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Published in:
Pacing and Clinical Electrophysiology

DOI:
10.1111/pace.13828

Publication date:
2019

Document version:
Accepted manuscript

Citation for published version (APA):

Go to publication entry in University of Southern Denmark's Research Portal

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Download date: 15. Sep. 2023
Quality of life, depression and anxiety in patients with a subcutaneous versus transvenous defibrillator system

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Word count (text only): 4028

Total number of tables and figures: 5

Short title: Patient-reported outcomes in S-ICD patients

Funding

The EFFORTLESS S-ICD Registry is sponsored in its entirety by Boston Scientific Corporation, St. Paul, Minnesota, USA. The MIDAS study was supported with a VENI grant (451-05-001) from the Netherlands Organization for Scientific Research (NWO) and a VIDI grant (91710393) from the Netherlands Organization for Health Research and Development (ZonMw), the Hague, the Netherlands to Professor Susanne S Pedersen.
Conflicts of interest

SSP has served as a consultant for Boston Scientific and has in the past received speaker’s fees from Servier and Astra-Zeneca, and independent research grants from Medtronic and Boston Scientific.

NC is an employee of Boston Scientific.

CB has no disclosures to report.

MS has no disclosures to report.

PDL serves as a consultant for Boston Scientific and have educational grants from Boston Scientific, St. Jude Medical and Medtronic. He is supported by UCLH Biomedicine NIHR.

LB serves as a consultant for Boston Scientific.

JBJ has no disclosures to report.

DAMJT serves as a consultant for Boston Scientific and has received research grants from Boston Scientific, Biotronik, and St. Jude Medical.

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Abstract

Background: Use of the subcutaneous implantable defibrillator (S-ICD) has increased since the device received US Food and Drug Administration approval in 2012, but we still know little about whether the quality of life (QoL) of patients with an S-ICD versus a transvenous ICD (TV-ICD) is comparable. We compared S-ICD patients with TV-ICD patients on QoL, depression, and anxiety up to 12 months’ follow-up.

Methods: A matched cohort of S-ICD (N=167) and TV-ICD patients (N=167) completed measures on QoL, depression, anxiety and personality at baseline, 3-, 6- and 12 months post implant. Data were analyzed using multivariate modelling with repeated measures.

Results: In adjusted analyses, we found no statistically significant differences between cohorts on physical and mental QoL and depression (all ps>0.05), while S-ICD patients reported lower anxiety than TV-ICD patients (p=0.0007). Both cohorts experienced improvements in physical and mental QoL and symptoms of depression and anxiety over time (all ps<0.001), primarily between implant and 3 months. These improvements were similar for both cohorts with respect to physical and mental QoL and anxiety (ps>0.05), while S-ICD patients experienced greater reductions in depressive symptoms (p=0.0317).

Conclusion: The QoL and depression levels were similar in patients with an S-ICD and a TV-ICD up to 12 months’ follow-up, while S-ICD patients reported lower anxiety levels and a greater reduction in depression over time as compared to TV-ICD patients. This knowledge may be important for patients and clinicians, if the indication for implantation allows both the S-ICD and the TV-ICD, making a choice possible.

Keywords: Anxiety; depression; implantable cardioverter defibrillator; quality of life.

Abstract word count: 249
**Background**

The entirely subcutaneous implantable defibrillator (S-ICD) received approval from the US Food and Drug Administration in 2012. Since FDA approval and the international Evaluation of Factors Impacting Clinical Outcome and Cost Effectiveness of the S-ICD (EFFORTLESS S-ICD) Registry, designed to evaluate the clinical and system performance of the S-ICD and patients' quality of life (QoL) in the “real world” (1; 2), use of the S-ICD has increased (3). While awaiting randomized controlled trials comparing the safety and efficacy of the S-ICD as compared to the transvenous (TV)-ICD system (4), initial observational studies indicate that the S-ICD is safe and effective (2; 3). The S-ICD is included in the European and American guidelines (5; 6). In the European guidelines, the S-ICD is a Class IIa level C indication in patients not dependent on pacing therapy for bradycardia, antitachycardia, or resynchronization therapy and a Class IIb level C indication in patients with inadequate vascular access, high risk of infection, and young patients.

Data on QoL and depression and anxiety in patients with an S-ICD are still scarce, albeit recommendation that the assessment of QoL and patient reported outcomes (PROs) is important in clinical studies (7; 8). For patients and clinicians, knowledge of potential differences in QoL, depression and anxiety, may be important, in particular if the indication for implantation allows both the S-ICD and the TV-ICD, making a choice possible. We have previously compared S-ICD patients to patients with an TV-ICD system on QoL up to 6 months of follow-up and found no statistically significant differences (9). The QoL of both cohorts improved significantly between time of implant and 3 months and 6 months, respectively, but not between 3 and 6 months. To our knowledge, Köbe and colleagues are the only other investigators that have compared the QoL of patients with the S-ICD to a matched cohort with a TV-ICD system, using a cross-sectional study design examining also potential differences in psychological disorders (10).
To our knowledge, we have no data on QoL beyond 6 months of follow-up and no prospective data on psychological disorders in patients with an S-ICD. Hence, in the current study, we compared patients with an S-ICD from the EFFORTLESS QoL sub study to patients with a TV-ICD system from the MIDAS cohort (Mood and personality as precipitants of arrhythmia in patients with an Implantable cardioverter Defibrillator: A prospective Study) on QoL and symptoms of depression and anxiety and examined the predictors of these study endpoints up to 12 months of follow-up.

Methods

Study design and participants

We used a matched case-control cohort design. Details of the two cohorts have been published elsewhere (1; 9). In brief, the S-ICD patients (N=167; mean age=54.0 ± 15.7; 73.1% men) were recruited between March 2011 and July 2014 from 29 sites in Europe and New Zealand for the international EFFORTLESS S-ICD registry and were eligible for inclusion if they also participated in the QoL sub study. In addition to the inclusion and exclusion criteria applied to the EFFORTLESS ICD registry, patients were not eligible to participate in the QoL sub study if they were retrospective enrollments (1). The EFFORTLESS S-ICD Registry QoL was designed to use the MIDAS cohort as a comparison group (1). The TV-ICD patients (N=167; mean age=53.8 ± 13.2; 71.9% men) were also first-time implant patients and recruited as part of the MIDAS study between August 2003 and February 2010 from the Erasmus Medical Center, Rotterdam, the Netherlands (11; 12). Both cohorts were matched on a priori selected baseline characteristics including baseline physical and mental QoL scores, using propensity score matching. Prior to matching, MIDAS patients with an indication for bradycardia or resynchronization therapy were excluded, as these patients would not be eligible for an S-ICD system (5).

Measures
Information on demographic and clinical variables were captured either from patients' electronic health records or purpose-designed questions (e.g. on seeing a mental health professional) that patients were asked to complete as part of a questionnaire package that also contained standardized and validated measures.

We assessed QoL with the Short Form Health Survey 12 (SF-12), which is a frequently used measure of QoL in the general population and patients with chronic diseases (13). The SF-12 is a generic measure that consists of 12 items. Based on an algorithm, the 12 items are converted to a scale from 0-100 that contribute to the Physical Component Summary (PCS) score and the Mental Component Summary (MSC) score, respectively. For both QoL dimensions, 100 represents the best QoL. The validity and reliability of the SF-12 has previously been established in patients with heart disease (14). Patients completed the SF-12 at 4 timepoints (i.e., at baseline, 3-, 6- and 12 months post implant).

We measured symptoms of depression and anxiety with the Hospital Anxiety and Depression Scale (HADS) (15). The HADS is comprised of 14 items that are answered on a four-point Likert scale from 0-3, with 7 items contributing to the depression score and 7 items contributing to the anxiety score (score range for both is 0-21). A higher symptom score indicates more depression and anxiety symptom severity. The HADS has frequently been used to assess anxiety and depression in the general population, patients with somatic disease, including heart disease, and primary care and psychiatric patients (16; 17). It has been shown to perform well in assessing both caseness of anxiety and depression disorders and symptom severity in these populations (16; 17) and to predict mortality in patients with acute coronary syndrome (18; 19) and in patients with ICD (20). Patients completed the HADS at 4 timepoints (i.e., at baseline, 3-, 6- and 12 months post implant). A cut-off of 8 or higher for both the depression and anxiety subscale is most commonly used, reflecting a mild level of symptomatology and also the best balance between sensitivity and specificity (17).
Type D personality – also called the *distressed personality type* – was assessed with the 14-item Type D Scale (DS14) (21), which with 7 items contribute to the negative affectivity (e.g. ‘I often feel unhappy’) and social inhibition (e.g. ‘I am a closed kind of person’) subscales, respectively. Items are rated on a 5-point Likert scale from 0-4, with the score range for each of the traits being 0-28. A score of ≥10 on both traits typify those who have a Type D personality, with Item Response Theory showing this cut-off to be the most optimal (21; 22). The validity and internal consistency of the DS14 have been demonstrated previously, with Cronbach’s alpha of 0.80 for negative affectivity and 0.86 for social inhibition (21). As Type D personality has been associated with poor compliance, increased risk of depression and anxiety, and poor QoL and premature death in patients with heart disease and patients with an ICD (12; 23), it was included in both the MIDAS study and the EFFORTLESS S-ICD registry due to its potential association with PROs and clinical outcomes. Patients only completed the DS14 at baseline.

**Permissions**

Medical ethics committees in each participating country of the EFFORTLESS S-ICD Registry study approved the study protocol. The medical ethics committee of the Erasmus Medical Center, Rotterdam, the Netherlands, approved the MIDAS study protocol (MEC # 231.491/2003/148 - September 9, 2003). The EFFORTLESS S-ICD Registry was also registered on [http://www.ClinicalTrials.gov](http://www.ClinicalTrials.gov) (NCT01085435). Both the EFFORTLESS S-ICD Registry and the MIDAS study were conducted according to the Helsinki Declaration. All patients received oral and written information about the study and provided written informed consent.

**Statistical analysis**

As patients with an indication for cardiac resynchronization therapy, bradycardia, or a secondary prevention indication due to monomorphic VTs are not eligible for an S-ICD system, these patients were excluded from the MIDAS cohort prior to propensity score
matching. Subsequently, EFFORTLESS and MIDAS patients were matched 1:1 on a priori selected variables that included age, gender, indication for ICD (primary versus secondary), ischemic versus non-ischemic etiology, and baseline mental and physical QoL. We used the Greedy Matching Algorithm with the recommended caliper width by Austin when performing the propensity score matching (24). Data on QoL, depression and anxiety across baseline, 3-, 6-, and 12 months were analyzed using multivariable modeling with repeated measures. In the multivariable modeling, we also considered the time by ICD system (S-ICD versus TV-ICD) interaction, provided that it was statistically significant ($p<0.05$). For all study endpoints (i.e., mental QoL, physical QoL, depression, and anxiety), two models were run. In model 1, we adjusted for Type D personality, shocks (any) during 12 months’ follow-up, New York Heart Association (NYHA) functional class III-IV, low educational level, amiodarone, mental health treatment, and cardiac rehabilitation attendance. These variables were selected a priori based on the literature. In model 2, we added all baseline variables that were systematically different between the EFFORTLESS and MIDAS cohorts despite matching to the variables in model 1. All data were analyzed using SAS version 9.4.

Results

**Baseline characteristics stratified by ICD system**

As indicated in Table 1, patients with an S-ICD system did not differ systematically from patients with a TV-ICD system on the majority of baseline characteristics. However, S-ICD patients were less likely to have ventricular fibrillation as index arrhythmia (20% vs. 30%, $p=0.0480$) and to be on statins (30% vs. 45%, $p=0.0047$) but more likely to have ventricular tachycardia as index arrhythmia (5% vs. 1%, $p=0.0426$), diabetes (19% vs. 10%, $p=0.0183$), heart failure (41% vs. 17%, $p<0.0001$) and to be on diuretics (48% vs. 34%, $p=0.0105$) as compared to TV-ICD patients. S-ICD patients had a shorter QRS duration (105 ± 21 vs. 112 ± 27, $p=0.0071$) and a lower score on anxiety as compared to TV-ICD patients (mean ±SD 5.3±3.8 vs. 6.5±3.7, $p=0.0047$).
**Shocks during follow-up stratified by ICD system**

During the 12 months’ follow-up period, 20 (12.3%) of the matched S-ICD patients experienced a shock (appropriate or inappropriate) versus 21 (12.6%) of the matched TV-ICD cohort ($p = 0.9331$).

**Comparison of physical and mental quality of life of S-ICD versus TV-ICD patients**

There was no significant interaction effect for time by device type with respect to physical and mental QoL (both $p$s>0.05), indicating that the change in mean scores over time was similar for both S-ICD and TV-ICD patients. Hence, the interaction term was not included in the multivariable models. When comparing patients with an S-ICD versus a TV-ICD system on QoL during the course of 12-months’ follow-up, S-ICD patients experienced somewhat lower physical QoL than the TV-ICD patients, while there was no significant difference on mental QoL between the two cohorts (Table 2, model 1). When adjusting for a priori selected covariates and baseline differences between the two cohorts, there were no statistically significant differences between S-ICD and TV-ICD patients on physical nor mental QoL (Table 2, model 2).

Both physical ($p<0.0001$) and mental ($p<0.0001$) QoL improved in both cohorts over time. For physical QoL, there was a significant improvement between baseline and 3 months ($p<0.0001$), baseline and 6 months ($p<0.0001$), baseline and 12 months ($p<0.0001$), but not between 3 and 6 months, 3 and 12 months, and 6 and 12 months (all $p$s>0.05). Similar results were found for mental QoL, except that there was a significant improvement between 6 and 12 months ($p=0.0141$). The largest improvements were found between implant and 3 months.

To examine the relative influence of device type, NYHA class, shock, and personality, respectively, on physical and mental QoL, we subtracted the scores for each of the four groups, generating a difference in mean score. This was done for all 4 measurement points.
(baseline, 3-, 6- and 12 months follow-up), with the reported range across follow-up representing the lowest and the highest difference per parameter. Figure 1. shows unadjusted mean scores and standard deviations for physical and mental QoL during the course of 12 months’ follow-up, stratified by ICD system (S-ICD versus TV-ICD), heart failure (NYHA class I-II versus III-IV), personality (Type D versus non-Type D), and shocks during follow-up (shocks versus no shocks). For physical QoL, differences in mean scores between the two ICD systems (range: 0.1-2.7), heart failure class (range: 7.9-10.3), personality type (range: 3.8-6.6), and shocks (range: 1.2-4.2) across follow-up show that the greatest difference in physical QoL is between NYHA class I-II and III-IV and the least difference between the two ICD systems. For mental QoL, the differences in mean scores between the two ICD systems (range: 0.3-2.4), heart failure class (range: 4.0-6.1), personality (range: 8.9-10.2), and shocks (range: 0.9-2.9) across follow-up show that the greatest difference in mental QoL is between Type D versus non-Type D and the least difference between the two ICD systems.

Independent correlates of physical and mental quality of life

Type D (distressed) personality, severe heart failure (NYHA III-IV), use of diuretics, and diabetes were independently associated with poor physical QoL (all ps<0.05). Type D personality, severe heart failure (NYHA III-IV), low educational level, being treated for depression / anxiety were independently associated with poor mental QoL, while use of statins and increased QRS duration were associated with better mental QoL.

Comparison of symptoms of depression and anxiety in S-ICD versus TV-ICD patients

The interactions for time by device type with respect to depression (p=0.0088) and time by device type with respect to anxiety (p=0.0374) were both significant and thus included in Model 1 (Table 3, model 1). Once the models were additionally adjusted for baseline differences (Table 3, model 2), the interaction term for depression remained significant (p=0.0317) but not for anxiety (p=0.0539). Hence, the interaction term for time by device type
was added to the fully adjusted model for depression but not anxiety. We found no statistically significant differences between S-ICD and TV-ICD patients on depression ($p=0.3354$), but a difference on anxiety ($p=0.0007$), with S-ICD patients scoring lower on anxiety (Table 3, model 2).

Both symptoms of depression and anxiety decreased in both cohorts over time. The improvements were found between baseline and 3 months, baseline and 6 months, baseline and 12 months (all $p$s<0.01), but not between 3 and 6 months, 3 and 12 months, and 6 and 12 months (all $p$s>0.05). The largest improvements were found between implant and 3 months. The evolution in mean anxiety scores over time was similar for both cohorts ($p=0.0539$). For depression scores, the interaction for time by study cohort was significant ($p=0.0317$), with S-ICD patients experiencing greater reductions in depressive symptoms over time.

Figure 2. shows unadjusted mean scores and standard deviations for symptoms of depression and anxiety during the course of 12 months' follow-up, stratified by ICD system (S-ICD versus TV-ICD), heart failure class (NYHA class I-II versus III-IV), personality (Type D versus non-Type D), and shocks during follow-up (shocks versus no shocks). For depression, differences in mean scores between the two ICD systems (range: 0-0.5), heart failure class (range: 1.5-1.9), personality type (range: 3.4-4.2), and shocks (range: 0.7-1.2) across follow-up show that the greatest difference in depression is between Type D versus non-Type D and the least difference between the two ICD systems. For anxiety, differences in mean scores between the two ICD systems (range: 1.2-2.1), heart failure class (range: 0.2-0.6), personality type (range: 3.2-4.5), and shocks (range: 0.1-1.2) across follow-up show that the greatest difference in anxiety is between Type D versus non-Type D, followed by device type, while the least difference was found between heart failure class I-II versus III-IV.

Independent correlates of depression and anxiety
Type D (distressed) personality, dilated cardiomyopathy, and psychological treatment were independent correlates of depression (all $p_s < 0.05$). Type D and psychological treatment were associated with increased depression scores while dilated cardiomyopathy was associated with decreased depression scores. Type D personality was the only independent correlate of anxiety ($p < 0.0001$), with risk being increased in patients with this personality profile. Neither severe heart failure (NYHA III-IV) nor shocks during follow-up were significantly associated with depression and anxiety ($p_s > 0.05$).

**Discussion**

In the current study, we examined potential differences in QoL, depression and anxiety in patients with an S-ICD versus TV-ICD system and the association between device type, personality, heart failure severity, and shocks on QoL, depression, and anxiety up to 12 months’ follow-up, using data from the international EFFORTLESS registry and the MIDAS study. We found no statistically significant differences in physical and mental QoL and depression between S-ICD and TV-ICD patients between time of implant and up to 12 months’ follow-up, adjusting for potential confounders. However, we did find a difference in anxiety, with S-ICD patients scoring lower on anxiety at all time points. S-ICD patients also experienced greater reductions in depressive symptoms over time. Overall, both cohorts experienced improvements in physical and mental QoL and a decrease in depression and anxiety symptoms from the time of implant to 12 months’ follow-up, which may reflect an adaptation to living with the device, as has also been found by others (25; 26).

Previously, we examined the physical and mental QoL of S-ICD versus TV-ICD patients and found no differences up to 6 months’ follow-up (9). The results of the current study support and extend these results, as S-ICD and TV-ICD patients reported similar physical and mental QoL up to 12 months and experienced similar QoL improvements between implant and follow-up. A recent cross-sectional case-control study comparing 60 S-ICD patients to 60 TV-ICD patients on QoL and psychological disorders, including posttraumatic disorder, found no
differences between groups on psychological disorders and mental QoL, while physical QoL was more impaired in TV-ICD patients (10). To our knowledge, our previous study, the current study and that of Köbe and colleagues (10) represent the only studies that have compared the QoL and the prevalence of psychological disorders in patients with an S-ICD versus a TV-ICD. While we await the results of the ongoing large-scale, randomized, controlled, multicenter, prospective PRAETORIAN trial that also include QoL as a secondary endpoint (4), available studies point towards at least similar QoL and mental health in S-ICD patients as compared to TV-ICD patients. When the S-ICD was initially launched, there was great concern in the arrhythmia community that the size and the weight of the device would lead to poorer QoL in these patients (27), which we have not been able to confirm. In addition, the size and weight of the S-ICD has been reduced with the second generation EMBLEM™ S-ICD system.

In the current study, the associations between factors, such as personality (Type D) and heart failure class, and physical and mental QoL and symptoms of depression and anxiety were greater than associations between type of device (S-ICD versus TV-ICD) and shocks during follow-up and these endpoints. This result is consistent with that of other studies in TV-ICD patients, showing that severity of heart failure (28), lower perceived control (29; 30), anxiety (29), depression (29), and Type D personality (30) are more strongly associated with QoL than e.g. shocks. One study that examined the relative association between heart failure versus device placement on QoL – comparing patients with an ICD without heart failure, patients with heart failure but no ICD, and patients with heart failure and ICD – found that disease severity was more strongly associated with QoL than having a device (28).

Nevertheless, we found that patients with an S-ICD system reported lower anxiety scores and experienced a greater reduction in their depression score than TV-ICD patients. In a smaller study of 42 pairs of S-ICD and TV-ICD patients, Köbe and colleagues found no differences in panic disorders, anxiety disorders and post-traumatic stress disorder (10).
We can only speculate why S-ICD patients experienced less anxiety than TV-ICD patients in the current study. Boston Scientific User’s manuals for their S-ICDs and TV-ICDs, respectively, are very similar in terms of information given to patients, although S-ICD patients recover faster with respect to movement of their left-arm, as there is no lead in-grow period, which is the case for TV-ICDs. Despite the similarities in instructions, this does not rule out that health care professionals may provide different (additional) information to patients pre- and post-implant or that patients may have specific perceptions about their device and treatment that could influence their anxiety levels negatively or positively. On the one hand, S-ICD patients may have more body image concerns and distress due to the S-ICD being larger, but this might be offset by less concerns, as the S-ICD does not have leads in and on the vasculature of the heart, leading patients to perceive the S-ICD as “less invasive” as compared to the TV-ICD. A recent scoping review on body image concerns found little to no evidence for an association between body image concerns and anxiety, with the overall impact of body image on patients’ lives being variable (31). Many other factors have also been shown to contribute to anxiety, among others ICD shocks directly or indirectly (e.g., through ICD-related concerns and perceived control) (32), symptomatic heart failure (33), female gender (34), and personality (35). Taken together, there is an urgent need to further explore the challenges that patients experience with an S-ICD as compared to patients with a TV-ICD and whether these challenges are different and how we can best help patients manage these challenges, in particular due to evidence that anxiety, depression and poor QoL are associated with adverse prognosis at least in patients with a TV-ICD (20; 36; 37).

The current study has some limitations. The S-ICD patients were recruited internationally across multiple centers, while the TV-ICD patients from the MIDAS cohort were recruited from a single center and during the course of 7 years as compared to 3 years for the EFFORTLESS S-ICD patients. However, the mean QoL scores of the MIDAS cohort were similar to those found in other cohorts with a TV-ICD system (38; 39). Since completion of
recruitment to the MIDAS study, new ICD programming strategies have been implemented, reducing inappropriate and unnecessary shocks. Nevertheless, similar levels of distress as in the current study were reported in the recent ENHANCED-ICD study that used the novel programming strategies (40). As the indication for an S-ICD differs from that of a TV-ICD system, patients from the MIDAS cohort with an indication for cardiac resynchronization therapy, bradycardia, or a secondary prevention indication due to monomorphic VTs were excluded prior to propensity score matching, as they are not eligible for an S-ICD system. Despite matching on a priori selected characteristics, the two cohorts differed on some characteristics that we adjusted in the statistical analyses. Given an established minimal clinical important difference on the HADS of 1.7 points, the differences between the S-ICD and TV-ICD patients on anxiety were clinically relevant at 3 months (1.82) and 12 months (1.71) in the final adjusted model (41). However, we cannot rule out that this difference is not due to the differences between the two cohorts. We did not have information about the use of anti-depressants and anxiolytics in either cohort, which might potentially have influenced their levels of depression and anxiety. However, we did have information about the number of patients seeing a mental health professional by means of a purpose-designed question administered at baseline. No systematic difference was found between the two cohorts with respect to seeing a mental health professional. The current study also has several strengths. To our knowledge, it is the first prospective study that compares S-ICD versus TV-ICD patients on physical and mental QoL and depression and anxiety with data up to 12 months’ follow-up. The two cohorts are also well described both with respect to their demographic, clinical and psychological profile, and medication use.

In conclusion, these first results on prospective data up to 12 months of follow-up of S-ICD versus a TV-ICD system on QoL, depression, and anxiety show that patients with an S-ICD experience similar QoL and are not at greater risk of experiencing depression as compared to patients with an TV-ICD system. With respect to anxiety and reductions in depressive symptoms during the course of follow-up, S-ICD patients seem to have a more favorable
course with less anxiety and greater reduction in depressive symptoms during follow-up, although these results warrant replication in randomized studies. If this can be confirmed in e.g. the ongoing PRAETORIAN trial that also include QoL as a secondary endpoint (4) and trials to follow on the S-ICD device, this information may be important for patients and clinicians if the indication for implantation allows both the S-ICD and the TV-ICD, making a choice possible.
Acknowledgements

We would like to thank all of the Investigators in the EFFORTLESS S-ICD Registry who contributed with patients to the Quality of Life sub study.
References


**Table 1.** Baseline characteristics for the EFFORTLESS (S-ICD) and MIDAS (TV-ICD) cohorts

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>EFFORTLESS (S-ICD system) (n = 167)</th>
<th>MIDAS (TV-ICD system) (n = 167)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>122 (73%)</td>
<td>120 (72%)</td>
<td>0.8065</td>
</tr>
<tr>
<td>Age, mean ±SD (years)</td>
<td>54 ± 16</td>
<td>55 ± 13</td>
<td>0.8831</td>
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<td>Low education (&lt;13 years)</td>
<td>73 (45%)</td>
<td>90 (55%)</td>
<td>0.0597</td>
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<tr>
<td>Clinical, comorbidities and previous events</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Primary prevention indication</td>
<td>123 (74%)</td>
<td>115 (69%)</td>
<td>0.3334</td>
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<tr>
<td>Ventricular fibrillation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>as index arrhythmia</td>
<td>32 (20%)</td>
<td>50 (30%)</td>
<td>0.0480</td>
</tr>
<tr>
<td>Ventricular tachycardia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>as index arrhythmia</td>
<td>8 (5%)</td>
<td>2 (1%)</td>
<td>0.0426</td>
</tr>
<tr>
<td>QRS duration</td>
<td>105 ± 21</td>
<td>112 ± 27</td>
<td>0.0071</td>
</tr>
<tr>
<td>Severe heart failure (NYHA III-IV)</td>
<td>20 (12%)</td>
<td>24 (15%)</td>
<td>0.5313</td>
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<tr>
<td>Heart failure</td>
<td>69 (41%)</td>
<td>28 (17%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>36 (22%)</td>
<td>30 (18%)</td>
<td>0.4097</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>31 (19%)</td>
<td>16 (10%)</td>
<td>0.0183</td>
</tr>
<tr>
<td>Renal failure (60 ml/kg/1.73m²)</td>
<td>13 (8%)</td>
<td>23 (14%)</td>
<td>0.0841</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>or stroke</td>
<td>13 (8%)</td>
<td>8 (5%)</td>
<td>0.2781</td>
</tr>
<tr>
<td>Dilated cardiomyopathy</td>
<td>25 (15%)</td>
<td>39 (23%)</td>
<td>0.0516</td>
</tr>
<tr>
<td>Ischemic cardiomyopathy</td>
<td>12 (7%)</td>
<td>12 (7%)</td>
<td>1.0000</td>
</tr>
<tr>
<td>Hypertrophic cardiomyopathy</td>
<td>22 (13%)</td>
<td>18 (11%)</td>
<td>0.5002</td>
</tr>
</tbody>
</table>
Previous myocardial infarction | 66 (40%) | 68 (40%) | 0.8223
Previous percutaneous coronary intervention | 32 (19%) | 42 (25%) | 0.1877
Previous coronary bypass | 17 (10%) | 17 (10%) | 1.0000

**Medication**

Angiotension converting enzyme inhibitors | 92 (55%) | 106 (64%) | 0.1190
Beta-blockers | 125 (75%) | 133 (80%) | 0.2964
Statins | 50 (30%) | 75 (45%) | **0.0047**
Diuretics | 80 (48%) | 57 (34%) | **0.0105**
Amiodarone | 15 (9%) | 12 (7%) | 0.5470
Digoxin | 10 (6%) | 17 (10%) | 0.1600

**Other treatment**

Cardiac rehabilitation | 7 (4%) | 11 (7%) | 0.3593
Mental health treatment | 9 (5%) | 14 (8%) | 0.2798

**Psychological and QoL**

Type D personality | 44 (27%) | 35 (21%) | 0.2461
Physical QoL, mean ±SD | 41 ± 12 | 41 ± 11 | 0.9787
Mental QoL, mean ±SD | 42 ± 12 | 43 ± 12 | 0.8697
Depression\(^2\) mean ±SD | 4.6±3.9 | 4.2±3.6 | 0.3504
% depression (cut-off ≥8) | 38 (23%) | 28 (17%) | 0.1691
Anxiety\(^2\), mean ±SD | 5.3±3.8 | 6.5±3.7 | **0.0047**
% anxiety (cut-off ≥8) | 41 (25%) | 56 (34%) | 0.0703

---

\(^1\) Currently seeing a social worker, psychologist or psychiatrist for psychological problems (purpose-designed question)

\(^2\) Assessed with the Hospital Anxiety and Depression Scale (HADS)
Table 2. Physical and mental quality of life of patients with an S-ICD system versus a TV system up to 12 months post implant

<table>
<thead>
<tr>
<th></th>
<th>EFFORTLESS (S-ICD system)</th>
<th>MIDAS (TV-ICD system)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean [95% CI]</td>
<td>Mean [95% CI]</td>
<td></td>
</tr>
<tr>
<td>Physical QoL (PCS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>39.36 [37.75-40.96]</td>
<td>41.61 [40.02-43.21]</td>
<td>0.0329</td>
</tr>
<tr>
<td>3 months</td>
<td>42.40 [40.84-43.95]</td>
<td>44.65 [43.10-46.20]</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>42.29 [40.69-43.90]</td>
<td>44.55 [42.95-46.14]</td>
<td></td>
</tr>
<tr>
<td>12 months</td>
<td>42.95 [41.26-44.64]</td>
<td>45.21 [43.55-46.86]</td>
<td></td>
</tr>
<tr>
<td>Mental QoL (MCS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>41.70 [40.11-43.29]</td>
<td>42.92 [41.33-44.51]</td>
<td>0.2353</td>
</tr>
<tr>
<td>3 months</td>
<td>45.11 [43.52-46.71]</td>
<td>46.33 [44.75-47.91]</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>44.56 [42.88-46.23]</td>
<td>45.78 [44.11-47.45]</td>
<td></td>
</tr>
<tr>
<td>12 months</td>
<td>45.87 [44.17-47.57]</td>
<td>47.09 [45.41-48.75]</td>
<td></td>
</tr>
</tbody>
</table>

Model 1<sup>a</sup>

Model 2<sup>b</sup>

Physical QoL (PCS)

Baseline | 40.46 [38.66-42.27]   | 41.00 [39.35-42.67]   | 0.6665  |
3 months  | 43.48 [41.69-45.27]   | 44.02 [42.38-45.65]   |         |
<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months</td>
<td>43.38 [41.55-45.21]</td>
<td>43.91 [42.24-45.59]</td>
</tr>
<tr>
<td>12 months</td>
<td>43.94 [42.04-45.83]</td>
<td>44.47 [42.75-46.20]</td>
</tr>
</tbody>
</table>

**Mental QoL (MSC)**

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>42.44 [40.63-44.25]</td>
<td>42.54 [40.87-44.20]</td>
</tr>
<tr>
<td>3 months</td>
<td>45.75 [43.92-47.58]</td>
<td>45.85 [44.16-47.53]</td>
</tr>
<tr>
<td>6 months</td>
<td>45.13 [43.22-47.04]</td>
<td>45.23 [43.46-47.00]</td>
</tr>
<tr>
<td>12 months</td>
<td>46.32 [44.50-48.36]</td>
<td>45.52 [44.75-48.29]</td>
</tr>
</tbody>
</table>

*a adjusted for a priori selected covariates*

*b adjusted for a priori selected covariates and baseline differences between the two cohorts*

*a + b For specific details on the covariates adjusted for, we refer the reader to the statistical analysis section*
**Table 3.** Depression and anxiety of patients with an S-ICD system versus a TV-ICD system up to 12 months post implant

<table>
<thead>
<tr>
<th></th>
<th>EFFORTLESS (S-ICD system)</th>
<th>MIDAS (TV-ICD system)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><em>Mean [95% CI]</em></td>
<td><em>Mean [95% CI]</em></td>
<td></td>
</tr>
<tr>
<td><strong>Model 1</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Depression</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>4.60 [4.08-5.11]</td>
<td>4.19 [3.67-4.71]</td>
<td>0.7264</td>
</tr>
<tr>
<td>3 months</td>
<td>3.73 [3.19-4.27]</td>
<td>4.19 [3.63-4.74]</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>4.16 [3.60-4.72]</td>
<td>4.08 [3.50-4.66]</td>
<td></td>
</tr>
<tr>
<td>12 months</td>
<td>3.69 [3.16-4.23]</td>
<td>4.19 [3.59-4.80]</td>
<td></td>
</tr>
<tr>
<td><strong>Anxiety</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>5.31 [4.80-5.83]</td>
<td>6.46 [5.94-6.99]</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>3 months</td>
<td>3.76 [3.22-4.31]</td>
<td>5.62 [5.06-6.18]</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>4.32 [3.74-4.91]</td>
<td>5.46 [4.85-6.06]</td>
<td></td>
</tr>
<tr>
<td>12 months</td>
<td>3.81 [3.26-4.35]</td>
<td>5.60 [4.98-6.21]</td>
<td></td>
</tr>
<tr>
<td><strong>Model 2</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Depression</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>4.83 [4.29-5.38]</td>
<td>4.02 [3.42-4.62]</td>
<td>0.3354</td>
</tr>
<tr>
<td>3 months</td>
<td>3.96 [3.39-4.54]</td>
<td>3.91 [3.27-4.55]</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>4.40 [3.81-4.99]</td>
<td>3.78 [3.11-4.45]</td>
<td></td>
</tr>
<tr>
<td><strong>Anxiety</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>5.43 [4.89-5.98]</td>
<td>6.55 [5.94-7.16]</td>
<td>0.0007</td>
</tr>
<tr>
<td>3 months</td>
<td>3.87 [3.30-4.45]</td>
<td>5.69 [5.04-6.33]</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>4.44 [3.82-5.06]</td>
<td>5.50 [4.80-6.20]</td>
<td></td>
</tr>
<tr>
<td>12 months</td>
<td>3.92 [3.34-4.50]</td>
<td>5.63 [4.94-6.33]</td>
<td></td>
</tr>
</tbody>
</table>

*a* adjusted for the interaction effect for time by study and a priori selected covariates

*b* adjusted for the interaction effect for time by study (for depression only), a priori selected covariates and baseline differences between the two cohorts

*a + b* For specific details on the covariates adjusted for, we refer the reader to the statistical analysis section
Figure 1. Mean (SD) scores on physical and mental quality of life (QoL) stratified by ICD system, NYHA class, Type D personality and shocks during 12 months’ follow-up*

* QoL score range is 0-100 (100=best QoL)
Figure 2. Mean (SD) scores on depression and anxiety stratified by ICD system, NYHA class, Type D personality and shocks during 12 months’ follow-up*

* Depression and anxiety score range is 0-21 (21=worst symptom score)