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ORIGINAL ARTICLE

Quality of Life in Subcutaneous or Transvenous Implantable Cardioverter-Defibrillator Patients: A Secondary Analysis of the PRAETORIAN Trial

Reinoud E. Knops, MD, PhD*; Jolien A. de Veld, MD*; Abdul Ghani, MD, PhD; Lucas V.A. Boersma, MD, PhD; Juergen Kuschyk, MD; Mikhael F. El Chami, MD; Hendrik Bonnemeier, MD, PhD; Elijah R. Behr, MD; Tom F. Brouwer, MD, PhD; Stefan Kääb, MD, PhD; Suneet Mittal, MD; Shari Pepplinkhuizen, MD; Anne-Floor B.E. Quast, MD, PhD; Lonneke Smeding, PhD; Willeke van der Stuijt, MD, PhD; Anouk de Weger, MSc; Nick R. Bijsterveld, MD, PhD; Sergio Richter, MD; Marc A. Brouwer, MD, PhD; Joris R. de Groot, MD, PhD; Kirsten M. Kooiman, MPA; Pier D. Lambiase, MD, PhD; Petr Neuzil, MD, PhD; Kevin Vernooy, MD, PhD; Marco Alings, MD, PhD; Timothy R. Betts, MD; Frank A.L.E. Bracke, MD, PhD; Martin C. Burke, DO; Jonas S.S.G. de Jong, MD, PhD; David J. Wright, MD; Ward P.J. Jansen, MD, PhD; Zachary I. Whinnett, MD, PhD; Peter Nordbeck, MD; Michael Knaut, MD; Berit T. Philbert, MD; Jurren M. van Opstal, MD, PhD; Alexandru B. Chicos, MD; Cornelis P. Allaart, MD, PhD; Alida E. Borger van der Burg, MD, PhD; Jose M. Dizon, MD; Marc A. Miller, MD; Dmitry Nemirovksy, MD; Ralf Surber, MD; Gaurav A. Upadhyay, MD; Jan G.P. Tijssen, MD, PhD; Arthur A.M. Wilde, MD, PhD; Louise R.A. Olde Nordkamp, MD, PhD; on behalf of the PRAETORIAN Investigators

BACKGROUND: The subcutaneous implantable cardioverter-defibrillator (S-ICD) was developed to overcome the risk of lead-related complications associated with the transvenous implantable cardioverter-defibrillator (TV-ICD). In contrast to the TV-ICD, the S-ICD is a completely extrathoracic device. Subsequently, complications differ between these 2 implantable cardioverter-defibrillators, which might impact patient perceptions of the therapies. This prespecified secondary analysis of the PRAETORIAN trial evaluates differences in quality of life.

METHODS: The PRAETORIAN trial (A Prospective, Randomized Comparison of Subcutaneous and Transvenous Implantable Cardioverter Defibrillator Therapy) randomized patients with an implantable cardioverter-defibrillator indication, without the need for pacing to S-ICD or TV-ICD therapy. Two questionnaires were collected at baseline, discharge, 12 months, and 30 months. The Duke Activity Status Index measures cardiac-specific physical functioning, and the 36-Item Short Form Health Survey measures physical and mental well-being, with the subscales bodily pain and mental health being of interest in this analysis. Mann-Whitney *U* tests were used to compare study arms, and a mixed model was used to describe the questionnaire outcomes over time.

RESULTS: Patients were randomized to S-ICD (n=426) and TV-ICD (n=423). In the S-ICD group, 20% were women versus 19% in the TV-ICD group. The median age was 63 (interquartile range, 54–69) years in the S-ICD group versus 64 (interquartile range, 56–69) years in the TV-ICD group. There were no significant differences in the Duke Activity Status Index and 36-Item Short Form Health Survey subscales for bodily pain and mental health between the groups at any time point. Patients with a shock in the last 90 days had significantly lower scores for social functioning (P=0.008) and role limitations due to emotional problems (P=0.001) than patients without a shock, but this effect did not differ between treatment arms.

Correspondence to: Jolien A. de Veld, MD, Department of Cardiology, Amsterdam University Medical Centers, Location AMC, Room D3-221, PO Box 22700, Meibergdreef 9, 1105 AZ Amsterdam, the Netherlands. Email j.a.develd@amsterdamumc.nl
*R.E. Knops and J.A. de Veld contributed equally.
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CONCLUSIONS: In a large randomized cohort of patients with an S-ICD or TV-ICD, no difference in overall quality of life was observed. However, implantable cardioverter-defibrillator shocks resulted in a reduction in quality of life, regardless of the device type or appropriateness.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT01296022.

Key Words: arrhythmias, cardiac ■ defibrillators, implantable ■ mental health ■ quality of life

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WHAT IS KNOWN

- Generator size and type of complications differ between the subcutaneous implantable cardioverter-defibrillator and transvenous implantable cardioverter-defibrillator.
- Conflicting results have been reported regarding differences in quality of life between these 2 therapies.

WHAT THE STUDY ADDS

- Randomized data of the subcutaneous implantable cardioverter-defibrillator and transvenous implantable cardioverter-defibrillator with prospectively assessed quality of life.
- No differences in quality of life between the 2 devices.
- Contribution to shared decision-making in clinical practice.

Nonstandard Abbreviations and Acronyms

BMI	body mass index
DASI	Duke Activity Status Index
ICD	implantable cardioverter-defibrillator
IQR	interquartile range
QoL	quality of life
SF-36	36-Item Short Form Health Survey
S-ICD	subcutaneous implantable cardioverter-defibrillator
TV-ICD	transvenous implantable cardioverter-defibrillator

The use of implantable cardioverter-defibrillators (ICDs) significantly improves the life expectancy of appropriately selected patients at substantial risk for sudden cardiac death.[1–3] For years, the transvenous ICD (TV-ICD) was the standard of care, but over the past decades, the subcutaneous ICD (S-ICD) has been shown to be a safe and effective device for the termination of potentially lethal ventricular arrhythmias.[4] Nevertheless, there are substantial differences between the 2 devices. The TV-ICD is implanted in the subclavicular region with ≥1 leads implanted in the heart through the venous system. In contrast, the S-ICD is a completely extracardiac device, with the lead implanted on the sternum and the generator on the left side of the thoracic wall.[4] This results in the need for a higher energy output for the S-ICD and a subsequently larger generator compared with the TV-ICD.

Multiple differences between the S-ICD and TV-ICD might impact a patient's daily activities and quality of life (QoL). First, due to its larger size, the S-ICD generator is more visible, especially in patients with a low body mass index (BMI), and it might also cause a larger area of skin erosion in older patients who are more prone to skin lesions.[5] In addition, in female patients, the implant location of the S-ICD can interfere with the location of the bra, which may cause irritation and discomfort.[6] Furthermore, the 2 devices differ in the incidence and type of complications. In transvenous devices, complications are frequently related to the lead and more often require invasive interventions, while in patients with an S-ICD, pocket hematomas are more common.[7] Finally, fewer patients with a TV-ICD receive appropriate shocks due to the ability to give antitachycardia pacing with the transvenous device, but antitachycardia pacing may potentially induce electrical storms.[8] Besides this, patients with an S-ICD receive numerically more inappropriate shocks, which are associated with a reduction in QoL.[9] It is unclear whether the mentioned device characteristics cause differences in QoL between S-ICD and TV-ICD recipients.

The randomized PRAETORIAN trial showed that the S-ICD is noninferior to the TV-ICD with regard to the composite end point of device-related complications and inappropriate shocks.[10] However, it is unclear whether the differences between the devices have an effect on QoL. Previously, nonrandomized smaller studies with shorter follow-up durations have shown conflicting results, ranging from reduced QoL in patients with an S-ICD to no significant differences between the S-ICD and TV-ICD.[11–13] In this prespecified analysis of the PRAETORIAN trial, we investigate the impact of S-ICD and TV-ICD therapy on QoL.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Patient Population and Study Overview

The PRAETORIAN trial enrolled 849 patients with a class I or IIa indication for ICD therapy for both primary and secondary prevention, aged ≥18 years, in 39 centers in Europe and the United States. Patients with a pacing indication or a known ventricular tachycardia below 170 bpm, or with therapy-refractory monomorphic ventricular tachycardia, were excluded from the trial. Trial design with complete inclusion and exclusion criteria, was published elsewhere.[10] The study was approved by the institutional review boards of the participating centers, and all participants provided written informed consent. The study subjects in this trial were randomly allocated to subcutaneous (n=426) or transvenous (n=423) defibrillator therapy, with stratification according to the center. ICD programming was mandated by protocol. Patients were enrolled between March 2011 and January 2017 and followed until December 2019, with a median follow-up duration of 49.1 months. Data on shocks, complications, and questionnaires were collected.

Questionnaires

The validated 36-Item Short Form Health Survey (SF-36; version 1) and the Duke Activity Status Index (DASI) questionnaires were used to collect self-reported QoL and functional capacity. Questionnaires were distributed during hospital visits, sent by mail, or occasionally administered by the research staff via a telephone call. The DASI reflects cardiac-specific physical functioning and scores from 0 (worst) to 58 (best), with direct questions rather than a recall of prior activities.[14] This questionnaire was used to investigate whether the device size and location would have an impact on the daily activities, under the premise that this would also affect QoL. The SF-36 yields 8 subscales, all covering different areas of mental health and physical well-being, ranging from 0 (worst) to 100 (best), with a recall period of 4 weeks.[15] These scales include role limitations (both physical and emotional), physical functioning, bodily pain, social functioning, mental health, vitality, and general health. The questionnaire gives an indication of overall QoL and is widely used in the literature, as well as in other ICD trials.[16] Questionnaires were completed at baseline, discharge, 12 months, and 30 months. QoL at baseline was assessed before randomization. For the comparison between the S-ICD and TV-ICD, we used the outcomes of the DASI and the SF-36 subscales mental health and bodily pain, as the largest differences were expected to be found in these subscales due to the larger size and location of the S-ICD generator, which may cause discomfort and aesthetic issues. The minimal clinically important difference is considered 4 points for the DASI.[14,16] For the SF-36, this is one-quarter of an SD, which is ≈5 points for mental health and 7 points for bodily pain in this cohort.[15]

Shocks and Complications

By definition, shocks were appropriate when given for ventricular tachycardia/ventricular fibrillation and inappropriate if given for anything other than ventricular tachycardia/ventricular fibrillation. The complications included in this analysis were all major complications requiring invasive interventions. Lead and device repositioning, lead and device replacements, device extractions, pocket explorations, and drain insertions after the initial implantation attempt were considered invasive interventions.[7] For both shocks and complications, only patients who had a shock or complication within 90 days before filling out a questionnaire were included, as the impact of these events decreases after a longer period of time.[16,17] To determine differences between patients with and without shocks, the SF-36 subscales social functioning, mental health, and role limitations due to emotional problems were used. For differences due to complications, the DASI and subscales physical functioning, role limitations due to physical health problems, and bodily pain were analyzed.

Statistical Analysis

Descriptive statistics are presented as mean with SD or median with interquartile range (IQR) for continuous variables and as proportions and percentages for categorical variables. Baseline variables were compared using a Mann-Whitney *U* test, χ^2 test, Fisher exact test, or Student *t* test, as appropriate. DASI questionnaires were not used if >2 questions were unanswered. For the SF-36, we calculated the subscales separately, so that if all questions for 1 subscale were answered, the subscale was calculated. Data were not imputed if missing. Mann-Whitney *U* tests were used to compare absolute questionnaire scores between study arms. A mixed model for repeated measures over time was used to describe the course of the questionnaire outcomes, corrected for device type, BMI, age, NYHA class, ischemic cardiomyopathy, hypertension, diabetes, atrial fibrillation, history of coronary artery bypass grafting, left ventricular ejection fraction, and primary/secondary prevention. In this model, subjects were fitted as random effect and time was fitted as a fixed effect. Absolute scores were included in the model and time was treated as a categorical variable. Regression models and *P* values for interaction were used for subgroup analysis based on sex, BMI, and age for both 12- and 30-month follow-up. To compare QoL between patients with and without a shock or with and without a complication, changes in scores compared with baseline were calculated. A 2-sided $P<0.05$ was considered statistically significant. All statistical analyses were performed using R software, version 4.0.3.

RESULTS

Patient Population

In total, 824 of 849 (97%) patients completed questionnaires at baseline, 772 of 849 (91%) at discharge, 716 of 815 (88%) at 12 months, and 582 of 776 (75%) at 30 months of follow-up (Figure 1). The baseline characteristics of all patients who completed at least 1 questionnaire at baseline are shown in the Table. The median age was 63 (IQR, 54–69) years in the S-ICD group and 64 (IQR, 56–69) years in the TV-ICD group, women made up 20% of the S-ICD group and 19% of the TV-ICD group (sex assigned at birth), and the median left ventricular ejection fraction was 30% (IQR, 25–35) in both arms. There were no significant differences in baseline characteristics between the S-ICD and TV-ICD, except for BMI (27 [IQR, 25–30] versus 28 [IQR, 25–32]; $P=0.003$).

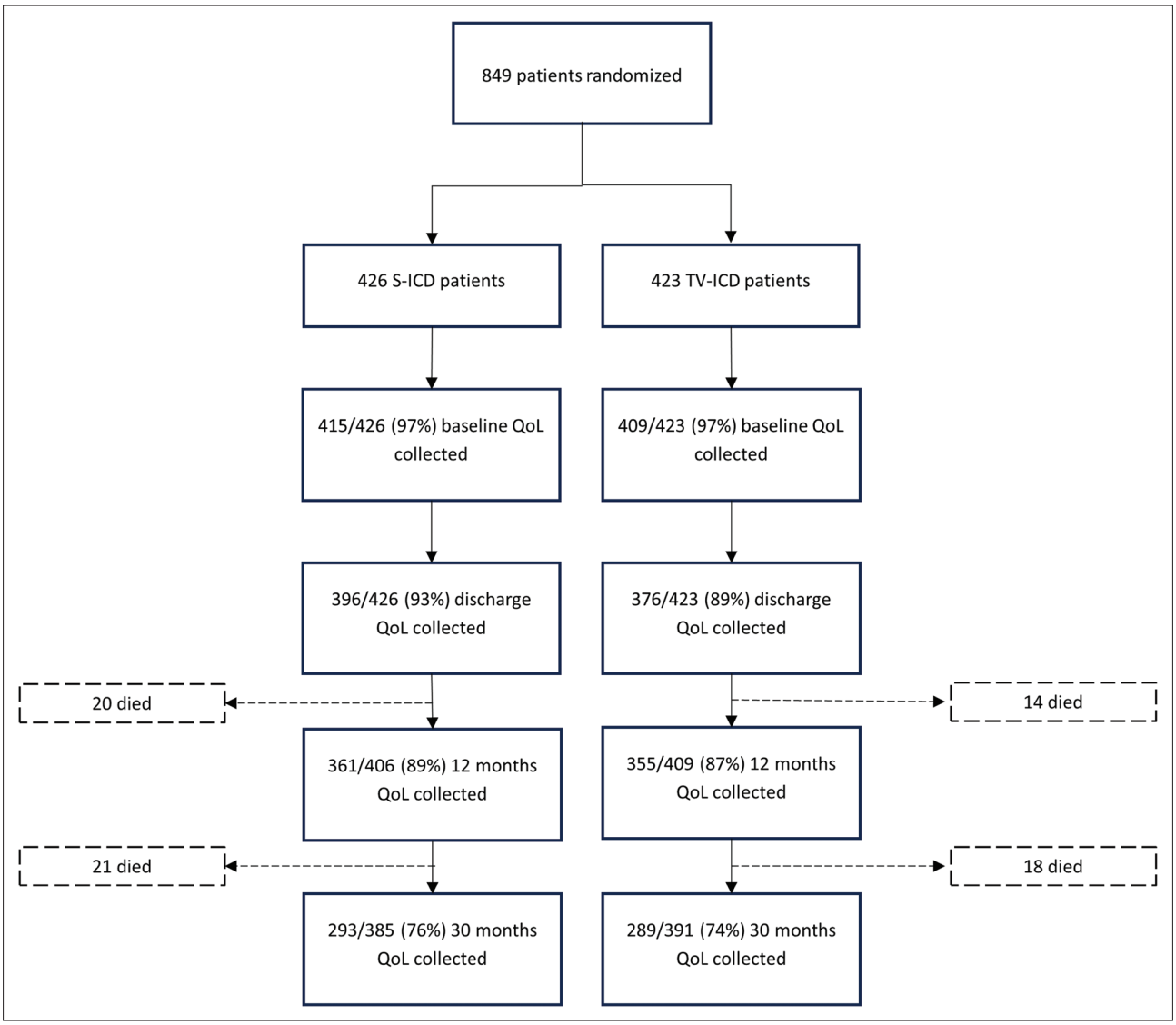

Figure 1. Flowchart of questionnaire completion.
Questionnaires were considered completed if at least 1 36-Item Short Form Health Survey subscale was available. QoL indicates quality of life; S-ICD, subcutaneous implantable cardioverter-defibrillator; and TV-ICD, transvenous implantable cardioverter-defibrillator.

QoL and DASI Over Time and in Subgroups

There were no significant differences in the DASI, mental health and bodily pain scores between the S-ICD and TV-ICD at baseline, discharge, 12 months, and 30 months (Figure 2).

A mixed model for repeated measures over time corrected for BMI, age, NYHA class, ischemic cardiomyopathy, hypertension, diabetes, atrial fibrillation, history of coronary artery bypass grafting, left ventricular ejection fraction, and primary/secondary prevention showed similar results. The outcomes of the other 6 SF-36 subscales are provided in Figure S1.

At 12 months, there were no significant differences in scores across subgroups based on sex, BMI, and age (Figure S2). At 30 months, subgroup analysis showed that patients with a BMI <25 kg/m^2 had significantly better mental health when implanted with a TV-ICD (P=0.02; Figure 3). No other differences were found between subgroups.

Regardless of device type, between baseline and discharge, there was a significant decrease of 4.9 (95% CI, −6.3 to −3.6) points on the DASI (P<0.001) and a significant decrease of 6.8 (95% CI, −9.5 to −4.1) points on the SF-36 subscale bodily pain (P<0.001). This was not seen for mental health (−0.4, points [95% CI, −2.0 to 1.2]; P=0.63). At 12 and 30 months, there were no significant differences compared with baseline in the DASI and SF-36 subscales bodily pain and mental health (Figure S3).

Effect of Shocks on QoL

Appropriate shocks were experienced by 21 patients within 90 days before a questionnaire (14 in the S-ICD

Table. Baseline Characteristics

	Subcutaneous ICD, n=415	Transvenous ICD, n=409
Median age, IQR; y	63 (54–69)	64 (56–69)
Female sex, n (%)	84 (20)	76 (19)
Median LVEF, IQR; %	30 (25–35)	30 (25–35)
Median body mass index, IQR; kg/m^2	27 (25–30)	28 (25–32)
Secondary prevention, %	76 (18)	82 (20)
Diagnosis, n/total n (%)		
Ischemic CMP	280/415 (67)	288/409 (70)
Nonischemic CMP	98/415 (24)	94/409 (23)
Genetic arrhythmia syndrome	20/415 (5)	18/409 (4)
Congenital heart disease	3/415 (1)	3/409 (1)
Other	14/415 (3)	6/409 (1)
NYHA class, n/total n (%)		
Class I	141/412 (34)	129/407 (32)
Class II	198/412 (48)	216/407 (53)
Class III	70/412 (17)	60/407 (15)
Class IV	3/412 (1)	2/407 (0)
Other conditions, n/total n (%)		
Hypertension or the use of antihypertensive drugs	223/413 (54)	232/405 (57)
Hypercholesterolemia or use of lipid-lowering drugs	155/408 (38)	171/404 (42)
Current or recent smoking	116/396 (29)	135/390 (35)
Diabetes	110/415 (27)	120/407 (29)
History of atrial fibrillation	112/415 (27)	90/406 (22)
History of nonsustained ventricular tachycardia	45/413 (11)	44/403 (11)

CMP indicates cardiomyopathy; ICD, implantable cardioverter-defibrillator; IQR, interquartile range; LVEF, left ventricular ejection fraction; and NYHA, New York Heart Association.

group and 7 in the TV-ICD group). In total, 8 patients had an inappropriate shock within 90 days before completing a questionnaire (4 in the S-ICD group and 4 in the TV-ICD group). Patients who received a shock had a significantly larger decrease on the subscales social functioning (P=0.008; median of −12.5 points for TV-ICD and −6.25 points for S-ICD) and role limitations due to emotional problems (P=0.001; median of 0 points for TV-ICD and 0 points for S-ICD) but not on mental health (P=0.104; median of −4 points for both TV-ICD and S-ICD; Figure 4). These differences were not apparent after expanding the time window between the shock and QoL assessment to 12 months. There were no significant differences between treatment arms in the QoL of patients who experienced a shock (P>0.05). Furthermore, there were no differences in QoL between patients with inappropriate or appropriate shocks (Figure S4).

Effect of Complications on QoL

There were 22 patients who had a complication requiring invasive intervention within 90 days before completing a questionnaire (8 in the S-ICD group and 14 in the TV-ICD group). Among these patients, 16 had a complication before discharge (6 in the S-ICD group and 10 in the TV-ICD group). At discharge, there were no significant differences between patients with and without a complication on the DASI and SF-36 subscales physical functioning, role limitations due to physical problems, or bodily pain. There were also no differences between the S-ICD and TV-ICD among patients with a complication. These results were consistent during follow-up (Figure S5).

DISCUSSION

This is the first randomized trial that compared the QoL of patients implanted with an S-ICD or TV-ICD. The main finding of this study was that there were no significant differences in QoL between the S-ICD and TV-ICD. At discharge, both arms had a significantly lower QoL compared with baseline, which was not reported during longer-term follow-up. Besides this, patients who experienced a shock had a lower QoL within 90 days after the shock than patients without a shock, regardless of device type. Furthermore, low BMI was associated with better mental health in patients with a TV-ICD at the 30-month follow-up.

Previous smaller nonrandomized studies on QoL between patients with an S-ICD and TV-ICD have shown conflicting results. Thienel et al[12] reported an impaired QoL in patients implanted with an S-ICD, while other studies by Köbe et al[18] and Pedersen et al[11,13] showed no significant differences between patients with S-ICD and TV-ICDs, or even better physical well-being with the S-ICD. Our study, the largest study to date, shows no differences in QoL between patients with an S-ICD and TV-ICD. The conflicting results may be caused by the use of varying questionnaires assessing QoL. Thienel et al specifically focused on discomfort and the sense of security created by the ICD. Pederson et al and Köbe et al both used the SF-12 questionnaire, which is a shorter adaption of the SF-36 that was used in our study. The SF-36 is a validated QoL questionnaire that focuses on overall QoL, whereas the use of specific questions has the risk of focusing only on aspects related to a specific hypothesis while overlooking aspects for which no difference is expected.

Effect of Shocks and Complications on QoL

Earlier studies reported a decrease in QoL in patients after ICD shocks.[16,17,19] Our data confirmed a significantly lower QoL in social functioning and role limitations due to emotional problems in patients within 90 days after a shock. Furthermore, patients who experienced a shock showed a larger decrease in QoL compared with baseline on mental health, even though it was not significant. This is possibly due to the relatively low number of patients

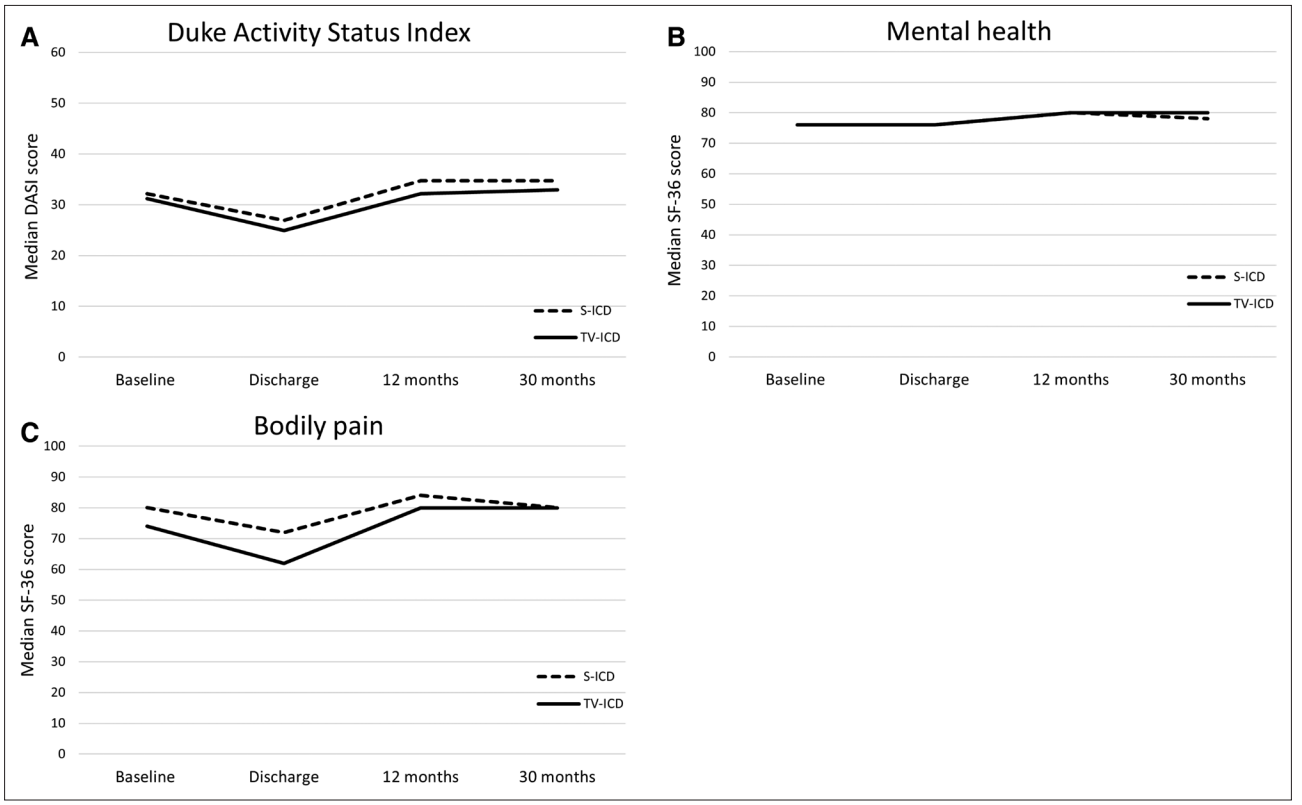

Figure 2. Outcomes between subcutaneous implantable cardioverter-defibrillator (S-ICD) and transvenous implantable cardioverter-defibrillator (TV-ICD) over time.

Questionnaire outcomes over time between the S-ICD and TV-ICD. **A**, Duke Activity Status Index (DASI). **B**, Mental health subscale of 36-Item Short Form Health Survey (SF-36). **C**, Bodily pain subscale of SF-36. The course of all remaining subscales can be found in Supplemental Material (Figure S1).

who experienced a shock within the 90-day time frame. Expanding the time frame would likely have led to a larger group of patients with shocks, but the effect of shocks on QoL is expected to be smaller when the event occurred longer ago.[16] This assumption was supported by our results not showing significant differences after prolonging the time window to 12 months. Furthermore, the fact that we found no difference in QoL between patients with inappropriate or appropriate shocks underlines that attention should be paid to avoiding inappropriate shocks, as these shocks have the same negative effect on QoL as appropriate shocks but are useless for the termination of ventricular arrhythmia. Inappropriate shocks are associated with increased mortality and can be proarrhythmic.[9,20,21] Earlier studies showed that inappropriate shocks are more common in S-ICD recipients, although better programming and new software algorithms have substantially decreased the inappropriate shock rate.[22,23] Our results indicate that QoL is reduced by the experience of a shock in general and the fact that an appropriate shock is life-saving does not counteract this effect. However, the data must be interpreted with caution, as the number of patients with a shock shortly before a questionnaire was low.

Surprisingly, unlike ICD shocks, complications were not associated with a lower QoL. This might be due to the fact that most complications occurred during or immediately after implantation, such that it is not possible to make a distinction between the effect of the implantation itself with subsequent discomfort and complications related to the implantation. The effect of a recent implantation procedure might be larger than the effect of a complication, which could be the explanation for an overall similar QoL between patients with and without complications.

Subgroup Analysis

It has been reported that female patients with an S-ICD experience various physical, aesthetic, and social issues, due to the generator and lead. Nevertheless, our subgroup analysis based on sex showed no difference between the S-ICD and TV-ICD, underlining that issues might also be present in men and in patients with a TV-ICD or that these issues do not reduce overall QoL. Among women with an S-ICD, patients with a lower BMI are less positive about the visibility of the S-ICD.[6] Furthermore, low BMI results in less tissue and potentially thinner skin overlying a cardiovascular implantable electronic device, which is associated with skin erosion.[24] Thinner skin is also more prevalent among older patients, which could lead to a

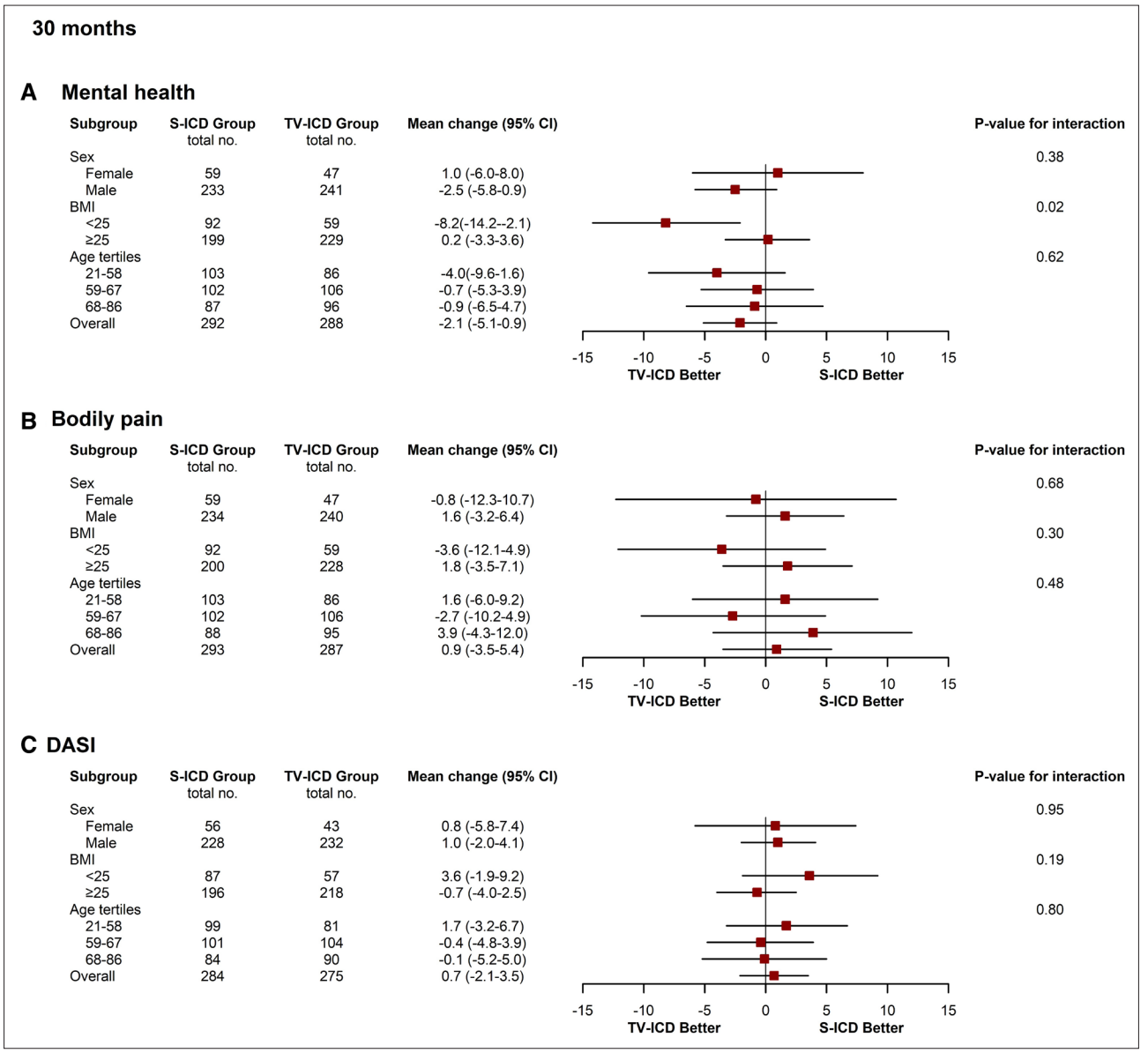

Figure 3. Subgroup analysis at 30 months.
Subgroup analysis at 30-month follow-up. **A**, Mental health. **B**, Bodily pain. **C**, Duke Activity Status Index (DASI). BMI indicates body mass index; SF-36, 36-Item Short Form Health Survey; S-ICD, subcutaneous implantable cardioverter-defibrillator; and TV-ICD, transvenous implantable cardioverter-defibrillator.

lower QoL in higher age groups.[5] On the contrary, the aesthetic and physical issues may be more prevalent in younger patients, affecting their QoL. Our subgroup analysis showed no differences based on age but did show significantly better mental health among patients with a BMI <25 kg/m^2 at 30 months of follow-up in the TV-ICD group compared with the S-ICD group. Even though this study was not powered for this type of subgroup analysis, these results underline that the generator size and location should be discussed with patients undergoing S-ICD implantation, and special attention should be given to the S-ICD implant position in thinner patients. In these patients, a subserratus or intermuscular position should be considered.

Clinical Implications

As no significant differences in QoL were observed between the S-ICD and TV-ICD in this study, this could help patients and their physicians in their shared decision-making process about which device is more suitable for a specific patient. Furthermore, the implantation of an ICD, in general, has no negative effect on QoL after 30 months, as no significant differences were reported between baseline and follow-up.

Limitations

This study has several limitations. First, as this was a secondary outcome measure, the study was not

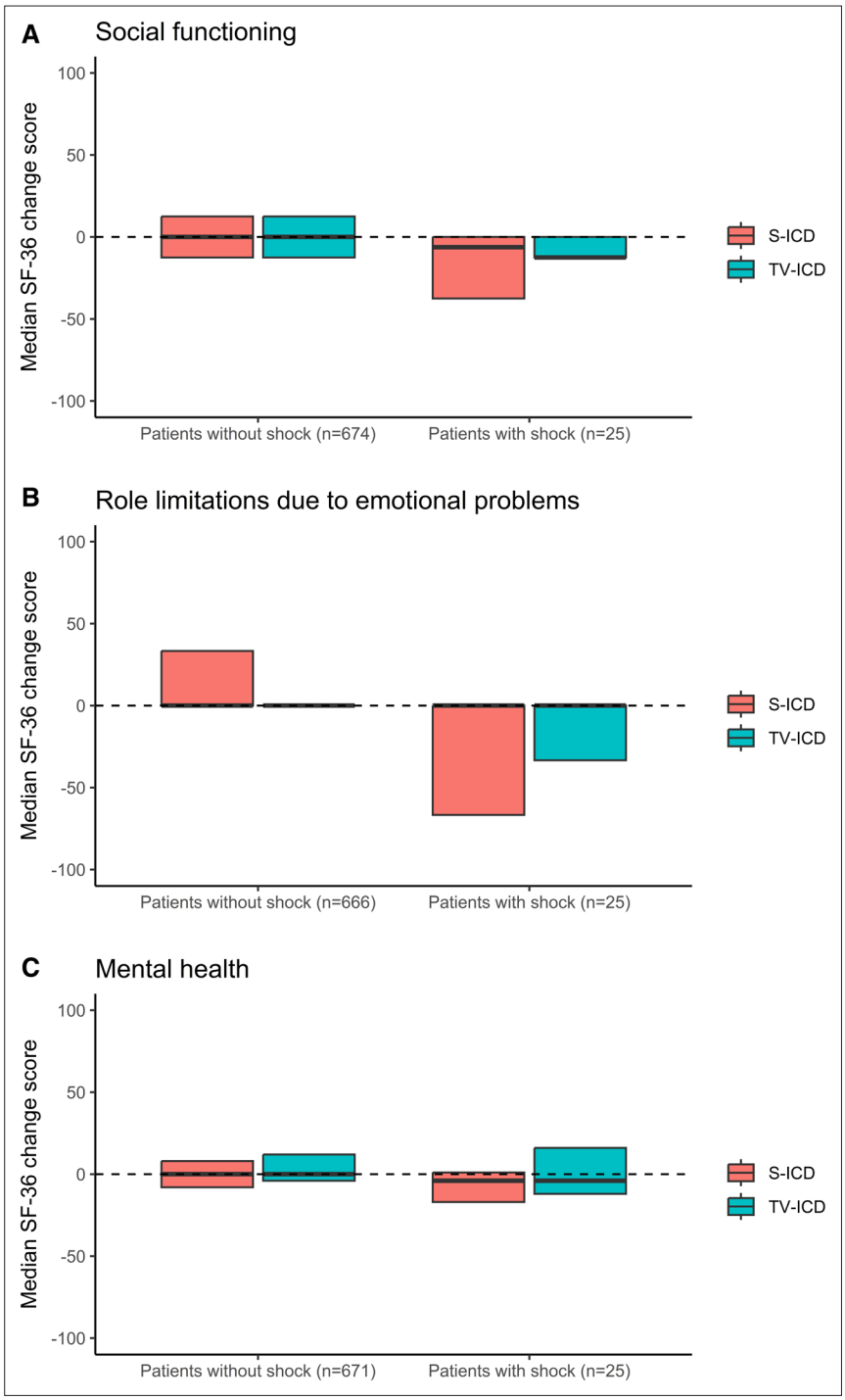

Figure 4. Quality of life after a shock. Median change score (dark line), presented with interquartile range. **A**, Social functioning. **B**, Role limitations due to emotional problems. **C**, Mental health. Orange, subcutaneous implantable cardioverter-defibrillator (S-ICD); blue, transvenous implantable cardioverter-defibrillator (TV-ICD). For patients without a shock, their change score from baseline to 12 months was used. An analysis using the change score from baseline to 30 months showed comparable results. Numbers of patients without a shock differ as not all subscales were completed by all patients. One patient with a shock did not complete the SF-36. Three patients had both an appropriate and an inappropriate shock.

powered to test the effect of ICD type on QoL. Second, as the protocol did not specifically collect questionnaires after a shock or after complications, there were limited data available on patients with shocks and complications. Third, this study is limited by the low number of female patients, making the results less generalizable. Fourth, interpreting significant differences in this study should be performed with caution, as *P* values were uncorrected for multiple testing. Fifth, the SF-36 and DASI are generic questionnaires and are not validated specifically for patients with an ICD. Although these questionnaires focus on the impact on daily activities, mental health, and bodily pain, which we hypothesized would be impacted in patients with an ICD, these questionnaires may not be sensitive enough to detect any meaningful differences. Sixth, the follow-up duration of the questionnaires was until 30 months after implantation, whereas the longevity of both the S-ICD and TV-ICD is much longer. Last, both patients and physicians were not blinded to the study arms.

Conclusions

In this randomized analysis, we report no significant difference in QoL between patients implanted with an S-ICD or TV-ICD. QoL is reduced after implantation and may be transiently impacted by shocks, but these effects do not persist.

ARTICLE INFORMATION

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Affiliations

Department of Cardiology, Amsterdam Cardiovascular Sciences Heart Failure and Arrhythmias, Amsterdam University Medical Centers Location University of Amsterdam, Heart Center, the Netherlands (R.E.K., J.A.d.V., L.V.A.B., T.F.B., S.P., A.-F.B.E.Q., L.S., W.v.d.S., A.d.W., J.R.d.G., K.M.K., J.G.P.T., A.A.M.W., L.R.A.O.N.). Department of Cardiology, Isala Heart Centre, Zwolle, the Netherlands (A.G.). Department of Cardiology, St. Antonius Hospital, Nieuwegein, the Netherlands (L.V.A.B.). First Department of Medicine, University Medical Center Mannheim, Germany (J.K.). German Center for Cardiovascular Research, Partner Site Heidelberg, Mannheim, Germany (J.K.). Division of Cardiology, Section of Electrophysiology, Emory University, Atlanta, GA (M.F.E.C.). Klinik für Innere Medizin III, Schwerpunkt Kardiologie und Angiologie, Universitätsklinikum Schleswig-Holstein, Campus Kiel, Germany (H.B.). St George's University of London, United Kingdom (E.R.B.). St George's University Hospitals NHS Foundation Trust, London, United Kingdom (E.R.B.). Department of Medicine I, Ludwig-Maximillians University Hospital, München, Germany (S.K.). German Center for Cardiovascular Research, Munich Heart Alliance, Germany (S.K.). European Reference Network for Rare, Low Prevalence and Complex Diseases of the Heart (S.K., A.A.M.W.). The Valley Health System, Ridgewood, NJ (S.M.). Department of Cardiology, Flevoziekenhuis, Almere, the Netherlands (N.R.B.). Department of Electrophysiology, Heart Center at University of Leipzig, Germany (S.R.). Heart Surgery, Heart Center Dresden, Carl Gustav Carus Medical Faculty, Dresden University of Technology, Germany (S.R.). Department of Cardiology, Radboud University Medical Center, Nijmegen, the Netherlands (M.A.B.). Office of the Director of Clinical Electrophysiology Research and Lead for Inherited Arrhythmia Specialist Services, University College London and Barts Heart Centre, United Kingdom (P.D.L.). Department of Cardiology, Homolka Hospital, Prague, Czech Republic (P. Neuzil). Department of Cardiology, Cardiovascular Research Institute Maastricht, Maastricht University Medical Center, the Netherlands (K.V.). Department of Cardiology, Amphia Hospital, Breda, the Netherlands (M.A.). Werkgroep Cardiologische Centra Nederland, Utrecht, the Netherlands (M.A.). Oxford Biomedical Research Centre, Oxford University Hospitals NHS Trust, United Kingdom (T.R.B.). Department of Electrophysiology, Catharina Hospital Eindhoven, the Netherlands (F.A.L.E.B.). CorVita Science Foundation, Chicago, IL (M.C.B.). Department of Cardiology, OLVG, Amsterdam, the Netherlands (J.S.S.G.d.J.). Liverpool Heart and Chest Hospital, United Kingdom (D.J.W.). Department of Cardiology, Tergooi Medisch Centrum, Blaricum, the Netherlands (W.P.J.J.). National Heart and Lung Institute, Imperial College London, United Kingdom (Z.I.W.). University and University Hospital Würzburg, Germany (P. Nordbeck). Heart Surgery, Heart Center Dresden, Carl Gustav Carus Medical Faculty, Dresden University of Technology, Germany (M.K.). Department of Cardiology, The Heart Centre, Rigshospitalet, University of Copenhagen, Denmark (B.T.P.). Medical Spectrum Twente, Enschede, the Netherlands (J.M.v.O.). Division of Cardiology, Northwestern Memorial Hospital, Northwestern University, Chicago, IL (A.B.C.). Department of Cardiology, and Amsterdam Cardiovascular Sciences, Amsterdam University Medical Centers, Location VUMC, the Netherlands (C.P.A.). Medisch Centrum Leeuwarden, the Netherlands (A.E.B.v.d.B.). Department of Medicine—Cardiology, Columbia University Irving Medical Center, New York, NY (J.M.D.). Icahn School of Medicine at Mount Sinai, Mount Sinaï Hospital, New York, NY (M.A.M.). Cardiac Electrophysiology Division, Department of Medicine, Englewood Hospital and Medical Center, NJ (D.N.). Department of Internal Medicine I, Jena University Hospital, Germany (R.S.). Center for Arrhythmia Care, Heart and Vascular Institute, University of Chicago Pritzker School of Medicine, IL (G.A.U.).

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Supplemental Material

Figures S1–S5

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