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# Emotional distress, positive affect, and mortality in patients with an implantable cardioverter defibrillator

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ABSTRACT

*Background:* Little is known about the relationship between emotional distress and mortality in patients with an implantable cardioverter defibrillator (ICD). Our aim was to examine the predictive value of general negative and positive affect, and depressive symptoms (including its components somatic symptoms and cognitive-affective symptoms) for mortality.

*Methods:* ICD patients (N = 591, 81% male, mean age = 62.7 ± 10.1 years) completed the Global Mood Scale to measure the independent dimensions negative and positive mood, and the Beck Depression Inventory to measure depressive symptoms. Covariates consisted of demographic and clinical variables.

*Results:* During the median follow-up of 3.2 years, 96 (16.2%) patients died. After controlling for covariates, negative affect was significantly related to all-cause mortality (HR = 1.034, p = 0.002), whereas positive affect was not (HR = 1.007, p = 0.61). Depressive symptoms were also independently associated with an increased mortality risk (HR = 1.031, p = 0.030) and somatic symptoms of depression in particular (HR = 1.130, p = 0.003), but cognitive-affective symptoms were not associated with mortality (HR = 0.968, p = 0.29). When entering both significant psychological predictors in a covariate-adjusted model, negative mood remained significant (HR = 1.039, p = 0.009), but somatic symptoms of depression did not (HR = 0.988, p = 0.78). Similar results were found for cardiac-related death. Of covariates, increased age, CRT, appropriate shocks were positively related to death.

*Conclusions:* Negative affect in general was related to mortality, but reduced positive affect was not. Depression, particularly its somatic symptoms, was also related to mortality, while cognitive-affective symptoms were not. Future research may further focus on the differential predictive value of emotional distress factors, as well as on mechanisms that relate emotional distress factors to mortality.

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## 1. Introduction

The implantable cardioverter defibrillator (ICD) constitutes the main treatment of patients with ventricular arrhythmias. This treatment has clear medical benefits [1], but psychological problems exist, with 25% to 33% of ICD patients experiencing anxiety or depressive symptoms [2–4]. These emotions seem to emanate from the psychological profile of the patient [2] and to a lesser extent from ICD shocks and advisories [5,6].

Little is known about the consequences of increased emotional distress in ICD patients. An increased risk for life-threatening arrhythmias has been found in patients with anxiety [7], depression [8], and clustering of chronic distress factors [9]. Emotional distress may also increase the risk for mortality in ICD patients. Findings from clinical trials suggest that poor quality of life is associated with mortality in the first year post-implantation [10]. In addition, mortality rates may be higher in patients with a high level of ICD concerns [11], post-traumatic stress symptoms [12], or a distressed personality (i.e., patients who inhibit the expression of negative emotions) [11].

Depression may also be related to mortality. Although one study did not find this relationship in ICD patients [13], depression has been related to mortality in patients with heart failure [14,15], and acute coronary syndrome [16]. Depression has also been related to mortality in the general population [17], as well as mortality in other patient populations, such as patients with cancer [18] or diabetes [19,20]. A distinction has to be made between somatic symptoms of depression (e.g., sleep difficulties and fatigue) and cognitive-affective symptoms of depression (e.g., shame, guilt, and a negative self-image). Both symptom dimensions have been independently

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associated with mortality [21], although the risk associated with somatic symptoms may be higher as the risk associated with cognitive-affective symptoms of depression [22].

Besides negative mood states, positive mood states (e.g. feeling active or cheerful) may also influence the mortality risk. Studies in coronary patients have shown that reduced positive affect (that is, anhedonia) is associated with an increased risk for major adverse cardiac events and mortality [23,24]. Notably, positive affect is a different dimension than negative affect and these relatively independent mood states may differentially affect outcomes.

The objectives of the current study were to examine 1) the association between positive and negative mood and mortality, and 2) the association between depressive symptoms and mortality, with depression also being subdivided into two symptom dimensions, i.e., somatic symptoms and cognitive-affective symptoms. Both all-cause and cardiac-related deaths were included. We hypothesize that 1) negative mood as well as reduced positive mood will be related to mortality, and 2) depression, and particularly somatic symptoms of depression, will be related to increased mortality.

## 2. Methods

### 2.1. Patient sample

Patients who underwent ICD implantation between May 2003 and February 2009 were included from two referral hospitals in the Netherlands (Amphia Hospital, Breda and Catharina Hospital, Eindhoven). Inclusion criteria were implantation with an ICD and age between 18 and 80 years. Exclusion criteria were significant cognitive impairments (e.g. dementia), life-threatening comorbidities (e.g. cancer), and insufficient knowledge of the Dutch language.

The study was approved by the Medical Ethics Committee of both participating hospitals. The study was conducted in accordance with the Helsinki Declaration, and all patients provided written informed consent.

The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [25].

### 2.2. Psychological measures

Patients completed psychological measures at the time of implantation (between 1 day prior to implantation and 3 weeks after implantation), and at 2, 12 and 18 months follow-up.

#### 2.2.1. Mood states

The Global Mood Scale (GMS) is a 20 item self-report questionnaire, with 10 items measuring negative mood states (characterized by fatigue and malaise; e.g. feeling listless, wearied, helpless) and 10 items measuring positive mood states (characterized by energy and sociability; e.g. feeling active, lively, enterprising) [26]. On a 5-point Likert scale, ranging from 0 — *not at all* to 4 — *extremely*, patients rate to what extent they experienced each mood state lately. Total scores for each subscale range from 0 to 40. The GMS is a reliable and valid measure of positive and negative mood states [26]. The GMS was developed to measure emotional distress in cardiac patients, as an alternative to traditional psychometric scales that may be burdensome to complete for cardiac patients who are not psychiatric patients and may not recognize themselves in the traditional psychometric scales, but do report feelings of fatigue [26]. These mood states represent independent mood dimensions.

#### 2.2.2. Depressive symptoms

The Beck Depression Inventory (BDI) is a 21-item self-report questionnaire that assesses the presence and severity of depressive symptoms [27]. The BDI can be subdivided in two subscales, with items 1–13 measuring cognitive-affective symptoms of depression (e.g., feeling guilty, shame, pessimism, sense of failure) and items 14–21 measuring somatic symptoms of depression (e.g., sleep disturbance, fatigue, loss of appetite, loss of libido) [27]. Each BDI item is rated on a Guttmann scale from 0 to 3, with total BDI scores ranging from 0 to 63 and scores $\geq$10 indicating clinically relevant levels of depressive symptoms [27]. The BDI is a reliable and valid measure of depressive symptomatology and it is most frequently used in cardiac patients.

### 2.3. Demographic and clinical variables

Demographic variables included gender, age, and marital status (having a partner vs. not having a partner) and were obtained via self-report. Clinical variables included ICD indication (primary vs. secondary prevention), cardiac resynchronization therapy (CRT; ICD vs. CRT-D), etiology (ischemic vs. non-ischemic cardiomyopathy), decreased ejection fraction (LVEF $\leq$35% vs. >35%), diabetes, smoking, ACE inhibitors, and beta blockers. These clinical variables were obtained from medical records at baseline, except for smoking which was assessed via self-report.

The occurrence of shocks was obtained from medical records, with electrophysiologists judging the appropriateness of ICD therapies on the basis of intracardiac electrograms. Only the most aggressive treatment per episode was counted, meaning that if a patient experienced a ventricular arrhythmia for which first ATPs were delivered and then shocks, this episode was only counted as one shock.

These demographic and clinical variables were selected as covariates, because they are related to mortality, are of importance in the ICD population, and have been used in other studies that investigated the relationship between distress and mortality in cardiac patients.

### 2.4. Mortality

Medical records were checked to see when the patient had last visited the hospital or when a patient had died. If information from the hospital was inaccurate or when a patient had died, the treating cardiologist or general practitioner was consulted for mortality status and cause of mortality. Both all-cause and cardiac-related mortalities were included as endpoints.

### 2.5. Statistical analyses

The frequency distribution of each variable is first examined for missing data. Cases with missing values on most of the baseline measurements of GMS items, BDI items and clinical variables are excluded from the analysis. If a case has a missing value on follow-up measurements for GMS and BDI, this missing value was imputed with the average of existing scores. In total, 21 patients had no score at the 2-month timepoint, 38 patients at 12-months and 66 patients at 18-months follow-up.

Baseline characteristics of the patients with respect to the mortality status of the patients at the end of the study are examined. The Chi-square test is used to compare binary categories while a t-test for independent samples is used to compare the averages of alive and dead patients on baseline continuous variables.

We fit a series of Cox regression models using the baseline measurements to determine the univariable effect of each variable on mortality over time. Next, multivariable Cox regression models are fitted, including GMS Negative Mood and GMS Positive Mood in the first model, the BDI total score in the second model, and BDI Somatic Symptoms and BDI Cognitive-Affective Symptoms in the third model. The first series of analyses include baseline measurements of GMS and BDI scales and the secondary series of analyses include the follow-up measurements on GMS and BDI scales as time dependent variables. In determining the independent effects of GMS and BDI scales on mortality, we decided a priori to control for the demographic variables age, gender and relationship, and the clinical variables indication, CAD, CRT, LVEF, diabetes, smoking, beta-blockers, ACE inhibitors, appropriate shocks, and inappropriate shocks. Finally, if two or more GMS or BDI subscales were significantly related to mortality, these were entered in one covariate-adjusted model to determine their independent predictive value for mortality. The hazard ratio (HR) and 95% confidence intervals for the HR are reported. To illustrate the results using plots of survival functions, categorical variables were constructed for the psychological variables that were significantly related to mortality. The categories were made with the median score at baseline as cut-off, with patients with a score below or equal to the median value being classified to the low group and those patients with scores greater than the median value being classified in the high group. All analyses were performed for all-cause mortality and cardiac-related mortality.

All tests are two sided and a p-value below 0.05 indicates a statistically significant effect. All analyses were performed using SPSS.17 for Windows.

## 3. Results

### 3.1. Patient characteristics and mortality

Among 645 patients whose data on demographic and clinical variables are obtained at baseline as well as GMS and BDI assessments at follow-up, 591 (91.6%) are included in the analysis. Patients who were not included in the analysis had missing data on the baseline measurements, on GMS and/or BDI items and/or on clinical variables. Included patients differed from patients who were not included on age (62.6 $\pm$ 10.1 years vs. 66.8 $\pm$ 9.6 years, $t = 3.0$, $df = 643$, $p = .003$), marital status (not having a partner: 26.8% vs. 13.2%, chi-square = 7.6, $df = 1$, $p = .006$), and ICD indication (secondary prevention: 52.8% vs. 35.7%, chi-square = 6.1, $df = 1$, $p = .013$). No differences were found on other baseline variables.

The median follow-up period is 1150 days (range 281 to 2384 days) or about 3.2 years (range 0.8 to 6.5 years). By the end of the study period (at least January 1, 2009), 16.2% (n = 96) of the patients had died from all-causes and 11.7% (n = 69) had died from cardiac-related causes. Table 1 shows demographic, clinical, and psychological characteristics of both the total sample (n = 591) and

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**Table 1**
Summary of patient characteristics by all-cause mortality.

| Characteristics | N (%) | Mortality (%) | p |
|---|---|---|---|
| Total | 591 | 16.2 | |
| Gender | | | |
| Male | 477 (80.7) | 17.0 | 0.320 |
| Female | 114 (19.3) | 13.2 | |
| Relationship | | | |
| Yes | 511 (86.5) | 16.2 | 0.999 |
| No | 80 (13.5) | 16.3 | |
| Smoker | | | |
| No | 486 (82.2) | 16.3 | 0.987 |
| Yes | 105 (17.8) | 16.2 | |
| CRT | | | |
| No | 412 (69.7) | 12.6 | **<0.001** |
| Yes | 179 (30.3) | 24.6 | |
| Diabetes | | | |
| No | 483 (81.7) | 14.9 | 0.062 |
| Yes | 108 (18.3) | 22.2 | |
| LVEF | | | |
| >35% | 102 (17.3) | 8.8 | **0.026** |
| ≤35% | 489 (82.7) | 17.8 | |
| Indication | | | |
| Primary | 380 (64.3) | 16.3 | 0.949 |
| Secondary | 211 (35.7) | 16.1 | |
| CAD | | | |
| No | 161 (27.2) | 11.8 | 0.073 |
| Yes | 430 (72.8) | 17.9 | |
| Beta-blockers | | | |
| No | 106 (17.9) | 22.6 | **0.049** |
| Yes | 485 (82.1) | 14.8 | |
| ACE-inhibitors | | | |
| No | 191 (32.3) | 17.8 | 0.478 |
| Yes | 400 (67.7) | 15.5 | |
| Appropriate shock (18 months) | | | |
| No | 528 (89.3) | 15.0 | **0.014** |
| Yes | 63 (10.7) | 27.0 | |
| Inappropriate shock (18 months) | | | |
| No | 561 (94.9) | 16.2 | 0.949 |
| Yes | 30 (5.1) | 16.7 | |

| | Combined Mean ± SD | Dead Mean ± SD | Alive Mean ± SD | p-value |
|---|---|---|---|---|
| Age (years) | 62.7 ± 10.1 | 66.6 ± 8.5 | 61.9 ± 10.3 | **<0.001** |
| GMS Negative Mood | 14.2 ± 10.4 | 18.1 ± 10.7 | 13.4 ± 10.2 | **<0.001** |
| GMS Positive Mood | 19.6 ± 9.0 | 18.3 ± 9.1 | 19.8 ± 8.9 | 0.111 |
| BDI total score | 8.7 ± 6.7 | 10.6 ± 6.9 | 8.3 ± 6.5 | **0.002** |
| BDI Cognitive-Affective Symptoms | 3.6 ± 4.2 | 4.1 ± 4.3 | 3.5 ± 4.2 | 0.245 |
| BDI Somatic Symptoms | 4.6 ± 3.1 | 6.0 ± 3.3 | 4.4 ± 3.0 | **<0.001** |

CAD = coronary artery disease; CRT = cardiac resynchronization therapy; LVEF = left ventricular ejection fraction; N = number; SD = standard deviation.
Significant p-values are highlighted in bold face.

stratified by all-cause mortality status at the end of the study. Based on p-values, age, CRT, LVEF, beta-blockers, appropriate shocks, GMS Negative Mood, BDI total score, and BDI Somatic Symptoms were significantly associated with all-cause mortality status. Similar results were found for cardiac-related mortality, although only a trend was found for LVEF ($p = 0.096$) and non-significance was found for appropriate shocks ($p = 0.130$). These comparisons do not take time until death into account, nor do they control for the effect of the other variables.

### 3.2. Univariable predictors of all-cause and cardiac-related mortality

Univariable Cox regression analyses showed that GMS Negative Mood was statistically significant related to mortality rate (all-cause death: HR = 1.040, 95% CI = 1.020–1.059, $p<0.001$; cardiac-related death: HR = 1.053, 95% CI = 1.029–1.077, $p<0.001$), with patients with higher negative mood dying sooner, while GMS Positive Mood was not (all-cause death: HR = 0.984, 95% CI = 0.962–1.006, $p = 1.153$; cardiac-related death: HR = 0.981, 95% CI = 0.956–1.007, $p = 0.156$). BDI Cognitive-Affective symptoms were also not significantly related to mortality rate (all-cause death: HR = 1.024, 95% CI = 0.980–1.069, $p = 0.290$; cardiac-related death: HR = 1.024, 95% CI = 0.973–1.076, $p = 0.354$), while the BDI total score (all-cause death: HR = 1.040, 95% CI = 1.014–1.067, $p = 0.003$; cardiac-related death: HR = 1.049, 95% CI = 1.019–1.080, $p = 0.001$) and BDI Somatic Symptoms (all-cause death: HR = 1.136, 95% CI = 1.074–1.200, $p<0.001$; cardiac-related mortality: HR = 1.176, 95% CI = 1.105–1.251, $p<0.001$) were related to mortality, with higher BDI scores entailing a higher mortality risk.

Age (all-cause death: HR = 1.057, 95% CI = 1.032–1.083, $p<0.001$; cardiac-related death: HR = 1.054, 95% CI = 1.025–1.084, $p<0.001$), CRT (all-cause death: HR = 1.994, 95% CI = 1.334–2.980, $p = 0.001$; cardiac-related death: HR = 2.421, 95% CI = 1.509–3.884, $p<0.001$), LVEF (all-cause death: HR = 2.417, 95% CI = 1.215–4.805, $p = 0.012$; cardiac-related death: HR = 2.200, 95% CI = 1.006–4.813, $p = 0.048$), diabetes (all-cause death: HR = 1.682, 95% CI = 1.059–2.672, $p = 0.028$), and use of beta blocker (cardiac-related death: HR = 0.563, 95% CI = 1.332–0.955, $p = 0.033$) appear to be related to mortality rate among the demographic and clinical variables. Appropriate shocks (all-cause death: HR = 1.637, 95% CI = 0.968–2.767, $p = 0.066$; cardiac-related death: HR = 1.456, 95% CI = 0.764–2.778, $p = 0.254$) were marginally related to mortality and inappropriate shocks (all-cause death: HR = 1.092, 95% CI = 0.443–2.689, $p = 0.848$; cardiac-related death: HR = 1.546, 95% CI = 0.622–3.847, $p = 0.349$) were not related to mortality.

### 3.3. Multivariable predictors of all-cause mortality

The first multivariable model indicated that the GMS Negative Mood was still significantly related to mortality (Table 2), with a 1 unit increase in the baseline GMS Negative Mood score increasing the hazard rate by 3.4%, keeping other variables constant. Baseline GMS Positive Mood was not related to mortality. The second multivariate model showed that the baseline BDI total score was significantly related to the rate of mortality (HR = 1.031, 95% CI = 1.003–1.059, $p = 0.030$) (table not shown). The third model showed that baseline BDI Somatic Symptoms were still significantly related to mortality (Table 2), with a 1 unit raise in score increasing the mortality rate by 13.0% keeping the other variables in the model constant. BDI Cognitive-Affective symptoms were not predictive. The final multivariable model with GMS Negative Mood and BDI Somatic Symptoms showed that GMS Negative Mood remained significant (HR = 1.039, 95% CI = 1.010–1.068, $p = 0.009$) but BDI Somatic Symptoms did not (HR = 0.988, 95% CI = 0.911–1.073, $p = 0.78$) (table not shown). These latter results should be interpreted with caution given the high correlation between GMS Negative Mood and BDI Somatic Symptoms ($r = 0.69$).

Secondary analyses showed similar results, with a significant increased risk for the time-varying covariates of GMS Negative Affect (HR = 1.047, 95% CI = 1.024–1.069, $p<0.001$), BDI total score (HR = 1.038, 95% CI = 1.012–1.065, $p = 0.004$), and BDI Somatic Symptoms (HR = 1.150, 95% CI = 1.069–1.237, $p<0.001$), indicating that a 1 unit increase in for instance GMS Negative Affect at any of the follow-up time points is associated with a 4.7% increase in mortality risk.

Older age, CRT, and appropriate shocks were significantly related to mortality rate in multivariable baseline and follow-up Cox models among the demographic and clinical variables.

Fig. 1 shows the plots of survival functions, with separate curves for low and high groups of GMS Negative Mood and BDI Somatic Symptoms after keeping demographic and clinical variables constant. The difference is large and clearly visible for both variables, with death occurring sooner in patients with high scores on these variables.

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**Table 2**
Multivariable Cox regression models for all-cause death.

| | GMS scales | | | BDI scales | | |
|---|---|---|---|---|---|---|
| | HR | 95% CI | *p* | HR | 95% CI | *p* |
| Centered age (years) | 1.053 | 1.025, 1.081 | <**0.001** | 1.046 | 1.018, 1.074 | <**0.001** |
| Gender (female) | 0.804 | 0.451, 1.430 | 0.457 | 0.770 | 0.434, 1.366 | 0.371 |
| Relationship (yes) | 0.850 | 0.460, 1.571 | 0.605 | 0.902 | 0.488, 1.667 | 0.742 |
| Secondary prevention | 0.874 | 0.533, 1.432 | 0.593 | 0.859 | 0.524, 1.409 | 0.548 |
| CAD | 1.278 | 0.736, 2.217 | 0.383 | 1.347 | 0.777, 2.333 | 0.288 |
| CRT | 1.571 | 0.995, 2.479 | 0.052 | 1.582 | 1.071, 2.541 | **0.024** |
| LVEF≤35% | 1.402 | 0.637, 3.086 | 0.402 | 1.421 | 0.648, 3.117 | 0.381 |
| Diabetes | 1.349 | 0.826, 2.204 | 0.232 | 1.398 | 0.861, 2.271 | 0.175 |
| Smoker | 1.136 | 0.657, 1.964 | 0.647 | 1.091 | 0.632, 1.885 | 0.754 |
| Beta-blockers | 0.644 | 0.402, 1.033 | 0.068 | 0.712 | 0.439, 1.155 | 0.169 |
| ACE-inhibitors | 0.770 | 0.502, 1.182 | 0.232 | 0.760 | 0.496, 1.164 | 0.207 |
| Appropriate shocks | 2.304 | 1.308, 4.060 | **0.004** | 2.206 | 1.248, 3.599 | **0.006** |
| Inappropriate shocks | 0.921 | 0.369, 2.300 | 0.860 | 0.872 | 0.350, 2.173 | 0.769 |
| GMS negative mood[a] | 1.034 | 1.012, 1.056 | **0.002** | | | |
| GMS positive mood[a] | 1.007 | 0.981, 1.033 | 0.605 | | | |
| BDI Somatic Symptoms[a] | | | | 1.130 | 1.042, 1.226 | **0.003** |
| BDI Cognitive-affective Symptoms[a] | | | | 0.968 | 0.910, 1.028 | 0.289 |

CAD = coronary artery disease; CI = confidence interval; CRT = cardiac resynchronization therapy; HR = Hazard ratio; LVEF = left ventricular ejection fraction.
[a] Baseline measurement.

### 3.4. Multivariable predictors of cardiac-related mortality

Table 3 shows that similar results were found for cardiac-related mortality, with a 1 unit increase being associated with a 4.0% increased risk of mortality for baseline GMS Negative Affect, a 3.9% increased risk for baseline BDI total score (data not shown) and a 21.3% increased risk for BDI Somatic Symptoms. Also, independent predictive risks were found for follow-up GMS Negative Affect (HR = 1.054, 95% CI = 1.028–1.081, p<0.001), BDI total score (HR = 1.047, 95% CI = 1.017–1.078, p = 0.002), and BDI Somatic Symptoms (HR = 1.191, 95% CI = 1.096–1.294, p<0.001).

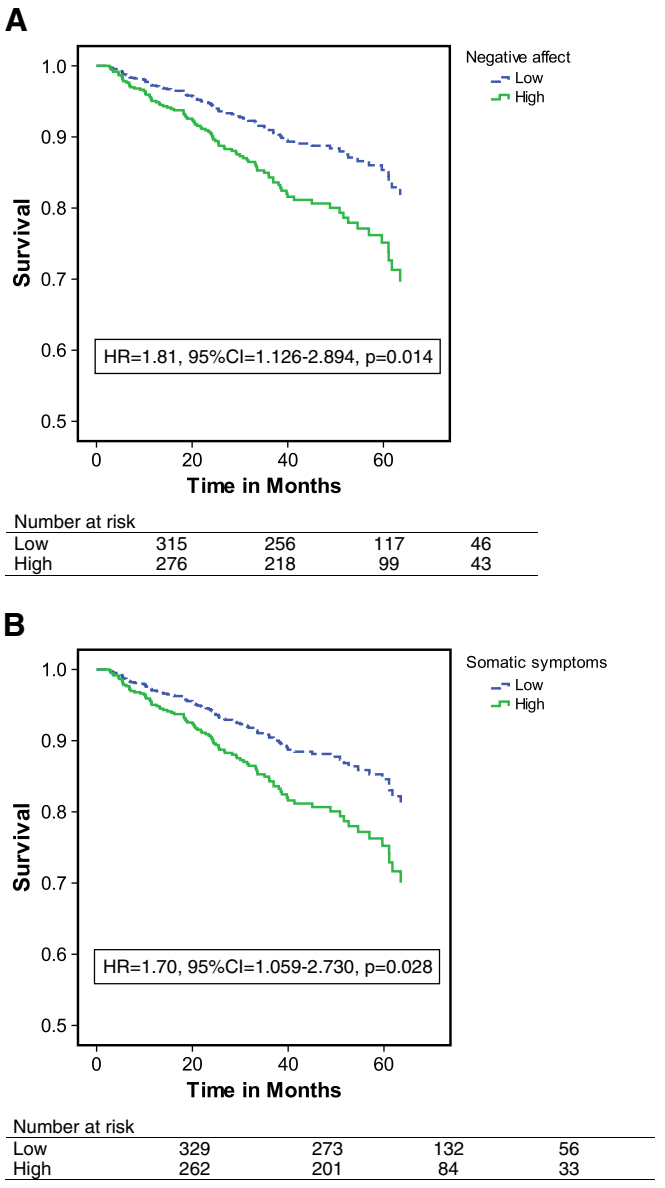


**Fig. 1.** Curves of survival probability over time for GMS Negative Mood [A] and BDI Somatic Symptoms [B] in multivariable models.

## 4. Discussion

The findings of this prospective study indicate that emotional distress is related to all-cause as well as cardiac-related mortalities in patients with an ICD. Particularly general negative mood and somatic symptoms of depression predicted mortality.

Positive mood as measured by the GMS was not related to mortality. This corroborates results from at least one study in coronary patients that also used the GMS and demonstrated that changes in positive mood were unrelated to mortality [28], but it is in contrast to other studies that demonstrated a higher mortality risk in cardiac patients with reduced positive mood [23,24]. We can only speculate why we found no association. The actual effect of reduced positive mood for mortality may be small and our sample may have been too small to detect this effect. It is also possible that the GMS and the Hospital Anxiety and Depression Scale, which was used in one of the positive studies, are fundamentally different measures of positive mood.

Previous studies have shown that psychological factors, such as ICD concerns [11], the distressed personality [11], and impaired quality of life [10] are associated with mortality in ICD patients. We extend the literature in ICD patients with the current findings that general negative mood is also associated with mortality. A total score of depression has been related to mortality in other cardiac populations [14,16], but not in the ICD population [13] or in cancer population [18,29]. The depression-associated risk of mortality may be more driven by somatic symptoms of depression, rather than cognitive affective symptoms of depression [22], which we were able to confirm in this cohort of ICD patients. The mortality risk associated with somatic symptoms may only be partially attributable to markers of disease status, as the risk was independent of ICD indication, CRT, CAD, LVEF and occurrence of shocks, and thus independent of disease severity, which was also found in previous studies [22].

Several behavioral and clinical factors may serve as mechanisms in the relationship between negative mood and mortality. Results among cardiac patients suggest that patients who were depressed

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**Table 3**
Multivariable Cox regression models for cardiac-related death.

| | GMS scales | | | BDI scales | | |
|---|---|---|---|---|---|---|
| | HR | 95% CI | p | HR | 95% CI | p |
| Centered age (years) | 1.048 | 1.017, 1.081 | **0.002** | 1.038 | 1.006, 1.070 | **0.018** |
| Gender (Female) | 0.869 | 0.452, 1.670 | 0.673 | 0.796 | 0.415, 1.528 | 0.492 |
| Relationship (yes) | 0.908 | 0.450, 1.833 | 0.789 | 1.024 | 0.509, 2.062 | 0.946 |
| Secondary prevention | 1.015 | 0.565, 1.822 | 0.961 | 1.003 | 0.556, 1.811 | 0.992 |
| CAD | 1.148 | 0.616, 2.139 | 0.663 | 1.247 | 0.669, 2.327 | 0.487 |
| CRT | 1.857 | 1.081, 3.189 | **0.025** | 2.007 | 1.172, 3.436 | **0.011** |
| LVEF≤35% | 1.225 | 0.495, 3.033 | 0.660 | 1.192 | 0.481, 2.951 | 0.705 |
| Diabetes | 1.157 | 0.638, 2.099 | 0.631 | 1.176 | 0.650, 2.127 | 0.592 |
| Smoker | 1.212 | 0.643, 2.285 | 0.553 | 1.176 | 0.624, 2.216 | 0.615 |
| Beta-blockers | 0.570 | 0.332, 0.981 | **0.043** | 0.651 | 0.373, 1.135 | 0.130 |
| ACE-inhibitors | 0.854 | 0.512, 1.424 | 0.544 | 0.841 | 0.505, 1.403 | 0.508 |
| Appropriate shocks | 1.976 | 0.989, 3.948 | 0.054 | 1.826 | 0.910, 3.665 | 0.090 |
| Inappropriate shocks | 1.410 | 0.556, 3.576 | 0.469 | 1.261 | 0.499, 3.192 | 0.624 |
| GMS Negative Mood[a] | 1.049 | 1.023, 1.076 | <**0.001** | | | |
| GMS Positive Mood[a] | 1.013 | 0.983, 1.044 | 0.413 | | | |
| BDI Somatic Symptoms[a] | | | | 1.213 | 1.106, 1.330 | <**0.001** |
| BDI Cognitive-affective Symptoms[a] | | | | 0.932 | 0.867, 1.003 | 0.059 |

CAD = coronary artery disease; CI = confidence interval; CRT = cardiac resynchronization therapy; HR = Hazard ratio; LVEF = left ventricular ejection fraction.
[a] Baseline measurement.

displayed poor medication adherence [30] and physical inactivity [14]. Patients with mood disorders may have more comorbidities than patients without mood disorders [14]. In addition, disturbed autonomic balance, indicated by low heart rate variability, may be an important mediator in the relationship between depression and mortality in cardiac patients [31,32], including ICD patients [33]. Specifically somatic symptoms of depression have been related to lower heart rate variability in patients with stable coronary heart disease, while cognitive depressive symptoms were not [34]. This finding could explain why only somatic symptoms of depression are related to mortality. Finally, the relationship between negative emotions and mortality may be explained by the increased risk of arrhythmias and ICD shocks in patients with chronic levels of negative emotions [9] and depression [8]. Shocks were related to mortality in the current study, as well as in previous studies [35]. The increased arrhythmia risk in these distressed patients may again be related to disturbed autonomic balance.

A number of limitations must be acknowledged. First, we did not have information on physical activity and medication adherence, which are shown to be related to depressive mood [14,30]. Second, depression was assessed with a self report questionnaire where a diagnostic interview may perform better in classifying patients as depressed. Third, information on heart failure symptomatology (i.e., NYHA class) was incomplete and therefore not included in analyses. However, other variables that are related to heart failure severity were included, such as ejection fraction, CRT, and presence of CAD. Of note, CRT, but not EF, was an independent predictor of mortality. Presumably, this is the result of the strong interrelatedness between EF and CRT, with 35.5% of patients with CRT having a low EF compared to 2.0% of patients without CRT ($p<.001$). Fourth, patients that were included in the study were slightly younger and more often married and more often had received the ICD for secondary purposes. However, the impact of these differences on the results is unknown, but may have been small. The strengths of this prospective study include its relatively long follow-up period, the large sample size, and the validated assessment of psychological variables.

Future studies are warranted to further study the relationship between psychological factors and mortality in ICD patients, as this study is only one of the few studies investigating this topic. Future studies should examine the impact of a clinical diagnosis of depression as assessed with a structured interview. In addition, research should focus on behavioral and clinical mechanisms that may explain this relationship. When research is directed at the impact of depression, it seems important to differentiate somatic symptoms of depression from cognitive-affective symptoms of depression. Finally, future research may examine whether the impact of emotional distress on mortality is age-dependent.

Awareness and timely identification of ICD patients with general negative mood states and specifically somatic symptoms of depression seems warranted, as depressed patients have an increased risk for mortality, which has been shown in several studies in other cardiac and non-cardiac patients, and for new life-threatening arrhythmias. Patients may be screened for depression with the BDI and for negative mood with the GMS, which are short self-report questionnaires that can easily be interpreted by the health care profession, such as an ICD nurse. Unfortunately, results from large intervention trials in cardiac patients have shown mixed findings. The majority of studies failed to show an improvement of cardiovascular outcomes after treatment of depression [36,37], which may have been caused by a substantial group of patients at increased risk for mortality who did not respond to the depression intervention [38]. Similarly, studies in ICD patients have not yet demonstrated a beneficial effect of psychological interventions on prevention of shocks and mortality [39, 40]. Results from comparable studies in other patient populations are sparse, but point in the same direction [41,42]. Nevertheless an argument has been made that depression is a burden on its own and as such cardiac patients should screened and treated for depression [36,37].

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The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [25].

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