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The Relation between the Variety of Stress And Arrhythmias

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ABSTRACT

Patients (n=190) having ventricular arrhythmias with implanted cardioverter-defibrillator (ICD), were involved in the investigation to determine what kind of stress (physical or emotional) is more dangerous for developing arrhythmias. Patients were given the specialized Hedge's diary. The emotional status was estimated on the base of Patterson's scale. Sixty-one patients showed 187 kinds (shocks) with ICD. It is interesting that only anger and anxiety were really associated with the high danger of shock development, compared to worry, sadness, positive and a number of negative emotions. Besides, only weak or moderate physical activity, but not expressed, promoted to the risk of shock developing.

Keywords: emotional stress, physical stress, arrhythmia, implanted cardioverter-defibillator, Hedge's diary, five-point Likert's rating scale, Patterson's scale.

INTRODUCTION

Epidemiological studies have shown direct correlation between sudden cardiac death (SCD) and emotionally devastating disasters (e.g., earthquake, war, etc.) [*Meisel S., et al., 1991; Leor J. et al., 1996*]. SCD correlates in epidemiological studies with vigorous exercise, particularly in less active persons [*Albert C. et al., 2000*]. It is very important to mention that stress increases sympathetic nervous system activation [*Meisel S. et al., 1991; Albert C. et al., 2000; Lampert R. et al., 2000*]. Coronary artery disease (CAD) as well as arrhythmia could provide the physiological link among stressors, catecholamines and SCD. Both anger [*Mittleman M. et al., 1995; Moller J. et al., 1999*] and vigorous exercise [*Mittleman M. et al.*, 1993] can trigger transient non fatal ischemia, as well as myocardial infarction [*Gabbay F. et al., 1996; Gullette E. et al., 1997*].

So, what kind of stress (emotional or physical) can directly trigger SCD and how frequently this occurs, had not been previously investigated in a practical manner.

Circuitous evidence suggests that emotional stressors do precipitate arrhythmic events [*Senan M., 2010*]. Ventricular tachycardia (VT) or ventricular fibrillation (VF) occurs more frequently on the beginning of the workweek in patients (pts) with implantable cardioverter-defibrillators (ICDs) [*Peters R. et al., 1996*]. Moreover, atrial and ventricular ectopy, nonsustained arrhythmias are increasing during the stress of being on-call in medical interns [*Stamler J. et al.,1992*] and in the period of exposure to a hostile environment in animals [*Sgoifo A. et al., 1997*]. In invasive studies psychological stress triggers the induction of VT, makes hard termination of it [*Kirby D. et al., 1991*]. VT [*Lampert R. et al., 1994*] like SCD [*Muller J. et al., 1987*] occurs more frequently duringsunrise time – the time of peak catecholamine levels [*Turton M. et al., 1974*]. Lowest vagal tone [*Huikuri H. et al., 1994*] consequently showed that sympathetic nervous system "arousal" facilitates fatal arrhythmias.

Thus, to investigate what kind of stress (emotional or physical) could activate dangerous arrhythmias in pts with ICDs, using a case-crossover design, we conducted a standard, controlled, diary-based study of the events and emotions preceding VT/VF that caused shock. A number of factors make this population exclusively suited to investigate potential arrhythmia triggers. Various pts "anecdotally" report psychological or physical stressors preceding ICD shock. The generally

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rapid and successful termination of arrhythmic events leaves the patient with full recall of preceding events, unlike many cardiac arrest survivors. Shock also identifies the occurrence of potentially fatal arrhythmias, and diagnostic data stored by the device, confirms the presence of VT/VF [*Kovach J. et al., 2001*].

MATERIAL AND METHODS

Patients (n=190) who had received ICDs for standard indications (clinical or inducible ventricular arrhythmias) were invited to participate in our study. Exclusion criteria were significant psychiatric illness and inability to read or be interviewed in English. All pts gave informed consent. The procedures followed were in accordance with standard guidelines [*Kovach J. et al., 2001*].

Pts were given a prepared diary to record their activities as well as mood states, described and validated by Hedges and his colleagues [*Hedges S. et al., 1990*] used in earlier studies on triggers of cardiac events. The diary included so called five-point Likert rating scale of intensity evaluating levels of anger, anxiety, worry, sadness, happiness, feelings of challenge, interest, and being in control (explained during diary orientation as "the ability to effectively respond to circumstances"). Emotion's impacting was defined as a recording more than three, representing higher levels. The diary is also an incorporated checklist of specific activities. It was classified into five levels of physical intensity, validated with activity monitoring, described by Patterson and his colleagues [*Patterson S., et al., 1993*]. Level One corresponds to sleep or rest; Level Two – usual daily living, talking, or office work; Level Three – driving; Level Four – sluggish walking, leisure activity, housework, shopping, moderate sex, etc. and Level Five – expressed walking and dynamic activity. Exposure to activity was defined as recording more than four (mild-to-moderate). Pts were instructed to complete a diary page for two predefined hazard periods, when they experienced a shock: the 15-minute period preceding shock and the 15-120 minutes period preceding shock.

Pts were enrolled at the time of first ICD follow-up (about 60 days after implantation) and were given diaries. Pts with earlier implants were enrolled at ICD by phone. All pts received comprehensive orientation to the diary at enrollment. Pts were asked to call on any day of shock received, then they were contacted by the study coordinator within 48-86 hours to review the diary questions with them and give guidance as needed. Pts were asked to fill out the second diary page to serve a control for a period corresponding to the same day of the week and time of a day, when they had received shock, but one week later. These pts received another call on that day as a reminder.

Data analysis was performed using case-crossover method [*Maclure M., 1991*]. In this approach, which has been used previously in studies on triggers of cardiac events, "case" information gathered at the time of interest as compared with "control" information from the same patient gathered at the comparable time (e.g., 7-10 days later). In our study, the two predefined hazard periods (0-15 minutes before shock and 15-120 before shock) were compared for each patient with the same periods at the same time, but one week later.

Data stored by the ICD, including Echo-CG and event details, were reviewed to determine the rhythm at the time of shock. Only events showing VT/VF, for which shock was received were included in our analysis. An arrhythmia requiring more than one shock termination was counted as a single shock event.

Assessment of the hazard *versus* control period for mood states and physical activity, dichotomized as above, was done by the McNemar test for matched case-control data. Crude odds ratios (OR) were calculated in the standard manner for matching case-control study [*Fleiss J., 1981; Kovach J. et al., 1997*]. Conditional logistic regression with person stratifying variableswas used to adjust multiple events occurring within a single individual, and adjusted ORs and 95% confidence intervals (CI) were calculated from the conditional logistic regression models. Multivariable analysis to determine independence of association for variables with significant univariate associations was performed with nominal logistic regression, with interaction terms included, where necessary (e.g., emotional level by physical activity level).

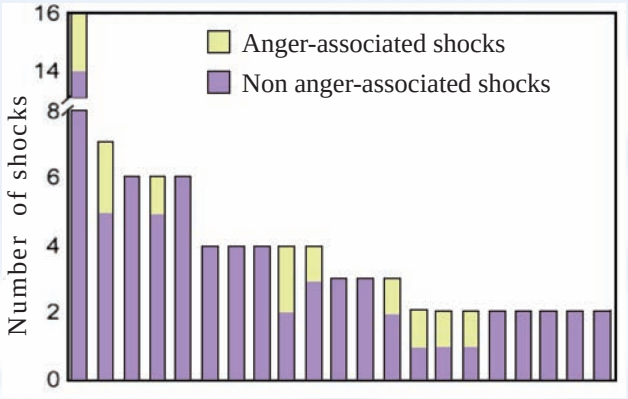

Figure 1. *Distribution of all shocks and shocks associated with anger in the 15-minute hazard period preceding shocks in pts with >1 shock. Each column represents one patient; 21 additional pts reported one shock each, of which 5 were anger-associated.*

Table 1.

Patients' characteristics (n=42)

Male sex (n)	33
Age mean ± SD (y)	55±17
Coronary artery disease	78%
Indication for ICD (100 %)	
Sustained VT	50%
VF or cardiac arrest	24%
NSVT or syncope with inducible VT	26%

RESULTS AND DISCUSSION

Diaries were recorded by 61 pts for 187 shock events, each occurring on different days; 80 events were excluded for different reasons (absence of therapy – "phantom shocks"; "antitachycardia pacing" events that were incorrectly interpreted by the pts as shock; lead malfunction and in cases of absence of ECG). The remaining 107 shocked ventricular arrhythmia events from 42 pts and their matched control data comprise the analysis. Distribution of shock frequencies among the pts is shown in Figure 1. Patient characteristics are shown in Table 1.

Tables 2 and 3 show the associations between each mood state in the preshock periods compared with the paired control periods, for the 0-15 minutes and 15-120 minutes hazard periods, respectively. Moderate anger (Level more than Two) occurred during 15% of the 0-15 minutes preshock hazard periods, 3% of control periods, and 1% of both periods ($p<0.03$ in unadjusted analysis). The 17 anger-associated shocks occurred in 14 pts, with 3 pts reporting 2 anger-associated shocks and 11 pts one each. The distribution of anger-associated shocks is shown in Figure 1. Anger was significantly associated with shock after adjustment multiple events occurring within single individual (OR 1.8; 95% CI, 1.04 to 3.16; $p<0.04$). Intense anger (Level Five) was reported less frequently, occurring in 8% of 0-15 minutes preshock hazard periods compared with 1% of control periods (Figure 2); this difference was significant in unadjusted analysis ($p<0.03$), although it was not significant after adjustment (OR. 2.4; 95% CI, 0.94 to 6.0; p=NS).

Among 17 shocks, for which control data were

Table 2.

Frequency of emotions in the 15 minutes preceding shock compared with Control period

	Shock Only %	Control Only %	Both %	OR (Unadjusted)	OR (Adjusted)	*P*
Anger	15	3	1	5.33	1.83	<0.04
Anxiety	19	7	2	2.86	1.51	0.09
Worry	13	8	4	1.55	1.16	NS
Sadness	7	4	2	2.0	1.22	NS
Happiness	11	19	52	0.6	0.87	NS
Challenge	20	9	7	2.1	1.24	NS
Interest	13	12	44	1.07	1.02	NS
In control	12	11	62	1.08	1.02	NS

NOTES: *OR indicates odds ratio: CI 95% of confidence intervals. Mood states are dichotomized at Level more than Two. Unadjusted (crude) ORs calculated from McNemar X^2. Adjusted ORs and P values calculated with conditional logistic regression.*

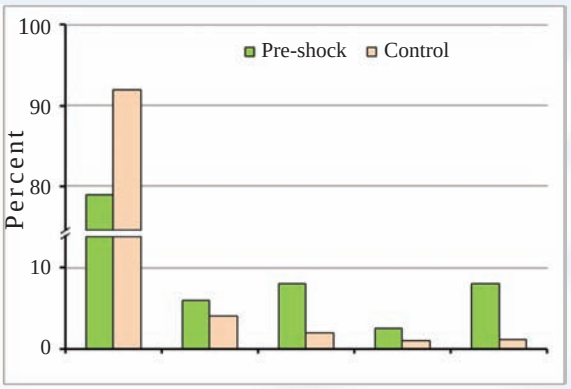

Figure 2. *Description of anger levels during the period of 15 minutes preceding shock and during the control period. In analysis of anger level was dichotomized at 3, anger was significantly associated with the preshock period.*

not available, 2 were associated with anger more than 3 and 2 with anxiety more than 3 (12% for each). This did not differ from the proportion of shocks with control data comparing with anger or anxiety (p=NS).

In unadjusted analysis, anxiety was significantly associated with shock in both - 15-minutes and 102-minutes hazard periods. The association of anxiety with shock did not remain significant after adjustment (for the 15-minutes period: OR 1.5; 95% CI, 0.93 to 2.42; for the 102-minutes period: OR 1.40; 95% CI 0.87 to 2.2). No difference was observed in levels of other mood states (worry, sadness, happiness, feelings of challenge, interest, or being in control) between the hazard period and the control period. Specific activities reported preceding shock were potentially associated with emotional arousal, including driving (n=6), arguing (n=2), gambling, and receipt of bad news (n=1 each).

Dynamic activity (Level Five) or control periods (n=1) were seldom reported during preshock (n=2), and it was not significantly associated with shock. Pts were engaged in mild-to-moderate physical activity (level 4 or more) within the 15 minutes preceding 53% of shocks and during 32% of control periods (OR 3.87; 95% CI, 1.97 to 14.8; $p<0.001$) After adjustment the multiple events, this level of activity remained associated with shock (OR 1.46; 95% CI; 1.02 to 2.08; $p<0.04$).

Activity was associated with the preshock period independent of emotions, and there was no active and emotional interaction (p=NS for interaction). Specific physical activities were reported more commonly in the 15 minutes preceding shock than during control periods, including walking slowly (40 *versus* 19), physical activity at work (9 *versus* 4), vigorous walking (2 *versus* 1) and recreational activity (7 *versus* 5). Activity in 120 minutes period did not differ between preshock and control periods.

Moderate levels of anger were more likely for spontaneous VT/VF pts during the period of preceding shock than during a paired control one week later, suggesting a triggering of arrhythmia by anger in a group of pts with a history of arrhythmia. Ventricular arrhythmia was also associated with mild-to-moderate activity occurring in daily life. Vigor-

Table 3.

Frequency of emotions in the 15 to 120 minutes preceding shock compared with Control periods

	Shock Only %	Control Only %	Both %	OR (Unadjusted)	OR (Adjusted)	*P*
Anger	10	4	3	2.75	1.35	NS
Anxiety	15	5	8	3.2	1.39	NS
Worry	8	8	3	1	1.00	NS
Sadness	12	5	0	2.6	1.54	NS
Happiness	10	18	52	0.57	0.86	NS
Challenge	23	12	10	1.92	1.24	NS
Interest	13	10	42	1.27	1.05	NS
In control	15	6	58	2.28	1.20	NS

NOTES: *OR indicates odds ratio: CI 95% of confidence intervals. Mood states are dichotomized at Level more than Two. Unadjusted (crude) ORs calculated from McNemar* X^2. *Adjusted ORs and P values were calculated with conditional logistic regression.*

ous activity was reported rarely in our study.

Previous studies have not directly suggested an association between emotions and arrhythmias. Several serious studies have shown a link between SCD and stressful *stimuli*, such as disasters and personal grief, though in these studies, real mode of death was unknown and whether CAD or arrhythmia provided the physiological link could not be determined [*Meisel S. et al., 1991; Leor J. et al., 1996; Albert C. et al., 2000; Jain D. et al., 2001*]. Although CAD has previously been shown to be triggered by psychological factors [*Stamler J. et al., 1992*; *Mittleman M. et al., 1993; Gabbay F. et al., 1996; Peters R. et al., 1996.*], whether arrhythmia can be similarly triggered had remained unknown. In one case series [*Leor J. et al., 1996*], 19% of pts were interviewed after cardiac arrest or symptomatic VT and they described episodes of emotional distress, mostly anger, in the 24 hours preceding the event. However, that study was not controlled and relied only on memories of pts.

In our study, each person held his own control, using the case-crossover approach and the quick therapy, achieved by the ICD, excluded the retrograde amnesia, often experienced by cardiac arrest survivors. Though benign arrhythmias have been shown to increase in times of stress in pts with normal hearts [*Toivonen L. et al., 1997; Kovach J. et al., 2001*], our study describes life-threatening ventricular arrhythmia spontaneously triggered by emotions of anger in pts with known susceptibility. Very similar results were obtained by Rachel Lampert and associates [*Lampert R. et al., 2002*].

Some trials show that electrophysiological properties can be altered by stress suggesting potential mechanisms, through which triggering of arrhythmia may occur. L. Toivonen and coworkers [*Toivonen L. et al., 1997*]. The trials also showed changes in repolarization in healthy medical interns exposed to the sudden stress of an on-call alarm. T-wave alternant (known as marker of repolarization heterogeneity correlates with risk of arrhythmia, has been shown to increase induction of an anger-like state in animals [*Kovach J. et al., 2001*]. Alterations in the signal-averaged ECG have also been seen during mental stress, implying stress-induced changes in conduction [*Folino A. et al., 1994*]. Our group has used an anger recal task to examine changes in induced arrhythmias during ICD, testing in the electrophysiological laboratory. Anger altered the VT circuit, accelerating VT and/or rendering it more difficult to terminate; these changes correlated with increases in catecholamine levels [*Folino A. et al., 1994*]. These electrophysiological changes in repolarization and conduction brought on by anger or stress may lead to the triggering of VT/VF seen in our study.

CONCLUSION

It is important to understand that arrhythmia triggered by emotional factors may help leading therapeutic strategies that will decrease arrhythmia, shock frequency in pts with ICDs and, potentially, the incidences of SCD. Our study showed an association between mild-to-moderate activity, such as usual walking or shopping and incidences of arrhythmia. Together with previous studies showing that these activities can be associated with ambulatory ischemia [*Fleiss J., 1981; Maclure M., 1991*], these data suggest that even modest activities occurring in our daily life, can provide sufficient sympathetic nervous system activation for triggering cardiovascular events.

Thus, anger and physical exertion can trigger arrhythmias.

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