ Definitely not so much now
- ❑ Not at all

5. Worrying thoughts go through my mind:

- ❑ A great deal of the time
- ❑ A lot of the time
- ❑ From time to time but not too often
- ❑ Only occasionally

6. I feel cheerful:

- ❑ Not at all
- ❑ Not often
- ❑ Sometimes
- ❑ Most of the time

7. I can sit at ease and feel relaxed:

- ❑ Definitely
- ❑ Usually
- ❑ Not often
- ❑ Not at all

8. I feel as if I am slowed down:

- ❑ Nearly all the time
- ❑ Very often
- ❑ Sometimes
- ❑ Not at all

9. I get a sort of frightened feeling like "butterflies" in the stomach:

- ❑ Not at all
- ❑ Occasionally
- ❑ Quite often
- ❑ Very often

10. I have lost interest in my appearance:
    - ❑ Definitely
    - ❑ I don't take so much care as I should
    - ❑ I may not take quite as much care
    - ❑ I take just as much care as ever
11. I feel restless as if I have to be on the move:
    - ❑ Very much indeed
    - ❑ Quite a lot
    - ❑ Not very much
    - ❑ Not at all
12. I look forward with enjoyment to things:
    - ❑ As much as I ever did
    - ❑ Rather less than I used to
    - ❑ Definitely less than I used to
    - ❑ Hardly at all
13. I get sudden feelings of panic:
    - ❑ Very often indeed
    - ❑ Quite often
    - ❑ Not very often

- ❑ Not at all

14. I can enjoy a good book or radio or TV program:

    - ❑ Often
    - ❑ Sometimes
    - ❑ Not often
    - ❑ Very seldom

FFMQ-15

Please rate each of the following statements using the scale provided. Write the number in the blank that best describes your own opinion of what is generally true for you

1	2	3	4	5
never or very rarely true	rarely true	sometimes true	often true	very often or always true

When I take a shower or a bath, I stay alert to the sensations of water on my body _____

I am good at finding words to describe my feelings _____

I do not pay attention to what I am doing because I'm daydreaming, worrying, or otherwise distracted _____

I believe some of my thoughts are abnormal or bad and I should not think that way _____

When I have distressing thoughts or images, I "step back" and am aware of the thought or image without getting taken over by it. _____

I notice how foods and drinks affect my thoughts, bodily sensations, and emotions _____

I have trouble thinking of the right words to express how I feel about things _____

I do jobs or tasks automatically without being aware of what I am doing _____

I think some of my emotions are bad or inappropriate and I should not feel them _____

When I have distressing thoughts or images, I am able just to notice them without reacting. _____

I pay attention to sensations, such as the wind in my hair or sun on my face _____

Even when I am feeling terribly upset I can find a way to put it into words _____

I find myself doing things without paying attention _____

I tell myself I should not be feeling the way I am feeling _____

When I have distressing thoughts or images, I just notice them and let them go _____

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