

ORIGINAL ARTICLE

Subcutaneous or Transvenous Defibrillator Therapy

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ABSTRACT

BACKGROUND

The subcutaneous implantable cardioverter-defibrillator (ICD) was designed to avoid complications related to the transvenous ICD lead by using an entirely extrathoracic placement. Evidence comparing these systems has been based primarily on observational studies.

METHODS

We conducted a noninferiority trial in which patients with an indication for an ICD but no indication for pacing were assigned to receive a subcutaneous ICD or transvenous ICD. The primary end point was the composite of device-related complications and inappropriate shocks; the noninferiority margin for the upper boundary of the 95% confidence interval for the hazard ratio (subcutaneous ICD vs. transvenous ICD) was 1.45. A superiority analysis was prespecified if noninferiority was established. Secondary end points included death and appropriate shocks.

RESULTS

A total of 849 patients (426 in the subcutaneous ICD group and 423 in the transvenous ICD group) were included in the analyses. At a median follow-up of 49.1 months, a primary end-point event occurred in 68 patients in the subcutaneous ICD group and in 68 patients in the transvenous ICD group (48-month Kaplan-Meier estimated cumulative incidence, 15.1% and 15.7%, respectively; hazard ratio, 0.99; 95% confidence interval [CI], 0.71 to 1.39; $P=0.01$ for noninferiority; $P=0.95$ for superiority). Device-related complications occurred in 31 patients in the subcutaneous ICD group and in 44 in the transvenous ICD group (hazard ratio, 0.69; 95% CI, 0.44 to 1.09); inappropriate shocks occurred in 41 and 29 patients, respectively (hazard ratio, 1.43; 95% CI, 0.89 to 2.30). Death occurred in 83 patients in the subcutaneous ICD group and in 68 in the transvenous ICD group (hazard ratio, 1.23; 95% CI, 0.89 to 1.70); appropriate shocks occurred in 83 and 57 patients, respectively (hazard ratio, 1.52; 95% CI, 1.08 to 2.12).

CONCLUSIONS

In patients with an indication for an ICD but no indication for pacing, the subcutaneous ICD was noninferior to the transvenous ICD with respect to device-related complications and inappropriate shocks. (Funded by Boston Scientific; PRAETORIAN ClinicalTrials.gov number, NCT01296022.)

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*A full list of the PRAETORIAN investigators is provided in the Supplementary Appendix, available at [NEJM.org](https://www.nejm.org).

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IMPLANTABLE CARDIOVERTER–DEFIBRILLATORS (ICDs) have been proven to be efficacious in the prevention of sudden cardiac death.^{1–3} Transvenous lead placement for cardiac sensing and defibrillation has been the standard for ICD design for several decades. However, important limitations of the technique include complications related to lead insertion, such as pneumothorax and cardiac perforation, and long-term complications, such as lead endocarditis and lead dysfunction.⁴ To avoid such complications, an entirely subcutaneous ICD was introduced as an alternative.⁵ The extrathoracic placement of the subcutaneous ICD circumvents the need to enter the heart and vasculature but makes it impossible for the device to deliver pacing therapy.

Class IIa recommendations for the subcutaneous ICD in U.S. and European guidelines for patients in whom pacing therapy for bradycardia, cardiac resynchronization, or antitachycardia pacing is not indicated are based on experience from observational studies.^{6–9} The Prospective Randomized Comparison of Subcutaneous and Transvenous Implantable Cardioverter Defibrillator Therapy (PRAETORIAN) trial evaluated whether the subcutaneous ICD would be noninferior to the transvenous ICD with regard to short-term and long-term device-related complications and inappropriate shocks.

METHODS

TRIAL DESIGN AND OVERSIGHT

We conducted this investigator-initiated, international, randomized, noninferiority trial in the United States and Europe. The principal coordinating investigators were responsible for the design of the trial, which has been published previously.¹⁰ The Academic Medical Center Amsterdam was responsible for site contracting, data collection, monitoring, and management. Trial design and execution were overseen by a steering committee, and the conduct of the trial and the safety of the patients were overseen by an independent data and safety monitoring board. The protocol, which is available with the full text of this article at NEJM.org, was approved by the institutional review board at all participating centers.

This trial was funded by Boston Scientific, which had no role in the design of the trial,

analysis of the data, or the drafting and submission of the manuscript. The principal investigators analyzed the data in accordance with the statistical analysis plan and prepared the manuscript. The authors vouch for the accuracy and completeness of the data and for the fidelity of the trial to the protocol.

TRIAL POPULATION

Patients were eligible for entry into this trial if they were 18 years of age or older and had a class I or IIa indication for ICD therapy for primary or secondary prevention, according to the guidelines from the American College of Cardiology–American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society or those from the European Society of Cardiology.^{6,8} Key exclusion criteria were previous ICD implantation, unsuitability for subcutaneous ICD therapy according to QRS-T-wave sensing analysis (see the Supplementary Appendix, available at NEJM.org), and indications for either bradycardia pacing or biventricular pacing. We also excluded patients with known ventricular tachycardia at a rate below 170 beats per minute or with refractory recurrent monomorphic ventricular tachycardia that could not be managed with medication or ablation therapy because, for such patients, antitachycardia pacing was considered to be an especially important therapeutic option. Detailed inclusion and exclusion criteria are provided in the Supplementary Appendix. All the patients provided written informed consent.

RANDOMIZATION AND PROCEDURES

Eligible patients were randomly assigned in a 1:1 ratio to receive either a subcutaneous ICD or transvenous ICD, with stratification according to center. Block sizes ranging from two to eight were used to conceal treatment assignments. All subcutaneous ICDs were manufactured by Cameron Health–Boston Scientific. The choice of transvenous ICD manufacturer was at the discretion of the physician performing the implantation. All transvenous ICDs were single-chamber devices unless a dual-chamber device was deemed to be necessary for the discrimination of arrhythmia. The procedures regarding implantation, defibrillation testing, and hospital discharge followed local clinical practice. All the patients were seen at a follow-up visit with-

in 4 months after implantation. Thereafter, ICDs were interrogated at least twice per year, and patients had at least one annual visit to the outpatient clinic.

ICD PROGRAMMING

Programming of the parameters for the detection of ventricular tachycardia or ventricular fibrillation and for therapeutic variables was standardized and based on the best available evidence at the time of protocol development.¹¹ Programming strategies were comparable between the two treatment groups. The cutoff for the fast ventricular tachycardia zone was set as close to 182 beats per minute as possible, given differences in manufacturer programming options, with one burst of antitachycardia pacing for the transvenous ICD. The cutoff for the ventricular fibrillation zone was 250 beats per minute. Deviation from the recommended device programming was allowed in order to fit the specific characteristics of the patient. Details are provided in the Supplementary Methods section in the Supplementary Appendix.

END POINTS

The composite primary end point of the trial consisted of device-related complications and inappropriate shocks. Complications included device infection that led to the extraction of the lead or generator; pocket hematoma that led to drainage, blood transfusion, or prolongation of hospitalization; device-related thrombotic events; pneumothorax or hemothorax that led to intervention or prolongation of hospitalization; cardiac perforation or tamponade; lead repositioning or replacement; and other complications related to the lead or generator that led to medical or surgical intervention. An ICD shock was classified as inappropriate when it was delivered for any rhythm other than ventricular fibrillation or ventricular tachycardia. Secondary end points included the individual components of the primary end point, death from any cause, appropriate ICD therapy (including antitachycardia pacing), major adverse cardiac events, hospitalization for heart failure, and crossover between the assigned devices.

A clinical-events committee consisting of three electrophysiologists who were not otherwise involved in the trial adjudicated all clinical and arrhythmic events. Shock therapy and other ar-

rhythmic events that were derived from regular device interrogation were classified as being either appropriate or inappropriate according to the rhythm that initiated the therapy. Hence, shocks without electrograms were not adjudicated. A complete overview of trial end points and definitions is provided in the Supplementary Appendix.

STATISTICAL ANALYSIS

The trial was designed to test the hypothesis of noninferiority of the subcutaneous ICD as compared with the transvenous ICD with respect to the time from device implantation to the first occurrence of a primary end-point event. The noninferiority margin for the upper boundary of the 95% confidence interval for the hazard ratio was set at 1.45. The estimation of cumulative incidence and sample-size justification have been reported previously.¹⁰ We estimated that the occurrence of a primary end-point event in the transvenous ICD group would be 17.2% at 48 months.^{1,11} Assuming that 5% of patients would discontinue the trial, we calculated that the enrollment of 425 patients in each group would provide the trial with 85% power to show noninferiority of the subcutaneous ICD at a one-sided alpha level of 0.025. A superiority analysis was prespecified if noninferiority was established.

Analyses for all the end points were performed in the modified intention-to-treat population, which included patients according to the group to which they had been randomly assigned, regardless of the device they received. Patients who did not receive either device after randomization or who underwent randomization in error were excluded from the analyses. A sensitivity analysis was performed in the as-treated population, which included patients according to the treatment that they first received. Additional sensitivity analyses included, among others, a competing-risks analysis to account for death and incomplete follow-up, an analysis to account for missing electrographic data from the device, and a multiple imputation analysis by fully conditional specification.¹²

For the time-to-event analyses, cumulative incidence curves were constructed with the use of the Kaplan–Meier method, and hazard ratios and 95% confidence intervals were calculated by Cox proportional-hazards models. For these analyses, missing data were presumed to be missing

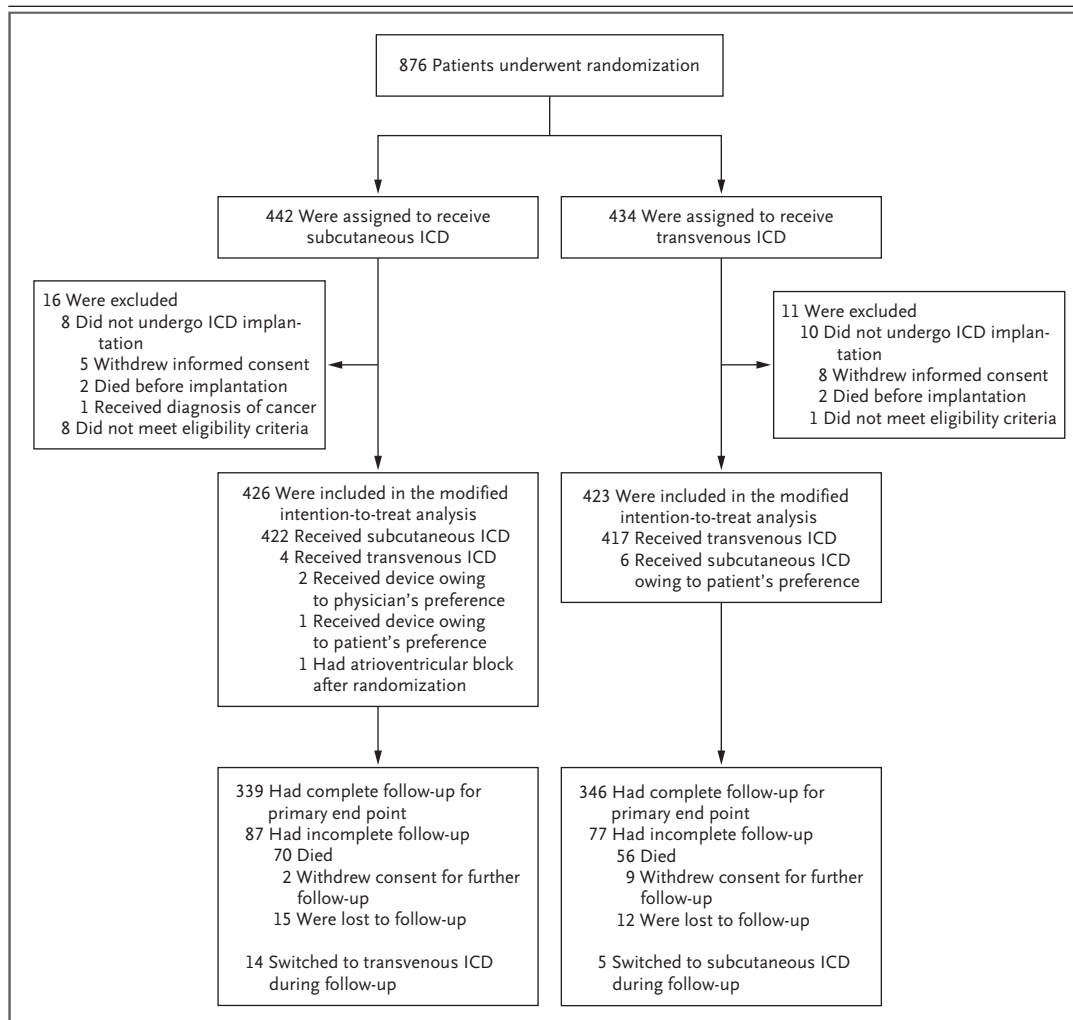


Figure 1. Randomization, Implantation, and Follow-up of the Patients.

Screening details and the reasons for exclusion are presented in Figure S1 and Table S2, respectively. A total of 16 patients in the group that was assigned to receive the subcutaneous implantable cardioverter–defibrillator (ICD) and 11 patients in the group that was assigned to receive the transvenous ICD were excluded from the modified intention-to-treat analysis because they either did not undergo ICD implantation or had undergone randomization in error. A total of 4 patients in the subcutaneous ICD group and 6 patients in the transvenous ICD group never underwent any attempt to implant the assigned device but instead received the alternate device. A total of 70 patients in the subcutaneous ICD group and 56 patients in the transvenous ICD group died before having a composite primary end-point event (device-related complication or inappropriate shock).

at random, and data were censored for patients with incomplete follow-up on the last known event-free day. The confidence intervals were not adjusted for multiplicity and therefore should not be used to infer definitive treatment effects. Prespecified subgroups that were defined according to age, sex, and body-mass index were analyzed for the occurrence of a primary end-point event. Additional information regarding the statistical analyses is provided in the Supple-

mentary Appendix. Statistical analyses were performed with the use of R software, version 3.6.2 (R Core Team).

RESULTS

PATIENTS AND IMPLANTATIONS

From March 2011 through January 2017, a total of 876 patients were enrolled at 39 centers in Europe and the United States (Fig. 1 and Table S1

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Subcutaneous ICD (N=426)	Transvenous ICD (N=423)
Median age (IQR) — yr	63 (54–69)	64 (56–70)
Female sex — no. (%)	89 (20.9)	78 (18.4)
Diagnosis — no. (%)		
Ischemic cardiomyopathy	289 (67.8)	298 (70.4)
Nonischemic cardiomyopathy	99 (23.2)	98 (23.2)
Genetic arrhythmia syndrome	20 (4.7)	18 (4.3)
Hypertrophic cardiomyopathy	15 (3.5)	7 (1.7)
Idiopathic ventricular fibrillation	11 (2.6)	5 (1.2)
Congenital heart disease	3 (0.7)	3 (0.7)
Other†	4 (0.9)	1 (0.2)
Secondary prevention — no. (%)	80 (18.8)	84 (19.9)
Median ejection fraction (IQR) — %	30 (25–35)	30 (25–35)
Mean QRS duration — msec	105±19	105±20
NYHA class — no./total no. (%)		
I	144/423 (34.0)	134/421 (31.8)
II	205/423 (48.5)	223/421 (53.0)
III or IV	74/423 (17.5)	64/421 (15.2)
Median body-mass index (IQR)‡	27.0 (24.5–30.5)	27.9 (25.2–31.7)
Hypertension or use of antihypertensive drugs — no./total no. (%)	227/424 (53.5)	240/419 (57.3)
Hypercholesterolemia or use of lipid-lowering drugs — no./total no. (%)	161/419 (38.4)	175/418 (41.9)
Current or recent smoking — no./total no. (%)	119/406 (29.3)	139/401 (34.7)
Diabetes mellitus — no./total no. (%)	112/426 (26.3)	126/421 (29.9)
Previous CABG — no./total no. (%)	86/425 (20.2)	85/421 (20.2)
History of atrial fibrillation — no./total no. (%)	115/426 (27.0)	93/420 (22.1)
History of nonsustained ventricular tachycardia — no./total no. (%)	46/423 (10.9)	44/417 (10.6)
History of syncope — no./total no. (%)	23/420 (5.5)	33/418 (7.9)
Site location — no. (%)		
Europe	394 (92.5)	395 (93.4)
United States	32 (7.5)	28 (6.6)
Median time from randomization to device implantation (IQR) — days	7.5 (1.0–29.0)	6.0 (1.0–26.5)

* Plus-minus values are means ±SD. CABG denotes coronary-artery bypass grafting, ICD implantable cardioverter-defibrillator, IQR interquartile range, and NYHA New York Heart Association.

† The patients in this category had ventricular fibrillation due to coronary spasm (one patient in the subcutaneous ICD group and one in the transvenous ICD group), coronary dissection (one in the subcutaneous ICD group), ischemic stroke (one in the subcutaneous ICD group), and myocarditis (one in the subcutaneous ICD group).

‡ The body-mass index is the weight in kilograms divided by the square of the height in meters.

in the Supplementary Appendix). Information about patients who underwent screening and reasons for exclusion are provided in Figure S1 and Table S2. Of the 876 patients enrolled, 27 were excluded from the primary analysis; 18 did not undergo ICD implantation and 9 had undergone randomization in error. A total of 849 pa-

tients were included in the primary analysis; of these patients, 426 were randomly assigned to the subcutaneous ICD group and 423 to the transvenous ICD group (Fig. 1). The clinical characteristics of the patients at baseline were similar in the two groups (Table 1). The median age of the patients was 63 years (interquartile

range, 55 to 70); 19.7% of the patients were women, and 69.1% had ischemic cardiomyopathy. The median left ventricular ejection fraction was 30%.

Details of the initial implantation procedure are provided in Table S3. Of the patients in the transvenous ICD group, 48 (11.3%) received a dual-chamber device at initial implantation. A total of 10 patients crossed over to the other device without any attempt to implant the assigned device. Five additional patients crossed over shortly after initial implantation, and 14 patients crossed over during follow-up. Details of all the crossovers are provided in Table S4. Details of adherence to the device programming protocol are provided in Table S5.

FOLLOW-UP AND PRIMARY END POINT

Follow-up of the trial was completed on December 1, 2019. A total of 339 patients in the subcutaneous ICD group and 346 patients in the transvenous ICD group had complete follow-up (Fig. 1). The median duration of follow-up was 49.1 months (48.0 months in the subcutaneous ICD group and 50.6 months in the transvenous ICD group). The primary end point occurred in 68 patients in the subcutaneous ICD group and in 68 patients in the transvenous ICD group (48-month Kaplan–Meier estimated cumulative incidence, 15.1% and 15.7%, respectively). The hazard ratio for the primary end point was 0.99 (95% confidence interval [CI], 0.71 to 1.39; non-inferiority margin, 1.45; $P=0.01$ for noninferiority; $P=0.95$ for superiority) (Fig. 2A and Table 2).

Device-related complications occurred in 31 patients in the subcutaneous ICD group and in 44 patients in the transvenous ICD group (cumulative incidence, 5.9% and 9.8%, respectively; hazard ratio, 0.69; 95% CI, 0.44 to 1.09) (Fig. 2B). The incidence of complications within the first 30 days was 3.8% in the subcutaneous ICD group and 4.7% in the transvenous ICD group. The incidence of complications related to the ICD lead was lower in the subcutaneous ICD group than in the transvenous ICD group (1.4% vs. 6.6%) (Fig. S2).

Inappropriate shocks occurred in 41 patients in the subcutaneous ICD group and in 29 patients in the transvenous ICD group (cumulative incidence, 9.7% and 7.3%, respectively; hazard ratio, 1.43; 95% CI, 0.89 to 2.30) (Fig. 2C). The first occurrences of inappropriate shocks in the

subcutaneous ICD group were most frequently caused by cardiac oversensing (in 58.5% of the patients with an inappropriate shock), whereas inappropriate shocks in the transvenous ICD group were more commonly triggered by supraventricular arrhythmia (in 93.1%) (Table 2). Deviations from the programming protocol at the time of first inappropriate shocks are described in the Supplementary Results section in the Supplementary Appendix; the findings indicated that two episodes of inappropriate shocks in the transvenous ICD group may have been prevented if the prespecified programming had been used.

The findings of the primary analysis were consistent in the as-treated population (Fig. S3). There were no between-group differences in the occurrence of the primary end point across prespecified subgroups (Fig. S4). Results of the competing-risks analyses, multivariable analyses, and sensitivity analyses that account for missing data are provided in Tables S6 through S11.

SECONDARY END POINTS

During the course of the trial, 83 patients in the subcutaneous ICD group and 68 patients in the transvenous ICD group died (hazard ratio, 1.23; 95% CI, 0.89 to 1.70) (Table 3 and Fig. S5). Causes of death are presented in Table S12. In each group, 18 patients died suddenly.

Appropriate ICD shocks were more frequent in patients in the subcutaneous ICD group than in those in the transvenous ICD group (19.2% vs. 11.5%; hazard ratio, 1.52; 95% CI, 1.08 to 2.12) (Table 3 and Fig. S6) and included subcutaneous ICD shocks due to oversensing of ventricular tachycardia below the programmed therapy zone in 11 patients. Appropriate antitachycardia pacing was delivered in 12.9% of the patients in the transvenous ICD group and successfully terminated 55% of all treated episodes of ventricular tachycardia. A total of 5 patients in the subcutaneous ICD group underwent implantation of a transvenous device for pacing for the treatment of bradycardia. There were no between-group differences in the cumulative incidence of major adverse cardiac events, hospitalization for heart failure, or total crossovers (Table 3), although there were numerically more crossovers during follow-up (shortly after the implantation attempt or later in follow-up) from the subcutaneous ICD to the transvenous ICD (14 patients) than vice versa (5 patients).

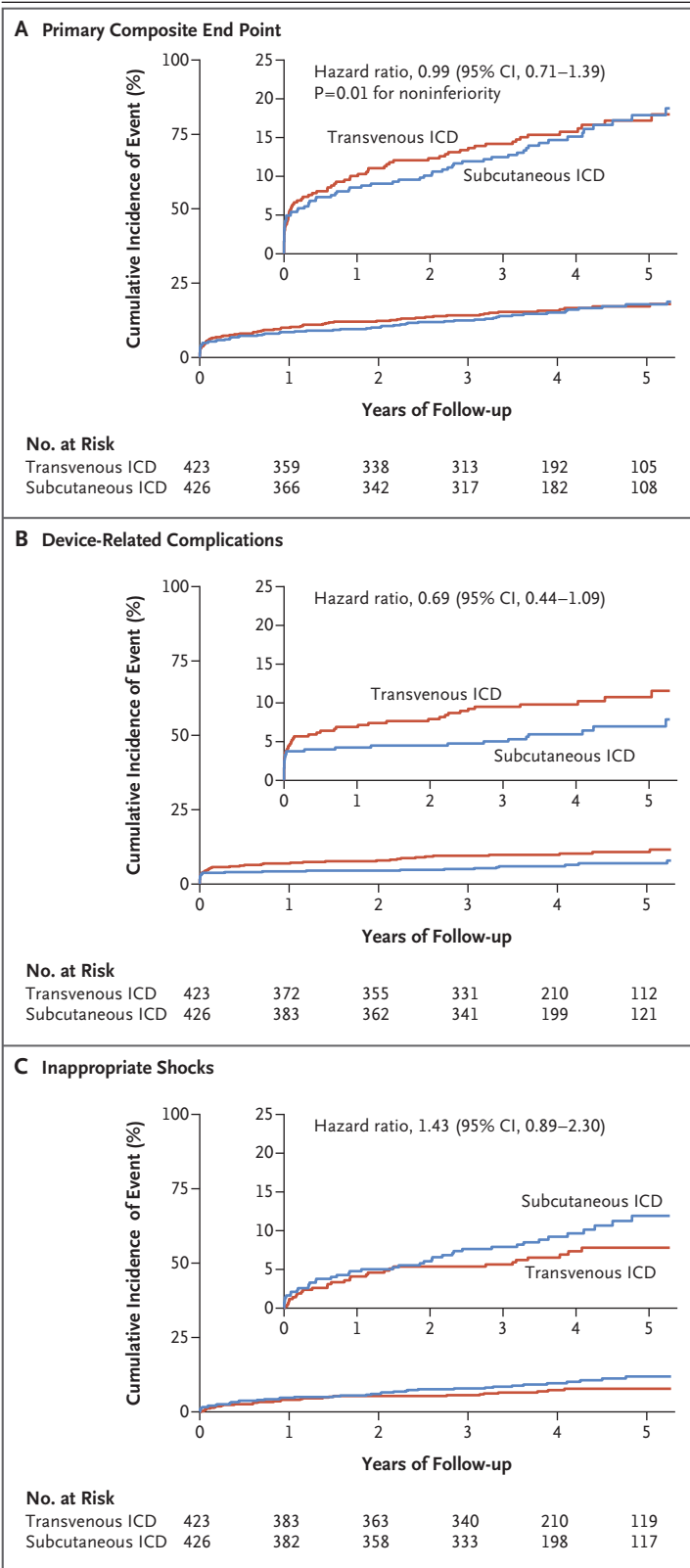


Figure 2. Time-to-First-Event Curves for the Primary End Point and Its Components.

Shown is the cumulative incidence of the first occurrence of the composite primary end point (Panel A) and its components, the first device-related complication (Panel B) and the first inappropriate shock (Panel C). Hazard ratios were derived from Cox regressions and indicate the relative risk (subcutaneous ICD vs. transvenous ICD) of the end point. The 95% confidence intervals were not adjusted for multiple comparisons and therefore should not be used to infer definitive treatment effects. Insets show the same data on an enlarged y axis.

DISCUSSION

In this trial, we found that the subcutaneous ICD was noninferior to the transvenous ICD with respect to device-related complications or inappropriate shocks in patients with an indication for defibrillator therapy but with no indication for pacing. The results were consistent in several sensitivity analyses and subgroup analyses. We observed equal numbers of sudden cardiac deaths in the two groups, but there were numerically more deaths from other causes in the subcutaneous ICD group than in the transvenous ICD group.

With respect to the two components of the primary outcome, there was a higher cumulative incidence of device-related complications in the transvenous ICD group and a higher cumulative incidence of inappropriate shocks in the subcutaneous ICD group, although the trial was not powered for these comparisons. Perspectives may vary among physicians and patients about which component poses a heavier burden: whereas complications are associated primarily with physical distress, ICD shocks can have profound psychological implications.¹³

The overall incidence of complications in this trial was as anticipated and was similar to that in previous studies.^{4,14,15} Fewer lead-related complications (including infection, perforation, lead dislodgement, and lead dysfunction) and subsequent surgical reinterventions occurred in the subcutaneous ICD group than in the transvenous ICD group, but this effect was counterbalanced by more frequent pocket hematomas with the subcutaneous ICD. The use of general anesthesia and defibrillation testing was much greater with the subcutaneous ICD than with the

Table 2. Primary Composite End Point.*

End point	Subcutaneous ICD (N=426)	Transvenous ICD (N=423)	Hazard Ratio (95% CI)
Primary composite end point — no. (%)	68 (15.1)	68 (15.7)	0.99 (0.71–1.39)†
Components of primary end point			
Device-related complication — no. (%)	31 (5.9)	44 (9.8)	0.69 (0.44–1.09)
Infection — no.‡	4	8	
Bleeding — no.	8	2	
Thrombotic event — no.	1	2	
Pneumothorax — no.§	0	4	
Lead perforation — no.§	0	4	
Tamponade — no.	0	2	
Lead repositioning — no.§	2	7	
Other lead or device complication — no.	19	20	
Lead replacement¶	3	9	
Device malfunction	4	6	
Sensing issues	4	0	
Pacing indication	5	1	
Implantation failure	0	3	
Defibrillation test failure**	3	0	
Pain or discomfort	2	3	
Inappropriate shock — no. (%) ††	41 (9.7)	29 (7.3)	1.43 (0.89–2.30)
Atrial fibrillation or supraventricular tachycardia — no.	11	27	
Cardiac oversensing — no.‡‡	24	2	
Noncardiac oversensing — no.§§	8	0	

* Percentages are 4-year cumulative incidences based on Kaplan–Meier estimates in time-to-first-event analyses. Multiple end points could occur in one patient; only the first end point was included in the estimation of the cumulative incidence. For all end points, the sample included all the patients in the trial group. The widths of the 95% confidence intervals have not been adjusted for multiplicity and therefore should not be used to infer definitive treatment effects.

† P=0.01 for noninferiority; P=0.95 for superiority.

‡ This category included lead-related infections in one patient in the subcutaneous ICD group and in five in the transvenous ICD group.

§ This end point was included in the composite end point “lead-related complications” (Fig. S2).

¶ In the subcutaneous ICD group, lead replacements were due to dislocation in two patients and to myopotential oversensing in one. In the transvenous ICD group, lead replacements were due to lead dysfunction in six patients and to lead dislodgement in three.

|| In the subcutaneous ICD group, three patients received a pacemaker, one received a cardiac-resynchronization therapy device with a defibrillator (CRT-D), and one crossed over to transvenous ICD therapy — all for pacing for the treatment of bradycardia. In the patient in the transvenous ICD group who had previously crossed over to subcutaneous ICD therapy, sick-sinus syndrome later developed, for which a pacemaker was implanted.

** This category included defibrillator test failures that led to surgical reintervention.

†† The subcutaneous ICD sensing filter (SMART Pass) was not activated or was unavailable in 78% of the first inappropriate shocks in the subcutaneous ICD group.

‡‡ This category included T-wave and P-wave oversensing and includes shock on atrial fibrillation or supraventricular tachycardia below the detection limit in five patients in the subcutaneous ICD group.

§§ This category included myopotential and noise oversensing.

transvenous ICD. Longer-term follow-up of this cohort will be important because the incidence of lead-related complications increases over time

with the transvenous ICD¹⁶ and because battery longevity is a limiting factor for the subcutaneous ICD.¹⁷

Table 3. Secondary End Points.*

End Point	Subcutaneous ICD (N = 426)	Transvenous ICD (N = 423)	Hazard Ratio (95% CI)
Death from any cause — no. (%)	83 (16.4)	68 (13.1)	1.23 (0.89–1.70)
Sudden cardiac death — no.†	18	18	
Death from other cardiovascular causes — no.	34	28	
Death from noncardiovascular causes — no.	31	22	
Appropriate shock therapy — no. (%)	83 (19.2)	57 (11.5)	1.52 (1.08–2.12)
Ventricular fibrillation — no.	32	22	
Ventricular tachycardia within therapy zone — no.	57	41	
Ventricular tachycardia below therapy zone — no.‡	11	0	
Antitachycardia pacing — no. (%)§			
Appropriate	6 (0.6)	54 (12.9)	
Inappropriate	1 (0.3)	30 (7.2)	
Major adverse cardiac event — no. (%)	64 (13.3)	80 (16.4)	0.80 (0.57–1.11)
Hospitalization for heart failure — no. (%)	79 (17.4)	74 (16.1)	1.08 (0.79–1.49)
Crossover to other study device — no. (%)	18 (4.3)	11 (2.7)	1.64 (0.77–3.47)
Before initial implantation — no.	4	6	
During implantation or follow-up — no.	14	5	
Upgrade to CRT-D — no. (%)	16 (3.5)	21 (4.2)	

* Percentages are 4-year cumulative incidences based on Kaplan–Meier estimates in time-to-first-event analyses. For all end points, the sample included all the patients in the trial group. The widths of the 95% confidence intervals were not adjusted for multiplicity and therefore should not be used to infer definitive treatment effects.

† This category included death from unexplained causes.

‡ These shocks were delivered on ventricular tachycardia below the programmed therapy limit with oversensing of cardiac signals. The sensing filter (SMART Pass) was not activated or was unavailable in 91% of the first occurrences of such events.

§ Patients who received antitachycardia pacing in the subcutaneous ICD group had previously crossed over to transvenous ICD therapy or had received a CRT-D.

Patients with a subcutaneous ICD had a higher risk of inappropriate shock than anticipated; the shocks were most frequently precipitated by oversensing of cardiac signals (predominantly T waves) and noncardiac signals. Although shocks on supraventricular arrhythmias can generally be managed with device reprogramming or medication, shocks caused by cardiac or noncardiac oversensing are less modifiable. However, a sensing filter that attenuates oversensing, which resulted in a 50% reduction of first inappropriate shocks in an earlier study, was introduced in a later stage of the trial.¹⁸ This filter was unavailable or not activated in the majority (78%) of patients with a subcutaneous ICD during their first inappropriate shock. Therefore, this trial could not assess the potential benefit of the sensing filter. Such changes to

device technology may improve the future performance of the subcutaneous ICD.

We observed a higher cumulative incidence of appropriate shocks with the subcutaneous ICD than with the transvenous ICD, which was, for the most part, explained by the inability of the subcutaneous ICD to deliver antitachycardia pacing. Antitachycardia pacing terminated ventricular tachycardia in more than half the pacing attempts with the transvenous ICD. In addition, the sensing of the subcutaneous ICD, which is based on morphologic features, can result in double-counting of slow ventricular tachycardia occurring at a rate below the programmed therapy zone, thus causing the sensed rate (if both QRS complexes and T waves are counted) to exceed the therapy threshold. According to the end-point definition, which was based on earlier

ICD trials, these shocks were classified as appropriate but — although occasionally clinically desirable — could be considered to be unnecessary.^{19,20}

This trial has several limitations. First, the members of the clinical-events committee were aware of the trial-group assignments. Second, device technology evolved throughout the trial, and practitioners who performed the implantations had less experience with the subcutaneous ICD than with the transvenous ICD, which could have affected clinical outcomes. Third, screening data were incomplete, and thus selection bias could not be ruled out. Fourth, 27 patients were excluded before device implantation, 38 patients were lost to follow-up, and 126 patients died before having a primary end-point event. However, sensitivity analyses yielded consistent results. Fifth, it is debatable whether the magnitude of the possible between-group difference as reflected by the noninferiority margin is clinically acceptable. Finally, the median follow-up of 48 months was too limited to provide information on chronic complications. Long-term follow-up is therefore warranted and is ongoing.

The results of our trial showed that among patients with an indication for ICD therapy but not for pacing therapy, the subcutaneous ICD was noninferior to the transvenous ICD with respect to the cumulative incidence of the primary end point of device-related complications or inappropriate shocks.

A data sharing statement provided by the authors is available with the full text of this article at NEJM.org.

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APPENDIX

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