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Sex differences in the course of implantable cardioverter defibrillator concerns (Results from the Danish national DEFIB-WOMEN study)

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ABSTRACT

Objective: The implantable cardioverter defibrillator (ICD) is used to treat malignant ventricular arrhythmias. Since 33% of patients experience ICD-related concerns, we examined sex differences in ICD concerns and correlates of ICD concerns during 24 months of follow-up after implantation of an ICD.
Methods: Patients from the DEFIB-WOMEN study ($n = 1515$; 81.6% male patients) completed questionnaires on ICD concerns, anxiety, depression, and Type D personality at five measure points (baseline, 3-, 6-, 12- and 24-months post-implantation).
Results: Male patients scored on average 7.0 (6.8) points on ICD concerns at the time of implantation and female patients scored on average 10.5 (8.2) points. We found statistically significant sex differences in ICD concerns at all measurement points, with female patients scoring 2.77 points (8.7% of the maximum score of 32) higher than male patients. ICD concerns decreased in both sexes the first 6 months and then levelled out. For both sexes, ICD concerns at baseline were significantly correlated with ICD concerns at 24-months follow-up. Anxiety at baseline was correlated with ICD concerns in female patients, while depression at baseline and at least one experienced shock correlated with ICD concerns in male patients.
Conclusion: Female patients reported more ICD concerns at all measurement points compared to male patients, but for both sexes ICD concerns decreased in the first 6 months. ICD shock, anxiety, depression, and ICD concerns at baseline were correlates of ICD concerns at 24-months follow-up.

1. Introduction

Patients who are at risk of or have survived ventricular tachyarrhythmias are offered an implantable cardioverter defibrillator (ICD) to treat the ventricular tachyarrhythmias and thereby improve the patient's survival and clinical outcomes [1,2]. One- and five-year survival rates after implantation are 92% and 68%, respectively [3]. Most patients adapt well to living with an ICD [4] but 20%–30% of patients experience psychological distress, such as anxiety and depression [5]. The distress is partly attributed to the experience or fear of ICD shocks and procedural- and device-related complications (e.g., infection, lead dislodgement, and inappropriate shocks), referred to as ICD concerns. An inappropriate

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shock is defined as the occurrence of shock without any life-threatening arrhythmia, which may lead to patients losing confidence in their device [6,7]. Patients who experience shocks or fear shocks may exhibit avoidance behaviours, live a sedentary lifestyle, experience sexual problems, and have poor quality of life [8]. Distress (e.g., anxiety and depression) in ICD patients is also associated with increased risk of life-threatening arrhythmias and premature death [9–11].

The level of distress that patients experience is associated with their general psychological profile [4], including personality, such as Type D personality (i.e., tendency to experience increased negative emotions paired with emotional non-expression) [12] and lack of optimism [13].

Female patients report higher levels of ICD concerns during the first year following implantation compared to male patients [14]. However, little is known about the evolution of ICD concerns for male and female patients beyond the first 12 months post implantation, and the correlates of ICD concerns.

The objectives of this study were to (i) examine sex differences in the course of ICD concerns 24 months post-implantation and (ii) identify correlates of ICD concerns. We hypothesized that female patients would experience more ICD concerns than male patients during the follow-up period and that anxiety, depression, Type D personality and ICD shocks would be correlates of ICD concerns.

2. Methods

2.1. Design and population

The DEFIB-WOMEN study is a national, multi-centre, longitudinal study conducted in Denmark. A total of 1598 patients were eligible for inclusion into the study. See Fig. S1 displaying the flowchart of number of patients included in the study and the analyses. Patients had an ICD implanted either as primary or secondary prevention between June 2010 and April 2013 at one of the five university hospital implanting centres in Denmark (Aalborg, Aarhus, Odense, Copenhagen, and Gentofte). Inclusion criteria were patients with a first-time ICD or ICD with cardiac resynchronization therapy (CRT—D), >18 years, sufficient Danish language proficiency to complete questionnaires, and providing written informed consent. Exclusion criteria were history of severe psychiatric disorders (e.g., psychosis), on the waiting list for a heart transplant, or having a left ventricular assist device [15].

2.2. Study procedure

Patients were approached for participation the day after their ICD implantation. Participants completed five questionnaires at the following time points: T0 baseline (first week after implantation), T1 three months post-implantation, T2 six months post-implantation, T3 twelve months post-implantation, and T4 24 months post-implantation. Participants who did not return the questionnaire received a reminder one week later.

2.3. Measures

2.3.1. ICD concerns

ICD concerns were assessed at all time points with the eight-item ICD Patient Concerns Questionnaire (see Table S5), with a higher score indicating higher levels of device-related concerns [16]. Items are rated on a five-point Likert scale from 0 (not at all) to 4 (very much so) and summed up to a total score ranging from 0 to 32. Points on the scale can be converted to percentages by dividing number of points on the scale (x) by the maximum score of 32 and multiplying by hundred ($x/32 \times 100$).

2.3.2. Anxiety and depression

Self-reported symptoms of anxiety and depression were assessed at baseline with the Hospital Anxiety and Depression Scale (HADS). The HADS consists of 14 items with 7 items measuring symptoms of depression and 7 items measuring symptoms of anxiety. Each item is rated on a 4-point Likert scale with both anxiety scores and depression scores ranging from 0 to 21. A higher score indicates a higher burden of anxiety/depression symptoms. A cut-off ≥8 reflects a clinically relevant symptom level and has among ICD patients been associated with increased risk of mortality [18,19].

2.3.3. Type D personality

Type D personality was assessed at baseline with the 14-item Type D Scale (DS14) [20]. The DS14 consists of two 7-item subscales that measure negative affectivity (e.g., *"I often feel unhappy"*) and social inhibition (e.g., *"I am a closed kind of person"*). A cut-off ≥10 on both subscales classifies individuals as having a Type D personality, while individuals with a score ≤ 9 are classified as having a non-Type D personality.

2.3.4. Quality of life

Physical quality of life was assessed with the Short Form Health Survey 36 (SF-36) at baseline, 3-, 6-, 12-, and 24-months post implantation. The SF-36 comprises 36 items that can be divided into 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). It is further possible to create a physical component summary (PCS) and mental component summary (MCS) score based on a weighting system of all the 8 subscales [21,22]. In this study, we used the one item on General Health at baseline where patients rate how they in general would say their health is (scored on a 5-point Likert scale ranging from poor to excellent, see Table 1). We also used the aggregated norm PCS score (Dutch normative data were used). The scores range from 0 to 100 with 100 representing the best quality of life on the physical domain.

2.3.5. Demographic and clinical information

Information on demographic and clinical variables was obtained through all-purpose questions in the questionnaires, from patients' medical records, and from the Danish Pacemaker and ICD Register and the Danish National Patient Register. Demographic information includes sex, age, marital status, education, working status, smoking status (smoking now/previously), self-reported contact with a psychologist or psychiatrist.

Clinical information includes indication for ICD implantation (primary – i.e., in patients without previous ventricular tachycardia vs secondary – i.e., in patients with previous ventricular tachycardia), type of ICD (single or dual chamber ICD or CRT—D), shocks, QRS duration (>120 ms), symptomatic heart failure assessed with the New York Heart Association (NYHA) functional class (class I-IV), ischemic heart disease, self-reported medication (i.e., beta-blockers, statins, ACE-inhibitors, digoxin, diuretics, amiodarone, psychopharmaca), and left ventricular ejection fraction (LVEF) > 35%, previous coronary artery bypass surgery (CABG) and previous percutaneous coronary intervention (PCI).

2.4. Statistical analysis

Baseline demographic and clinical characteristics were assessed for sex differences using Student's *t*-test for continuous variables and the Chi-square test for categorical variables, where missing observations were excluded.

The effect of sex on ICD concerns over time was estimated in three multi-level linear mixed models with a random intercept per patient. The crude model (model 1) included only time point (five categories) and sex as fixed covariates, while the second model additionally included the interaction time by sex. The third model adjusted for the following covariates: age (continuous, per 10 years), secondary prevention indication, NYHA class III/IV, LVEF>35%, HADS-anxiety at baseline, HADS-depression at baseline, Type D personality at baseline,

Table 1
Baseline demographic and clinical characteristics of the study population ($N = 1515$), by sex. The reported p-values relate to Chi-square tests for categorical variables and t-tests for continuous variables, where missing categories were excluded.

Characteristics	n missing	Total	Male patients	Female patients	*P*-value
Demographic characteristics		1515 (100)	1236 (100)	279 (100)	
Age, mean (SD)	0	63.6 (10.9)	64.5 (10.0)	59.4 (13.3)	<0.001
Married/partner	6	1168 (77)	973 (79)	195 (70)	<0.001
Education/college level	25	463 (31)	372 (30)	91 (33)	0.281
Working status (yes)	18	304 (20)	256 (21)	48 (17)	0.241
Smoking status, now or previous (yes)	1	948 (63)	812 (66)	136 (49)	<0.001
Clinical characteristics					
ICD type	10				0.208
CRT-D		438 (29)	360 (29)	78 (28)	
Single chamber		708 (47)	587 (47)	121 (43)	
Dual chamber		359 (24)	282 (23)	77 (28)	
Secondary prevention indication	16	651 (43)	524 (42)	127 (46)	0.281
Symptomatic heart failure (NYHA)	157				<0.001
Class I		356 (23)	269 (22)	87 (31)	
Class II		668 (44)	571 (46)	97 (35)	
Class III		330 (22)	267 (22)	63 (23)	
Class IV		4 (0)	4 (0)		
Ischemic heart disease	9	1007 (66)	896 (72)	111 (40)	<0.001
QRS > 120 ms	9	509 (34)	423 (34)	86 (31)	0.305
LVEF>35%	11	467 (31)	351 (28)	116 (42)	<0.001
Previous CABG	16	387 (26)	360 (29)	27 (10)	<0.001
Previous PCI	24	595 (39)	526 (43)	69 (25)	<0.001
Medication and treatment					
Beta-blockers	72	1237 (82)	1028 (83)	209 (75)	0.002
Statins	72	1058 (70)	927 (75)	131 (47)	<0.001
ACE inhibitors	72	1158 (76)	980 (79)	178 (64)	<0.001
Digoxin	72	104 (7)	82 (7)	22 (8)	0.410
Diuretica	72	881 (58)	739 (60)	142 (51)	0.012
Amiodarone	72	152 (10)	132 (11)	20 (7)	0.091
Psychopharmaca	72	169 (11)	124 (10)	45 (16)	0.002
Psychological treatment	7	38 (3)	23 (2)	15 (5)	<0.001
Anxiety, depression, personality and health perception at baseline					
Mean score HADS-Anxiety (SD)	12	4.0 (3.7)	3.7 (3.5)	5.5 (4.2)	<0.001
Mean score HADS-Depression (SD)	12	3.0 (3.1)	2.8 (3.0)	3.8 (3.4)	<0.001
HADS-Anxiety cut-off ≥8	12	259 (17)	184 (15)	75 (27)	<0.001
HADS-Depression cut-off ≥8	12	137 (9)	99 (8)	38 (14)	0.003
	12	231 (15)	181 (15)	50 (18)	0.180
Mean Type D personality (DS-14) (SD)					
Mean PCS of SF-36 (SD)	127	42.0 (9.6)	42.4 (9.5)	40.2 (10.3)	<0.001
SF-36: General Health	40				0.278
Excellent		48 (3)	44 (4)	4 (1)	
Very good		267 (18)	220 (18)	47 (17)	
Good		642 (42)	527 (43)	115 (41)	
Fair		428 (28)	339 (27)	89 (32)	
Poor		90 (6)	73 (6)	17 (6)	

CRT-D: Cardiac Resynchronization Therapy - Device; NYHA: New York Heart Association functional class; LVEF: Left ventricular Ejection Fraction; CABG: Coronary Artery Bypass surgery; PCI: Percutaneous Coronary Intervention; ACE: Angiotensin-Converting Enzyme; HADS: Hospital Anxiety and Depression Scale; PCS: Principal Component Summary.

SF-36 PCS at baseline (continuous), SF-36 General Health item (categorical), as well as for the presence of shocks in the period before. No random coefficients were included in the models. In the third model, observations with missing covariate values were included in the respective reference category instead of excluding these observations.

To investigate the same correlates as above of high levels of ICD concerns at the end of study (i.e., at 24 months post implantation), we first defined high ICD concerns at 24 months as a score above the sex-specific 80th percentile. We then investigated the associations in logistic regression models, stratified by sex. Instead of shocks in the previous period, we considered the binary variable of "at least one shock during the whole period".

To indicate statistical significance, a p-value of <0.05 (two-tailed) was used. Data was analysed using Stata 15.0 (StataCorp LP, TX, USA).

2.5. Ethics

The study was carried out to conform the ethical guidelines of the Helsinki Declaration and participants received both oral and written information about the study, and all patients provided written informed consent. The study protocol for the DEFIB-WOMEN study was submitted to the Regional Committees on Health Research Ethics for Southern Denmark, who stated that no approval was required by Danish law as no biomedical intervention was performed and no biological material was collected. The study was approved by the Danish Data Protection Agency and the legal department at the Odense University Hospital (journal number: 18/25780).

3. Results

3.1. Participants

Of the 2914 patients who received an ICD in the study period, 1598 were eligible to participate in the study. A total of 83 patients were excluded from the analyses: one patient had an unknown vital status, one patient emigrated before baseline, two had their ICD removed before completing the first questionnaire, two reported a diagnosis of schizophrenia, 27 patients had missing scores on baseline ICD concerns, and 50 patients had no other measure of ICD concerns after baseline (Fig. S1). For patient characteristics see Table 1.

3.2. ICD concerns

Female patients scored consistently higher on ICD concerns than

male patients during the entire study period. Both male and female patients' score on ICD concerns decreased in the first 6 months and then levelled during the remaining 18 months (Fig. 1 and Table S1 – see also Table S2 for distribution of ICD concerns score). In regression model 1, the overall sex difference was estimated as 2.77 (95%CI: 2.06;3.48) points ($p < 0.001$), that is, female patients scored on average 2.77 points ($2.77/32 \times 100 = 8.7\%$) higher than male patients on ICD concerns (Table 2). The 2.77 points equals an increase of 67.5% in women compared to the male patients mean score of 4.1 points ($2.77/4.1 \times 100 = 67.5\%$). Introducing an interaction effect (model 2) or other adjustment variables (model 3) improved the model but did not change the overall results on sex. The complete estimation results for model 3 are presented in Table S3.

3.3. Factors correlating with ICD concerns 24 months after implantation

The distribution of ICD concerns as score and the classification into high ICD concerns (yes/no) based on the 80th percentile at 24 months after implantation, overall and by sex, is presented in Table 3. For both sexes, only baseline ICD concerns had a statistically significant association with high ICD concerns at 24 months, with adjusted odds ratios (aOR) of 1.16 (95%CI: 1.13–1.20) for male patients and 1.14 (95%CI: 1.08–1.20) for female patients. For male patients, also depression at baseline (aOR 2.43; 95%CI: 1.24–4.78), and at least one experienced shock during the follow-up period (aOR 3.06; 95%CI: 1.70–5.50) were significantly associated with a high level of ICD concerns at 24 months (for distribution of shocks over time and by sex see Table S4). For male patients, there was also a trend for an association between ICD concerns at 24 months and NYHA class III-IV (aOR 0.54; 95%CI: 0.32–0.93) at baseline. For female patients, there was an association with anxiety at baseline (aOR 2.87; 95%CI: 1.15–7.15). Since only few female patients and comparably many explanatory factors were included in this analysis, the scarcity of statistically significant results was to be expected.

3.4. Factors associated with change in ICD concerns score

A linear mixed model for ICD concerns over the 24-month period including time and sex and their interaction showed that patients experiencing a shock in the period had an increase of 2.79 (95%CI: 2.09;3.49) points in ICD concerns compared to patients not experiencing a shock. Moreover, patients experiencing anxiety scored 5.07 (95%CI: 4.32;5.82) points higher on ICD concerns compared to patients without anxiety, while patients with depression scored 1.87 (95%CI: 0.89;2.84) points higher on ICD concerns compared to patients with no depression. With respect to patients' rating of their own general health on the SF-36, we used the answer *good* as the reference category. Compared to the reference category *good,* those scoring their general health as *very good* scored 0.9 (95%CI: −1.61;-0.20) points lower on ICD concerns and those scoring their general health as *excellent* scored 3.01 (95%CI: −4.43;-1.58) points lower on ICD concerns. Also, patients classified as NYHA class III + IV scored 0.75 (95%CI: −1.38:-0.12) points lower on ICD concerns than patients classified as NYHA I + II. Finally, increased age was associated with lower scores on ICD concerns with patients scoring 0.35 (95%CI: −0.58; −0.11) points lower for every ten years difference (Table S3).

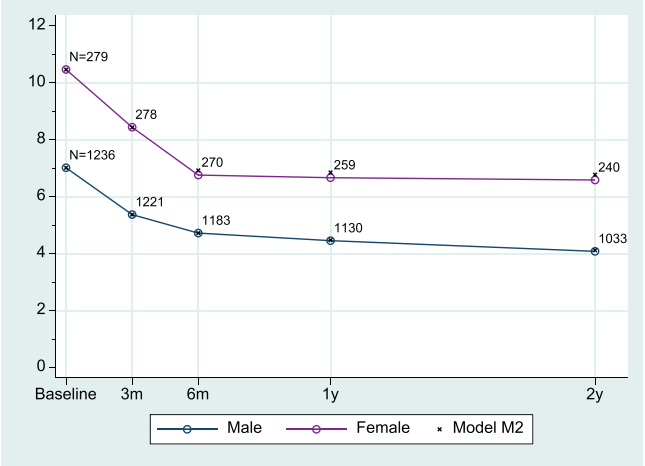

Fig. 1. Mean scores of ICD concerns for male patients and female patients from baseline to 24-months follow-up. The number of observations is presented above the respective mean estimates. Model estimates (M2) are added with small crosses.

Table 2
Estimates of three different linear mixed models for ICD concerns (score) over time. A random-intercept term (RI) for patients was included in all three models. M1: categorical time and sex; M2: categorical time and sex and interaction; M3: additional covariates included. P-values of likelihood ratio tests for M2 versus M1 and M3 versus M2 are <0.01. Full results for M3, including p-values, can be found in the supplementary material.

Variable	M1 ($N = 7129$)	M2 (N = 7129)	M3 (N = 7129)
	Coef (95% CI)	Coef (95% CI)	Coef (95% CI)
Baseline	Ref	Ref	Ref
Time and sex			
3 months	−1.72 (−1.97–1.46)	−1.64 (−1.92–1.36)	−1.70 (−1.98–1.42)
6 months	−2.52 (−2.78–2.27)	−2.29 (−2.58–2.01)	−2.32 (−2.60–2.04)
1 year	−2.74 (−3.00–2.48)	−2.54 (−2.83–2.25)	−2.61 (−2.90–2.33)
2 years	−3.04 (−3.31–2.78)	−2.90 (−3.19–2.60)	−2.99 (−3.29–2.70)
Female sex	2.77 (2.06–3.48)	3.45 (2.63–4.27)	2.33 (1.58–3.09)
Interaction terms for female sex:			
3 months		−0.39 (−1.04–0.26)	−0.42 (−1.07–0.23)
6 months		−1.25 (−1.91–0.59)	−1.23 (−1.89–0.58)
1 year		−1.07 (−1.74–0.40)	−1.04 (−1.70–0.37)
2 years		−0.80 (−1.48–0.11)	−0.76 (−1.44–0.08)
Intercept	7.14 (6.80–7.49)	7.02 (6.67–7.37)	9.52 (7.34–11.71)
Random effects			
RI (variance)	27.08 (25.03–29.29)	27.06 (25.01–29.27)	19.56 (18.03–21.22)
Residual variance	12.66 (12.20–13.14)	12.62 (12.16–13.10)	12.52 (12.06–12.99)
ICC	68.1	68.2	61.0

ICC: Interclass Correlation coefficient.

4. Discussion

4.1. Gender differences in ICD concerns over 24 months

In accordance with our hypothesis, we found that female patients reported significantly higher levels of ICD concerns over 24 months of follow-up post ICD implantation as compared to male patients. Female patients' mean score on ICD concerns was almost 3 points higher than the mean score of male patients between baseline and 24 months of follow-up, which equalled an increase of approx. 68% of the mean score for male patients. Other studies have found sex differences in ICD-related concerns [14,23,24]. Two cross-sectional studies have also found sex differences in ICD concerns with higher scores among female patients [23,24]. In a longitudinal study by Starrenburg et al. the authors found higher shock-related anxiety among female patients compared to male patients. However, this sex difference was only observed in the first two months after implantation, and after one year there was no longer any sex difference in shock-related anxiety [14].

Table 3
Adjusted Odds Ratios (aOR) for high ICD concerns at 24-months follow-up, stratified by sex. High ICD concerns are defined as ≥ the 80th percentile of ICD concerns (score) at 24 months.

	Male patients	Female patients	P-values for overall
N in regression	1033	240	
Variable	aOR (95% CI)	aOR (95% CI)	
ICD concerns at baseline (continuous score)	1.16 (1.13–1.20)	1.14 (1.08–1.20)	<0.001
Age (per 10 years)	0.92 (0.77–1.11)	1.10 (0.80–1.53)	0.669
Secondary prevention indication	0.66 (0.42–1.04)	0.82 (0.34–2.02)	0.092
NYHA class III + IV	0.54 (0.32–0.93)	1.12 (0.37–3.37)	0.052
LVEF>35%	1.27 (0.78–2.07)	1.80 (0.66–4.94)	0.229
HADS-anxiety at baseline (yes)	1.36 (0.81–2.27)	2.87 (1.15–7.15)	0.031
HADS-depression at baseline (yes)	2.43 (1.24–4.78)	0.87 (0.28–2.67)	0.034
Type D personality (DS14) at baseline (yes)	1.28 (0.79–2.09)	1.06 (0.37–3.07)	0.311
SF-36: PCS	0.99 (0.96–1.01)	1.00 (0.94–1.05)	0.326
SF-36: General Health			
Excellent	0.48 (0.09–2.39)	–	0.369
Very good	0.99 (0.57–1.71)	2.36 (0.65–8.55)	0.563
Good	Ref	Ref	
Fair	0.91 (0.57–1.46)	2.44 (0.91–6.56)	0.600
Poor	0.84 (0.36–1.95)	2.44 (0.48–12.39)	0.901
At least one shock in whole period	3.06 (1.70–5.50)	1.56 (0.43–5.75)	<0.001
Female sex			0.002

These results differ from the present study where the sex differences persisted during the entire 24-month follow-up period. A possible explanation for the different findings may be due to the smaller sample size in the study by Starrenburg et al.

The sex differences in ICD concerns found in the present study highlights yet another area of sex disparity regarding ICDs. It is well known that compared to men fewer women are recruited for ICD related studies and fewer are offered an ICD [25–28]. Further women are older when receiving and ICD and more women get ICD related complications compared to men [25–27,29]. Some of the reasons for these sex differences have been argued to be related to lower rates of ventricular arrhythmias and sudden cardiac death in women compared to men, varying results regarding the survival benefits of an ICD for women, as well as lower rates of appropriate shocks among female patients with an ICD [25,30,31]. ICD concerns may be another factor playing into the sex disparities among ICD recipients. More female patients may decline getting an ICD due to concerns about issues related to the device, body image, their role as caregivers and changes in physical functioning [32,33]. Also, the invasive nature of the treatment may cause more women to decline an ICD. Similar sex disparities are found in catheter ablation of atrioventricular nodal re-entry tachycardia where the whole course from symptom to ablation on average was four times longer for female patients, and more female patients expressed concerns about procedure-related complications [34]. An increase in psychosocial distress among women is not only seen among ICD recipients but generally found among women with cardiovascular disease [35,36].

4.2. Decrease in ICD concerns over time

The present study also found that for both sexes the ICD concerns levelled off after 6 months, indicating that adjusting to the new life situation with an ICD takes time and can be psychologically demanding. Although most patients adjust well to living with the ICD, it is important to identify those patients who continue to experience psychological distress, as elevated symptoms of anxiety and depression are related to poorer quality of life and increased risk of mortality [39–41]. A qualitative study looked at patients' experiences of living with an ICD [42]. Some patients expressed that the ICD felt like something foreign in the beginning but over time became an integrated part of their body. This indicate that acceptance of the ICD can take time. The patients also displayed different views of the ICD where some experienced improved quality of life with the ICD, whereas others expressed concerns about living with an ICD [42]. Different views and experiences of living with an ICD can play a part in how quickly the individual adapts to living with the device and how well.

4.3. Variables associated with ICD concerns at 24-months follow-up

In the current study, we found that baseline ICD concerns for both sexes, anxiety among female patients, and depression and receiving a shock (which may be experienced as distressing) for male patients were associated with higher levels of ICD concerns at 24-months follow-up. In the study by Starrenburg et al. they did not, however, find an association between receiving a shock and shock-related anxiety for either men and women [14].

Karczewska and Młynarska (2021) exaimed factors related to ICD concerns six months after implantation and found that younger age, insomnia, anxiety and negative emotions predicted higher levels of ICD concerns [43]. Together with the results from the present study this indicates an association between prior psychological distress (e.g., from baseline) and later ICD concerns. A study by Jokela et al. (2011) support that prior psychological distress is related to a progressively increasing risk of future distress in a dose-response manner [44]. This suggests that screening patients at baseline for psychological distress may help identify those who may adjust less well to life with an ICD. However, as shown in a recent paper, follow-up screenings may also be necessary, as 14.5% of patients with an ICD were identified with new onset anxiety and 11.3% with new onset depression during 24 months of follow-up [45]. Since patients with anxiety and depression have poorer quality of life and an increased risk of mortality [8–11], it is paramount to identify these patients early on and provide the appropriate support and treatment.

Information about the ICD and what to expect if the shock comes (i.e., having a shock plan) [46] may help patients adjust better to a life with an ICD and help mitigate their potential feelings of loss of control over their own life. As indicated in the guidelines [47,48] it is also important to discuss with patients – already at the time of implant – that a day may come where it may be necessary deactivate the ICD in order to avoid painful shocks – and that this can be done without further surgery and without deactivating the pacemaker function. Any decisions about deactivation should, however, always be a shared decision between the patient and their healthcare team taking the patient's individual circumstances into consideration.

Due to the sex disparities related to ICDs, a special effort may be required to prevent ICD concerns among female patients. A group cognitive behavioural therapy intervention developed to addressed both device-specific concerns, such as stress, anxiety, and fear, as well as female specific concerns, such as body image, sexual functioning, and relationship issues has shown promising results in reducing ICD concerns [32].

4.4. Strengths and limitations

There were systematic differences between patients who were included in the DEFIB-WOMEN study compared to those who were excluded or chose not to participate. Thus, the results cannot necessarily be generalized to the entire ICD population [15]. Due to the

observational design of the study, it is uncertain whether we included all relevant variables. Thus, the results could be influenced by other variables not measured. For example, the first assessment was in the first week after implantation. If there had been an assessment point just prior to implantation, this might have added additional information about the patients' mental state. On the other hand, as patients can be anxious before the procedure, especially those receiving it for secondary prevention, it was deemed more appropriate to examine their baseline measurements after the procedure.

During follow-up, patients dropped out of the study and/or did not answer the ICDC questionnaire, resulting in missing outcome values. This could have led to biased estimation results. Furthermore, it is not possible to determine the clinical relevance of sex differences in ICD concerns.

The study has several strengths. The study provides knowledge from a national "real world" cohort of ICD patients recruited from all ICD implanting centres in Denmark with a long follow-up period. The prospective study design allows for the examination of the course of ICD concerns over time and the correlates of high levels of concerns from the time of implantation to 24-months' follow-up. To our knowledge, the DEFIB-WOMEN study is also one of few studies designed explicitly to examine potential sex differences in patients with an ICD [15].

5. Conclusion

We found differences between female and male patients with respect to ICD concerns in the period from implantation to 24-months' follow-up, with female patients generally scoring 3 points higher than male patients at all time points. For both sexes, the ICD concerns decreased over the first 6 months and then reached a stable level. ICD concerns at baseline were associated with ICD concerns at 24 months for both female and male patients. For female patients, anxiety at baseline was associated with ICD concerns at 24 months, whereas for male patients both depression and having experienced a shock correlated with ICD concerns at 24 months' follow-up. These results speak to the value of being attentive to the mental health of patients scoring high on ICD concerns at baseline and maybe in particular to female patients as these concerns seem to continue to be an issue even years later.

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Disclosures

CMA: no conflict of interest.

JBJ: Relationship with Medtronic – consulting, advisory, speaking and lecture fees. Relationship with BIOTRONIK – consulting, advisory and lecture fees. Relationship with Merit Medical Systems Inc. – consulting, advisory and speaking and lecture fees.

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CRediT authorship contribution statement

Christina M. Andersen: Writing – original draft. **Jens Brock Johansen:** Conceptualization, Methodology, Resources, Data curation, Writing – review & editing, Funding acquisition. **Sonja Wehberg:** Formal analysis, Data curation, Writing – original draft. **Jens Cosedis Nielsen:** Writing – review & editing. **Sam Riahi:** Writing – review & editing. **Jens Haarbo:** Writing – review & editing. **Berit T. Philbert:** Writing – review & editing. **Susanne S. Pedersen:** Conceptualization, Methodology, Resources, Data curation, Writing – original draft, Project administration, Funding acquisition.

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