ORIGINAL ARTICLE

# Posttraumatic Stress Symptoms and Predicted Mortality in Patients With Implantable Cardioverter-Defibrillators

## *Results From the Prospective Living With an Implanted Cardioverter-Defibrillator Study*

*Karl-Heinz Ladwig, PhD, MD; Jens Baumert, PhD; Birgitt Marten-Mittag, PhD; Christof Kolb, MD; Bernhard Zrenner, MD; Claus Schmitt, MD*

**Context:** Cardiac disease and treatment with an implantable cardioverter-defibrillator (ICD) may be psychologically traumatic. Posttraumatic stress disorder (PTSD) is generally overlooked in cardiac patients, and no study to date (to our knowledge) has evaluated the effect of PTSD symptoms on the prognosis in patients with ICDs.

**Objective:** To test whether PTSD symptoms at baseline predict long-term mortality risk in patients with ICDs.

**Design:** Prospective cohort study with a mean follow-up period of 5.1 years, accounting for 743 person-years observed.

**Setting:** Data were derived from the Living With an Implanted Cardioverter-Defibrillator-Study, which initially included 211 patients with ICDs routinely attending the German Heart Center Munich outpatient clinic.

**Participants:** The Impact of Event Scale–Revised was used in 147 patients (125 men and 22 women) who qualified for the "A" criterion of PTSD (survival of a life-threatening event). Thirty-eight patients scoring in the upper quartile of the scale constituted the PTSD index group.

**Main Outcome Measures:** Mortality risk per 1000 person-years as assessed by Cox proportional hazards regression analysis based on an appropriate model fit (area under the curve, >0.80).

**Results:** Index patients experienced more anxiety and depression, had more cardiac symptoms, but showed no differences in left ventricular ejection fraction status or extent of ICD discharges compared with non–index patients. Forty-five patients (30.6%) died during the follow-up period. The relative mortality risk (multivariate adjusted for age, sex, diabetes mellitus, left ventricular ejection fraction, β-blocker prescription, prior resuscitation, ICD shocks received, depression, and anxiety) hazard ratio was 3.45 (95% confidence interval, 1.57-7.60; $P=.002$) for the PTSD group. Compared with 55 fatal events per 1000 person-years in patients without PTSD, the long-term absolute mortality risk accounted for 80 fatal events per 1000 person-years in patients with PTSD.

**Conclusion:** The adverse effect of PTSD symptoms on the long-term mortality risk in ICD-treated cardiac event survivors, independent of disease severity, supports the need for routinely applied interdisciplinary psychosocial aftercare.

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**Author Affiliations:** Department of Psychosomatic Medicine and Psychotherapy, Technische Universitaet Muenchen (Drs Ladwig and Marten-Mittag), and German Heart Center Munich, Technical University of Munich (Drs Kolb, Zrenner, and Schmitt), Munich, and Institute of Epidemiology, Helmholtz Zentrum National Research Center for Environmental Health, Neuherberg (Drs Ladwig and Baumert), Germany.

SURVIVAL FOLLOWING LIFE-threatening cardiovascular disease conditions (those with a rapid and unexpected onset) is a cause of acute distress and may result in a constellation of symptoms that qualify for the diagnosis of posttraumatic stress disorder (PTSD).[1-3] Besides exposure to a traumatic and life-threatening event (the "A" criterion of PTSD), the diagnosis of PTSD according to established international classification systems such as the *DSM-IV*[4] requires a patient's response to be characterized by intense fear, leading to the persistence of painful intrusive memories, avoidance behavior, and hyperarrousal.[5] In particular, survival of an out-of-hospital cardiac arrest bears traumatic properties that may result in a prevalence of PTSD ranging from 27% to 38%.[6,7] The effect of an acute myocardial infarction may be less pronounced but results in PTSD rates ranging from 8% to 20%.[8-12] The prevalence of PTSD among patients with myocardial infarction consulting at a primary care setting may range from 22% to 32%.[13] Among older patients with myocardial infarction, Chung et al[14] recently revealed prevalence rates of 30% for full PTSD and 42% for partial PTSD. Among heart transplant recipients, the transplant-related 12-month prevalence of PTSD was found to be roughly 16%.[15]



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A significant proportion of patients with an implantable cardioverter-defibrillator (ICD) have survived a cardiac arrest or an acute myocardial infarction.[16] Although ICDs are highly effective and life-saving in the treatment of lethal ventricular arrhythmias,[17] comorbid negative affectivity remains an enduring concern in patients under ICD treatment. The best-recognized affective mood states in patients with ICDs are panic disorders, anxiety, and depression.[18] Treatment with an ICD may act as a constant reminder of the underlying disease condition; therefore, patients with ICDs may be particularly prone to experience PTSD symptoms.[19]

Recently, a prospective association has been shown between PTSD symptoms and coronary heart disease (CHD) in apparently healthy men from the Veterans Affairs Normative Aging Study.[20] However, little is known about the effect of PTSD in patients with ICDs,[19] and no study to date (to our knowledge) has evaluated the long-term mortality risk conferred by PTSD in patients with ICDs. We sought to determine whether PTSD in patients with ICDs was associated with an increased subsequent total mortality risk. Because there is substantial overlap between symptoms of PTSD and those of depression and anxiety, any PTSD-mortality association in patients with ICDs may be largely influenced by comorbid negative affectivity.[20,21] Therefore, when evaluating the effect of PTSD symptoms on the long-term mortality risk in patients with ICDs, we adjusted for depression and anxiety.

## METHODS

### PATIENTS AND SETTING

The present data were derived from the Living With an Implanted Cardioverter-Defibrillator (LICAD) Study, which initially included 211 patients treated with an ICD. Patients attending the cardiology outpatient clinic of the German Heart Center Munich for a routine ICD checkup participated at the baseline examination between January 6, 1998, and May 31, 1998 (first survey), and between April 1, 2002, and June 30, 2002 (second survey). The mean (SD) time since implantation was 27 (21) months (range, 3-142 months).

Inclusion criteria for the present analysis were treatment with an ICD, time since implantation longer than 3 months (to avoid benign transitory adaptation reactions), and age older than 16 years. Furthermore, rapid onset of the CHD condition (cardiac arrest or acute myocardial infarction) was required to meet the A criterion of the PTSD.[4] Written informed consent was obtained from all patients. The study was approved by the ethics committee of the medical faculty of the Technical University of Munich.

Seven patients refused to participate in the study, and 2 patients had severe cognitive impairment, leaving 202 patients with eligible data. Among them, 166 patients had experienced a sudden onset of their disease condition. Of these, 19 patients (11.4%) with missing values to estimate their PTSD symptom burden were excluded from the analysis. The dropout analysis revealed no statistical differences in sex, age, or educational status compared with 147 patients (125 men and 22 women) with complete data; however, dropout patients had less frequently experienced out-of-hospital resuscitation. A multivariate Cox proportional hazards regression model for all patients (n=166) to assess whether patients with Impact of Event Scale–Revised (IES-R) data (n=147) vs patients without IES-R data (n=19) differed in mortality risk revealed a hazard ratio (HR) of 0.80 (95% confidence interval [CI], 0.31-2.06; $P$=.65), confirming that the findings were unaffected by missing values of IES-R data.

### PSYCHODIAGNOSTIC ASSESSMENT

All patients who had a potentially traumatic event (survival of a cardiac arrest or an acute myocardial infarction) during the course of disease before ICD implantation were asked to confirm that they had experienced a rapid-onset CHD condition. Immediate threat responses to the initial index event were not assessed retrospectively, but the patients' actual emotional involvement with the event (1 item [score range, 0-2]) and whether they had vivid recollections of it (1 item [score range, 0-2]) were measured. We used the IES-R,[22,23] a 22-item self-report inventory that indexes intrusive and avoidance symptoms (each subscale has 8 items [score range, 1-4]) and startle symptoms (6 items [score range, 1-4]). To ensure that IES-R symptoms were CHD event related, the IES-R was introduced by asking the patient to indicate sentiments related to the onset event. Patients rating in the upper quartile of the IES-R score distribution were assigned to the index group with severe PTSD symptoms. The effect of acute coronary syndromes results in rates of PTSD ranging from 8% to 20%, while survival of an out-of-hospital cardiac arrest may result in a PTSD prevalence ranging from 27% to 38%. These prevalence rates were assessed at different time points of the disease course using different methods and cutoff points. Therefore, using the upper quartile of scores on the IES-R as a cutoff point may be considered a conservative way to assess a tangible clinical population that experiences burdensome and clinically relevant psychosocial disability.

Intratrauma dissociation was assessed by a rater-administered 8-item version of the Peritraumatic Dissociative Experiences Questionnaire,[24] with scores ranging from 0 (low) to 8 (high). Test-retest reliability and internal consistency of the questionnaire are satisfactory, and convergent validity is moderate to strong.[25] Anxiety and depression symptoms were measured using the German version of the 14-item Hospital Anxiety and Depression Scale.[26,27] For both subscales, a cutoff value of 8 or higher proved to be optimal for anxiety (sensitivity, 0.89; specificity, 0.75; and area under the curve, 0.88) and for depression (sensitivity, 0.80; specificity, 0.88; and area under the curve, 0.97).[28] Furthermore, the phobic anxiety subscale of the Symptom Checklist,[29] a self-rated scale that consists of 8 psychiatric symptom domains, was applied. For all psychodiagnostic parameters, a missing value of an item was replaced with the mean of the other items if at least 70% of the components of the scale or module were answered.

### CLINICAL DATA ASSESSMENT

Patient records, including specific data regarding ICD treatment, were provided by the electrophysiological outpatient clinic of the German Heart Center Munich. Left ventricular ejection fraction (LVEF) was assessed echocardiographically or angiographically and was classified in 4 categories (normal, ≥0.35, 0.20 to <0.35, or <0.20). In a standardized interview, sociodemographic characteristics were assessed. Moreover, patients were asked whether they had experienced cardiac symptoms (palpitations, tachycardia, or racing heart), including chest pain (exertional, at rest, or at night), during the past 4 weeks before baseline examination.

### VITAL STATUS ASSESSMENT

The vital status of all patients was assessed by routine examinations in the outpatient clinic and by telephone interview with



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**Table 1. Baseline Characteristics by Posttraumatic Stress Disorder (PTSD) Level in the Study Population of 147 Patients With an Implantable Cardioverter-Defibrillator**

| Characteristic | Total No. | PTSD Level: Low or Moderate (n=109) | PTSD Level: High (n=38) | *P* Value |
|---|---|---|---|---|
| Age, mean (SD), y | 147 | 62.30 (12.25) | 57.45 (13.86) | .04[a] |
| Female, No. (%) | 147 | 15 (13.8) | 7 (18.4) | <.49 |
| Marital status, No. (%) | **145** | | | .71 |
| Unmarried | | 17 (15.9) | 4 (10.5) | |
| Married or living with partner | | 78 (72.9) | 29 (76.3) | |
| Divorced or widowed | | 12 (11.2) | 5 (13.2) | |
| Education level, No. (%) | **146** | | | .53 |
| ≤Secondary | | 58 (53.7) | 21 (55.3) | |
| High school education | | 16 (14.8) | 8 (21.1) | |
| University degree | | 34 (31.5) | 9 (23,7) | |
| Currently employed, No. (%) | 147 | 29 (26.6) | 10 (26.3) | .97 |

[a] *t* Test; $\chi^2$ test for all others.

their attending physician. Information from spouses or household members was validated by death certificates from the local health department. For this analysis, March 31, 2005, was set as the end point of the follow-up period, leading to a mean (SD) follow-up period of 5.1 (2.2) years. Three patients were censored at the date of their heart transplantation surgery.

## STATISTICAL ANALYSIS

Statistical associations between categorical variables were performed using the $\chi^2$ test; for continuous variables, group differences were analyzed using the *t* test. The person-years method was used to assess crude mortality rates. For multivariate adjustment, Cox proportional hazards regression analysis was applied to evaluate associations between PTSD symptoms at baseline examination and subsequent mortality. Proportional hazards assumption was tested using appropriate time interaction variables. Cox proportional hazards regression models were adjusted for age, sex, and survey (model 1), as well as for CHD diagnosis (yes or no), prior resuscitation (yes or no), number of shocks (0-4 or ≥5), and time of ICD implantation before enrollment (≤12 or >12 months) (model 2). To assess whether the effect of the IES-R score on mortality was altered by LVEF (normal, ≥0.35, 0.20 to <0.35, <0.20, or missing), depression (yes, no, or missing), and anxiety (yes, no, or missing), these factors were added to the factors of the prior model (model 3). Missing values for these 3 variables were included as a category in the Cox proportional hazards regression models to keep the maximum number of patients. All models were estimated for continuous IES-R scores and for categorical IES-R scores dichotomized at the upper quartile of the IES-R score distribution (<15 [low or moderate] or ≥15 [high]). Because differences between the approaches were marginal (although somewhat more pronounced in the categorical model), we report only the results of the model with categorical IES-R scores. The predictive value of the models was assessed by the area under the curve. For model calibration, the Hosmer-Lemeshow goodness-of-fit test was used. We computed several Cox proportional hazards regression models by implementing a growing number of adjustment variables. The predictive value increased by inclusion of IES-R score in the Cox proportional hazards regression model. The area under the curve increased from 0.75 in model 0 (adjusted for age, sex, and survey) to 0.76 in model 1 (adjusted for age, sex, survey, and PTSD). The Hosmer-Lemeshow goodness-of-fit test revealed a similar model fit.

All *P* values are 2-tailed, and all CIs are computed at the 95% level. All analyses were performed in parallel using commercially available statistical software (SPSS versions 14.0 and 8.02; SPSS Inc, Chicago, Illinois).

## RESULTS

All 147 patients enrolled in the study had survived rapid onset of their disease condition. Among them, 38 patients scored in the upper quartile of the IES-R and constituted the index group of patients with severe PTSD symptoms. The mean (SD) IES-R scores were 34.78 (16.80) in the index group and 4.70 (4.19) in the comparison group. Patients in the index group were younger compared with the patients with low levels of PTSD symptoms ($P>.05$). However, sex, marital status, education level, and employment status were not different between the groups (**Table 1**). Index group patients more frequently experienced chest pain and other cardiac symptoms. However, no measurable difference was found for LVEF status or classic CHD risk factors (**Table 2**). The extent of prior ICD shock discharge also had no influence on experiencing PTSD symptoms. The prescription of standard cardiac medication was not different between the groups except for β-blockers, with 28 of 38 index patients (73.7%) taking β-blocker medication compared with 59 of 109 patients without PTSD (54.1%) ($P=.04$, $\chi^2$ test).

However, significantly more patients in the index group (15 of 38 index patients [39.5%] vs 4 of 109 patients without PTSD [3.7%]) reported being burdened by memories of the disease onset ($P<.001$). As expected, they also experienced anxiety, phobic anxiety, and depression significantly more often (**Table 3**).

During a mean (SD) follow-up period of 5.1 (2.2 years) (range, 0.2-7.2 years) leading to 743 person-years of observation, 45 fatal events (30.6%) (in 39 men and in 6 women) were observed. The crude mortality rate for the total study group was 60.6 deaths per 1000 person-years. When stratifying for patients without PTSD (32 fatal events) and for patients with PTSD symptoms (13 fatal events), a remarkable difference in the absolute mortality risk was observed based on patient age (**Table 4**). Compared with 55 fatal events per 1000 person-years in patients without PTSD, the long-term absolute mortality risk accounted for 80 fatal events per 1000 person-years in patients with PTSD. For patients 60 years or younger at the baseline examination, the mortality increased from 21.7 deaths per 1000 person-years in patients without PTSD to 46.30 deaths in patients with PTSD symptoms. A similar observation was made for patients older than 60 years with ICDs (77.2 vs 145.5 deaths per 1000 person-years).

As summarized in **Table 5**, the basic crude model (adjusted for age, sex, and survey) revealed a relative mortality risk HR of 2.44 (95% CI, 1.24-4.80; $P=.01$) for pa-



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**Table 2. Clinical Characteristics and Implantable Cardioverter-Defibrillator (ICD) Features by Posttraumatic Stress Disorder (PTSD) Level in the Study Population**

| Variable | Total No. | PTSD Level, No. (%) Low or Moderate (n=109) | High (n=38) | *P* Value |
|---|---|---|---|---|
| ICD implantation before enrollment, mo | 147 | | | .63[a] |
| 3-6 | | 14 (12.8) | 3 (7.9) | |
| 7-12 | | 15 (13.8) | 7 (18.4) | |
| 13-24 | | 32 (29.4) | 12 (31.6) | |
| 25-48 | | 31 (28.4) | 13 (34.2) | |
| >48 | | 17 (15.6) | 3 (7.9) | |
| Resuscitation | 147 | 76 (69.7) | 32 (84.2) | .08[a] |
| ICD shocks | **147** | | | .16[a] |
| 0 | | 61 (56.0) | 21 (55.3) | |
| 1-4 | | 29 (26.6) | 11 (28.9) | |
| 5-9 | | 9 (8.3) | 6 (15.8) | |
| ≥10 | | 10 (9.2) | 0 | |
| Angina pectoris in previous 4 wk | 147 | 24 (22.0) | 18 (47.4) | <.001[a] |
| Cardiac symptoms in previous 4 wk[b] | 147 | 26 (23.9) | 17 (44.7) | <.02[a] |
| Classic coronary heart disease risk factors | | | | |
| Hypertension | | 18 (16.5) | 5 (13.2) | .62 |
| Smoking | | 6 (5.7) | 3 (8.6) | .69 |
| Diabetes mellitus | | 10 (9.2) | 3 (7.9) | >.99 |
| Hypercholesterol[c] | | 48 (44.0) | 15 (39.5) | .62 |
| Left ventricular ejection fraction[d] | 131 | | | .21[a] |
| Normal | | 12 (12.6) | 8 (22.2) | |
| ≥0.35 | | 5 (5.3) | 3 (8.3) | |
| 0.20 to <0.35 | | 56 (58.9) | 14 (38.9) | |
| <0.20 | | 22 (23.2) | 11 (30.6) | |

[a] $\chi^2$ Test.
[b] Palpitations, tachycardia, and racing heart.
[c] Number of patients taking lipid-lowering medication.
[d] Ninety-five patients with low-moderate PTSD levels; 36 patients with high PTSD levels.

**Table 3. Psychotraumatic and Affective Characteristics by Posttraumatic Stress Disorder (PTSD) Level in the Study Population**

| Characteristic | PTSD Level, Mean (SE) Low or Moderate (n=109) | High (n=38) | *P* Value[a] |
|---|---|---|---|
| Peritraumatic Dissociative Experiences Questionnaire[24] | 1.303 (0.194) | 2.130 (0.218) | .006 |
| Hospital Anxiety and Depression Scale[26,27] | | | |
| Anxiety | 3.473 (0.381) | 7.142 (0.427) | <.001 |
| Depression | 3.379 (0.403) | 6.397 (0.451) | <.001 |
| Symptom Checklist 90[29] phobic anxiety | 1.446 (0.334) | 3.958 (0.373) | <.001 |

[a] *t* Test, drawn from linear regression models adjusted for age, sex, and survey.

**Table 4. Mortality Rates by Age Class and by Posttraumatic Stress Disorder (PTSD) Level in the Study Population**

| PTSD Level | Deaths, No. (%) | Total No. | Follow-up Period, y | Person-Years | Mortality Rate per 1000 Person-Years |
|---|---|---|---|---|---|
| Age ≤60 y | | | | | |
| Low or moderate | 5 (12.8) | 39 | 5.9 | 230.0 | 21.7 |
| High | 5 (21.7) | 23 | 4.7 | 108.0 | 46.3 |
| Age >60 y | | | | | |
| Low or moderate | 27 (38.6) | 70 | 5.0 | 349.7 | 77.2 |
| High | 8 (53.3) | 15 | 3.7 | 55.0 | 145.5 |
| **Total** | **45** (30.6) | **147** | 5.1 | **742.7** | 60.6 |

tients with PTSD symptoms compared with patients without PTSD. When controlling for factors that mirror cardiac characteristics of the study patients (LVEF, CHD diagnosis, prior resuscitation, β-blocker prescription, number of ICD shocks, and time of ICD implantation before enrollment), the HR for patients with PTSD symptoms increased to 3.21 (95% CI, 1.56-6.62; *P*=.002) (model 2). The inclusion of depression and anxiety and further adjustment by noncardiac diseases (including diabetes mellitus) and β-blocker prescription at the baseline examination did not weaken the effect of PTSD level on the mortality risk (model 3) (HR, 3.45; 95% CI, 1.57-7.60; *P*=.002).

In addition, we performed an analysis using continuous data, which revealed a significant effect of the IES-R score on mortality risk. The goodness of fit of the models was similar to that of the models with PTSD in the dichotomous form (**Table 6**). The HR in the fully adjusted model was 1.03 (95% CI, 1.01-1.05; *P*=.01), meaning that the mortality risk increased by 3% per PTSD unit. As shown in **Figure 1**, stratification of continuous IES-R scores by subscales revealed that the intrusive recollections subscale alone contributed significantly to the excess mortality risk, with an HR of 1.09 (95% CI, 1.04-1.14), indicating a mortality risk increase of 9% per unit of the subscale.

**Figure 2** shows that the observed number of life-years lost because of PTSD increases as the duration of follow-up increases. To ensure that the observed associations were not affected by early deaths with specific conditions, we restricted the follow-up to a maximum of 3 years, leading to 20 deaths (in 16 men and in 4 women) within 3 years. Multivariate-adjusted HRs estimated from these models were similar to the HRs estimated for the entire observation period.

## COMMENT

To our knowledge, this is the first study to evaluate the effect of negative affectivity on the long-term mortality risk in patients with ICDs and is among the first follow-up studies in cardiac patient populations to apply PTSD symptoms as a mortality risk predictor. In 1999, Dew et al[15] showed that the risk among heart transplant recipients was substantially increased for patients who met criteria for PTSD related to the transplant. Our findings provide direct evidence for an independent influence of PTSD symptoms on fatal outcome in these patients. Experiencing PTSD symptoms conferred a 2.4-



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**Table 5. Effect of Posttraumatic Stress Disorder (PTSD) Symptoms on Mortality Risk Estimated by Cox Proportional Hazards Regression Models With Different Adjustments**

| Model and Adjustment | Hazard Ratio (95% Confidence Interval)[a] | *P* Value | Area Under the Curve | Hosmer-Lemeshow Goodness-of-Fit Test |
|---|---|---|---|---|
| Age, sex, survey | . . . | . . . | 0.75 | 12.4 |
| Model 1: age, sex, survey, PTSD | 2.44 (1.24-4.80) | .01 | 0.76 | 6.1 |
| Model 2: multivariate, PTSD[b] | 3.21 (1.56-6.62) | .002 | 0.83 | 6.1 |
| Model 3: multivariate, PTSD[c] | 3.45 (1.57-7.60) | .002 | 0.83 | 9.9 |

Abbreviation: Ellipses, not applicable.
[a] Hazard ratio of mortality in patients with a high PTSD level compared with a low or moderate PTSD level.
[b] Model 2 adjusted for age, sex, survey, coronary heart disease diagnosis, prior resuscitation, left ventricular ejection fraction, number of shocks, β-blocker prescription, time of implantable cardioverter-defibrillator implantation before enrollment, and PTSD.
[c] Model 3 adjusted for age, sex, survey, coronary heart disease diagnosis, prior resuscitation, left ventricular ejection fraction, number of shocks, β-blocker prescription, time of implantable cardioverter-defibrillator implantation before enrollment, noncardiac diseases, depression, anxiety, and PTSD.

**Table 6. Effect of Posttraumatic Stress Disorder (PTSD) Symptoms on Mortality Risk Estimated by Cox Proportional Hazards Regression Models With Different Adjustments and Using Continuous Data**

| Model and Adjustment | Hazard Ratio (95% Confidence Interval)[a] | *P* Value | Area Under the Curve | Hosmer-Lemeshow Goodness-of-Fit Test |
|---|---|---|---|---|
| Age, sex, survey | . . . | . . . | 0.75 | 12.4 |
| Model 1: age, sex, survey, PTSD | 1.03 (1.01-1.04) | .008 | 0.76 | 2.5 |
| Model 2: multivariate, PTSD[b] | 1.03 (1.01-1.05) | .002 | 0.82 | 6.2 |
| Model 3: multivariate, PTSD[c] | 1.03 (1.01-1.05) | .01 | 0.82 | 11.9 |

Abbreviation: Ellipses, not applicable.
[a] Hazard ratio of mortality in patients per PTSD unit increase.
[b] Model 2 adjusted for age, sex, survey, coronary heart disease diagnosis, prior resuscitation, left ventricular ejection fraction, number of shocks, β-blocker prescription, time of implantable cardioverter-defibrillator implantation before enrollment, and PTSD.
[c] Model 3 adjusted for age, sex, survey, coronary heart disease diagnosis, prior resuscitation, left ventricular ejection fraction, number of shocks, β-blocker prescription, time of implantable cardioverter-defibrillator implantation before enrollment, noncardiac diseases, depression, anxiety, and PTSD.

fold long-term age- and sex-adjusted mortality risk for patients with ICDs. Additional adjustment for indexes of the particular cardiac disease burden in patients with ICDs (LVEF, number of ICD shocks, and resuscitation) strengthened the association to a 3.2-fold HR.

As expected, patients experiencing severe PTSD symptoms in the present study exhibited substantially more negative affectivity than their nonaffected counterparts, which agrees with findings that provide evidence for a substantial overlap between PTSD, depression, and anxiety.[21] The influence of depressed mood on subsequent shock frequency in patients with ICDs has been demonstrated in a recent investigation[30] in which moderate to severe depression among 645 patients with ICDs was associated with a 3.5-fold risk of experiencing ICD shocks. Nevertheless, adjustment for depression and anxiety in the present analysis did not weaken the predictive accuracy of PTSD symptoms on the mortality end point. Therefore, the PTSD-mortality association may be largely independent of overlapping affective comorbidity.[19]

Reasons for the apparent effect of PTSD on survival in patients with ICDs have yet to be determined. Our study failed to find differences in baseline clinical characteristics that account for the remarkable survival gap between patients with and without PTSD symptoms. Left ventricular ejection fraction is a major contributor of long-term adverse outcomes in patients with ICDs[31-33] but did not contribute to the mortality risk among patients experiencing PTSD in our study. Furthermore, ICD shock frequency is a predictor of mortality and is an important determinant of impaired quality of life in patients with ICDs but was likewise unassociated with PTSD. Therefore, other unexamined factors may serve to increase survival risk in this particular patient population.

Patients with PTSD in the present investigation reported significantly more cardiac symptoms than their counterparts. Therefore, the perceived severity rather than the objective severity of a cardiac condition as determined by cardiac criteria may be associated with PTSD. These findings are in line with previous studies[8,34] among cardiac populations demonstrating that PTSD was associated less with objective clinical disease burden but more with subjective severity as indexed by chest pain.

The exact nature of PTSD provoked by medical conditions (eg, a life-threatening cardiac event) is unknown. Unlike many types of trauma, the threat to the patient's life and well-being is not one of experience but is persistent and enduring. Based on the considerations of Mundy and Baum,[1] PTSD threat in medical patients comprises a future-oriented aspect (in contrast to traditional traumas) that represents fears and worries about treatment, survival, recurrence, stigma, the persistence of life threat, and new dangers yet to come. Therefore, patients experiencing PTSD symptoms may be particularly stressed by agonizing rumination and by an involuntary preoccupation with the underlying disease process. This assumption is further supported by the finding that among possible PTSD core features (as measured by the IES-R subscales) illness onset–related intrusive memories accounted solely for the mortality prediction.

Further investigations are required to assess the behavioral and biologic pathways by which posttraumatic maladaptation contributes to the excess mortality risk in patients with ICDs. The PTSD symptoms may worsen medical outcome by decreased adherence to postinfarction medical regimens. Shemesh and colleagues showed that PTSD symptoms were associated with nonadherence to captopril[35] and aspirin[36] therapy. They suspect that cardiac medical recommendations may act as a "traumatic reminder" and are likely to be avoided. Contrary to these findings, compliance with treatment was unaffected by PTSD status among patients with myocardial



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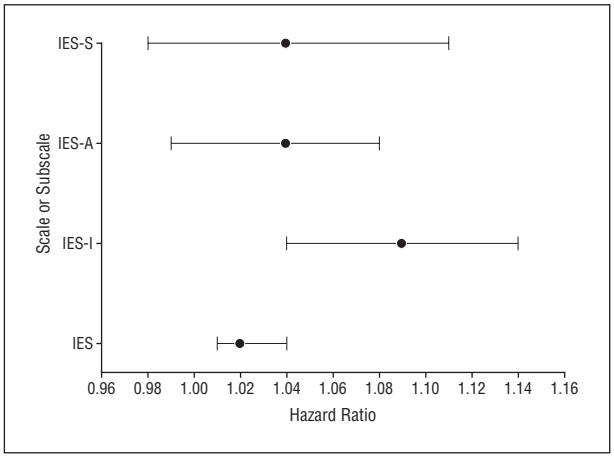


**Figure 1.** Hazard ratios of continuous Impact of Event Scale (IES)–Revised total scores and subscale scores on mortality risk of patients with an implantable cardioverter-defibrillator adjusted for age, sex, survey, anxiety, depression, number of shocks, prior resuscitation, posttraumatic stress disorder, left ventricular ejection fraction, and time of implantation before enrollment. IES-A indicates avoidance subscale; IES-I, intrusive subscale; and IES-S, startle subscale. Whiskers indicate 95% confidence intervals.

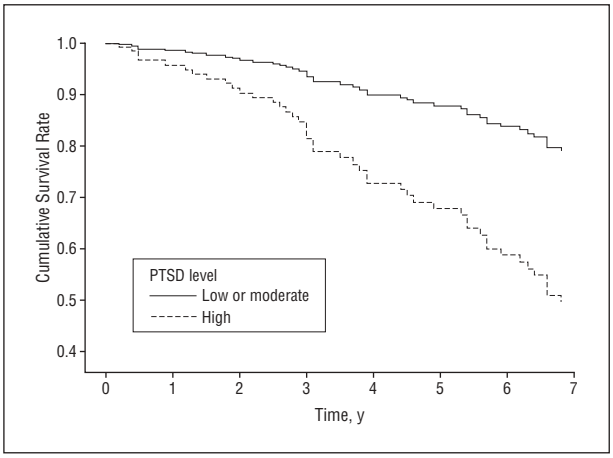


**Figure 2.** Long-term mortality risk in patients with an implantable cardioverter-defibrillator stratified for posttraumatic stress disorder (PTSD) symptoms (adjusted survival curve) adjusted for age, sex, survey, PTSD, anxiety, depression, prior resuscitation, number of shocks, left ventricular ejection fraction, and time of implantation before enrollment.

infarction in a 2007 British study by Jones et al,[13] possibly because of new United Kingdom primary care contracts by which index patients are actively identified and their conditions reviewed to manage risk factors. Physiologic activation may have become critically prolonged in subjects experiencing sustained intrusive rumination (eg, leading to impaired cardiac autonomic control with subsequent lowering of the cardiac threshold for severe arrhythmias[37] or to unfavorable immunologic activation[38]). Recent preliminary data point to an association of PTSD with endothelial dysfunction.[39]

The decision to use an IES-R cutoff point rather than a full psychiatric interview was guided by 3 considerations. First, it is far less burdensome to patients to answer a short self-report screen compared with a full interview, ensuring adequate and representative enrollment and retention of patients in the protocol. Second, the use of the IES-R is feasible in clinical settings for the screening of cardiovascular patients (while performing a full psychiatric interview is not), ensuring that the study has more immediate relevance to clinical implications. Third, there is no reason to believe that only PTSD "case-ness" is related to poor outcomes; symptom severity may be the more important marker, as demonstrated in previous studies[2,30,32] that linked PTSD symptoms to poor outcomes in cardiovascular patients. Furthermore, the assumption that the use of the upper quartile of scores on the IES-R identifies important psychopathologic conditions is borne out by the cross-referencing to other questionnaires applied in the present analysis.

Our study population is limited by a small number of patients with PTSD. However, the follow-up duration of 5.1 years accounted for a total observation period of 743 person-years. Furthermore, the model fit of the Cox proportional hazards regression models was appropriate, as evidenced by an area under the curve exceeding 0.80. Therefore, in multivariate models we were able to detect significant relationships between the experience of PTSD symptoms and subsequent mortality. However, the study is underpowered to conduct further subgroup analyses, especially for sex effects.

In the present investigation, we did not aim to identify "cases" with a full PTSD diagnosis but rather focused on symptom severity as assessed using the IES-R. Compared with performing a psychiatric interview such as the Structured Clinical Interview for *DSM-IV*, the pragmatic barriers for the IES-R screening instrument are substantially lower.

## CONCLUSIONS

Symptoms of PTSD, particularly intrusive recollections of adverse aspects of the disease course, have a substantial effect on survival in patients with ICDs. The absolute mortality risk of patients with ICDs experiencing PTSD is more than double the risk compared with patients without the PTSD symptom pattern. Survival analysis further revealed that, even after rigorous adjustment for ICD-specific factors and for affective morbidity, the relative mortality risk remains 3-fold higher in PTSD-prone patients with ICDs.

The findings underline the urgent need for routinely applied comprehensive and interdisciplinary psychosocial aftercare for patients with ICDs. In particular, the present data suggest that PTSD is an important source of psychological distress in patients with ICDs having symptoms persisting for many years that should not be overlooked. Although the serious mortality risk of PTSD in patients with ICDs needs to be further investigated before firm recommendations can be made, screening for PTSD symptoms in patients with ICDs is likely to be clinically beneficial, and treatment in selected patients should be attempted. Studies of PTSD treatment are indicated to determine whether specific treatment of PTSD might improve outcomes in these patients.

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**Correspondence:** Karl-Heinz Ladwig, PhD, MD, Insti-



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tute of Epidemiology, Helmholtz Zentrum National Research Center for Environmental Health, Ingolstaedter Landstrasse 1, 85764 Neuherberg, Germany (ladwig@helmholtz-muenchen.de).

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