Association of mood disturbance and arrhythmia events in patients after cardioverter defibrillator implantation

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Abstract:

Background: Life stresses and negative emotions, such as anxiety and depression, are associated with adverse cardiac events, including arrhythmia. Patients undergoing implantation of an automatic internal cardioverter defibrillator provide a unique opportunity to characterize these relationships since all tachyarrhythmia episodes are recorded by the device.

Objectives: The purpose of this study was to examine the association of emotional status after internal cardioverter defibrillator (ICD) implantation and subsequent arrhythmia events.

Methods: An analysis of data obtained in a prospective longitudinal study of responses to the ICD measured mood disturbance (Profile of Mood States; POMS) before implant and at 1, 3, 6, and 9 months postoperatively. Subjects included 144 men and 32 women with a mean age of 60 ± 13 years and a mean left ventricular ejection fraction (LVEF) of 33± 12%. Arrhythmia events were measured by self-report of shocks and by ICD device interrogation to obtain the number and type (defibrillation, cardioversion, and antitachycardia pacing) of therapies delivered by the ICD. For each time point, POMS scores of subjects who had arrhythmia events were compared with those who did not. For subjects who had ICD shocks, pre-event and post-event POMS scores were also compared. Multiple logistic regression was used at each time point to determine if clinical, demographic and psychological data could predict arrhythmia events.

Results: Patients with arrhythmia events had higher POMS scores throughout the 9 months of follow-up. Higher level of mood disturbance (specifically anxiety, fatigue, and confusion) at 1 and 3 months were independent predictors of subsequent arrhythmia events at 3 and 6 months after controlling for LVEF, the presence of coronary artery disease, pre-implant arrhythmia history, and the use of amiodarone and beta-blocking agents. There were no differences in POMS scores before and after ICD shocks, reinforcing the notion that negative emotions were a cause, rather than a consequence, of arrhythmia events.

Keywords: anxiety | ventricular arrhythmia | implanted cardioverter defibrillator | mood disturbance | depression

Article:

INTRODUCTION

More than 250,000 persons in the United States succumb to sudden cardiac death annually, usually as the result of ventricular tachycardia and ventricular fibrillation [Myerburg and Demirovic, 1995; American Heart Association, 1998]. Even if they are rescued, these patients have a high incidence of recurrent arrest. The implanted cardioverter defibrillator (ICD) has become the standard of care for these patients and also has been shown to prolong life when used in asymptomatic patients at high risk for malignant ventricular arrhythmias [Moss et al., 1996; AVID Investigators, 1997; Owens et al., 1997]. The ICD automatically detects and terminates tachyarrhythmias by using overdrive pacing or high-voltage shocks. In addition, the device stores both R-R intervals and intracardiac electrograms whenever tachyarrhythmia is detected. Interrogation of the ICD with an external programmer allows retrieval of these data at the time of the next follow-up visit.

Psychosocial studies of ICD patients reveal fairly high acceptance of the device by patients and families [Sneed and Finch, 1992; Luderitz et al., 1993, 1994; Pycha et al., 1986, 1990]. However, varying degrees of psychological distress have been recorded with 15–50% of ICD patients experiencing such responses as anxiety, anger, depression and withdrawal [Fricchione et al., 1989; Vlay et al., 1989; Keren et al., 1991; Morris et al., 1991]. These responses are attributed to feelings of vulnerability [Kuiper and Nyamathi, 1991; Burke et al., 1992; Sneed and Finch, 1992], lifestyle changes such as restricted driving [Finch et al., 1997], and experiences related to device discharge [Dougherty, 1995; Dunbar et al., 1993].

Psychological states as precursors to arrhythmia have been suspected for some time [Lown et al., 1980]. In the cardiac arrhythmia suppression trial (CAST-I), level of perceived social support was a predictor of mortality after myocardial infarction [Gorkin et al., 1993]. In a subset of patients studied within the GUSTO trial, anxiety measured in the first 48 hr after myocardial infarction was associated with subsequent in-hospital ischemia, sustained ventricular tachycardia and ventricular fibrillation [Moser and Dracup, 1996]. Intense, unexpected stimuli, such as

earthquakes, are followed by an increased incidence of sudden death and ICD activity [Leur and Loner, 1995; Nishimoto et al., 1995].

To determine whether emotional state was related to subsequent arrhythmia events in patients at high risk for recurrent ventricular arrhythmia, we performed a secondary analysis using data from a prospective study in which we originally followed ICD patients over the first 9 months after implantation [Dunbar, 1996]. The aim of this analysis was to examine the relationships between emotional states and arrhythmia events and ICD activations and whether subsequent arrhythmia events in the early recovery phase after ICD implantaion could be determined from emotional and clinical variables.

METHODS

SUBJECTS

Subjects for this analysis were drawn from a sample participating in a repeated measures, longitudinal study of coping, emotional, and functional outcomes in the first 9 months after ICD insertion [Dunbar, 1996]. Patients were eligible if they were receiving their initial ICD, had intact memory and cognitive function, could read and write English, and had no history of psychiatric illness requiring medication, psychotherapy, or hospitalization. The study protocol was approved by the Human Research Committee at Emory University and all subjects provided written consent. In the primary study, subjects (n=213) were men (83%) and women (17%) who received an initial ICD for treatment of ventricular arrhythmia at five participating hospitals in the southeastern and Midwestern United States. Ages ranged from 24–85 years with a mean age of 59 ± 13 years. Twenty-three percent had been resuscitated from cardiac arrest; 14% were taking amiodarone, and 18% were receiving beta adrenergic blockers at the time of enrollment. Most subjects were married (79%) and well educated, with 42% having completed some post-secondary education. All subjects who completed 9 months of follow-up and had data suitable for analysis were included in the current study.

Demographic and clinical variables for the primary and secondary samples are presented in Table 1. No differences were found, suggesting that the subset who completed the study were comparable to the cohort as a whole.

PROCEDURES AND MEASURES

Prior to receiving the ICD, subjects completed a battery of questionnaires selected to measure emotional status, functional status, perceptions of illness, and concerns. These instruments were completed again at 1, 3, 6, and 9 months after ICD implant [Dunbar et al., 1996; Dunbar et al., 1997; Dunbar et al., 1999]. Emotional status was measured by the Profile of Mood States (POMS) [McNair et al., 1993], which includes 65 adjectives that subjects rate on a five-point scale according to how well each adjective describes their feelings during the past week. Six emotional dimensions, including tension-anxiety, depression-dejection, anger-hostility, vigor-

activity, fatigue-inertia, and confusion-bewilderment are measured. Total Mood Disturbance (TMD) is measured by summing the six primary mood scores with vigor weighted negatively. Internal consistency for the six scales ranges from 0.84 to 0.95 in a normative population [McNair et al., 1993] and from 0.84-0.97 in this sample.

Subjects also completed and returned a device activation form [Dunbar et al., 1993] within 24 hr of receiving a shock from the ICD. These forms were used to track perceived shocks and to compare with results of ICD interrogation. Device interrogation provided precise information regarding the date and time of the arrhythmia and the type of therapy delivered. Subjects were considered to have had an arrhythmia event if antitachycardia pacing, cardioversion, or defibrillation had been delivered by the ICD during the follow-up time period.

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STATISTICAL ANALYSIS

All data were analyzed using the Statistical Package for Social Science (SPSS v.7.0). Subjects were divided into two groups (no arrhythmia events and arrhythmia events) at each follow-up time point according to whether or not they had received ICD therapy (antitachycardia pacing, cardioversion, or defibrillation). Demographic, clinical, and POMS subscale data were compared by group using chi square and Student's ttest for unpaired variables. To determine the influence of ICD shocks on emotional state, TMD scores before the first arrhythmia event were compared with TMD scores at the next follow-up visit using Student's t-test for paired data.

At each time point of 0, 1, 3, 6, and 9 months after ICD insertion, separate multiple logistic regression analyses were used to determine if emotional state (independent variable) could be used to predict the occurrence of an arrhythmia event (dependent variable) while controlling for selected clinical and demographic variables. Due to the wide range of possible scores on the POMS, the scaling of the TMD scores was converted into increments of 10. By using stepwise multiple logistic regression, the following variables were entered first as a block: history of cardiac arrest, history of coronary artery disease, left ventricular ejection fraction, and treatment with amiodarone or beta-adrenergic blocking drugs. The TMD score from the prior follow-up time point was then entered into the equation as the second step. Additional analyses occurred with each POMS subscale replacing the TMD score in separate logistic regression equations. Alpha was set at P£.05.

RESULTS

Of the 213 patients entering the study, 176 had data suitable for the analysis. Thirty-five subjects had an arrhythmia event by the 1 month follow-up period with 35, 32, and 23 experiencing events at the 3, 6, and 9 month periods, respectively. Thirty-one subjects had arrhythmia events in more than 1 time frame. There were no differences in the demographic or clinical characteristics between subjects who had arrhythmic events during follow-up as compared with

those who did not (Table 1). In contrast, TMD scores were consistently higher in the cohort with arrhythmia events at 1, 3, 6, and 9 month follow-up compared with those who were arrhythmia-free (Fig. 1).

Multiple logistic regression revealed that baseline TMD score did not predict arrhythmia event groups at 1 month. However, significant models were found for 3 and 6 month analyses. The 1 month TMD score was the only independent predictor of an arrhythmia event by the time of the 3 month follow-up (odds ratio 1.16, 95% CI 1.03 to 1.32, P=.01) (see Table 2). To determine specific effects of emotional status on arrhythmia events, subscale scores of anxiety, depression, anger, fatigue, confusion, and vigor were substituted for TMD in separate logistical regression analyses. Significant models were found when the emotional status variables were anxiety (odds ratio 1.07, 95% CI 1.01–1.13, P=.03), fatigue (odds ratio 1.10, 95% CI 1.03–1.17, P=.003), vigor (odds ratio .91, 95% CI .84–.98, P=.01), or confusion (odds ratio 1.13, 95%CI 1.04–1.25, P=.006). The relationships for total mood disturbance and subscale scores were such that the greater the score or presence of the emotional state, the greater the likelihood of arrhythmia events with vigor negatively weighted.

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Similarly, only the 3 month TMD score (OR=1.14, 95% CI 1.03–1.30, P=.04) was an independent predictor of arrhythmia events between 3 and 6 months (see Table 3). Similar to the three month predictive models, separate significant subscale models included anxiety (OR 1.07, 95% CI 1.01–1.14, P=.02), fatigue (OR 1.07 95% CI .99–1.15, P=.05), vigor (OR .90, 95% CI .84–.97, P=.002), and confusion (OR 1.14, 95% CI 1.02–1.26, P=.01). Neither anger nor depression were significant predictors at either the 3 or 6 month follow-up time points. For the 6–9 month follow up period, no significant predictors were found.

Although mood disturbance appeared to predict arrhythmia events, the converse was not true. Paired ttest revealed there was no difference in the POMS scores obtained at the follow-up visit before and just after an ICD shock (mean values = 26.3 vs 26.8; t =.143, P=.89). This was also the case if only the POMS scores before and after the first shock were considered for those subjects with more than one arrhythmia event.

DISCUSSION

Prospective evaluation of patients receiving devices for management of malignant ventricular arrhythmias revealed that the best predictor of arrhythmia events after ICD insertion was the emotional status of the patient at the prior follow-up visit. The greater the total mood disturbance, the greater the likelihood of experiencing an arrhythmia event that required antitachycardia pacing, cardioversion, or defibrillation by the ICD. Odds ratios suggested that for each tenpoint increase in TMD, the chance of arrhythmia increased by 10–20%. More specifically, the greater the anxiety, fatigue, and confusion subscale scores and the lower the vigor score at 1 and 3 months, the greater the likelihood of experiencing an arrhythmic event at 3

and 6 months. These findings are particularly compelling given the stepwise logistic regression approach which revealed the independent influence of mood after controlling for traditional arrhythmia risk factors of previous history of cardiac arrest, history of coronary artery disease, and poor LVEF [Furukawa et al., 1989; Myerburg and Demirovic, 1995].

Mood disturbance at the initial baseline assessment before ICD implant did not predict occurrence of arrhythmia events by the 1 or 3 month follow-up visit. This may be due to the multitude of possible, intervening variables that influence both the development of mood disturbance and the relationship between mood disturbance measured in the acute care setting and outcome during the early postoperative period. For example, the mood disturbance measured at baseline in the acute care setting reflects a more transient response to change in illness status and treatment options. Experiences occurring during the inpatient setting and early recovery period included learning about their high risk status and need for an ICD, therapeutic procedures such as electrophysiology studies, changes in antiarrhythmic medication doses, and device reprogramming after implantation, all of which could have influenced the relationship between baseline assessment and arrhythmia event. This study demonstrates the need for ongoing evaluation of emotional response to living with a highrisk arrhythmia and its treatment with the ICD. The distance from implant time, variation in emotional adaptation, and device reprogamming may have artificially attenuated the lack of influence of mood factors at nine months.

Dougherty et al. [1995] found that subjects who received shocks in the first year after ICD implantation had more anxiety, depression, and anger than patients who had not received shocks. Similarly, Keren and coworkers [1991] noted greater distress among patients who had experienced five or more shocks in the first year after implant. These findings are comparable to the observations made in the current study, in which the arrhythmia group had significantly higher degrees of mood disturbance than those who remained arrhythmia free during the 9 months of follow-up. The previous reports assumed that shocks were a cause of emotional distress. Results of the current study suggest that mood disturbance may, in fact, preceed arrhythmia events and that ICD shocks appear to have relatively little impact on overall mood disturbance. Differences in our findings and those of Doughtery and Keren may be due to improved standards of care over time and increased preparation of patients regarding what to expect with device therapy.

A number of studies have documented an association between emotion, stress, and adverse cardiac events. Several hypothesized mechanisms or pathways are suggested including neuroendocrine activation, myocardial ischemia, and platelet dysfunction. Mental stress and anger have a multitude of effects on the neuroendocrine and autonomic nervous systems which, in turn, may predispose to myocardial ischemia and arrhythmias [Furukawa et al., 1989; Ironson et al., 1992]. Ironson et al. [1992] suggest that anger may be one of the most potent emotions in that it reduces ejection fraction in patients with a history of coronary artery disease setting up an arrhythmogenic situation. In this study, the lack of influence of anger may be a function of the

length of time between its measurement and time of device therapy. Anger is an acute emotion with more immediate effects that may not have been captured in the measurement time points of this study. In addition, a portion of the subjects did not have a history of coronary artery disease as did all subjects in previous studies documenting the effects of anger [Furukawa et al., 1989; Ironson et al., 1992; Thomas et al., 1997].

Depression has been shown to be a very potent risk factor for arrhythmia and sudden cardiac death [Frasure-Smith et al., 1993; Frasure-Smith et al., 1995; Barefoot and Schroll, 1996; Thomas et al., 1997]. The lack of contribution of depressed mood to this arrhythmia events in this sample may be due to the low depressed mood scores in this sample, the measure of mood state versus clinical measurement of depression, and/or the hypothesized mechanisms through which depression exerts negative cardiac effects such as impaired serotonin levels and effects on platelets [Musselman et al., 1998]. Anxiety and tension, on the other hand, involves heightened sympathetic arousal and imbalances between the sympathetic and parasympathetic systems which mediates an arrhythmogenic environment [Goldberg et al., 1996]. Most studies of the effect of emotion on arrhythmia have been documented with acute, task-oriented provocations of emotions, and little is known about the more chronic effects of extended negative emotion, especially chronic anxiety. For a sustained arrhythmia to develop, an interaction is required between a trigger, substrate and other factors such as sympathetic and parasympathetic nervous system. The presence of ongoing chronic anxiety may heighten susceptibility to arrhythmia by sustained sympathetic stimulation or depressed vagal tone. Studies of the role of both acute and extended emotional distress in vulnerable patients, specific emotions and pathways are essential to better understand these mind-body interactions.

Another possible explanation for the findings could be that the patients who experienced arrhythmia events perceived themselves as sicker and with worse prognosis that those who did not experience events regardless of similar ejection fraction and clinical features. The higher total mood disturbance in the arrhythmia event group may be a reflection of the reciprocal nature of perception rather than a causative factor in events. Given the high POMS scores and the low LVEF, the influence of the fatigue and vigor scores may have reflected the combined interaction of compromised cardiac status and emotional distress. The opposite direction of the likelihood between arrhythmia event and scores of fatigue (positive) and vigor (negative) would be expected in terms of their hypothesized effects. Nevertheless, the association of negative emotion and arrhythmia events in this study suggests that the nature of the relationship deserves further attention in both research and clinical practice.

There are a number of important limitations to this study. The duration of follow-up was relatively brief and included new ICD patients. It is unknown whether prolonged mood disturbance continues to pose an ongoing risk of arrhythmia events and whether the findings are generalizable to long-term ICD patients. Multivariate analysis has shown a clear association between mood disturbance and arrhythmia events, but this technique does not prove cause and effect. It is possible that an uncontrolled co-morbid variable may have played an important role.

Prospective controlled trials of psychological states and intervention after ICD implantation will be required to demonstrate that reduction in mood disturbance will have an antiarrhythmic effect.

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