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ORIGINAL RESEARCH ARTICLE

Efficacy and Safety of Appropriate Shocks and Antitachycardia Pacing in Transvenous and Subcutaneous Implantable Defibrillators: Analysis of All Appropriate Therapy in the PRAETORIAN Trial

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BACKGROUND: The PRAETORIAN trial (A Prospective, Randomized Comparison of Subcutaneous and Transvenous Implantable Cardioverter Defibrillator Therapy) showed noninferiority of subcutaneous implantable cardioverter defibrillator (S-ICD) compared with transvenous implantable cardioverter defibrillator (TV-ICD) with regard to inappropriate shocks and complications. In contrast to TV-ICD, S-ICD cannot provide antitachycardia pacing for monomorphic ventricular tachycardia. This prespecified secondary analysis evaluates appropriate therapy and whether antitachycardia pacing reduces the number of appropriate shocks.

METHODS: The PRAETORIAN trial was an international, investigator-initiated randomized trial that included patients with an indication for implantable cardioverter defibrillator (ICD) therapy. Patients with previous ventricular tachycardia <170 bpm or refractory recurrent monomorphic ventricular tachycardia were excluded. In 39 centers, 849 patients were randomized to receive an S-ICD (n=426) or TV-ICD (n=423) and were followed for a median of 49.1 months. ICD programming was mandated by protocol. Appropriate ICD therapy was defined as therapy for ventricular arrhythmias. Arrhythmias were classified as discrete episodes and storm episodes (≥3 episodes within 24 hours). Analyses were performed in the modified intention-to-treat population.

RESULTS: In the S-ICD group, 86 of 426 patients received appropriate therapy, versus 78 of 423 patients in the TV-ICD group, during a median follow-up of 52 months (48-month Kaplan-Meier estimates 19.4% and 17.5%; *P*=0.45). In the S-ICD group,

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83 patients received at least 1 shock, versus 57 patients in the TV-ICD group (48-month Kaplan-Meier estimates 19.2% and 11.5%; *P*=0.02). Patients in the S-ICD group had a total of 254 shocks, compared with 228 shocks in the TV-ICD group (*P*=0.68). First shock efficacy was 93.8% in the S-ICD group and 91.6% in the TV-ICD group (*P*=0.40). The first antitachycardia pacing attempt successfully terminated 46% of all monomorphic ventricular tachycardias, but accelerated the arrhythmia in 9.4%. Ten patients with S-ICD experienced 13 electrical storms, versus 18 patients with TV-ICD with 19 electrical storms. Patients with appropriate therapy had an almost 2-fold increased relative risk of electrical storms in the TV-ICD group compared with the S-ICD group (*P*=0.05).

CONCLUSIONS: In this trial, no difference was observed in shock efficacy of S-ICD compared with TV-ICD. Although patients in the S-ICD group were more likely to receive an ICD shock, the total number of appropriate shocks was not different between the 2 groups.

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

Key Words: defibrillators, implantable ■ electrophysiology ■ tachycardia

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Clinical Perspective

What Is New?

- This is the first trial to study the shock efficacy of subcutaneous and transvenous implantable cardioverter defibrillator in a randomized population.
- Although efficacy of the first antitachycardia pacing attempt was 46% in monomorphic ventricular tachycardia, the number of shocks was not different between subcutaneous and transvenous implantable cardioverter defibrillator.

What Are the Clinical Implications?

- Shock efficacy is not statistically different between subcutaneous and transvenous implantable cardioverter defibrillator, and the decision for either device should be made in a shared decision-making process between patient and physician.
- Physicians are recommended to observe the efficacy of antitachycardia pacing in the individual patient. When antitachycardia pacing is repeatedly unsuccessful in terminating ventricular arrhythmias, we recommend limiting programming to a single antitachycardia pacing attempt.

Nonstandard Abbreviations and Acronyms

ATP	antitachycardia pacing
HR	hazard ratio
ICD	implantable cardioverter defibrillator
IQR	interquartile range
PRAETORIAN	A Prospective, Randomized Comparison of Subcutaneous and Transvenous Implantable Cardioverter Defibrillator Therapy
RR	relative risk
S-ICD	subcutaneous implantable cardioverter defibrillator
TV-ICD	transvenous implantable cardioverter defibrillator
VF	ventricular fibrillation
VT	ventricular tachycardia

Implantable cardioverter defibrillators (ICDs) improve survival in people at risk for ventricular arrhythmias and sudden cardiac death.[1–3] Subcutaneous ICD (S-ICD) is an effective extravascular alternative to traditional transvenous ICD (TV-ICD). The randomized controlled PRAETORIAN trial (A Prospective, Randomized Comparison of Subcutaneous and Transvenous Implantable Cardioverter Defibrillator Therapy) demonstrated noninferiority of S-ICD compared with TV-ICD with regard to inappropriate shocks and complications in patients with a Class I or IIa indication for ICD therapy according to current guidelines.[4] Antitachycardia pacing (ATP) has been developed as a painless method to terminate ventricular tachycardias (VTs) and might decrease the number of appropriate shocks.[5] Conversely, ATP might be given unnecessarily for VTs that would have ended spontaneously and might even accelerate VTs. The reported efficacy ranges from 52% to 81%, and some studies have observed higher mortality in patients treated by ATP.[6–10] Because of its extrathoracic design, S-ICD is incapable of providing pacing therapy, including ATP.[11,12] In this prespecified secondary analysis of the PRAETORIAN trial, we aimed to determine the efficacy and safety of ATP and shocks by comparing appropriate therapies in S-ICD and TV-ICD and investigated whether ATP reduced the number of appropriate ICD shocks.

METHODS

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

Design and Population of the PRAETORIAN Trial

The PRAETORIAN trial was an international, investigator-initiated, multicenter, randomized noninferiority trial that was conducted in the United States and Europe.[4] Enrollment started in March 2011 and ended in January 2017. Patients with a Class I or IIa indication for ICD therapy and without the need for bradycardia pacing or cardiac resynchronization therapy were eligible to participate. Patients with known VT at a rate below 170 beats per minute and patients with refractory recurrent monomorphic VT that could not be managed with medication or ablation therapy were excluded. Patients were randomly assigned in a 1:1 ratio to receive either S-ICD or TV-ICD, with stratification according to center. Programming of detection and therapy parameters was standardized and aimed to reduce avoidable appropriate and inappropriate shocks (Table 1). Deviation from the recommended device programming was allowed to fit the specific characteristics of the patient. The study protocol was approved by the institutional review committees and all patients provided written informed consent.

End Point Definitions

The main end points of this secondary analysis include total appropriate therapy and patients with appropriate therapy and first shock efficacy. A post hoc analysis was performed to evaluate the efficacy of ATP and the occurrence of electrical storms. Appropriate ICD therapy was defined as ATP or shock therapy for either VT or ventricular fibrillation (VF). Successful therapy was defined as a shock or ATP that is able to convert the ventricular arrhythmia to sinus rhythm or atrial fibrillation within 5 seconds. Shock efficacy was defined as the percentage of successful shocks of the total amount of shocks. ATP efficacy was calculated as the proportion of successful ATP attempts of the total ATP delivered on a monomorphic VT. ATP for polymorphic VT and VF were excluded from the calculation of ATP efficacy because ATP is not expected to be successful for these arrhythmias. The start of a ventricular arrhythmia marked the beginning of an episode and episodes end after conversion of the arrhythmia. Episodes were classified as discrete and storm episodes. An electrical storm was defined as ≥3 episodes of VT/VF within 24 hours.[13] Cardiac rhythm at time of ICD therapy was adjudicated by an independent clinical event committee consisting of 3 experienced electrophysiologists not otherwise involved in the trial. 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, but excluded patients who did not receive any ICD. An as-treated analysis that included patients according to the ICD that they first received, as well as a per protocol analysis that censors patients if they receive a different ICD at any moment in the study, were performed for the occurrence of electric storms in both groups and are included in the Supplemental Appendix.

Statistical Analyses

Descriptive statistics are reported as mean±SD or median with interquartile range (IQR) for continuous variables and numbers and percentages for categorical variables. Baseline variables were compared using the Fisher exact test, χ^2 test, Student *t* test, or Mann-Whitney *U* test, as appropriate. For time to event variables, Kaplan-Meier curves displaying the pattern of events are constructed and 4-year Kaplan-Meier estimates of the event rate are reported for both study groups and compared using log-rank tests. Participants without events are censored at their last known event-free time point. Hazard ratios (HRs) and 95% CIs were calculated by Cox proportional hazard models. Univariable and multivariable Cox proportional hazard models were performed to find predictors of appropriate therapy. Relative risks (RRs) and 95% CI were estimated using the Wald method. A negative binomial regression analysis was performed to assess the rate ratio of appropriate shocks between the groups. To adjust for multiple episodes per patient, shock and ATP efficacy estimations were adjusted using the generalized estimating equation method with exchangeable correlation matrix. A *P* value <0.05 was considered statistically significant. All statistical analyses were performed using R software version 4.0.3 (RStudio PBC). Detailed information on the statistical analyses can be found in the Supplemental Appendix.

RESULTS

In the PRAETORIAN trial, a total of 849 patients were included, of whom 426 patients were assigned to the S-ICD group and 423 patients to the TV-ICD group. Baseline characteristics of the population are presented in Table S1. Further details and results of the PRAETORIAN trial are published elsewhere.[4,14]

Table 1. Standardized Implantable Cardioverter Defibrillator Programming in the PRAETORIAN Trial

	S-ICD		TV-ICD		
	Conditional zone	Unconditional zone	Monitor zone	Fast VT zone	VF zone
Arrhythmia detection zones, beats/min	>180	>250	>167	>182	>250
Time to initiate therapy, s (charge for shock or ATP)	Fixed (18/24: 6 s)	Fixed (18/24: 4.3 s)	11	10	7.2
Therapy	Shocks at maximum output	Shocks at maximum output	No therapy	(1) 1 burst of ATP*; (2) shocks at maximum output	Shocks at maximum output
Pacing programming	Postshock pacing "on"		VVI 40 beats/min		

ATP indicates antitachycardia pacing; ICD, implantable cardioverter defibrillator; PRAETORIAN, A Prospective, Randomized Comparison of Subcutaneous and Transvenous Implantable Cardioverter Defibrillator Therapy; S-ICD, subcutaneous implantable cardioverter defibrillator; TV-ICD, transvenous implantable cardioverter defibrillator; VF, ventricular fibrillation; and VT, ventricular tachycardia.

*Consists of 8 intervals with a pacing length of 88% of the tachycardia length.

In the S-ICD group, 86 patients had a total of 256 episodes with appropriate therapy, versus 78 patients in the TV-ICD group with 348 episodes, during a median follow-up time of 52 months (IQR, 41.4–68.5 months). There was no statistical difference in the number of patients with appropriate therapy between the 2 groups (48-month Kaplan-Meier estimated cumulative incidence, 19.4% and 17.5%, respectively; HR, 1.12 [95% CI, 0.83–1.53]; *P*=0.45; Figure 1). Median time from start of arrhythmia to first therapy was 17.4 seconds in the S-ICD group (IQR, 15.0–20.4 seconds) versus 10.4 seconds in the TV-ICD group (IQR, 9.2–12.6 seconds).

In the S-ICD group, in 2 of 256 episodes (0.8%), the electrograms of appropriate therapy were not available, versus 106 of 348 episodes (30.5%) with an unavailable electrogram in the TV-ICD group. Three patients who received appropriate therapy were primarily implanted with a different device from the group to which they were randomized (0 of 86 in the S-ICD group versus 3 of 78 in the TV-ICD group). Five additional patients crossed over during follow-up (5 of 86 in the S-ICD group versus 0 of 78 in the TV-ICD group) and 13 patients received an upgrade to a cardiac resynchronization therapy defibrillator during follow-up (8 of 86 in the S-ICD group versus 5 of 78 in the TV-ICD group). A list of the crossovers is presented in Table S2.

The clinical characteristics at baseline of patients with appropriate therapy were similar in the 2 groups (Table 2). Median age was 63 years (IQR, 55–68), 17.1% were women, 68.3% had ischemic cardiomyopathy, and 28.1% received their ICD for a secondary prevention indication. The median ejection fraction was 28% (IQR, 20%–35%). A multivariable analysis showed that a secondary prevention indication for ICD therapy and a lower left ventricular ejection fraction at baseline were significantly associated with an increased risk for appropriate therapy (*P*<0.01 and *P*<0.01; Table S3).

Appropriate Shocks

In the S-ICD group, 83 patients were treated with at least 1 shock, versus 57 patients in the TV-ICD group (48-month Kaplan-Meier estimated cumulative incidence, 19.2% and 11.5%, respectively; HR, 1.52 [95% CI, 1.08–2.12]; *P*=0.02; Figures 2 and 3). A total of 254 shocks occurred in 242 episodes in the S-ICD group and 228 shocks occurred in 193 episodes in the TV-ICD group (0.60 versus 0.54 shock per patient; rate ratio, 1.11; *P*=0.68; Table S4). First and final shock efficacy were 93.8% and 97.9% in the S-ICD group versus 91.6% and 98.4% in the TV-ICD group (*P*=0.40 and *P*=0.70; Figure S1). The arrhythmias that were not terminated by the ICD all ended spontaneously after the

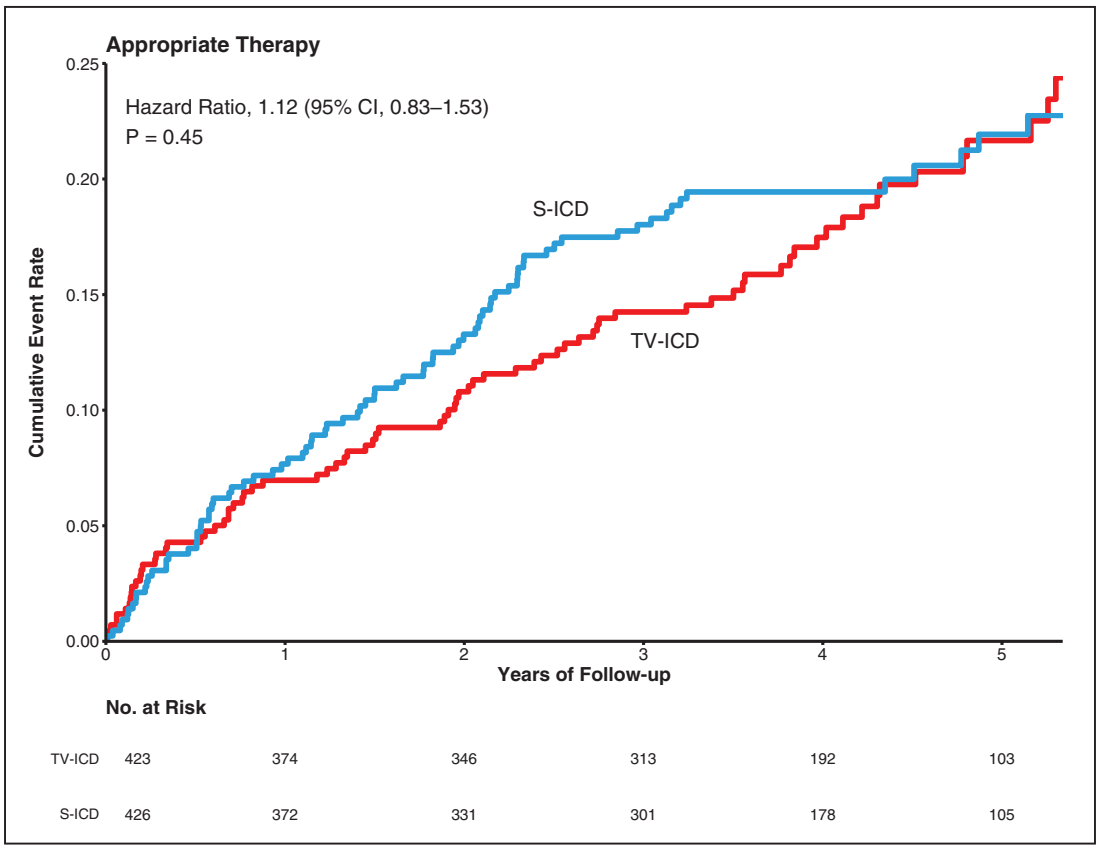

Figure 1. Kaplan-Meier curve of all patients with appropriate therapy in the PRAETORIAN trial.
CI indicates confidence interval; PRAETORIAN, A Prospective, Randomized Comparison of Subcutaneous and Transvenous Implantable Cardioverter Defibrillator Therapy; S-ICD, subcutaneous implantable cardioverter defibrillator; and TV-ICD, transvenous implantable cardioverter defibrillator.

Table 2. Characteristics of Patients With Appropriate Therapy

	Patients with appropriate therapy (n=164)		
	S-ICD (n=86)	TV-ICD (n=78)	*P* value
Age, y	63 (55–68)	63 (54–68)	0.90
Female	11 (12.8)	17 (21.8)	0.13
Diagnosis			0.91
Ischemic cardiomyopathy	58 (67.4)	54 (69.2)	
Nonischemic cardiomyopathy	21 (24.4)	18 (23.1)	
Genetic arrhythmia syndrome	4 (4.7)	4 (5.1)	
Idiopathic VF	1 (1.2)	2 (2.6)	
Congenital heart disease	1 (1.2)	0 (0.0)	
Other	1 (1.2)	0 (0.0)	
Secondary prevention	22 (25.6)	24 (30.8)	0.46
Ejection fraction	28 (20–35)	29 (22–35)	0.55
QRS duration	107±19	108±19	0.83
NYHA class			0.13
I	32/86 (37.2)	34/77 (44.2)	
II	38/86 (44.2)	37/77 (48.1)	
III/IV	16/86 (18.6)	6/77 (7.8)	
Body mass index*	27.2 (24.4–30.1)	27.4 (25.0–30.5)	0.52
Medication at discharge			
β-blocker	68 (79.1)	67 (85.9)	0.25
Amiodarone	6 (7.0)	4 (5.1)	0.87

Values are median (interquartile range), mean±SD, or n (%). NYHA indicates New York Heart Association; S-ICD, subcutaneous implantable cardioverter defibrillator; TV-ICD, transvenous implantable cardioverter defibrillator; and VF, ventricular fibrillation.

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

final shock and no deaths were observed resulting from an inefficient shock. Shock efficacy adjusted per multiple episodes per patient is described in Table S5A. This analysis included 11 patients with S-ICD who had 18 shocks on VTs below the programmed therapy zone because of cardiac oversensing. Details of the number of shocks across different arrhythmia rates are provided in Table S6. Median time from start arrhythmia to first shock was shorter in the TV-ICD group (17.8 seconds in the S-ICD group [IQR, 15.3–20.6 seconds] versus 13.8 seconds in the TV-ICD group [IQR, 11.6–17.1 seconds]).

Appropriate ATP

Because this analysis was performed on the modified intention-to-treat population, which included crossovers, 18 ATP attempts were observed in 5 patients in the S-ICD group. In the TV-ICD group, 328 ATP attempts occurred in 56 patients, of which 259 (79.0%) were first ATP attempts. Three of 86 patients (3.5%) in the S-ICD group and 21 of 78 patients (26.9%) in the TV-ICD group were treated by ATP only. Of the 259 total first ATP attempts, 234 (90.3%) were given on monomorphic VTs with an efficacy of 46% (95% CI, 39.9%–52.6%). The first ATP attempt on a monomorphic VT accelerated the tachycardia in 9.4% of all episodes, which affected 15 patients (19.2%; Figure 4). ATP efficacy decreased when multiple attempts were given (Table S5B). In total, 102 of 182 discrete episodes (56%) in the TV-ICD group were terminated by ATP only. Details of the efficacy of ATP across different arrhythmia rates are provided in Table S7.

Electric Storms

A total of 10 of 86 patients (11.6%) in the S-ICD group experienced 13 electric storms with 89 storm episodes in which 91 shocks were administered by the ICD. In the TV-ICD group, 18 of 78 patients (23.1%) experienced 19 electric storms with 166 storm episodes in which 149 shocks and 148 ATP attempts were delivered (Figure 5). Patients with appropriate therapy had an almost 2-fold increased RR of electric storms in the TV-ICD group compared with the S-ICD group (RR, 1.98 [95% CI, 0.98 –4.04]; *P*=0.05). These findings were consistent in the as-treated (RR, 1.99 [95% CI, 1.02–4.04]; *P*=0.04) and per protocol analyses (relative risk, 1.99 [95% CI, 0.98–4.04]; *P*=0.05; Table S8).

There were no significant differences in baseline characteristics of patients with an electric storm compared

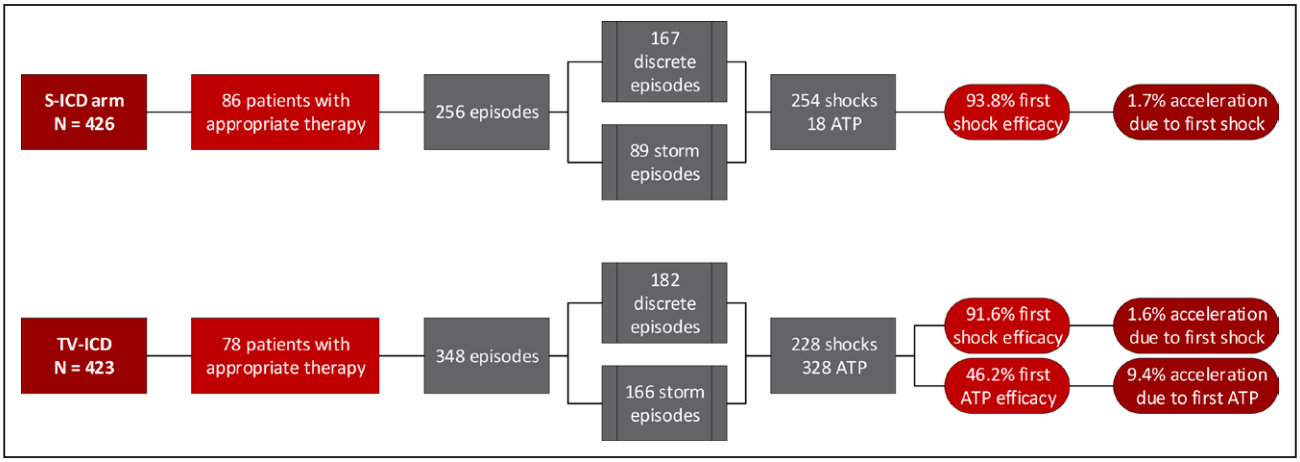

Figure 2. Overview of all patients with appropriate therapy, appropriate episodes, and therapies.
ATP indicates antitachycardia pacing; S-ICD, subcutaneous implantable cardioverter defibrillator; and TV-ICD, transvenous implantable cardioverter defibrillator.

with patients without an electric storm (Table S9). In 6 of 19 electric storms (32%) in the TV-ICD group, >1 ATP attempt per episode was given and ICDs were programmed with more than the single ATP attempt that was specified in the protocol. The first ATP attempt successfully terminated the monomorphic VT in 54.6% of the discrete episodes, versus 35.9% in storm episodes ($P<0.01$). In the TV-ICD group, 77 of 166 electrograms of storm episodes (46%) were overwritten owing to limited storage capacity of the device (Figures S2 and S3).

DISCUSSION

In this secondary analysis of the randomized PRAETORIAN trial, we found no statistical difference in number of patients treated with appropriate ICD therapy in the S-ICD group and TV-ICD group. Patients with S-ICD were more likely to receive an appropriate shock, but the overall number of appropriate shocks was comparable between the 2 groups, despite the inability of the S-ICD to deliver ATP. We observed no difference in first and final shock efficacy in the 2 groups. ATP successfully terminated approximately half of the monomorphic VTs and 1 in 4 patients could be treated by ATP only. The efficacy of ATP decreased after the first attempt and the first ATP attempt accelerated the arrhythmia in 9.4% of the episodes.

The median time from start of arrhythmia to first therapy and shock was shorter in the TV-ICD group compared with the S-ICD group, probably owing to a combination of a shorter time to detection, the delivery of ATP, and a shorter capacitor charge time of the TV-ICD. It is often postulated that a longer time to shock would result in a lower number of shocks, because it reduces the risk of needless treatment of unsustained ventricular arrhythmias. This was not confirmed by our results, as we showed a comparable number of shocks in the 2 groups.

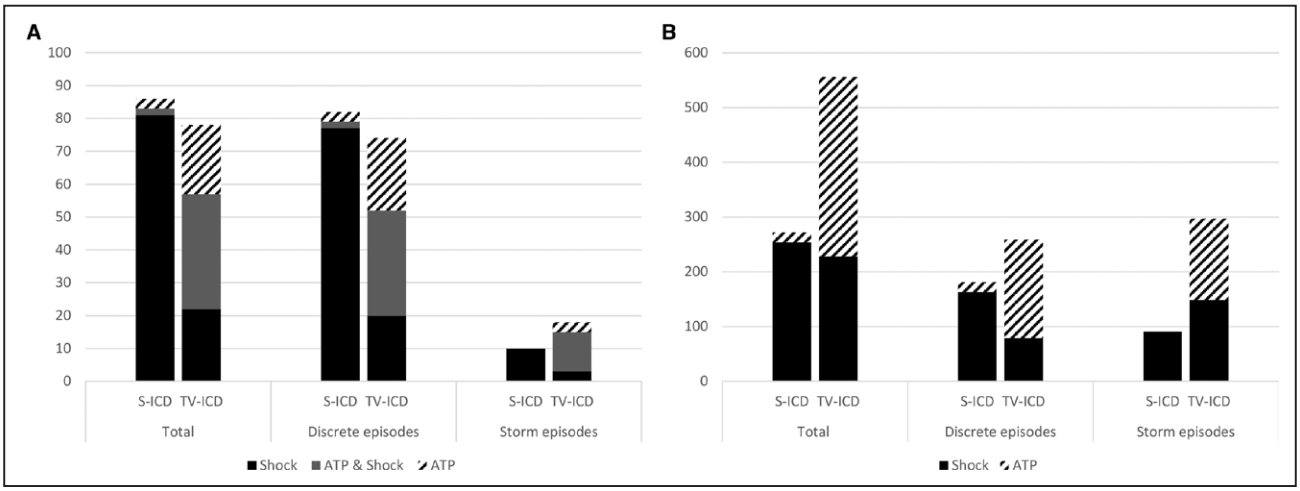

Figure 3. Total number of patients with appropriate therapy and total delivered therapy.
A, Total number of patients with appropriate therapy. Patients can be represented in both discrete and storm episodes. **B**, Total delivered therapy. ATP indicates antitachycardia pacing; S-ICD, subcutaneous implantable cardioverter defibrillator; and TV-ICD, transvenous implantable cardioverter defibrillator.

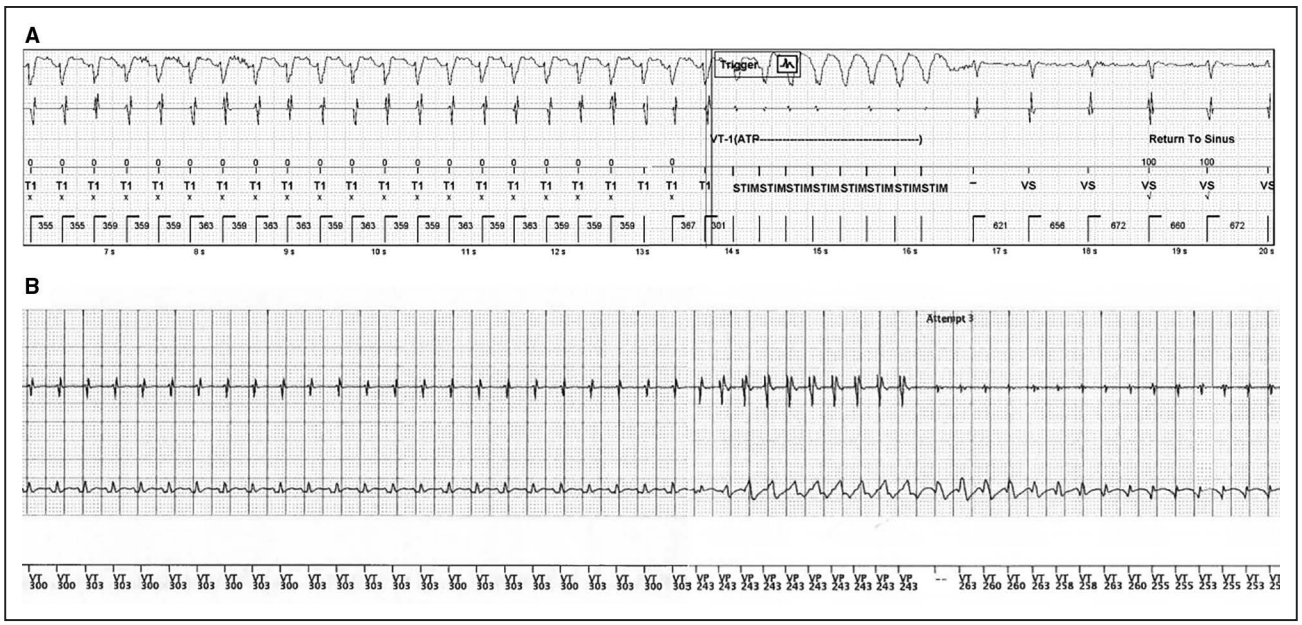

Figure 4. Successful conversion to sinus rhythm and acceleration of ventricular tachycardia after antitachycardia pacing.
A, Successful conversion to sinus rhythm after antitachycardia pacing (ATP). **B**, Acceleration of ventricular tachycardia (VT) after ATP, ultimately terminated by a shock (shock not shown).

ATP is recommended as preferred therapy for most patients with ICD and has been considered a safe and painless alternative to defibrillation shocks.[8,15] Our results show that a number of monomorphic VTs in patients in the TV-ICD group could be terminated by ATP only, without affecting the overall number of appropriate shocks compared with patients in the S-ICD group. There were more treated appropriate episodes in the TV-ICD group than in the S-ICD group, which may be the result of unnecessary treatment with ATP on ventricular arrhythmias that would otherwise have ended spontaneously. Although we observed that the first ATP attempt was successful in 46% of all episodes with a monomorphic VT, subsequent ATP attempts seem to yield little additional efficacy. The lower success rate, compared with previous studies,[6–8] can be explained by the patient selection in the PRAETORIAN trial, which excluded patients with VTs at a rate below 170 beats per minute or recurrent monomorphic VTs before implant. It has been indicated that VT acceleration by ATP might lead to electric storms and a higher mortality.[10] Whereas there was no difference in mortality in the PRAETORIAN trial,[4] patients with a TV-ICD indeed had a higher risk of electric storms compared with patients with an S-ICD,

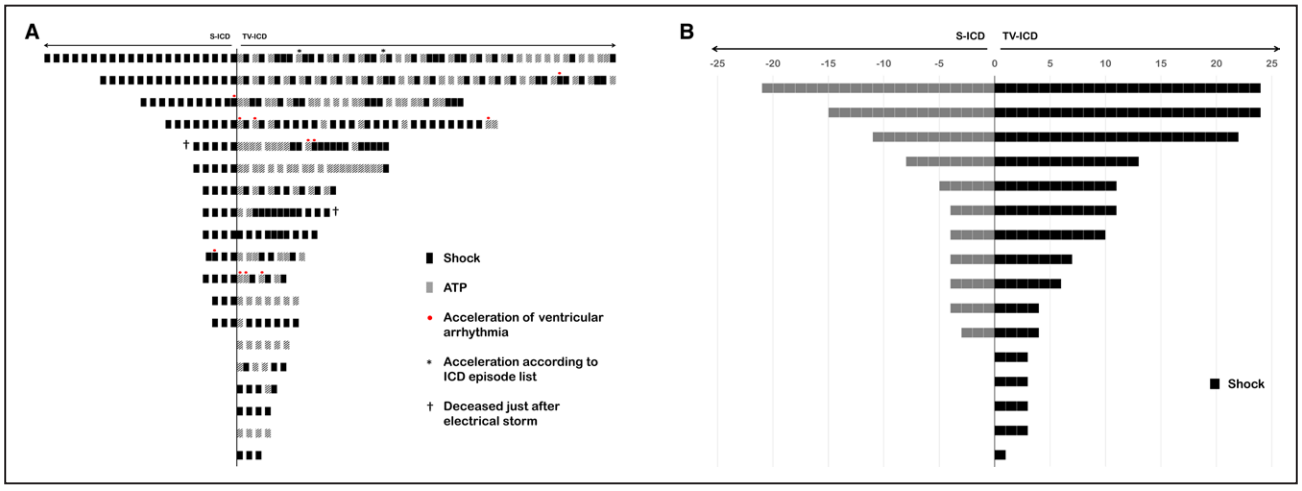

Figure 5. Electric storms in subcutaneous and transvenous implantable cardioverter defibrillator.
A, Number of shocks and antitachycardia pacings (ATPs) per episode per storm. Each horizontal row represents 1 electric storm. Therapies that accelerated the arrhythmia are shown with a dot above the therapy. **B**, Electric storms with only shocks. Each horizontal row represents 1 electric storm. Only electric storms with at least 1 shock are presented in the figure. There were 91 shocks in the subcutaneous implantable cardioverter defibrillator (S-ICD) group and 149 shocks in the transvenous implantable cardioverter defibrillator (TV-ICD) group.

despite the comparable baseline. In this study, ATP had a proarrhythmogenic effect in 9.4% of the episodes. In addition, we observed a significantly lower ATP efficacy in storm episodes compared with discrete episodes. The higher incidence of electric storms in the TV-ICD group could be associated with the capability of the TV-ICD to provide ATP, as 32% of the storms were given >1 ATP attempt per episode. Our data suggest that, in the studied population, ATP therapy should be limited to a single attempt to observe the efficacy in the individual patient. After a positive effect of ATP is demonstrated, ATP programming may be extended.

This analysis has several limitations. First, patients with known VT at a rate <170 beats per minute and patients with refractory recurrent monomorphic VT that could not be managed with medication or ablation therapy were not eligible to participate in the PRAETORIAN trial. It is therefore unclear whether the results of this analysis apply to all patients with ICD. Second, the majority of episodes with missing electrograms occurred in the TV-ICD group, as this device often overwrites previously stored episodes to preserve storage capacity. These episodes could not be adjudicated and lead to an underestimation of the amount and nature of appropriate therapy in the TV-ICD group. Third, the morphology of the electrograms of the TV-ICD does not resemble the surface ECG as much as the electrograms of the S-ICD. As a result, it is more difficult to discriminate between ventricular and supraventricular arrhythmias, which could have influenced the classification of appropriate therapy in the TV-ICD group.

Conclusions

The results of this analysis show that S-ICD is equally effective as TV-ICD in terminating ventricular arrhythmias. The capability to provide ATP in the TV-ICD group led to fewer patients with appropriate shocks, but the total number of appropriate shocks was not different in the 2 study groups. ATP is less effective during storm episodes than during discrete episodes and ATP efficacy is mainly a result of the first attempt. In addition, ATP can accelerate arrhythmias and more electric storms were observed in the TV-ICD group. In patients who are not expected to benefit from ATP, we suggest limiting ATP therapy to a single attempt.

ARTICLE INFORMATION

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Supplemental Material

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Figures S1–S3
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REFERENCES

1. Bardy GH, Lee KL, Mark DB, Poole JE, Packer DL, Boineau R, Domanski M, Troutman C, Anderson J, Johnson G, et al; Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) Investigators. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. *N Engl J Med.* 2005;352:225–237. doi: 10.1056/NEJMoa043399
2. Moss AJ, Hall WJ, Cannom DS, Daubert JP, Higgins SL, Klein H, Levine JH, Saksena S, Waldo AL, Wilber D, et al. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia: Multicenter Automatic Defibrillator Implantation Trial Investigators. *N Engl J Med.* 1996;335:1933–1940. doi: 10.1056/NEJM199612263352601
3. Moss AJ, Zareba W, Hall WJ, Klein H, Wilber DJ, Cannom DS, Daubert JP, Higgins SL, Brown MW, Andrews ML; Multicenter Automatic Defibrillator Implantation Trial II Investigators. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *N Engl J Med.* 2002;346:877–883. doi: 10.1056/NEJMoa013474
4. Knops RE, Olde Nordkamp LRA, Delnoy PHM, Boersma LVA, Kuschyk J, El-Chami MF, Bonnemeier H, Behr ER, Brouwer TF, Kääb S, et al; PRAETORIAN Investigators. Subcutaneous or transvenous defibrillator therapy. *N Engl J Med.* 2020;383:526–536. doi: 10.1056/NEJMoa1915932
5. Yee R, Klein GJ, Guiraudon GM, Jones DL, Sharma AD, Norris C. Initial clinical experience with the pacemaker-cardioverter-defibrillator. *Can J Cardiol.* 1990;6:147–156.
6. Arenal A, Proclemer A, Kloppe A, Lunati M, Martìnez Ferrer JB, Hersi A, Gulaj M, Wijffels MC, Santi E, Manotta L, et al. Different impact of long-detection interval and anti-tachycardia pacing in reducing unnecessary shocks: data from the ADVANCE III trial. *Europace.* 2016;18:1719–1725. doi: 10.1093/europace/euw032
7. Kleemann T, Strauss M, Kouraki K, Zahn R. Clinical course and prognostic relevance of antitachycardia pacing-terminated ventricular tachyarrhythmias in implantable cardioverter defibrillator patients. *Europace.* 2015;17:1068–1075. doi: 10.1093/europace/euv007
8. Wathen MS, DeGroot PJ, Sweeney MO, Stark AJ, Otterness MF, Adkisson WO, Canby RC, Khalighi K, Machado C, Rubenstein DS, et al; PainFREE Rx II Investigators. Prospective randomized multicenter trial of empirical antitachycardia pacing versus shocks for spontaneous rapid ventricular tachycardia in patients with implantable cardioverter-defibrillators: Pacing Fast Ventricular Tachycardia Reduces Shock Therapies (PainFREE Rx II) trial results. *Circulation.* 2004;110:2591–2596. doi: 10.1161/01.CIR.0000145610.64014.E4
9. Moss AJ, Schuger C, Daubert JP. A clinical trial of ICD programming. *N Engl J Med.* 2013;368:965–966. doi: 10.1056/NEJMc1300614
10. Schukro C, Leitner L, Siebermair J, Pezawas T, Stix G, Kastner J, Schmidinger H. Impact of accelerated ventricular tachyarrhythmias on mortality in patients with implantable cardioverter defibrillator therapy. *Int J Cardiol.* 2013;167:3006–3010. doi: 10.1016/j.ijcard.2012.09.015
11. Bardy GH, Smith WM, Hood MA, Crozier IG, Melton IC, Jordaens L, Theuns D, Park RE, Wright DJ, Connelly DT, et al. An entirely subcutaneous implantable cardioverter-defibrillator. *N Engl J Med.* 2010;363:36–44. doi: 10.1056/NEJMoa0909545
12. Weiss R, Knight BP, Gold MR, Leon AR, Herre JM, Hood M, Rashtian M, Kremers M, Crozier I, Lee KL, et al. Safety and efficacy of a totally subcutaneous implantable-cardioverter defibrillator. *Circulation.* 2013;128:944–953. doi: 10.1161/CIRCULATIONAHA.113.003042
13. Al-Khatib SM, Stevenson WG, Ackerman MJ, Bryant WJ, Callans DJ, Curtis AB, Deal BJ, Dickfeld T, Field ME, Fonarow GC, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines and the Heart Rhythm Society. *Circulation.* 2018;138:e272–e391. doi: 10.1161/CIR.0000000000000549
14. Olde Nordkamp LR, Knops RE, Bardy GH, Blaauw Y, Boersma LV, Bos JS, Delnoy PP, van Dessel PF, Driessen AH, de Groot JR, et al. Rationale and design of the PRAETORIAN trial: a Prospective, Randomized Comparison of Subcutaneous and Transvenous Implantable Cardioverter-Defibrillator Therapy. *Am Heart J.* 2012;163:753–760.e2. doi: 10.1016/j.ahj.2012.02.012
15. Wilkoff BL, Fauchier L, Stiles MK, Morillo CA, Al-Khatib SM, Almendral J, Aguinaga L, Berger RD, Cuesta A, Daubert JP, et al; Document Reviewers. 2015 HRS/EHRA/APHRS/SOLAECE expert consensus statement on optimal implantable cardioverter-defibrillator programming and testing. *Europace.* 2016;18:159–183. doi: 10.1093/europace/euv411