Clinical Investigations

Panic Disorders and Agoraphobia: Side Effects of Treatment with an Implantable Cardioverter/Defibrillator

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Summary

Background: Implantable cardioverter/defibrillator (ICD) treatment has reduced the mortality of patients with a high risk of sudden cardiac death. However, ICD discharges may cause anxiety with respect to new discharges and lead to preventive, for example, phobic, behavior. This study evaluated the frequency of panic disorders and agoraphobia in patients with ICD and assessed the risk factors in their development.

Hypothesis: Treatment with ICD represents a risk factor in the development of anxiety disorders.

Methods: Ninety patients with ICD were examined using a standardized lifetime Diagnostic Interview of Psychiatric Syndromes (DIPS). This interview makes it possible to estimate the incidence of panic disorders and agoraphobia. The impact of the severity of the underlying cardiac disease, the number of ICD discharges, and the subjective appraisal of the shock experience on the development of panic disorders and agoraphobia was assessed.

Results: Fifteen patients (16.7%) developed anxiety disorders after ICD implantation. The incidence was 21% in patients with and 6.9% in patients without ICD discharge. In patients with two or more ICD discharges annually, the incidence of panic disorders and agoraphobia was higher than

that in patients with a single ICD discharge annually (62 vs. 10%, $p < 0.01$). The intensity of self-observation of their body was significantly related to the development of anxiety disorders ($p < 0.001$).

Conclusion: Panic disorders and agoraphobia are frequent side effects of ICD treatment. Risk factors in the development of these disorders are two or more ICD discharges annually and a negative cognitive appraisal of ICD discharges. Therapeutic efforts should aim at reducing the number of ICD discharges and provide early psychological treatment.

Key words: ventricular tachyarrhythmia, implantable cardioverter/defibrillator, panic disorder, agoraphobia

Introduction

In the United States, more than 300,000 individuals die annually from sudden cardiac death,¹ and an estimated 500,000 people experience out-of-hospital cardiac arrest each year. Those who survive have a high recurrence rate of malignant arrhythmias or sudden death. Since its introduction 20 years ago, the implantable cardioverter/defibrillator (ICD) has been used in an increasing number of patients to prevent sudden death. Implantation of an ICD lowers overall mortality in patients with documented malignant ventricular tachyarrhythmias.^{2–4} In addition, ICD therapy improves survival in high-risk patients who had never previously experienced a sustained ventricular tachyarrhythmia.^{5,6} Thus, ICD treatment is becoming an increasingly important factor, both for the primary and the secondary prevention of sudden cardiac death.

Implantable cardioverter/defibrillator shock delivery for the termination of rapid ventricular tachyarrhythmias may cause sudden severe pain.⁷ Since the 1980s, there have been reports of patients with ICD suffering from symptoms of depression and anxiety.^{8,9} Some authors^{7,10} found a correlation between the number of shocks and anxiety, but others did not.^{8,11,12} The latter interpret anxiety symptoms as a consequence of cognitions, especially the fear of dying.¹²

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A major drawback in these studies is that anxiety symptoms were mainly assessed by self-rating instruments (e.g., Spielberger's state anxiety inventory).¹³ This, however, does not allow for the determination of a specific psychiatric disease. A clinical psychiatric examination has only been performed in small groups of patients with ICD.^{8,9,14} In these studies, no or only minimal association was found between shocks and psychiatric disorders. Furthermore, there was no information on whether these anxiety disorders developed after ICD implantation or whether they were related to the underlying heart disease or to the side effects of ICD therapy.

We therefore used a standardized diagnostic interview, together with multiple-level self- and observer-rating instruments, to assess psychiatric morbidity, especially the incidence of panic disorders and agoraphobia after ICD implantation, and to identify factors contributing to their development.

Materials and Methods

Patient Population

All patients with ICD currently involved in long-term outpatient monitoring at the Department of Cardiology at the Free University of Berlin and the German Heart Institute were asked to participate in the study. Patients were not included when (1) their place of residence was outside of Berlin, (2) ICD implantation was < 1 year previously, or (3) language or intellectual and/or physical restrictions were present that did not allow the diagnostic assessment used in the study.

Diagnostic Assessment

Patients were examined using the Diagnostic Interview of Psychiatric Disorders (DIPS),¹⁵ a semi-structured, standardized interview that focuses on the diagnosis of anxiety disorders and registers both the presence of a mental disorder and the time at which it developed (e.g., before or after ICD implantation). Therefore, DIPS allows the exact calculation of the prevalence and a good estimation of the incidence of psychiatric disorders. All patients participating in this study were well able to remember the start of their panic attacks. The interview is based on the diagnostic criteria in the revised Diagnostic Statistical Manual III (DSM-III-R). To fulfill the criteria for panic disorders, patients have to be subject to repeated attacks of anxiety with bodily sensations such as vertigo, sweating, and paresthesia; specific catastrophic thoughts like "I will die" or "I will fall down and nobody will help me;" and a continuous fear of new attacks.¹⁶ Agoraphobia is an anxiety disorder associated with avoidance of complex stimuli such as crowded places (e.g., supermarkets), crowds, and cramped spaces (e.g., elevators).¹⁶

Patients with a history of ICD discharges filled out a self-assessment scale on cognitive coping with shocks. The scale consisted of seven items that had to be answered on a five-point Likert scale ("I do not agree" to "I agree fully") (internal consistency: Cronbach's alpha 0.86). This instrument was designed

by us, as no other published instruments are available that adequately assess coping styles in patients with ICD discharges.

Implantable Cardioverter/Defibrillator Therapy Definitions

The patients were treated with third-generation ICDs capable of delivering shock therapy and antitachycardia pacing. All ICD devices were programmed with a ventricular tachycardia (VT) and a ventricular fibrillation (VF) zone. In the VT zone, usually four ramp sequences were programmed, followed by shock therapy. In the VF zone, only shocks with the maximum shock level of 30–34 J were programmed. If patients were not pacemaker dependent, the bradycardiac intervention frequency was programmed at 40 beats/min. The number of shocks and shock clusters delivered by the ICD were registered. A shock cluster is defined as being more than three discharges within 24 h. Shock episodes were classified as appropriate if symptoms such as presyncope or syncope occurred, if the evaluation of the ICD Holter monitor revealed a sudden-onset tachycardia and a stability < 30 ms, and if an intracardial electrogram from the ICD memory showed altered QRS complexes. If these criteria were not fulfilled, shock episodes were classified as "inappropriate" and defined as supraventricular tachyarrhythmias (i.e., sinus tachycardia or atrial fibrillation).

Statistical Analysis

The statistical evaluation was performed using the Statistical Package for Social Sciences, version 10.0 (SPSS Inc., Chicago, Ill., USA). Differences in continuous variables between subgroups of patients were assessed by *t*-tests. Associations between continuous variables or nominal variables were analyzed by chi-square tests. The Mann-Whitney U-test was used to compare ranges of cognitive shock appraisals in patients with as opposed to without anxiety disorders. A multivariate regression analysis was used to determine the effect of different variables on the development of panic disorders and agoraphobia. Statistical significance was defined for a *p* value of < 0.05.

Results

A total of 126 patients fulfilled the inclusion criteria. Thirty-three patients refused to take part in the study and three patients were excluded from the analysis because they had already suffered from an anxiety disorder prior to ICD implantation. Thus, 90 patients (mean age 59.5 years, 86.7% men) were included in the analysis. The characteristics of this patient population are given in Table I. Of the study patients, 56.7% had been resuscitated prior to ICD implantation; 67.8% of patients with ICD had experienced at least one ICD shock. There was no difference between included and excluded patients regarding age, gender, and ejection fraction.

Panic disorder and/or agoraphobia could be diagnosed in 15 patients (16.7%). According to DSM-III-R criteria, we found

an isolated panic disorder in two cases, an isolated agoraphobia in eight, and a combination of panic disorder and agoraphobia in five. Most of these disorders developed within the first year after ICD implantation. In addition, 12 depressive disorders, 2 social phobias, 6 specific phobias, and 1 alcohol dependency were diagnosed. Six depressive disorders developed after ICD implantation, whereas the other psychiatric disorders had developed prior to ICD implantation.

During follow-up, 61 of the 90 patients (68%) had ICD discharges. In these patients, the incidence of panic disorders and agoraphobia was 21% (13/61). In contrast, those patients without ICD discharge had a significantly lower incidence at 6.9% (2/29). As shown in Table II, patients with anxiety disorders had approximately four times as many ICD discharges compared with patients without anxiety disorders. The incidence of patients with two or more ICD discharges per year

TABLE I Patient characteristics (n = 90) (patients with and without implantable cardioverter/defibrillator discharges)

Mean age (years)	59.5 ± 11.1
Male (%)	78 (86.7)
FU after ICD implantation (years)	3.5 ± 2.0
Ejection fraction (%)	42.4 ± 16.5
ICD indication	
Cardiac arrest due to VT / VF (%)	51 (56.7)
Unstable VT (%)	29 (32.2)
Syncope, EPS+ (%)	10 (11.1)
History of ICD discharge in the first year after implantation	
Yes (%)	61 (67.8)
No (%)	29 (32.2)
Number of ICD discharges	
All patients	7.9 ± 18.1
Patients with a history of ICD discharges (n = 61)	12.0 ± 21.3
Patients with panic disorder and agoraphobia (n = 15)	20.0 ± 27.7
Number of inappropriate ICD discharges	
All patients	0.6 ± 1.2
Number of shock clusters	
All patients	0.5 ± 0.7
ICD discharges per year	
All patients	1.3 ± 2.2

Abbreviations: ICD = implantable cardioverter/defibrillator, VT = ventricular tachycardia, VF = ventricular fibrillation, EPS+ = inducibility during electrophysiologic study, FU = follow-up.

TABLE II Comparison of patients (n = 90) with and without anxiety disorders

	Anxiety disorder n = 15	No anxiety disorder n = 75	t Value	Level of significance (p)
Age	56.6 ± 7.2	60.0 ± 11.7	1.10	NS
Number of ICD discharges	20.7 ± 27.7	4.8 ± 14.2	−2.34	< 0.05
Number of inappropriate ICD discharges	0.9 ± 1.6	0.5 ± 1.1	−1.1	NS
Ejection fraction (%)	48.2 ± 15.8	41.4 ± 16.6	−1.21	NS
Follow-up after ICD implantation (years)	3.9 ± 2.0	3.4 ± 2.0	−0.96	NS
Gender				
Male	12	66		
Female	3	12	0.4	NS
ICD indication				
Cardiac arrest due to VT/VF	6	45		
Unstable VT	7	22		
Syncope, EPS+	2	8	2.1	NS
History of cardiac arrest and successful resuscitation				
Yes	6	45		
No	9	30	2.04	NS

Abbreviations as in Table I.

was 62% (8/13), whereas only 10% of patients (5/48) had less than two ICD discharges per year ($p < 0.01$). There was no difference between the two groups with regard to age, gender, underlying cardiac disease, ejection fraction, duration of follow-up after ICD implantation, or history of cardiac arrest with successful resuscitation.

Cognitive coping style with respect to ICD discharge was significantly related to the development of anxiety (Table III). Patients with anxiety disorders pay more attention to possible body changes and are constantly expecting the next discharge. In addition, patients with anxiety disorders report more affective symptoms; they feel depressed after ICD shocks and report more anxiety with regard to the next ICD discharge.

A multivariate logistic regression showed that the coping style (odds ratio 2.3) and the number of ICD clusters (odds ratio 2.3) are risk factors in the development of panic disorders and agoraphobia, predicting the difference between patients with and without anxiety disorders (Table IV).

Discussion

This study investigated the psychiatric status of patients with ICD and, using structured psychiatric assessment methods, analyzed the impact of psychological and somatic variables on the development of anxiety disorders. The main findings are that patients with ICD are under substantial risk of developing panic disorders and agoraphobia following ICD implantation, and that both the number of ICD discharges and catastrophic cognitions contribute to the development of these anxiety disorders.

Incidence of Anxiety Disorders

In our study, the incidence of panic disorders and/or agoraphobia in patients with ICD was 16.7%. This is approximately 100 times higher than that in the general population, in which the 1-year incidence of panic disorders has been found to be 0.14%.¹⁷ Other authors have reported a smaller incidence of panic disorders and agoraphobia (range 5–15%) in patients with ICD.^{8, 9, 14} However, the patient population in these studies was smaller and the follow-up shorter compared with our study. Furthermore, the reported number of shocks was lower (between 33 and 50%) of patients.^{8, 12} By contrast, in our study approximately two-thirds of the patients experienced ICD discharges. Overall, our results indicate that, in the context of ICD treatment, panic disorders and agoraphobia are frequent and may be both a characteristic finding in this severely sick patient population and, in part, a side effect of this life-saving therapy.

Relation between Implantable Cardioverter/Defibrillator Shocks and the Development of Anxiety Disorders

In our study, 68% of patients had ICD shocks after ICD implantation. In this group, the incidence of anxiety disorders was higher than in those patients who had not suffered shocks. There was no relation between the incidence of anxiety disorders and the underlying cardiac disease, left ventricular ejection fraction, or other cardiac parameters. These findings suggest that anxiety disorders are not primarily related to the severity of the underlying cardiac disease, but may be directly

TABLE III Cognitive appraisal of implantable cardioverter/defibrillator (ICD) discharges by 61 patients with ICD discharges

	Patients with anxiety disorders n = 13	Patients without anxiety disorders n = 48	U	Asymptotic significance (2-tailed)
The discharge was painful	3.8 ± 1.8	2.8 ± 1.5	196	0.044
The discharge saved my life	3.6 ± 1.8	3.8 ± 1.4	292	0.891
I can feel dangerous pulse irregularities	3.5 ± 1.4	2.5 ± 1.4	192	0.036
The discharge frightened me	4.5 ± 1.1	2.9 ± 1.5	128.5	0.001
I constantly expect the next discharge	3.8 ± 1.3	1.5 ± 1.0	57	0.000
I feel down after the discharge	4.0 ± 1.5	2.5 ± 1.4	146.5	0.003
I pay attention to bodily changes to avoid being surprised by the next discharge	4.3 ± 1.1	2.7 ± 1.5	117	0.000

TABLE IV Independent variables in the development of panic disorders and agoraphobia (according to a multivariate analysis) (n=61)

	Sign	Odds ratio	Confidence interval
"I pay attention to body changes to avoid being surprised by the next discharge"	<0.00	2.3	2.1–2.5
Number of ICD clusters (more than three shocks within 24 h)	<0.05	2.3	1.9–2.6
Age	0.19	0.95	0.99–1.01
Ejection fraction	0.68	1.01	0.98–1.04

Logistic regression, omnibus test: $F = 26.6$, $p < 0.000$.

associated with ICD shocks. Our data are consistent with some^{7, 10, 18} but not all previous studies.^{8, 9} In a small series of patients, Lüderitz *et al.*⁷ found that patients receiving more than five shocks showed a significant increase in anxiety during a 12-month follow-up. In another retrospective analysis, approximately 50% of patients with ICD reported anxiety related to ICD discharges, and for 30% of patients ICD shock delivery was the most distressing aspect of ICD treatment.¹⁰ Hermann *et al.* found that negative attitudes in patients with ICD are more frequent in those who have received shocks during follow-up.¹⁸ By contrast, Chevalier *et al.*⁸ found no relation between psychological well-being and ICD discharges. In their study, 10 patients suffered from a psychiatric illness (4 from depression, 2 from phobia, and 4 from a general anxiety disorder), but the authors could not show any relation with the number of shocks. However, in that study only 15 patients (45%) experienced a shock, and the total number of shocks is not reported. Another small study with only 20 patients could not show a correlation between psychiatric syndromes and the number of shocks, but there was a tendency for inadvertent shocks to be associated with psychiatric disorders such as depression or panic disorders.⁹

Our results suggest that the psychological theory of classic conditioning plays an important role as a potential mechanism for the development of anxiety disorders.¹⁹ This theory states that an aversive unconditioned stimulus such as an ICD discharge is associated with unpleasant body sensations. The sensations are linked to information on the environment of the patients (e.g., confined places), which then become conditioned and may subsequently evoke discomfort and anxiety even without the original stressor.²⁰ Patients then try to reduce this discomfort by avoiding certain stimuli that may indicate impending discomfort. This initiates an operant conditioning mechanism which may lead to progressive avoidance behavior, that is, phobic reactions.²¹

Catastrophic Fears—A Possible Risk Factor in the Development of Anxiety Disorders

Since avoidance behavior is mediated by cognitive processes, patients with anxiety tend to interpret body sensations as catastrophic events,^{22, 23} and more especially as indicators of impending catastrophes; as a consequence, they are prone to observe themselves more intensely.²⁴ We have also found these characteristics in our patients, who paid great attention to their bodies in order to avoid being surprised by an ICD discharge (Table IV). Our results are consistent with the data of Pauli *et al.*,¹² who reported that patients with ICD with high anxiety levels have increased catastrophic fears compared with healthy controls. Although patients with anxiety disorders do not have a different perception of their heart rhythm from that of normal subjects,²⁵ they are constantly trying not to overlook the prodroma of an ICD discharge. They also try to avoid potentially dangerous situations which may, in the final instance, lead to avoidance behavior. This operant negative reinforcement has been found to be the core process in the development of phobias. Thus, anxiety levels may be related more

closely to cognitive concepts than to objectively distressing experiences or medical complications.¹² These cognitive schemata may be both a consequence and expression of anxiety following psychological traumatization by ICD discharges and a premorbid characteristic shown by the patients; however, it could also be that higher anxiety levels and dysfunctional schemata increase the probability of shocks by triggering VT.

Another aspect of the development of anxiety disorder is that patients with malignant tachyarrhythmias, who have also experienced resuscitated cardiac arrest, have a fear of dying suddenly. Prior to ICD implantation, this is surely a realistic fear which should improve after ICD therapy is clearly not understood by all patients, since in one study¹² 26% of patients still suffer from a fear of dying, even after ICD implantation.

Diagnostic and Therapeutic Consequences

The diagnosis of anxiety disorders in patients with ICD can be a difficult clinical task, since anxiety problems are often reported by the patients. Complex avoidance behavior, as found in agoraphobia, is often misinterpreted by the patients themselves as successful coping. Furthermore, panic attacks rarely occur in medical settings because patients feel secure in such an environment.²⁷ Therefore, it is necessary to ask patients about certain anxiety characteristics and, in case of doubt, a psychiatrist should be consulted.

A reduction of ICD discharges, including optimal programming for each individual, probably reduces psychological distress and may therefore reduce the incidence of anxiety disorders. Thus, all efforts should be undertaken to avoid inappropriate or appropriate ICD discharges by ICD programming and, in some patients, by additional antiarrhythmic drug treatment.²⁸

Treatment with cognitive behavioral techniques²⁹ has been shown to be effective in the treatment of panic disorders and agoraphobia. Pharmacologic treatment options are serotonergic reuptake inhibitors (SSRI) such as paroxetine.³⁰ Benzodiazepines are a reasonable method of treatment for reducing acute anxiety states, mainly in panic disorders, although there is a risk of the patient developing a dependency. Bourke *et al.*¹⁴ reported on three patients with ICD with panic disorders or agoraphobia, who were successfully treated by cognitive behavioral therapy in combination with benzodiazepines and SSRI; however, controlled clinical trials on the treatment of anxiety disorders in patients with ICD have not been undertaken so far.

Limitations

A limitation of this study is the retrospective cross-sectional design and the variable time of patient exploration after ICD implantation. However, the estimation of the incidence of anxiety disorders was based on a validated psychiatric lifetime interview, which allows the starting point of psychiatric diseases to be determined.

Conclusion

The present study shows that panic disorders and agoraphobia are frequent after ICD implantation, and that the incidence of these disorders is related to the occurrence of ICD discharges. The results further support central psychological theories such as classical and operant conditioning with cognitive paradigms in the development of anxiety disorders. It is necessary to look carefully for psychiatric disorders in patients with ICD, so that treatment can start as early as possible.

References

- Myerburg RJ, Kessler KM, Castellanos A: Sudden cardiac death. Structure, function, and time-dependence of risk. *Circulation* 1992;85(1 suppl):12–10
- Kuck KH, Cappato R, Siebels J, Rüppel R: Randomized comparison of antiarrhythmic drug therapy with implantable defibrillators in patients resuscitated from cardiac arrest: Cardiac Arrest Study Hamburg (CASH). *Circulation* 2000;102:748–754
- Connolly SJ, Gent M, Roberts RS, Dorian P, Roy D, Sheldon RS, Mitchell LB, Green MS, Klein GJ, O'Brien B: Canadian Implantable Defibrillator Study (CIDS)—a randomized trial of the implantable cardioverter defibrillator against amiodarone. *Circulation* 2000;21:1297–1302
- The Antiarrhythmics versus Implantable Defibrillators (AVID) Investigators: A comparison of antiarrhythmic drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias. *N Engl J Med* 1997;337:1576–1583
- Moss AJ, Hall WJ, Cannom DS, Daubert JP, Higgins SL, Klein H, Levine JH, Saksena S, Waldo AL, Wilber D, Brown, MW, Heo M: Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. *N Engl J Med* 1996;335:1933–1940
- Buxton AE, Lee KL, Fisher JD, Josephson ME, Prystowsky EN, Hafley G: A randomized study of the prevention of sudden death in patients with coronary artery disease. Multicenter Unsustained Tachycardia Trial Investigators. *N Engl J Med* 1999;341:1882–1890
- Lüderitz B, Jung W, Deister A, Marneros A, Manz M: Lebensqualität nach Implantation eines Kardioverters / Defibrillators bei malignen Herzrhythmusstörungen. *Dtsch Med Wochenschr* 1993;118:285–289
- Chevalier P, Verrier P, Kirkorian G, Touboul P, Cottiaux J: Improved appraisal of quality of life in patients with automatic implantable cardioverter defibrillator: A psychometric study. *Psychother Psychosom* 1996;65:49–56
- Morris PL, Badger J, Chmielewski C, Berger E, Goldberg RJ: Psychiatric morbidity following implantation of the automatic implantable cardioverter defibrillator. *Psychosomatics* 1991;32:58–64
- Schöhl W, Trappe HJ, Lichtlen PR: Acceptance and quality of life after implantation of an automatic cardioverter / defibrillator. *Z Kardiol* 1994;83: 927–932
- Keren R, Aarons D, Veltri EP: Anxiety and depression in patients with life-threatening ventricular arrhythmias: Impact of the implantable cardioverter-defibrillator. *Pacing Clin Electrophysiol* 1991;14:181–187
- Pauli P, Wiedemann G, Dengler W, Blaumann-Benninghoff G, Kuhlkamp V: Anxiety in patients with an automatic implantable cardioverter defibrillator: What differentiates them from panic patients? *Psychosom Med* 1999; 61:69–76
- Spielberger CD: *State-Trait-Anger-Expression-Inventory*. Palo Alto, Calif.: Consulting Psychologist Press, 1988
- Bourke JP, Turkington D, Thomas G, McComb JM, Tynan M: Florid psychopathology in patients receiving shocks from implanted cardioverter-defibrillators. *Heart* 1997;78:581–583
- Margraf J: *Diagnostic Interview of Psychiatric Disease (DIPS)*. Berlin: Springer, 1994
- American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders* (3rd edition - revised). Washington, DC: American Psychiatric Association, 1987
- Eaton WW, Anthony JC, Romanski A, Tien A, Gallo J, Cai G, Neufeld K, Schlaepfer T, Laugharne J, Chen LS: Onset and recovery from panic disorder in the Baltimore Epidemiologic Catchment Area follow-up. *Br J Psychiatry* 1998;173:501–507
- Herrmann C, von zur Muhlen F, Schaumann A, Buss U, Kemper S, Wentzen C, Gonska BD: Standardized assessment of psychological well-being and quality-of-life in patients with implanted defibrillators. *Pacing Clin Electrophysiol* 1997;20:95–103
- Mackintosh NJ: *Conditioning and Associative Learning*. Oxford: Oxford University Press, 1983
- Eysenck, HJ: The conditioning model of neurosis. *Behav Brain Sci* 1979; 2:155–199
- Mowrer OH: *Learning Theory and Behavior*. New York: J. Wiley, 1960
- Ahmad T, Wardle J, Hayward P: Physical symptoms and illness attribution in agoraphobia and panic. *Behav Res Ther* 1992;30:493–500
- Clark DM: A cognitive model of panic attacks. In *Panic: Psychological Perspectives* (Eds. Rachman S, Maser JD). New Jersey: Lawrence Erlbaum Associates, 1988
- Ehlers A, Margraf J, Roth WT, Taylor CB, Maddock RJ, Sheikh J, Kopell ML, McClenahan KL, Gossard D, Blowers GH: Lactate infusions and panic attacks: Do patients and controls respond differently? *Psychiatry Res* 1986;17:295–308
- Rapee RM, Brown TA, Antony MM, Borlow DH: Response to hyperventilation and inhalation of 5.5% carbon dioxide-enriched air across the DSM-III-R anxiety disorders. *J Abnorm Psychol* 1992;101:538–552
- Vlay SC, Olson LC, Fricchione GL, Friedman R: Anxiety and anger in patients with ventricular tachyarrhythmias. Responses after automatic internal cardioverter-defibrillator implantation. *Pacing Clin Electrophysiol* 1989;12: 366–373
- Chambles DL, Goldstein A: The treatment of agoraphobia. In *Handbook of Behavioral Interventions* (Eds. Goldstein A, Foa EB). New York: J. Wiley, 1980
- Pacífico A, Hohnloser SH, Williams JH, Tao B, Saksena S, Henry PD, Prystowsky EN: Prevention of implantable-defibrillator shocks by treatment with sotalol. D,1-Sotalol Implantable Cardioverter-Defibrillator Study Group. *N Engl J Med* 1999;340:1855–1862
- Ost LG, Westling BE: Applied relaxation vs. cognitive behaviour therapy in the treatment of panic disorder. *Behav Res Ther* 1995;33:145–158
- Bakker A, van Dyck R, Spinhoven P, van Balkom AJ: Paroxetine, clomipramine, and cognitive therapy in the treatment of panic disorder. *J Clin Psychiatry* 1999;60:831–838