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Triggering Effect of Physical and Mental Stress on Spontaneous Ventricular Tachyarrhythmias in Patients with Implantable Cardioverter-Defibrillators

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Summary

Background: Physical and mental stress as well as sexual activity are potential triggering factors of acute coronary events and sudden cardiac death.

Hypothesis: These factors may also trigger recurrence of spontaneous ventricular tachyarrhythmias in patients with implantable cardioverter-defibrillators (ICDs).

Methods: We performed a case-crossover study in 43 consecutive patients with 95 symptomatic, ICD-documented tachyarrhythmic events and calculated the relative risk of tachyarrhythmia recurrence during physical and mental stress. Physical and mental activity was graded on a 4-step intensity scale, and stress was defined as physical exertion or mental stress with an intensity grade ≥ II during or up to 1 h before arrhythmia recurrence. Relative risk was determined taking into account the habitual weekly stress frequency of each patient.

Results: Physical stress was present in 26% (n = 25), mental stress in 24% (n = 23), and sexual activity in 2% (n = 2) of analyzed events. The weekly habitual stress frequency was 8 ± 8 (median 7) for physical stress, 6 ± 6 (median 4) for mental stress, and 0.5 ± 0.5 (median 0.25) for sexual activity. Thus, relative risk of arrhythmia recurrence during the presence of stress was 7.5 for physical activity (95% confidence interval [CI] 5.2–11.1), 9.5 (CI 6.3–14.5) for mental activity, and 7.5 (CI 2.3–24.8) for sexual activity.

Conclusions: Physical and mental stress as well as sexual activity are factors that significantly increase relative risk of spontaneous recurrence of sustained ventricular tachyarrhythmias in patients with ICDs. Consideration of this stress-related relative risk increase may contribute to avoidance of harmful shock delivery in ICD recipients.

Key words: ventricular arrhythmia, trigger, implantable defibrillator, case-crossover

Introduction

Physical and mental stress have been identified as potential triggering factors of acute myocardial infarction[1–6] and sudden cardiac death.[7–13] As sudden cardiac death is mostly caused by ventricular tachyarrhythmias,[14] stress can be expected to increase the relative risk of tachyarrhythmic episodes as well in patients with implantable cardioverter-defibrillators (ICDs). Recipients of ICDs who have mood disturbances seem to have more frequent tachyarrhythmias during long-term follow-up,[15] and preliminary data suggest that physical and mental stress actually may trigger tachyarrhythmias in these patients;[16] however, data to support this notion are lacking.

Thus, the aim of the present study was to evaluate the potential stress-induced increase of shock deliveries for sustained ventricular tachyarrhythmias in patients with ICDs.

Patients and Methods

Patients

We studied 43 consecutive patients (mean age 58 ± 13 years, 35 men [81%]) with ICDs presenting after appropriate shock delivery in our outpatient department. Coronary artery disease was present in 33 patients (77%) and idiopathic dilated cardiomyopathy in 6 patients (14%). In most patients, mean left ventricular ejection fraction was significantly depressed (mean value 36 ± 15%); 28 patients (65%) were in New York Heart Association (NYHA) class I or II and 15 patients (35%) in NYHA class III. The indications for device implantation were recurrent ventricular tachycardias in 13 patients (30%), ventricular fibrillation in 10 patients (23%), and both arrhyth-

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mias in 17 patients (34%). Twenty patients (47%) were receiving amiodarone and 25 patients (58%) were receiving beta blockers during shock delivery. No other antiarrhythmic drugs were used.

Devices

All devices used in this study were late-generation implantable cardioverter-defibrillators (Ventak PRx III, Mini and AV, Cardiac Pacemaker, Inc. [CPI], St. Paul, Minn., USA) providing endocardial electrogram storage of arrhythmic episodes.

Methods

Relative risk of stress-associated tachyarrhythmia recurrence was determined using a case-crossover method.[17] In such a study, patients serve as their own cases and controls. Relative risk is calculated by comparing the presence of potential triggering factors around the index event with the habitual exposure to the analyzed factors during daily life in a patient population. In previous studies using this relatively new but well accepted method, a 1–2 h induction interval has been found in which stress may increase the risk for cardiovascular events.[1–3, 6, 18] Thus, we analyzed the presence of physical and mental stress during or up to a prospectively defined risk period of 1 h before appropriate shock delivery.

As our patients suffered from heart failure of different degrees, the extent of physical activity was not classified following the estimated consumption of metabolic equivalents (MET) defined as the energy expended per min by a resting subject. Taking into account individual cardiovascular performance, a certain physical activity may be easy for one person but highly strenuous for another. Classifying certain activities as strenuous and others as nonstrenuous following the consumption of METs would result in underestimation of physical stress in patients with highly depressed ventricular function (35% of our patients were in NYHA class III).

Therefore physical stress was defined and graduated as follows:

0 = no physical activity
I = physical activity not perceived strenuous
II = physical activity perceived strenuous but not accompanied by sweating and/or dyspnea
III = sweating and/or dyspnea caused by physical activity.

Mental stress was defined as the presence of negative emotions (tension/nervousness, depression, or anger) and graduated on a 4-point intensity scale:

0 =none, I = light, II = moderate, III = heavy.

In cases of physical activity or negative emotions, ≥ grade II, "stress" was considered to be present.

As sexual activity usually requires both physical and mental activity and seems to be associated with an increased risk of cardiac death,[3, 19, 20] we also analyzed the frequency of appropriate shock delivery during or up to 1 h after sexual activity.

Statistical Analysis

The patients' usual frequency of physical and mental stress ≥ grade II as well as the individual frequency of sexual activity over the past year (estimated following the reported weekly frequencies) were compared with the actual presence of these hypothetical triggers during or up to 1 h before shock delivery. Assuming a hypothetical time period of 1 h of relative risk increase after exposure to stress, a habitual stress frequency of, for example, seven times weekly would result in 7 h of exposure to stress and in 161 unexposed hours per week. For each patient we calculated the observed odds of occurrence of a suspected trigger within 1 h before arrhythmia and the expected odds that the trigger would have occurred, given the usual trigger frequency during daily life. The relative risk of shock-treated arrhythmia associated with a suspected trigger was calculated with use of the Mantel-Haenszel procedure.[17]

Results

The situational context of 95 of 97 tachyarrhythmias as (2 ± 2 per patient, median 2) with episode termination by shock delivery could be clarified in structured interviews. In 55% of these episodes (n = 52) patients were active, and in 45% (n = 43) patients were at rest. Physical stress was present in 25 episodes (26%) and mental stress in 23 episodes (24%). In six episodes both potential triggers were affirmed.

The reported weekly stress frequency in the study group was 8 ± 8 (median 7) for physical and 6 ± 6 (median 4) for mental activities.

According to this habitual stress frequency and the frequency of stress during or before shock delivery, relative risk of arrhythmia recurrence associated with physical stress was 7.6 (95% confidence interval [CI] 5.2–11.1) and was 9.5 (95% CI 6.3–14.5) for exposure to mental stress.

In two patients, shock therapy was delivered during or immediately after sexual activity. Of the 43 patients, 32 (74%) reported to be sexually active. The frequency of sexual activity was reported to be less than once per week by 17 patients (53%), approximately once per week by 12 patients (38%) and more than once per week by 3 patients (9%). Considering these statements, the calculated relative risk of arrhythmia recurrence associated with sexual activity in the study patients was 7.5 (CI 2.3–24.8).

Taking into account the possibility of imprecise retrospective patient statements concerning the time interval (maximum 1 h) between the exposure to stress and shock delivery, we also calculated the relative risk for a hypothetical trigger presence up to 2 h before device therapy. For example, if the presence of stress is remembered within a time interval of 1 h before shock delivery but actually has been present within 2 h prior, the estimated time for habitual exposure to stress has to be doubled for calculation of relative risk. In this case, the method works less sensitively, but even then the analyzed triggers were found to increase the relative risk of arrhythmia recurrence significantly (Table I).

TABLE I Relative risk according to the reported time interval of exposure to stress and shock-treated tachyarrhythmias

Exposure to stress before shock delivery	RR for physical stress	RR for mental stress	RR for sexual activity
1 Hour	7.5 (CI 5.2–11.1)	9.5 (CI 6.3–14.5)	7.5 (CI 2.3–24.8)
2 Hours	3.6 (CI 2.4–5.4)	4.5 (CI 2.9–7.2)	3.7 (CI 1.0–13.7)

Abbreviations: RR = relative risk, CI = confidence interval.

Comparison of the relative risk of stress-associated tachyarrhythmia recurrence in patients who do or do not receive amiodarone or beta blockers revealed a lower relative risk for patients on antiarrhythmics, suggesting a protective effect of amiodarone and beta blockers (Table II). Relative risk of arrhythmia recurrence associated with physical stress was more than twice as high in patients without antiarrhythmics. The difference in relative risk for tachyarrhythmia recurrence in patients with and without antiarrhythmics was less pronounced for exposure to mental stress. Because of the small number of gender-associated arrhythmic events, this subgroup analysis could not be performed for sexual activity.

Discussion

The present study is the first that provides detailed results of a case-crossover analysis in patients with ICDs. Relative risk of ventricular tachyarrhythmia recurrence was found to be between 3.6 and 9.5 for the analyzed triggering factors.

Relative Risk of Cardiovascular Events in Previous Case-Crossover Studies

The extent of relative risk increase in this study is comparable with the results of other case-crossover studies dealing with the potential influence of physical and mental stress on the frequency of cardiovascular events.[1–3, 6, 18] Mittleman *et al.*[2] reported a relative risk of 5.9 for those engaged in strenuous physical activity within 1 h before myocardial infarction, and Willich *et al.*[6] found a relative risk of 2.1 in a comparable study. Muller *et al.*[3] reported a relative risk of 2.5 for triggering myocardial infarction by sexual activity, and Mittleman *et al.*[1] found episodes of anger to be capable of triggering the onset of acute myocardial infarction with a relative risk of 2.3. In a study by Gullette *et al.*,[18] mental stress was shown to increase the risk of myocardial ischemia in the subsequent hour (relative risk 2.6–3.0), and Moller *et al.*[21] reported a relative risk of 9.0 for triggering acute myocardial infarction within 1 h after the outburst of anger. By contrast, in a preliminary study of Lampe *et al.*,[16] a relative risk of 119 (CI 70–203) was reported for appropriate shock episodes in patients with ICDs following heavy physical exertion. This seems particularly high, but cannot be discussed further as detailed information on results and methodology are not available.

Mental Stress and Tachyarrhythmias

The physiologic link between mental stress and spontaneous ventricular tachyarrhythmias remains unexplained. Coronary ischemia may be one factor facilitating development of tachyarrhythmias that are clearly associated with myocardial infarction. Numerous studies have demonstrated potential triggering of myocardial ischemia by mental stress,[22–27] and susceptibility to transient myocardial ischemia in our patients can be expected to be high, as most of them had coronary artery disease. The hypothesis of partly ischemia-associated arrhythmic events seems to be supported by studies reporting mental stress-induced platelet activation and plasma coagulation[28–30] which may prove disadvantageous to coronary blood flow. On the other hand, Lampert *et al.*[31] monitored ICD recipients electrographically and measured left ventricular ejection fraction noninvasively in an experimental stress setting (mental arithmetic and anger recall), but did not find signs of ischemia in 9 of 10 patients (8 of these had coronary artery disease). In this study, ventricular tachyarrhythmias were faster and more difficult to terminate, but could not be induced more easily during mental stress. This is no real contradiction to our results, as the setting of a noninvasive electrophysiologic study during experimental stress in a small number of patients does

TABLE II Relative risk in patients with and without antiarrhythmics (amiodarone or beta blockers)

Exposure to stress before shock delivery	RR for physical stress	RR for mental stress
30 Patients on antiarrhythmics (65 events)		
1 Hour	5.6 (CI 3.1–10.3)	9.8 (CI 5.3–18.2)
2 Hours	2.7 (CI 1.5–4.8)	4.6 (CI 2.5–8.6)
13 Patients without antiarrhythmics (30 events)		
1 Hour	14.9 (CI 6.6–33.6)	11.6 (CI 4.5–29.6)
2 Hours	7.2 (CI 3.2–16.1)	5.7 (CI 2.2–14.5)

Abbreviations as in Table I.

not seem to be comparable with a mental stress case-crossover analysis in everyday life. Furthermore, the definition of mental stress in this study was different and the degree of mental stress actually induced remained undefined.

Another mental stress-associated arrhythmogenic factor may be sympatho-adrenergic activation, which has been demonstrated in the laboratory setting by measuring increase of norepinephrine levels during mental stress.[31, 32]

Physical Stress, Sexual Activity, and Tachyarrhythmias

The same mechanisms discussed as potential links between mental stress and tachyarrhythmias (transient myocardial ischemia and sympatho-adrenergic activation) may be also involved in tachyarrhythmia recurrence associated with physical and sexual activity. Both activities naturally activate the sympatho-adrenergic system, and physical activity (usually part of sexual activity) is the most frequent reason for coronary ischemia in everyday life. Furthermore, it can be speculated that physical stress-related increases in myocardial wall stress in patients with heart failure might facilitate triggering of ventricular tachyarrhythmias.

Subgroup analysis of patients on antiarrhythmics suggests a protective effect of amiodarone and beta blockers. Taking these drugs may allow patients to continue exposure to stress in daily life instead of practicing avoidance behaviors.

Limitations and Methodological Remarks

The retrospective character of this study and the inclusion of a relatively small number of patients are limitations of the study. However, the methodology of case-crossover studies is generally accepted and supposed to provide reliable data despite the imprecision that is naturally involved when patients are interviewed.[1–3, 6, 18] It must be emphasized that in a case-crossover study all patients serve as their own controls, giving the same statistical weight independent of the number of events counted to each patient. This ensures that results are not biased by differences in arrhythmogenic risk factors in the study and the control group, or by a different interpretation of the 4-point stress scale. As the habitual stress frequency and the arrhythmia-associated presence of stress were determined in the same interview, it seems probable that patients reported realistically the habitual frequency of exposures to comparable stress levels during daily life. The question of the extent to which relative risk may be influenced by the combined occurrence of potential triggering factors (in this study 6 of 95 cases [6 %]) cannot be answered as we could not ascertain the habitual frequency of these combined trigger occurrences; this seems not to be determinable retrospectively in an interview with sufficient reliability.

Conclusions

In the present study, physical and mental stress as well as sexual activity are identified as potential triggering factors of ventricular tachyarrhythmia recurrence in patients with ICDs. The relative risk of shock delivery during exposure to stress is a function of the absolute risk of arrhythmia recurrence, which may widely vary intra- and interindividually. In clinical practice, intensified antiarrhythmic drug therapy is the treatment of choice in patients with frequent shock episodes. This may be effective according to the results of this study. However, in some patients with a persistent high absolute arrhythmia risk, avoidance of strenuous physical activity may be helpful in reducing the number of painful shock deliveries. In selected cases, for example, in patients with ICDs with frequent recurrent shocks and who are evidently under heavy mental stress, even an accompanying psychologic treatment may be helpful.

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