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New onset anxiety and depression in patients with an implantable cardioverter defibrillator during 24 months of follow-up (data from the national DEFIB-WOMEN study)

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ABSTRACT

Objective: To examine the cumulative incidence of and covariates’ association with new onset anxiety and depression in implantable cardioverter defibrillator (ICD) patients during 24 months of follow-up in patients without depression and anxiety at implant.

Methods: Patients (n = 1040; 155 (14.9%) women; mean age: 64.2 ± 10.6) with a first-time ICD enrolled in the national, multi-center prospective observational DEFIB-WOMEN study comprised the study cohort. We obtained information on demographic and clinical data from the Danish Pacemaker and ICD Register.

Results: During 24 months of follow-up, 138 (14.5%) patients developed new onset anxiety and 109 (11.3%) new onset depression. Age ≥ 60 [HR:0.60;95%CI:0.40–0.90] and an anxiety score between 3 and 4 [HR:2.85; 95%CI:1.71–4.75] and 5–7 [HR:5.97; 95%CI:3.77–9.45] on the Hospital Anxiety and Depression Scale (HADS) were associated with different hazards of new onset anxiety during follow-up. Age ≥ 60 [HR:0.62;95%CI:0.42–0.93] and a HADS depression score between 3 and 4 [HR:2.99;95%CI:1.80–4.95] and 5–7 [HR:6.45; 95%CI:4.12–10.10] were associated with different hazards of new onset depression.

Conclusion: During 24 months of follow-up, respectively 14.5% and 11.3% of patients developed new onset anxiety and depression, suggesting that screening patients at several timepoints, and in particular those with even minimally elevated HADS scores at baseline, may be warranted to identify patients at risk for poor health outcomes.

1. Introduction

The implantable cardioverter defibrillator (ICD) is the treatment of choice for primary and secondary prevention of sudden cardiac death in patients at risk of life-threatening arrhythmias due to significant risk reductions in arrhythmic death and all-cause mortality compared to anti-arrhythmic drugs [1]. Overall, patients adjust well to living with an implantable cardioverter defibrillator (ICD) but 10%–20% report clinically relevant levels of anxiety and depression [2–4] that may compromise their quality of life (QoL) and increase risk of ventricular tachyarrhythmias and mortality [5,6].

Research in the ICD population has primarily focused on the prevalence of anxiety and depression at the time of implant or changes in symptoms over time. The literature shows that distress in patients tend to abate over time up to 3 months of follow-up post implant, after which symptom levels tend to stabilize. Although this is good news for patients,
this approach may have led us to overlook patients at risk. A study of
patients undergoing a percutaneous coronary intervention showed that
of patients free of depressive symptoms at 6 months (baseline in the
study) 8% developed depression up to 12 months [7]. New onset
depression could not be attributed to a new cardiac event during follow-
up. However, both diabetes and the distressed personality type (Type D)
were associated with new onset depression, with the incidence of
depression more than doubling per risk factor [7].

To our knowledge, no study has examined the incidence of new onset
anxiety and depression in ICD patients and the association of covariables
with the hazard of new onset. Identification of patients at risk of new
onset distress after implantation is important due to potential impair-
ments to their QoL [4,8], and risk of non-adherence, ventricular
tachyarrhythmias and mortality [5,6]. Hence, the aims of the current
study were to examine (i) the cumulative incidence of new onset anxiety
and depression during 24 months of follow-up, defined by an increased
symptom level (cut-off ≥8 on the Hospital Anxiety and Depression Scale
(HADS), as also used by others [9], referred to as anxiety and depres-
sion in the remainder of the article, and (ii) the association of covariables
with the hazard of new onset anxiety and depression in a national cohort
of ICD patients with a first-time ICD implant without clinical levels of
anxiety and depression at the time of implant. We hypothesized that
some patients, free of symptoms of anxiety and depression at the time of
implant, would develop new-onset symptoms during the follow-up
period, as shown in other cardiac populations [7,9].

2. Methods

2.1. Study design, eligibility criteria and recruitment

DEFIB-WOMEN (Utilization of implantable cardioverter DEFIBril-
lator therapy in the treatment of heart disease: Clinical and psycholog-
ical outcomes in WOMEN) is a national, multi-center, prospective,
observational study of patients with a first-time ICD, designed a priori to
examine potential sex differences in patient-reported outcomes (PROs)
[10]. A consecutive cohort of patients who received a first-time ICD
between June 2010 to April 2013 at one of the five implanting hospitals
(Odense University Hospital, Aarhus University Hospital, Aalborg Uni-
versity Hospital, Copenhagen University Hospital and Gentofte Uni-
versity Hospital) comprised the patient cohort [2]. Patients were
approached one day post implantation and prior to discharge from
hospital for study participation if they fulfilled all the inclusion criteria
and none of the exclusion criteria. All patients received written and oral
information about the study. Patients willing to participate were asked
to sign an informed consent form and complete a set of standardized and
validated questionnaires, which they were asked to return within one
week in a self-addressed, stamped envelope. Patients would receive a
reminder by mail including another questionnaire, if the first one was
not returned within one week. The same procedure was used for the
follow-up questionnaires. Information on demographic and clinical
characteristics was obtained from the Danish Pacemaker and ICD Reg-
ister or purpose-designed questions in the questionnaires.

Patients were eligible for inclusion, if they had a first-time single- or
dual-chamber ICD or ICD with cardiac resynchronization therapy (CRT-
D) and were ≈18 years of age. Patients were excluded, if they had a
history of severe psychiatric illness, were on the waiting list for heart
transplantation, had a left ventricular assist device, or insufficient
knowledge of the Danish language to complete the questionnaires. In
addition to the inclusion and exclusion criteria for the overall DEFIB-
WOMEN study, due to the objective of the current sub-study focusing
on new onset depression and anxiety, we chose for a conservative
strategy to ensure we had a "clean" cohort with no indication of psy-
chological issues. Hence, we also excluded patients with an indication of
a psychological condition (i.e., baseline symptoms of anxiety or
depression (cut-off ≥8 on the HADS), prescribed psychotropic medica-
tion, in treatment for a psychological condition), and patients with a
missing HADS-A or HADS-D score at baseline, patients with no other
measurement of HADS-A and HADS-D than at baseline, with missing
HADS-A and HADS-D measurements during follow-up. We do not know
if patients excluded due to these criteria had been diagnosed with prior
depression or anxiety, but that might be the case for some of the
excluded patients.

The study was conducted according to the principles of the Helsinki
Declaration. Permission was granted by the Danish Data Protection
Agency to conduct the study and we obtained permission to use data
from the Danish Pacemaker and ICD Register. The study protocol was
submitted to the Regional Committees on Health Research Ethics for
Southern Denmark. According to Danish law, official ethics approval
related to health research (14, 1), such as the DEFIB-WOMEN study, is
not required [decision on 25 February 2010].

2.2. Demographic and clinical variables

We obtained information on patients' demographic and clinical
variables from the Danish Pacemaker and ICD Register, patients' elec-
tronic health records, and via purpose-designed questions in the ques-
tionnaire that also included standardized and validated questionnaires,
as described in the following section. Information included age, sex,
marital status, working status, smoking, educational level, device type,
New York Heart Association (NYHA) functional class, left ventricular
ejection fraction (LVEF), indication for the ICD (secondary prophylactic
indication [e.g., patients with a history of dangerous sustained ventricular
arythmia] versus primary prophylactic indication [e.g., patients with a
medical condition that places them at increased risk for such arrhythmias and
sudden cardiac arrest] [1], QRS duration, cardiac diagnosis at implant,
procedures prior to implant (e.g., percutaneous coronary intervention
(PCI) and coronary artery bypass surgery (CABG)), medication, and
device therapies (e.g., shocks) during follow-up.

2.3. Description of questionnaires

2.3.1. The hospital anxiety and depression scale (HADS)

The Hospital Anxiety and Depression Scale (HADS) is a self-report
measure of symptoms of anxiety and depression that has been vali-
dated and frequently used in patients with heart disease [11]. The HADS
consists of 14 items, with 7 items contributing to the anxiety subscale
and 7 items contributing to the depression subscale. Items are rated on a
4-point Likert scale from 0 to 3, with the anxiety and depression subscale
scores ranging from 0 to 21. A high score indicates increased symptom
levels. In the current study, we used a cut-off ≥8 to classify patients with
anxiety and depression, as this cut-off reflects a clinically relevant
symptom level and has been associated with increased risk of mortality
in ICD patients [6]. Patients completed the HADS at baseline, 3-, 6-, 12-
and 24 months post implant.

2.3.2. The type D scale

The Type D Scale (DS14) is a 14-item scale that typifies individuals
into a Type D versus a non-Type D personality, based on scores on the
two sub-scales Negative Affectivity (NA) and Social Inhibition (SI). The
14 items are answered on a five-point Likert scale (0 = false, 4 = true),
with NA and SI sum scores ranging from 0 to 28 [12]. Item Response
Theory has shown that a cut-off of ≥10 on both sub-scales is the most
optimal for determining Type D [12]. Individuals with a Type D per-
sonality are prone to experience increased negative emotions and unease
(e.g., "I often feel unhappy") worries and irritation (e.g., "I often find
myself worrying about something"), feel discomfort (e.g., "I am a closed
kind of person") and lack of social confidence (e.g., "I often feel inhibited
in social interactions"). We assessed Type D, as patients with this per-
sonality type have been shown to report poorer PROs, including QoL,
anxiety and depression, and to have a worse prognosis, although more
recent studies show mixed results with respect to prognosis [13]. Pa-
ients completed the Type D Scale at baseline.
2.3.3. Short form health survey 36

We assessed physical QoL with the Short Form Health Survey 36 (SF-36) [14] at baseline and at 3-, 6-, 12-, and 24 months post implantation. The SF-36 consists of 36 questions that contribute to 8 subscales: Physical Functioning (PF), Role-Physical Functioning (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Role-Emotional Functioning (RE), and Mental Health (MH). Based on the 36-items, it is also possible to generate a Physical Component Summary (PCS) and Mental Component Summary (MCS). All 8 subscales contribute to both the PCS and MCS, based on a weighting system. Using an algorithm, responses to the individual items are transferred to scale scores that range from 0 to 100, with 100 representing the best QoL, except for Bodily Pain, where 100 reflects the total absence of pain. In the current study, we adjusted for PCS at baseline, as poor physical functioning has been associated with risk of anxiety and depression [15].

2.4. Statistical analyses

Differences on baseline demographic and clinical characteristics between patients stratified by sex were compared with the Chi-square test for categorical variables and student’s t-test for independent samples for continuous variables. Cox regression survival models and discrete survival models were used to estimate the association of covariates (i.e., sex, age, marital status, smoking, working, education, NYHA class, indication for ICD, Type D personality, ICD type, shocks during follow-up, physical functioning, cardiac diagnosis at implant, and baseline HADS scores) with the hazard of time to new onset anxiety and depression separately, treating deaths as censored. These covariates were selected a priori based on the literature (e.g., [5,8,13,16]). Both univariable and multivariable models were fitted. We intended to include the variable shocks as time-dependent variable during the 24-months follow-up period. However, shocks predicted non-failures perfectly for time to onset of depression. Therefore, only baseline covariates were included in the analysis of depression. We performed sensitivity analyses, using discrete cloglog survival models. We used Nelson-Aalen graphs to illustrate the cumulative hazard estimates for new onset anxiety and new onset depression for the total sample and stratified by sex. All statistical analyses were performed using StataCorp 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC. For all tests, a p-value of less than 0.05 was considered statistically significant.

3. Results

Of 2914 patients who received an ICD between June 2010 and April 2013 at one of the five implanting hospitals in Denmark, 1592 consented to participate in the study and did not withdraw their consent during the study period. Of these patients, 1040 were included in the statistical analyses (see flowchart in Fig. 1). Of the 1040 patients, 155 (14.9%) were women; mean age: 64.2 ± 10.6) and 885 were men; mean age: 65.0 ± 9.8). The number of women and men included in the current study reflects the ratio of women versus men implanted with an ICD in Denmark, as shown in the latest Annual Report from the Danish Pacing and ICD Register from 2017 to 2018, with 214 women (18.8%) and 927 (81.2%) implanted with an ICD [17].

We found some differences between patients included versus excluded in the analyses on sex, age, marital status, smoking, cardiac diagnosis at implant, indication for ICD implant, percutaneous coronary intervention (PCI) prior to implant, Type D personality, physical functioning, and shocks between 0 and 3 months, which was to be expected as the study objective warranted that we exclude patients who had included the variable shocks as time-dependent variable during the 24-months follow-up period. However, shocks predicted non-failures perfectly for time to onset of depression. Therefore, only baseline covariates were included in the analysis of depression. We performed sensitivity analyses, using discrete cloglog survival models. We used Nelson-Aalen graphs to illustrate the cumulative hazard estimates for new onset anxiety and new onset depression for the total sample and stratified by sex. All statistical analyses were performed using StataCorp 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC. For all tests, a p-value of less than 0.05 was considered statistically significant.

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anxiety or depression at baseline or received psychopharmaca (i.e., being treated for anxiety and depression), in order to have a cohort of patients who were free of anxiety and depression at baseline.

Baseline demographic and clinical characteristics of the study population stratified by sex are shown in Table 1 (supplementary material). Men were more likely to be married, to have ischemic heart disease as cardiac diagnosis at implant, to have had a PCI or coronary artery bypass graft surgery (CABG), but less likely to have a LVEF >35% as compared to women. Men were more likely to be in the middle and upper tertile of physical functioning, while women were more likely to be in the lower tertile. Men were also more likely to be prescribed beta-blockers, angiotension-converting enzyme (ACE) inhibitors, and statins as compared to women. We also found differences between men and women on age, with more women being in the age groups 20–49 and 50–59, while men were more likely to be in the age groups 60–69 and ≥70.

Fig. 2 (supplementary material) shows the cumulative hazard estimates for new onset anxiety and new onset depression for the total sample. Fig. 3 (supplementary material) shows the cumulative hazard estimates for new onset anxiety and new onset of depression stratified by sex. These results represent raw percentages, with the number of patients at risk changing per assessment time, not considering patients who died during follow-up or were lost to follow-up. For this reason, we have added Table 1 that takes into account the change in number of patients at risk for new onset anxiety and depression per assessment time (i.e., at 3, 6, 12, and 24 months). As shown in Table 1, during 24 months of follow-up, 138 (14.5%) patients developed new onset anxiety and 109 (11.3%) new onset depression. The covariates age >60 years [HR:0.60; 95%CI: 0.40–0.90] and a HADS baseline anxiety score between 3 and 4 [HR:2.85; 95%CI: 1.71–4.75] and 5–7 [HR:5.97; 95%CI: 3.77–9.45] were associated with different hazards of new onset anxiety during follow-up in adjusted cox regression models (Table 2). Higher age was associated with a 40% reduced risk of new onset anxiety, and a HADS score from 3 to 4 or from 5 to 7 with a higher risk. These results were confirmed in sensitivity analyses using discrete survival models. As shown in Table 3, age >60 years [HR:0.62; 95%CI: 0.42–0.93] and a HADS depression score between 3 and 4 [HR:2.99; 95%CI: 1.80–4.95] and between 5 and 7 [HR:6.45; 95%CI:4.12–10.10] were associated with different hazards of new onset depression. Higher age was associated with a 38% reduced risk of new onset depression, and a HADS score from 3 to 4 or from 5 to 7 with a higher risk. Sensitivity analyses using discrete survival models confirmed these results.

4. Discussion

In the current study, we examined the cumulative incidence of new onset anxiety and new onset depression during 24 months of follow-up in patients with a first-time ICD enrolled in the national DEFIB-WOMEN study without clinical levels of anxiety and depression at the time of implant and the association of covariates with the hazard of new onset anxiety and depression. During 24 months of follow-up, 138 (cumulative incidence: 14.5%) patients developed new onset anxiety and 109 (cumulative incidence: 11.3%) new onset depression. This compares to an average incidence of depression in Denmark in 2010–2012 of 4000 in women and 6500 in men in a population of 5,560,628 [18], equal to 0.7% in women and 0.1% in men. In the same period, the average incidence of anxiety was 10,000 in women and 6500 in men, equal to 1.8% in women and 1% in men [18].

The incidence of depression found in the current study is similar to that found in patients undergoing PCI with drug-eluting stents [7]. In the latter study, the risk associated with Type D personality was 3-fold, while in the current study Type D was not significantly associated with new onset anxiety and depression, likely due to the adjustment of baseline anxiety and depression scores in the current study and the overlap between Type D and HADS. The association of covariates with the hazard of new onset anxiety and depression were similar. Age ≥60 years was protective for both new onset anxiety and depression, while baseline HADS scores between 3 and 4 and 5–7 as compared to a score between 0 and 2 were associated with greater risk of both new onset anxiety and depression. Screening for anxiety and depression with HADS at the time of implant would be useful to identify patients at risk for new onset anxiety and depression, in particular given the finding that a HADS score that is considered mild (3–4 and 5–7) in the current study shows that these patients are at increased risk. A recent study using routine practice data from the British Heart Foundation National Audit of Cardiac Rehabilitation (NACR) found that 20% of patients without initial depression developed new onset depression [19]. Factors associated with risk of onset depression included increased anxiety, physical inactivity, male sex, deprivation, and comorbidities, such as diabetes, stroke, and chronic back pain [19]. The incidence of new onset anxiety and depression found in this study was slightly lower, with 138 (cumulative incidence: 14.5%) and 109 (cumulative incidence: 11.3%), respectively in the first 24 months post implant. In addition, the latter study did not adjust for baseline HADS scores, as was done in the current study, which likely has an influence on the few number of covariate associations found in the current study. Taken together, the identified patients with new onset anxiety and depression and the 459 excluded patients who had anxiety or depression already at baseline or received psychopharmaca in the current study indicate that a considerable number of patients has clinically relevant symptoms of psychological distress that may go unnoticed and untreated [20], unless we screen patients not only at baseline but also several times during follow-up.

4.1. Clinical and research implications

Since we identified the majority of patients with new onset anxiety and depression in the first year post implant and few in the second year, one might argue that it is not worthwhile to screen ICD patients beyond one year post implant. However, given that anxiety and depression are associated with poor QoL and risk of morbidity and mortality in ICD patients [5,6], it is paramount that we identify the subset of patients at risk and offer them treatment for their psychological symptoms as also

### Table 1

<table>
<thead>
<tr>
<th>Months FU</th>
<th>N at risk</th>
<th>No</th>
<th>Yes</th>
<th>Total</th>
<th>Incidencea</th>
<th>New onset anxiety</th>
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<td>6</td>
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<td>64</td>
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<tr>
<td>12</td>
<td>903</td>
<td>74</td>
<td>32</td>
<td>106</td>
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<td>24</td>
<td>797</td>
<td>777</td>
<td>20</td>
<td>797</td>
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<tr>
<td>Total</td>
<td>902</td>
<td>138</td>
<td>1040</td>
<td></td>
<td>14.5%</td>
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</table>

<table>
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<tr>
<th>Months FU</th>
<th>N at risk</th>
<th>No</th>
<th>Yes</th>
<th>Total</th>
<th>Incidencea</th>
<th>New onset depression</th>
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<tr>
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<td>816</td>
<td>800</td>
<td>16</td>
<td>816</td>
<td>2.0%</td>
<td></td>
</tr>
</tbody>
</table>

FU = Follow-up.

* As the number of patients at risk declines per follow-up assessment, the incidence (%) is calculated per follow-up assessment with cases of new onset anxiety and depression in the numerator and the total number of patients at risk in the denominator (e.g., for anxiety, the denominator at 3 months is 1040–73 = 967 and at 6 months 1040–73–64 = 903, respectively).
Table 2: Covariates with associations with new onset anxiety, univariable and multivariable models (Cox regression model and discrete survival model).

**Table 2**

<table>
<thead>
<tr>
<th>Table 2 (continued)</th>
</tr>
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<tbody>
<tr>
<td><strong>Cox regression model</strong></td>
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<tr>
<td><strong>Deaths during follow-up</strong></td>
</tr>
<tr>
<td>REF</td>
</tr>
<tr>
<td>CRT-D (ICD with cardiac resynchronization therapy)</td>
</tr>
<tr>
<td>CRT-D (ICD with cardiac resynchronization therapy) = reference category. 2 Middle = reference category.</td>
</tr>
</tbody>
</table>

For analyses purposes, missings are placed in the largest category.

ICD: Implantable cardioverter defibrillator; NYHA: New York Heart Association functional class; PCS: Physical Component Summary Score (SF-36).

recommended in the guidelines for the management of patients with ventricular arrhythmias [1]. These symptoms are often unrecognized and undertreated [20] partly because systematic screening has not yet been implemented in clinical cardiology practice [21]. In addition, it is important to emphasize that we also had more follow-up and measurement points in the first year (i.e., at 3, 6 and 12 months), while in the second year we only had one measurement point (i.e., at 24 months of follow-up). Potentially, some patients may have developed new onset distress between 12 months and 24 months that we were not able to detect. From a clinical practice perspective, it may be relevant for health care professionals and patients to know that a subset of patients may develop anxiety and depression even up to 24 months post implant. This can be seen as part of patient education and empowerment, so that patients can seek help from their general practitioner in time.

Future studies in ICD patients are warranted to investigate if the results of the current study are replicable in other ICD cohorts and in other countries. We would recommend including more follow-ups than we did in the second year of the DEFIB-WOMEN study to ascertain whether more patients would develop new onset of anxiety and depression symptoms beyond the first year after implant than demonstrated in our study. It will also be important to explore whether screening ICD patients for anxiety and depression combined with psychological treatment lead to better health outcomes. Several societies in Europe and the US have published advisories recommending screening patients with heart disease for anxiety and depression (e.g., [22-24]). This has led to discussions and criticism, as there is no evidence to support this recommendation due to lack of randomized controlled trials combining screening with treatment [25,26]. The CODIACS-QoL study (Comparison of Depression Interventions After Acute Coronary Syndrome: Quality of Life) in patients with ischemic heart disease is the study that the field has been waiting for, as it examined the impact of systematic screening and treatment, however, showing no substantial improvement in QoL, depression free days, mortality, or patient-reported harms [27]. To our knowledge no such study has been conducted in ICD patients, although results will soon be available from the ACQUIRE-ICD study that offered a comprehensive intervention to ICD patients, including systematic screening for anxiety and depression followed by treatment (cognitive behavioral therapy) for the subset of patients who screened positive for anxiety and/or depression [28]. In the future, it would be important to explore whether systematic screening and treatment combined with cardiac rehabilitation would improve outcomes of ICD patients, as some patients post implant feel insecure about engaging in physical activity, increasing the risk of a sedentary lifestyle, anxiety, and depression. Unfortunately, in Denmark, currently ICD patients are not systematically referred to cardiac rehabilitation, as such a program is not yet available.

Table 2: Covariates with associations with new onset anxiety, univariable and multivariable models (Cox regression model and discrete survival model).

<table>
<thead>
<tr>
<th>Cox regression model</th>
<th>Unadjusted HR [95% CI]</th>
<th>p-value</th>
<th>Adjusted HR [95% CI]</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Deaths during follow-up</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>REF</td>
<td>1.00</td>
<td></td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>CRT-D (ICD with cardiac resynchronization therapy)</td>
<td>1.16</td>
<td>0.061</td>
<td>1.27</td>
<td>0.062</td>
</tr>
<tr>
<td>CRT-D (ICD with cardiac resynchronization therapy) = reference category. 2 Middle = reference category.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Covariate associations with new onset depression, univariable and multivariable models (Cox regression model and discrete survival model)

<table>
<thead>
<tr>
<th>Table 3 continued</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cox regression model</td>
</tr>
<tr>
<td>---------------------</td>
</tr>
<tr>
<td>5–7</td>
</tr>
<tr>
<td>7.62 (4.86–11.95)</td>
</tr>
</tbody>
</table>

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a As none of the patients with new onset depression received a shock, this cannot be estimated and was not included in the model.

1 CRT-D [ICD with cardiac resynchronization therapy] = reference category.

2 Middle = reference category.

4.2. Strengths and limitations

The results of the current study should be interpreted with the following limitations in mind. Given the observational study design, we cannot be certain that we included all relevant variables, with the risk that the results might have been influenced by variables that we did not access during follow-up (e.g., acute myocardial infarction and procedures such as PCI and CABG). Another limitation of the study is that the results cannot necessarily be generalized to the entire ICD population, since 54% of patients declined to participate in the study. We did not include other time-dependent variables in the multivariable analyses than shocks during follow-up in order to prevent overfitting of the regression models [29]. We did consider patients who died during follow-up, but it was not possible to make a formal competing risk analysis due to incomplete information on the cause of loss to follow-up, which might influence risk estimates. In addition, we used a self-report measure – the HADS – and a cut-off ≥ 8 to classify patients with anxiety and depression and not a diagnostic interview. However, this cut-off reflects a clinically relevant symptom level and not only a diagnosis but also increased symptom levels have been associated with increased risk of mortality in ICD patients [6]. We used a conservative approach to determine patients at risk for new onset depression and anxiety in order to ensure a “clean” and homogenous group without indication of psychological challenges. Thus, it is only possible to generalize the results to this subset of patients.

Other limitations include that we did not have a control group and therefore cannot say if the new onset rates are normal in the background population. However, when comparing with Danish data from the general population published by the National Board of Health [18], the incidence of new onset depression and anxiety is much higher in the current ICD population. In addition, we decided to analyze onset of anxiety and depression separately, even though some patients develop both. However, we wanted to explicitly investigate differences between these two outcomes with respect to their separate hazard ratios. Given some systematic differences between patients included versus excluded in the analyses, the results cannot be generalized to the entire ICD population. However, these differences were expected given that we excluded patients with a previous psychological condition, those prescribed psychotropic medication or in treatment for a psychological condition, and patients with missing anxiety and depression data.

Despite these limitations, the results of the current study contribute to the existing literature, as to our knowledge this is the first study to examine the incidence of new onset anxiety and depression in patients with an ICD.

5. Conclusion

Taken together, our results show that in clinical practice screening ICD patients at one timepoint (e.g., at the time of implant) will not be sufficient, as 14.5% experienced new onset anxiety and 11.3% new onset anxiety.
depression the first 24 months post implant. Moreover, adding those who were excluded, we reach a substantial number of patients with psychological challenges that may warrant treatment. Our findings also show that patients with even minimally elevated HADS scores at baseline are at greater risk of new onset anxiety and depression, indicating that re-screening this subset of patients may be particularly warranted, as they may be at risk of poor health outcomes. Thus, we may have to consider screening patients at multiple timepoints, which can be done with a brief measure, such as the 4-item Patient Health Questionnaire (PHQ-4) that assesses both symptoms of anxiety and depression [30], when the patient is seen in the outpatient clinic [21,31]. If the patient screens positive, further evaluation may be needed by a mental health professional either as part of the multi-disciplinary team or through a referral, ensuring the correct management and treatment of the patient’s symptoms.

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Declaration of Competing Interest

SSP: Supported with a grant (09-10-R75-A2713-22565) from the Danish Heart Foundation. Consultancy for ReCor Medical (Ultrasound Denervation Therapies).

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.genhosppsych.2021.07.003.

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[18] Authority DH. Disease-burden in Denmark [Disease Burden in Denmark]. 2015.


