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What factors lead to the acceleration of ventricular tachycardia during antitachycardia pacing?—Results from over 1000 episodes

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Abstract

Introduction: Ventricular tachycardia (VT) acceleration due to antitachycardia pacing (ATP) therapy could be often observed in patients with implantable cardioverter defibrillator (ICD), which usually results in additional shock. However, few studies focused on the risk factors for VT acceleration caused by ATP therapy. The purpose of this study was to investigate risk factors for VT acceleration due to ATP delivery.

Methods: We retrospectively reviewed 1056 ATP episodes in 33 patients with structural heart diseases, of whom clinical characteristics and episodes details were evaluated.

Results: At individual patient level, number of VT morphologies recorded in electrograms during follow-up was a risk factor with cutoff point of 1 (AUC 0.79, sensitivity 72.7%, specificity 77.3%, $P < .001$) to predict ATP acceleration (OR 3.50, $P = .008$). From episode-based analysis, VT cycle length (VTCL) and mean variation in VTCL were risk factors to predict ATP acceleration (OR 0.98, $P < 0.001$ vs OR 1.06, $P < .001$, respectively), with cutoff points of 347 ms (AUC 0.67, sensitivity 82.5%, specificity 47.6%, $P < .001$) and 7.3 ms (AUC 0.66, sensitivity 77.5%, specificity 56.7%, $P < .001$), respectively. In addition, VTs with cycle length less than 347 ms were more likely to be accelerated by burst stimulation with more pulse numbers (OR 3.31, $P < .001$).

Conclusions: Number of VT morphologies, VTCL, and mean variation in VTCL are risk factors predicting ATP acceleration. Burst stimulation with less pulse numbers should be performed in VTs with cycle length less than 347 ms.

KEYWORDS
acceleration, antitachycardia pacing, degeneration, implantable cardioverter defibrillator, ventricular tachycardia

1 | INTRODUCTION

Implantable cardioverter defibrillators (ICDs) play a significant role in the diagnosis and treatment of malignant ventricular tachyarrhythmias in patients at high risk of sudden cardiac death.[1] Although ICD shocks could terminate those arrhythmias immediately, they would result in both physical and psychological damages and even increase the mortality and hospitalization as proved in some previous studies.[2–4]

As a method of painless therapy and a supplement of ICD shocks, antitachycardia pacing (ATP) has been demonstrated to be as effective as ICD shocks with no increase in mortality and improve patients' quality of life.[5] However, not all ATPs could terminate ventricular arrhythmias and some ATPs may even lead to the acceleration of ventricular tachycardias (VTs) or degeneration of those to ventricular fibrillations (VFs), which might result in more ICD shocks or even "ICD storms." According to previous studies, the rate of ATP acceleration ranged from 1.2% to 21%,[5–8] but few researches focused on the predictors of ATP acceleration. The purpose of our study was to examine what factors led to VT acceleration by ATP therapy.

2 | METHODS

2.1 | Study population

Eighty-six consecutive patients undergoing ICD or cardiac resynchronization defibrillator (CRT-D) implantation in the First Affiliated Hospital of Nanjing Medical University from January 2007 to September 2014 were reviewed. Patients were enrolled according to the following criteria: (i) Structural heart disease complied with the indication of secondary prevention of ICD or CRT-D[9–11] and (ii) ATP therapies delivered due to monomorphic VTs during the follow-up. Patients were excluded in line with the following criteria: (i) age<18, (ii) without structural heart disease, (iii) with ionic channel disease, (iv) ICD or CRT-D implantation because of primary prevention, (v) without ATP therapies during the follow-up, (vi) only with ATP therapies due to polymorphic VTs, and (vii) only with inappropriate ICD therapies due to supraventricular tachycardias. The study complied with the Declaration of Helsinki and followed acceptance of the protocol by the institutional review board. All the patients provided informed consent, and the enrollment is shown in Figure 1.

2.2 | Data collection

Clinical baseline characteristics and implantation records were collected during patients' hospitalization. During the follow-up, all available stored episodes were collected, including VT cycle length (VTCL), mean variation in VTCL, variation degree of VTCL, and number of VT morphologies recorded in electrograms (EGMs). These episodes were analyzed by 2 experienced physicians. Episodes exceeding the storage of device memory due to electrical storms were excluded as they could not be read. If electrophysiological (EP) study was performed before device implantation or catheter ablation during the follow-up because of ventricular arrhythmias, the EP data would also be collected.

2.3 | Device implantation and programming

All patients received implantations of single-chamber, dual-chamber ICD or CRT-D (Medtronic, Boston Scientific, and Biotronik). The
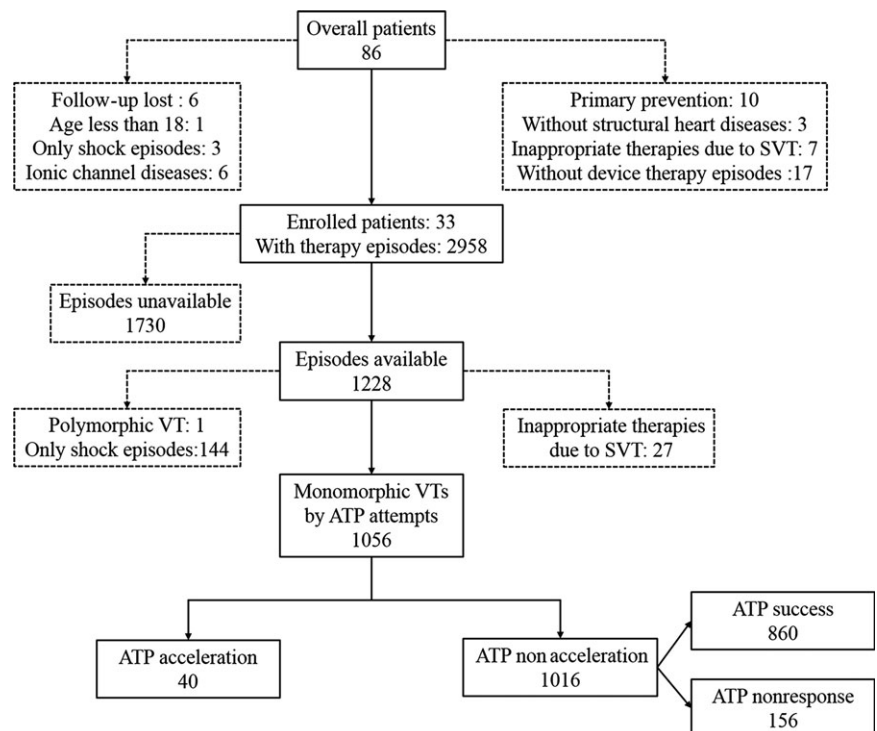

FIGURE 1 Patient population and device therapy episodes. ATP, antitachycardia pacing; SVT, supraventricular tachycardia

right ventricular intravenous leads were positioned either in apex or in septum. The devices were programmed with either 2 or 3 tachyarrhythmia detection zones based on the preoperative VT rate. Moreover, ATPs were chosen as the first-line therapy for monomorphic VTs. There were 2 types of ATP deliveries, burst stimulation and ramp (ramp$^+$) stimulation. Burst stimulation was programmed at 66%-91% of VTCL with 4-15 pulses of each sequence, while ramp stimulation was set at 72%-91% with 4-8 pulses.

2.4 | Classification and definitions

ATP acceleration was defined as VTCL decreased by>10% or VT degenerated to ventricular flutter or VF after ATP attempt. ATP-successful therapy was defined as both the ventricular rhythm was converted and the termination standard of the device was met after ATP therapy of VT. ATP-nonresponse therapy referred to those episodes with increase or no change in VT cycle length after ATP therapy (Figure 2). In addition, followings are the instructions of several parameters that will be estimated in this study.

2.4.1 | VTCL

VT cycle length, defined by the mean value of the last 12 RR intervals preceding the first ATP therapy.

2.4.2 | M-VTCL

Mean variation in VTCL, defined by the mean difference between 2 adjacent RR intervals in 13 RR intervals before the first ATP delivery.[12]

2.4.3 | V-VTCL

Variation degree of VTCL, dividing M-VTCL by VTCL.

2.4.4 | Prop-nonresponse

The proportion of ATP-nonresponse episodes, which was calculated by dividing the numbers of ATP-nonresponse episodes by the total numbers of ATP episodes in each individual.

2.5 | Study design

Patients were classified into 2 groups according to the existence of ATP acceleration. Those who experienced at least 1 ATP acceleration episode were allocated to acceleration group, while those without were allocated to nonacceleration group. Episodes were also divided into 2 groups according to the existence of ATP acceleration: ATP acceleration group and ATP nonacceleration group. The ATP nonacceleration group was further divided into 2 subgroups: ATP success group and ATP-nonresponse group. Thereafter, we analyzed different information and parameters in patient grouping and episode grouping, respectively.

2.6 | Statistical analysis

Continuous variables were described by means and standard deviations if normally distributed or medians (interquartile range) if not. Categorical variables were expressed as numbers and percentages. Student's *t* test or Mann-Whitney *U* test was used for normal or nonnormal continuous variables, respectively. Fisher's exact test was used for categorical variables. Receiver-operating characteristic (ROC) curves were graphed to establish the cutoff point with the best specificity and sensitivity. Multivariate analysis was accomplished by logistic regression tests including the following variables: number of VT morphologies and Prop-nonresponse in patient estimation, VTCL and M-VTCL in ATP episode analysis, and pulse number and width in burst stimulation analysis. $P < .05$ was considered statistically significant.

3 | RESULTS

3.1 | Patient population and individual-level analysis

A total of 33 patients were enrolled, of them 11 suffered from at least 1 ATP acceleration event, whereas the remaining 22 did not have any acceleration episode. The baseline characteristics and analysis of patients between 2 groups are shown in Table 1. Of all the 33 patients, EP studies (EPS) were performed in 22 patients. The median number of VT morphologies induced by EPS in those with ATP acceleration events was 3.0 (2.3, 5.0), and in those without acceleration, it was 1.0 (1.0, 1.0) ($P = .001$). Furthermore, number of VT morphologies recorded in EGMs during the follow-up was also more in the acceleration group. In addition, the proportion of ATP-nonresponse episodes was greater in acceleration group than in nonacceleration group (Table 1). By the logistic regression analysis, number of VT morphologies in EGMs was proved to be a predictor of ATP acceleration (Table 2A). ROC curve was generated to estimate significance of different numbers of VT morphologies in ATP acceleration. The cutoff point was 1 with the best sensitivity and specificity of 72.7% and 77.3%, respectively (AUC 0.79, $P < .001$) (Figure 3A).

3.2 | Device therapies

During a median follow-up of 22 (11.5, 44.5) months, there were 2958 therapy episodes, of which 1228 were available because of limited device memory. Among these available episodes, there were 144 shock-only episodes and 27 inappropriate therapies attributed to supraventricular tachyarrhythmias. One episode was detected as polymorphic VT accelerated by the ATP first, then terminated by shock. The finally left 1,056 episodes were all with ATP events, in which 40 (3.7%) monomorphic VTs were accelerated by ATPs, 860 events were terminated by them, and 156 monomorphic VTs did not respond to ATP attempts (Figure 1).
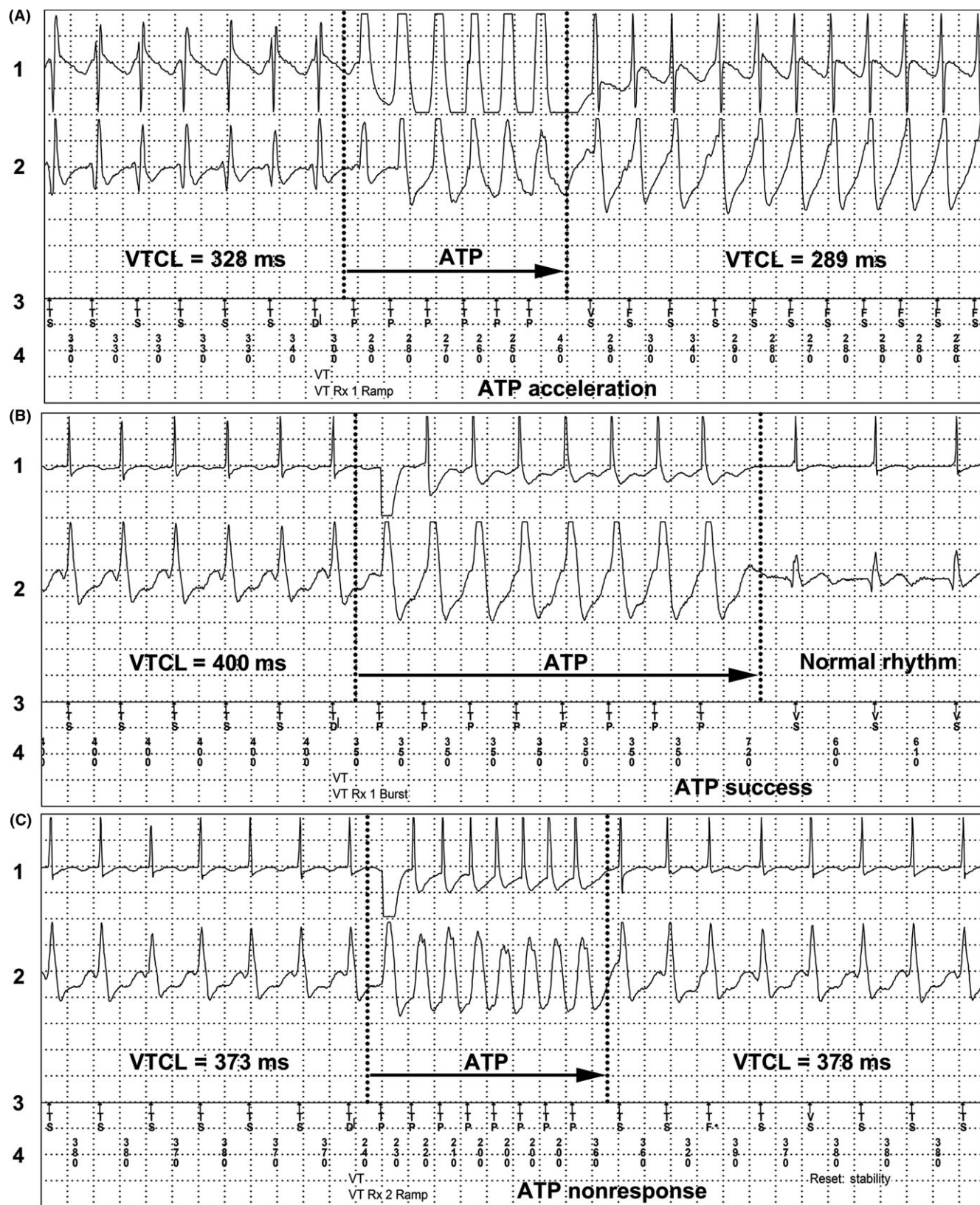
FIGURE 2 Different ATP behaviors. A, VT was accelerated by ATP. B, VT was terminated by ATP. C, VT was not disturbed by ATP. ATP, antitachycardia pacing; EGM, electrogram; VT, monomorphic ventricular tachycardia; VTCL, ventricular tachycardia cycle length

TABLE 1 Baseline characteristics and analysis of patients

	n (%)		
	ATP acceleration (n = 11)	ATP nonacceleration (n = 22)	P value
Implantation age (y)	52.6 ± 13.0	50.4 ± 11.7	.629
Male	8 (72.7%)	20 (90.9%)	.304
Coronary artery disease	2 (18.2%)	1 (4.5%)	.252
Dilated cardiomyopathy	3 (27.3%)	9 (40.9%)	.703
Hypertrophic cardiomyopathy	1 (9.1%)	1 (4.5%)	1.000
ARVC	4 (36.4%)	9 (40.9%)	1.000
Other structural heart disease[a]	0 (0%)	2 (9.1%)	.542
NYHA class	1.7 ± 0.8	1.6 ± 0.8	.706
LVEDD (mm)	54.0 (51.0, 69.0)	52.0 (46.8, 65.0)	.243
LVEF (%)	50.5 (36.8, 63.4)	59.9 (41.8, 65.0)	.456
Induced VT morphologies during EP test	3.0 (2.3, 5.0), n = 8	1.0 (1.0, 1.0), n = 14	.001
Number of VT morphologies in EGMs	3.0 (1.0, 4.0)	1.0 (1.0, 1.3)	.002
Patients with ATP-nonresponse episodes	9 (81.8%)	10 (45.5%)	.067
Prop-nonresponse (%)	13.9 (5.9, 26.9)	0.3 (0.0, 8.1)	.040

ARVC, arrhythmogenic right ventricular cardiomyopathy; ATP, antitachycardia pacing; EGMs, electrograms; EP, electrophysiological; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; Prop-nonresponse, proportion of ATP-nonresponse episodes; VT, monomorphic ventricular tachycardia.
[a]Two patients had congenital heart disease and sarcoidosis, respectively.

TABLE 2 A, Multivariate analysis (logistic regression) of ATP acceleration predictors by patients; B, multivariate analysis (logistic regression) of ATP acceleration predictors by events

(A)

Variable	Odds ratio	95% Confidence interval	P value
Number of VT morphologies	3.50	1.38 − 8.85	.008
Prop-nonresponse (%)	1.01	0.99 − 1.04	.309

(B)

Variable	Odds ratio	95% Confidence interval	P value
VTCL (ms)	0.98	0.97 − 0.99	<.001
M-VTCL (ms)	1.06	1.04 − 1.09	<.001

ATP, antitachycardia pacing; M-VTCL, mean variation in VTCL; VTCL, ventricular tachycardia cycle length; Prop-nonresponse, proportion of ATP-nonresponse episodes.

3.3 | ATP acceleration

Of the 40 acceleration episodes, 32 VTs were accelerated with VTCL shortened, 7 was degenerated to VFs, and 1 was accelerated by the first ATP delivery and degenerated to VF by the second ATP stimulus. The median acceleration degree was 15.3% (12.7%, 22.0%) with minimum and maximum degree of 10.1% and 42.9%, respectively. 29, 5, 3, 1, and 2 episodes were accelerated by the first, second, third, fifth, and seventh ATP deliveries, respectively. There were 28 and 4 events terminated by shocks and subsequent ATP attempts, respectively. There were 7 episodes terminated spontaneously and 1 VT episode slowing down with the CL out of tachycardia detection of intervals.

3.4 | Analysis by ATP episodes

The different parameters between 2 groups of episodes are shown in Table 3. Based on the univariate analysis, the logistic regression analysis showed that the VTCL and mean variation in VTCL were both predictors of ATP acceleration (Table 2B). ROC curves were performed to estimate significance of different VTCL and mean variation in VTCL in ATP acceleration. The cutoff point of VTCL was 347 ms with the optimal sensitivity and specificity of 82.5% and 47.6%, respectively (AUC 0.67, P < .001) (Figure 3B). The cutoff point of mean variation in VTCL was 7.3 ms with the best sensitivity and specificity of 77.5% and 56.7%, respectively (AUC 0.66, P < .001) (Figure 3C).

3.5 | Analysis of ATP stimulation

Parameters of different ATP stimulation between ATP acceleration group and ATP success group are compared in Table 4. We found that the pulse number of burst stimulation was more in acceleration group than in success group within both the overall events and those with VTCL<347 ms. The similar findings were seen in the episodes that could be terminated by one-sequence ATP delivery (Table 5).

4 | DISCUSSION

The purpose of this study was to find the factors that may lead to VT acceleration by ATP therapies. It showed that number of
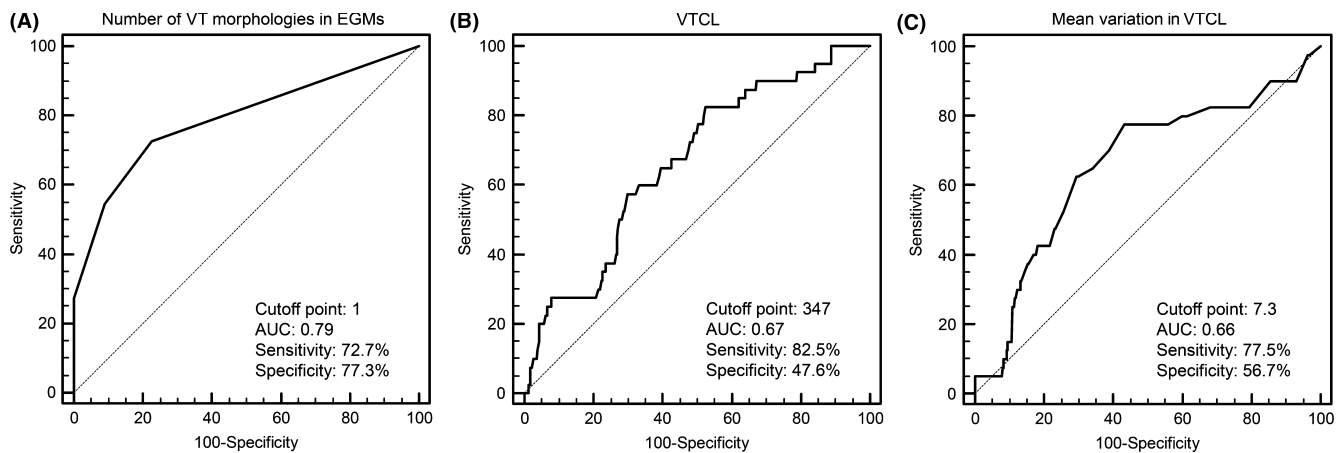
FIGURE 3 Receiver-operating characteristic (ROC) curve. A, ROC curve of number of VT morphologies recorded in EGMs for ATP acceleration. B, ROC curve of VTCL for ATP acceleration. C, ROC curve of mean variation in VTCL for ATP acceleration. AUC, area under the curve; VTCL, ventricular tachycardia cycle length

TABLE 3 Analysis of different parameters of ATP episodes recorded in EGMs

	ATP acceleration (n = 40)	ATP nonacceleration (n = 1016)	P value
VTCL (ms)	316.5 ± 40.3	347.1 ± 54.2	<.001
M-VTCL (ms)	10.8 (7.5, 21.5)	6.7 (3.3, 10.8)	.001
V-VTCL (%)	3.5 (2.0, 6.9)	1.9 (0.9, 3.4)	<.001

ATP, antitachycardia pacing; EGM, electrogram; M-VTCL, mean variation in VTCL; VTCL, ventricular tachycardia cycle length; V-VTCL, M-VTCL/VTCL, variation degree of VTCL.

VT morphologies recorded in EGMs, VTCL, and mean variation in VTCL were the risk factors that could predict ATP acceleration. Besides, patients with more morphologies of induced VTs during EP test were more likely to experience ATP acceleration. In addition, for VT with cycle length less than 347 ms, burst stimulation with more pulse numbers was more likely to cause ATP acceleration.

4.1 | Incidence of ATP acceleration

Based on previous researches, the acceleration rate in spontaneous VT was found no more than 7% [13] and the rate of 3.7% in our study was similar to those studies. Although it seemed to be low, most of the accelerated episodes were eventually terminated by shocks, which could do greater harm to patients. Therefore, it is indispensable to decrease the acceleration incidence in order to relieve patients' agony.

4.2 | Number of VT morphologies and ATP acceleration

This study showed that the more number of VT morphologies, the higher rate of ATP acceleration. Clemens et al [14] reported that, in patients with secondary prevention of ICD implantation due to

monomorphic VT, the acceleration of VT by ATP was 1.1%, 3.2%, or 8.1% with 1, 2, 3, or more morphologies of VT, respectively. Our study found that if a number of VT morphologies were ≥2 in a single patient during the follow-up, acceleration was easier to be caused with a sensitivity and specificity of 72.7% and 77.3%, respectively. Therefore, it seems not reasonable to switch on ATP in patients with ≥2 morphologies of VT, and antiarrhythmic drugs (AADs) and catheters ablation should be performed to eliminate VTs as soon as possible.

4.3 | VTCL and ATP acceleration

Most researches suggested that ATP acceleration was correlated with short VTCL.[6,8,15] It has been demonstrated that reentrant VT responds better to ATP therapy.[13,16] Josephson [17] summarized that the most important factors of ATP terminating reentrant VT is the VTCL. Shorter VTCLs are associated with less possibility for ATP to penetrate the excitable gap of the reentrant circuit. Hammill et al [15] and Calkins et al [8] reported that the incidence of ATP acceleration in VTs with VTCL<300 ms was higher than with VTCL ≥300 ms in induced VTs. However, Peters et al [6] failed to find the same result in spontaneous VTs with VTCL<300 ms. In the current study, we found the optimal cutoff point of 347 ms in VTCL to predict ATP acceleration with the sensitivity of 82.1%, which indicates that VTs>347 ms are unlikely to be accelerated by ATP attempts. In such scenario, conservative therapies should be considered.

4.4 | Variation in VTCL and ATP acceleration

Our findings showed that VTs with larger cycle length variation were more likely to be accelerated by ATP stimulation. However, it was different in the study by Jimenez-Candil et al,[12] in which with the increase in variation degree of VTCL, the acceleration incidence decreased. The mechanism of VTCL variation contributing to ATP

TABLE 4 A, Analysis of ATP stimulation in overall episodes; B, analysis of ATP stimulation in episodes with VTCL<347 ms; C, multivariate analysis (logistic regression) of ATP acceleration predictors by burst stimulation

(A)

	ATP acceleration (n = 40)	ATP success (n = 860)	*P* value
ATP category (burst stimulation)	17 (42.5%)	328 (38.1%)	.619
Pulse number	8 (8, 9)	8 (6, 8)	.005
Coupling interval (%)	88 (84, 91)	88 (84, 91)	.735
ATP amplitude (V)	8.0 (8.0, 8.0)	8.0 (8.0, 8.0), n = 853	.146
ATP pulse width (ms)	1.5 (1.5, 1.6)	1.5 (1.5, 1.6), n = 853	.187
Burst stimulation			
Pulse number	8 (8, 10), n = 17	8 (8, 8), n = 328	<.001
Coupling interval (%)	88 (84, 88), n = 17	88 (84, 88), n = 328	.967
ATP amplitude (V)	8.0, n = 17	8.0 (8.0, 8.0), n = 321	.316
ATP pulse width (ms)	1.5, n = 17	1.5 (1.5, 1.6), n = 321	.001
Ramp stimulation			
Pulse number	8 (6, 8), n = 23	8 (6, 8), n = 532	.818
Coupling interval (%)	91 (91, 91), n = 23	91 (88, 91), n = 532	.504
ATP amplitude (V)	8 (8, 8), n = 23	8 (8, 8), n = 532	.291
ATP pulse width (ms)	1.6 (1.6, 1.6), n = 23	1.6 (1.5, 1.6), n = 532	<.001

(B)

	ATP acceleration (n = 33)	ATP success (n = 502)	*P* value
ATP category (burst stimulation)	16 (48.5%)	228 (45.4%)	.857
Pulse number	8 (8, 9.5)	8 (8, 8)	.002
Coupling interval (%)	91 (86, 91)	91 (88, 91)	.303
ATP amplitude (V)	8.0 (8.0, 8.0)	8.0 (8.0, 8.0)	.825
ATP pulse width (ms)	1.5 (1.5, 1.6)	1.5 (1.5, 1.6)	.697
Burst stimulation			
Pulse number	9 (8, 10), n = 16	8 (8, 8), n = 228	<.001
Coupling interval (%)	88 (84, 88), n = 16	88 (88, 88), n = 228	.053
ATP amplitude (V)	8.0, n = 16	8.0 (8.0, 8.0), n = 228	.348
ATP pulse width (ms)	1.5, n = 16	1.5 (1.5, 1.6), n = 228	.004
Ramp stimulation			
Pulse number	8 (8, 8), n = 17	8 (8, 8), n = 274	.889
Coupling interval (%)	91 (91, 91), n = 17	91 (91, 91), n = 274	.497
ATP amplitude (V)	8 (8, 8), n = 17	8 (8, 8), n = 274	.416
ATP pulse width (ms)	1.6 (1.6, 1.6), n = 17	1.6 (1.5, 1.6), n = 274	.007

(C)

	Odds ratio	95% Confidence interval	*P* value
In total			
Pulse number	1.33	1.08 – 1.64	.007
ATP pulse width (ms)	0.14	0.01 – 3.70	.238
VTCL<347 ms			
Pulse number	3.31	1.93 – 5.68	<.001
ATP pulse width (ms)	0.12	0.00 – 17.77	.405

ATP, antitachycardia pacing; VTCL, ventricular tachycardia cycle length.

acceleration is not clear. The discrepancy between 2 studies may be due to the disease entities. 62% of the enrolled patients in their study had coronary artery diseases (CADs), which increased the likelihood of spontaneous termination of VT in patients with higher degree of RR interval fluctuations.[18] However, in the current study, nonischemic structural heart diseases took a large proportion

TABLE 5 A, Analysis of ATP stimulation in one-sequence ATP episodes; B, analysis of ATP stimulation in one-sequence ATP episodes with VTCL<347 ms; C, multivariate analysis (logistic regression) of ATP acceleration predictors by burst stimulation

(A)

	ATP acceleration (n = 29)	ATP success (n = 742)	P value
ATP category (burst stimulation)	16 (55.2%)	286 (38.5%)	.082
Pulse number	8 (8, 9)	8 (6, 8)	<.001
Coupling interval (%)	88 (86, 91)	88 (84, 91)	.550
ATP amplitude (V)	8.0 (8.0, 8.0)	8.0 (8.0, 8.0), n = 736	.052
ATP pulse width (ms)	1.5 (1.5, 1.6)	1.5 (1.5, 1.6), n = 736	.408
Burst stimulation			
Pulse number	8 (8, 10), n = 16	8 (8, 8), n = 286	< 0.001
Coupling interval (%)	88 (84, 88), n = 16	88 (84, 88), n = 286	.923
ATP amplitude (V)	8.0, n = 16	8.0 (8.0, 8.0), n = 280	.326
ATP pulse width (ms)	1.5, n = 16	1.5 (1.5, 1.6), n = 280	.001
Ramp stimulation			
Pulse number	8 (7, 8), n = 13	8 (6, 8), n = 456	.466
Coupling interval (%)	91 (91, 91), n = 13	91 (88, 91), n = 456	.073
ATP amplitude (V)	8 (8, 8), n = 13	8 (8, 8), n = 456	.170
ATP pulse width (ms)	1.6 (1.6, 1.6), n = 13	1.5 (1.5, 1.6), n = 456	.001

(B)

	ATP acceleration (n = 27)	ATP success (n = 454)	P value
ATP category (burst stimulation)	15 (55.6%)	214 (47.1%)	.432
Pulse number	8 (8, 10)	8 (8, 8)	.001
Coupling interval (%)	88 (88, 91)	91 (88, 91)	.308
ATP amplitude (V)	8.0	8.0 (8.0, 8.0)	.292
ATP pulse width (ms)	1.5 (1.5, 1.6)	1.5 (1.5, 1.6)	.746
Burst stimulation			
Pulse number	9 (8, 10), n = 15	8 (8, 8), n = 214	<.001
Coupling interval (%)	88 (84, 88), n = 15	88 (88, 88), n = 214	.115
ATP amplitude (V)	8.0, n = 15	8.0 (8.0, 8.0), n = 214	.347
ATP pulse width (ms)	1.5, n = 15	1.5 (1.5, 1.6), n = 214	.005
Ramp stimulation			
Pulse number	8 (8, 8), n = 12	8 (8, 8), n = 240	.633
Coupling interval (%)	91, n = 12	91 (91, 91), n = 240	.580
ATP amplitude (V)	8, n = 12	8 (8, 8), n = 240	.580
ATP pulse width (ms)	1.6, n = 12	1.5 (1.5, 1.6), n = 240	<.001

(C)

	Odds ratio	95% Confidence interval	P value
In total			
Pulse number	1.35	1.07 – 1.70	.012
ATP pulse width (ms)	0.17	0.01 – 5.26	.312
VTCL<347 ms			
Pulse number	3.01	1.74 – 5.21	<.001
ATP pulse width (ms)	0.13	0.00 – 18.31	.419

ATP, antitachycardia pacing; VTCL, ventricular tachycardia cycle length.

(90.9%). Besides, it has been reported that substrate of ischemic heart disease is more stable than that of nonischemic heart disease.[19] The pathological changes in nonischemic heart disease are progressively developing and the substrate is more complex which might cause the instability of VTCL and more incidence of ATP acceleration.

4.5 | Burst stimulation and ATP acceleration

In our study, we found that burst stimulation with more pulse numbers was more likely to cause VT acceleration, especially in those with cycle length<347 ms. Cycle length of ATP stimulus, number of ATP pulse, and site of ATP stimulation were all contribution factors of the efficacy of ATP therapies.[16] In a study with induced VT, with more pulses in ramp stimulation, the incidence of ATP acceleration was higher, but there were no similar findings in burst stimulation.[15] In spontaneous VT study, Nasir et al [20] found no difference between different burst numbers in ATP acceleration either. However, ADVANCE-D trial [21] showed that the incidences of ATP acceleration increased with more burst pulses in both fast VT episodes and overall VT episodes. Unfortunately, they both failed to show statistical significance. Our study suggested that burst pulse numbers affected the result of ATP therapy *per se*. In VT with cycle length<347 ms, acceleration was more likely to be caused by burst stimulation with higher pulse number.

4.6 | Clinical implications

In our study, number of VT morphologies, VT cycle length (VTCL), and variation in VTCL were proved to be risk factors predicting ATP acceleration, and VTs with VTCL less than 347 ms were more likely to be accelerated by burst stimulation with more pulse numbers. Therefore, more considerations should be taken to reprogram ATP therapies for patients with such risk factors, as to lower or eliminate the incidence of VT acceleration by ATP therapies. For instance, radical ATP settings should not be performed in patients with VT of faster heart rate and more numbers of morphologies.

4.7 | Study limitations

First, this study is retrospective and nonrandomized. ATP algorithms were programmed based on individual empirical discretion and previous clinical studies which might cause bias. During the follow-up, ATP algorithms might also be adjusted due to the occurrence of VT episodes. Thus, more randomized controlled trials should be conducted to further confirm these results. Second, due to the limitation of device memory, we did not get whole ATP episodes in patients, which might influence grouping of patients and analysis of data. Third, compared with the control group, the sample size of ATP acceleration episodes was too small, which may weaken the statistical power, although we had used rank sum test and Fisher's exact test to minimize the effect. Fourth, AADs were not unified and might be changed during the follow-up, so the influence of AADs to the ATP therapy was inevitable. Therefore, more studies are needed to standardize regimen of drug therapies in order to get more precise results.

5 | CONCLUSIONS

We concluded that in patients of structural heart disease with ICD or CRT-D implantation for secondary prevention, number of VT

morphologies recorded in EGMs, VTCL, and its mean variation are risk factors predicting ATP acceleration. VT with cycle length<347 ms is more likely to get acceleration by burst stimulation with more pulse numbers. These findings provide the evidence to optimize ATP reprogramming or choose other invasive or noninvasive methods for the purpose of preventing ATP acceleration.

CONFLICTS OF INTEREST

Authors declare no Conflict of Interests for this article.

DISCLOSURE

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