Electrocardiographic Parameters Indicating Worse Evolution in Patients with Acquired Long QT Syndrome and Torsades de Pointes

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Background: Acquired long QT syndrome (a-LQTS) is associated with life-threatening ventricular arrhythmias, mainly torsades de pointes (TdP). ECG parameters predicting evolving into ventricular fibrillation (VF) are ill defined.

Aims: To determine ECG parameters preceding and during TdP associated with higher risk of developing VF.

Methods: We analyzed 151 episodes of TdP, recorded in 28 patients with a-LQTS (mean QTc 638 ms $\pm$ 57).

Results: All 28 patients had prolonged QT interval, (mean QTc 638 ms $\pm$ 57) ranging from 502 ms to 858 ms correcting by Bazett's formula. The mean TdP heart rate was 218 bpm $\pm$ 38 (mean cycle length of TdP 274 $\pm$ 47 ms). We classified TdPs episodes into "slower"-TdP (s-TdP) < 220 bpm (range from 145–220 bpm) observed in 81 (53.6%) episodes and "faster"-TdP (f-TdP) $\geq$ 220 bpm (ranged from 221–281 bpm) observed in 70 (46.4%) episodes. Among 151 episodes of TdP, 21 (13.9%) were unstable (converted into VF). Out of 81 episodes of "slower"-TdP only 2 (2.5%) episodes converted into VF. The mean coupling interval (CI) of the PVC initiating TdP was 510 ms $\pm$ 118, the pause-RR interval was 1147 ms $\pm$ 335, the prematurity index (PI) of PVC that initiated TdP was 0.45 $\pm$ 0.13. The mean cycle length variability of TdP (VRV-TdP) was 30.79 ms $\pm$ 19.7. U wave was observed in 86 episodes (56.9%), among that in 69 episodes, the U/T wave ratio was > 1. Macro T wave alternans was observed in 4 patients. The QT interval was not different in patients with VF(+) and VF(–) episodes, 633 $\pm$ 60 and 639 $\pm$ 57, respectively.

Conclusions: Some electrocardiographic parameters can be helpful in determining the risk of TdP evolving into VF. The slower ventricular rate (< 220 bpm), the higher rate instability (VRV > 30 ms) and the short episodes < 20 beats could predict benign evolution.

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torsades de pointes; acquired long QT syndrome; ventricular fibrillation; ventricular rate variability

INTRODUCTION

Acquired long QT syndrome (a-LQTS) and congenital long QT syndrome (c-LQTS) are associated with

life-threatening ventricular arrhythmias, mainly torsades de pointes (TdP).^{1,2} Prolonged QT interval by itself may not be enough to provoke this dangerous arrhythmia; and clinical conditions may

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Figure 1. Electrocardiographic parameters estimated for each episode of TdP: pause-RR interval, the coupling interval, the first cycle length of TdP, and ventricular rate variability (VRV).

predispose to TdP.^{3,4} These clinical conditions have been described elsewhere and are not the focus of the present manuscript. Rather, we will analyze ECG clues that would help the clinicians to identify patients at higher risk of developing more serious arrhythmias. Many episodes of TdP are self-terminating but eventually they can evolve into ventricular fibrillation (VF).

The aim of our study was to determine ECG parameters preceding and during TdP associated with higher risk of developing VF.

METHODS AND DEFINITIONS

ECG recordings of 28 patients with a-LQTS from two centers (Gorlice, Cracow from 2003 to 2012) were analyzed. Standard 12-lead ECGs or 24 hour Holter recordings (three leads) and monitor strips using a paper speed of 25 and 50 mm/s were used. All analyzed parameters were assessed using the caliper. ECG interpretation was performed using the lead with the highest T wave amplitude. TdP episodes with at least five consecutive beats were included in the analysis. The following parameters were evaluated:

- (1) The RR interval pause preceding TdP (pause-RR) defined as the maximal RR interval immediately before the TdP episode. (Fig. 1).
- (2) The coupling interval (CI) of the premature beat that initiated TdP; defined as the time from the QRS onset of the last sinus beat just before the TdP to the onset of the premature QRS that initiated TdP (Fig. 1).
- (3) The prematurity index (PI) calculated as the CI divided by the pause-RR.
- (4) The T_p - T_{iTdP} interval; that was defined as the time from the peak of the T wave of the beat immediately preceding TdP to the onset of the QRS initiating TdP; inscribed in the descending portion of the T-U wave complex or after it.
- (5) The mean RR interval/mean heart rate during the whole episode of TdP (RR-TdP/HR-TdP).
- (6) The minimal RR interval within the TdP (min RR-TdP).
- (7) The number of beats within the TdP episode.
- (8) The first cycle length duration during the episode (f-CL-TdP).
- (9) The ventricular rate variability of the TdP; calculated as the mean difference between consecutive RR intervals within the whole TdP episode (VRV-TdP).

- (10) The corrected QT interval before the TdP (QTc).
- (11) The presence of U waves in the normal beats preceding the TdP. (Fig. 2).
- (12) The amplitude of the U wave and the ratio of the U wave/T wave. (Fig. 2).
- (13) The mode of TdP onset classified as (i) short-long-short sequence (S-L-S), (ii) single premature ventricular contraction or sudden onset, and (iii) multiple premature ventricular contractions (PVCs) preceding TdP.
- (14) The TdP termination mode: classified as (i) deceleration mode (decel-mode) if the mean HR-TdP_{term} assessed from the four last RR intervals before TdP termination was slower than the mean HR-TdP_{term-1} assessed from the three consecutive RR intervals before the last four beats of TdP (Fig. 2), (ii) acceleration mode (accel-mode) if the mean HR-TdP_{term} assessed from the four last RR intervals before TdP termination was faster than the mean HR-TdP_{term-1} assessed from the three consecutive RR intervals before the last four beats of TdP, and (iii) the stable mode, if the mean HR-TdP_{term} of the four last RR intervals and the mean HR-TdP_{term-1} of the three consecutive RR intervals before four last beats of TdP was the same or the difference was < 10 bpm.
- (15) The morphology of the first and the second PVC within the TdP episode, classified as (i) "monomorphic-type" and (ii) "polymorphic-type" (Fig. 3).

All TdP episodes were also classified according to hemodynamic stability as:

- i. "stable" – event (–) and
- ii. "unstable" – event (+) degenerating into VF or causing collapse.

Statistical Analysis

Continuous parameters were normally distributed and compared between groups using unpaired Student's *t*-test and within groups using paired *t* tests. A 2-sided value of *P* < 0.05 was considered significant.

RESULTS

We analyzed 151 episodes of TdPs, recorded in 28 patients. Clinical data are shown in Table 1.

Figure 2. Termination of a TdP episode. The mode of termination of TdP depicted in this picture is classified as "deceleration mode (decel-mode)." The heart rate of this episode of TdP is slowing down before termination.

Almost 14% of the episodes degenerated into VF and/or hemodynamic collapse.

Electrocardiographic Parameters

All 28 patients had prolonged QT interval, (mean QTc 638 ms ± 57) ranging from 502 to 858 ms correcting by Bazett's formula. The mean TdP heart rate was 218 bpm ± 38 (mean cycle length of TdP 274 ± 47 ms). The mean CI of the PVC initiating TdP was 510 ms ± 118, the pause-RR interval was 1147 ms ± 335, and the PI of PVC that initiated TdP was 0.45 ± 0.13. The mean cycle length variability of TdP (VRV-TdP) was 30.79 ms ± 19.7. The mean T_p-T_{iTdP} interval was 57.3 ms ± 52.0. U wave was observed in 86 episodes (56.9%), among that in 69 episodes, the U/T wave ratio was > 1. Macro T wave alternans was observed in four patients. The QT interval was not different in patients with VF(+) and VF(–) episodes, 633 ± 60 and 639 ± 57 ms, respectively.

Mode of Onset of Torsades de Pointes

S-L-S was observed in 137 (90.1%) episodes and sudden onset in 12 (7.9%). In two episodes, the ECG strip did not contain the minimum required of three beats before TdP and were not included in the analysis. In the S-L-S group, 24 episodes consisted of salvos of multiple PVCs, 92 presented bigeminy (91 ventricular and 1 supraventricular), and 21 episodes presented trigeminy. The TdPs were

Figure 3. Mode of TdP onset. (A) Bold black arrow shows a prominent U wave before TdP and thin black arrow shows the T wave. In this episode of TdP, U wave amplitude is higher than T wave amplitude (U wave amplitude is 5 mm). Mode of TdP onset presents short-long-short (S-L-S) pattern. The morphology of the initial PVC is “monomorphic-type”; the first and the second PVC during TdP present both the same morphology. (B) Mode of TdP onset presents S-L-S pattern but the morphology of the initial PVC is “polymorphic-type.” (C) Mode of TdP onset shows sudden onset. The morphology of the initial PVC is “polymorphic-type.”

initiated by monomorphic PVCs in 92 episodes (60.9%) and by polymorphic PVCs in 59 (39.1%).

Mode of Termination of Torsades de Pointes

We observed decel-mode in 87 episodes (57.6%) and accel-mode in 33 (21.8%), and the stable mode was found in 14 (9.3%) episodes. In the remaining 17 (11.3%) episodes, the mode of termination could not be determined because of degeneration into VF. Decel-mode TdP was longer than accel-mode TdP (8.6 vs 15.3 beats per episode, $P = 0.0000$). There were no differences between decel-mode TdP and accel-mode TdP regarding the mean HR-TdP, pause-RR, min RR-TdP, f-CL-TdP, VRV-TdP, and CI.

VF (-) and VF (+) Torsades de Pointes Episodes

Among 151 episodes of TdPs, 21(13.9%) were unstable - VF(+) episodes. The VF(+) episodes

were longer (number of beats per episode), $P < 0.001$, faster (the mean heart rate of torsades de pointes [HR-TdP]), $P < 0.001$, presented more stability of cycles length (lower VRV-TdP), $P = 0.003$, and had shorter minimal RR interval within the TdP, $P < 0.001$ than the VF(-) episodes. The pause-RR interval before VF(+) episodes was longer than of VF(-) ones, but did not reach statistical significance, $P = 0.075$. The time from peak of T-U complex to the depolarization of the PVC initiating TdP was shorter in VF(+) episodes versus VF(-) ones, but it did not reach statistical significance, $P = 0.102$. These results are depicted in Table 2.

Characteristic of Torsades de Pointes

The Heart Rate of TdP: Slower and Faster Torsades de Pointes

The mean HR-TdP was 218 ± 38 bpm. We classified TdP episodes into “slower”-TdP (s-TdP)

Table 1. Clinical Characteristic

	Patients, n	Patients with Event	Patients without Event
Study population	28	11	17
Male/female	3/25	1/10	2/15
Age (years)	69 ± 10	64.5 ± 11	67.3 ± 10
Potassium level (mmol/l)	3.19 ± 0.37	3.17 ± 0.32	3.19 ± 0.38
Drugs-related LQTS	Amiodarone – 14 Sotalol – 5	Amiodarone – 6 Sotalol – 2	Amiodarone – 8 Sotalol – 3
Other cardiac diseases or other conditions	CAVB – 4, AF – 20, Hypokalemia – 15, Remote MI – 3 CHF – 4, Acute CVE – 2 Hypothyreosis – 1, Aortic stenosis – 1, AVR – 1,	CAVB – 2 AF – 10 Hypokalemia – 6 Remote MI – 2 CHF – 3 Acute CVE – 1	CAVB – 2 AF – 10 Hypokalemia – 9 Remote MI – 1 CHF – 1 Acute CVE – 1, Hypothyreosis – 1, Aortic stenosis – 1, AVR – 1,

AF = atrial fibrillation; AVR = aortic valve replacement; CAVB = complete atrioventricular block; CVE = cerebro-vascular event; CHF = congestive heart failure; MI = myocardial infarction.

Table 2. Univariate Regression Analysis in Prediction of VF(+) Events

ECG parameters	All N = 151 Mean (SD)	VF (–) N = 130 Mean (SD)	VF (+) N = 21 Mean (SD)	Odds Ratio [95% CI]	P Value
Beats	18.7 (26.9)	10.8 (7.99)	67.7 (45.8)	3.29 [2.01;5.39] (per 10)	<0.001
CI-PVC	511 (118)	512 (118)	508 (124)	0.97 [0.66;1.44] (per 100)	0.891
HR-TDP	226 (41.7)	220 (39.7)	259 (38.2)	2.93 [1.66;5.15] (per 50)	<0.001
VRV-TDP	30.7 (19.7)	32.5 (20.6)	19.7 (5.86)	0.39 [0.21;0.72] (per 10)	0.003
Min RR-TdP	235 (50.0)	242 (43.8)	188 (61.0)	0.32 [0.18;0.54] (per 50)	<0.001
F-CL-TdP	306 (54.9)	310 (55.1)	287 (50.1)	0.65 [0.41;1.05] (per 50)	0.080
First-VRV	42.5 (30.5)	42.5 (30.8)	42.6 (29.5)	1.00 [0.86;1.16] (per 10)	0.988
Pause-RR	1148 (334)	1128 (341)	1270 (265)	1.14 [0.99;1.31] (per 100)	0.075
Prem.index	0.47 (0.14)	0.48 (0.14)	0.41 (0.12)	0.63 [0.41;0.97] (per 0.1)	0.035
T _p -T _{ITdP}	57.3 (52.0)	60.1 (53.5)	40.0 (39.0)	0.64 [0.37;1.09] (per 10)	0.102

Data are shown as mean value (SD). CI-PVC = coupling interval premature ventricular contraction; HR-TdP = heart rate of TdP; F-CL-TdP = first cycle length of TdP; min RR-TdP = minimal RR interval within TdP; pause-RR = pause RR interval; VRV = ventricular rate variability; Prem.index = prematurity index; T_p-T_{ITdP} = T peak to T itdp interval.

< 220 bpm (range from 145 to 220 bpm) observed in 81(53.6%) episodes and "faster"-TdP (f-TdP) ≥ 220 bpm (ranged from 221 to 281 bpm) observed in 70 (46.4%) episodes. The QTc interval was similar in both groups: (633 ± 60 vs 644 ± 58 ms, respectively). The episodes of f-TdP compared to s-TdP were longer (28.7 vs 8.5 beats per event, P = 0.0001) and had lower VRV-TdP (22.7 vs 37.8 ms, P = 0.0006). The following parameters: CI (460 vs 555 ms, P = 0.0001), f-CL-TdP (272.6 vs 335.0 ms, P = 0.0002), and min RR-TdP (197.7 vs 268.4 ms, P = 0.0004) intervals were shorter in f-TdP as compared to s-TdP. Out of s-TdP and f-TdP episodes, 2 (2.5%) and 20 (28.5%), respectively, P = 0.001, converted into VF. None of the TdP

episodes with HR-TdP < 206 bpm converted into VF. The mode of onset such as f-TdP as s-TdP was in the most episodes "the monomorphic-type" PVC, 62% and 60.5%, respectively.

Stability of TdP: "High" – and "Low"– Ventricular Rate Variability TdP

The mean VRV-TdP was 30.7 ± 19.7 ms. We classified TdP episodes into "high"-VRV-TdP (VRV-TdP ≥ 30 ms seen in 49 episodes) and "low"-VRV-TdP (VRV-TdP < 30 ms seen in 102 episodes). There were no differences between the "low"-VRV and the "high"-VRV regarding QTc interval (640 ± 55 vs 635 ± 57 ms, respectively), the CI, the PI,

and the pause-RR interval. The "low"-VRV-TdPs were longer ($P = 0.001$), had shorter f-CL-TdP ($P = 0.002$), and min RR-TdP ($P = 0.009$) than the "high"-VRV-TdPs (Table 3).

Predictors of Ventricular Fibrillation

The VFs(+) were observed in 17.6% episodes of "low" VRV-TdP and in 4.1% episodes of the "high"-VRV-TdP episodes ($P = 0.01$). None of the "high"-VRV-TdP with VRV-TdP > 35 ms degenerated into VF. Among 81 episodes of s-TdPs only 2 (2.5%) episodes converted into VF ($P = 0.001$). None of the TdP episodes with HR-TdP < 206 bpm converted into VF.

In univariate regression analysis, the predictors of VF (+) episodes were: number of beats within TdP (odds ratio [OR] = 3.29, $P < 0.001$), HR-TdP (OR = 2.93, $P < 0.001$), VRV-TdP (OR = 0.39, $P < 0.003$), min RR-TdP (OR = 0.32, $P < 0.001$), and PI (OR = 0.63, $P = 0.35$). The results are shown in Table 2.

We built four models consisting of electrocardiographic parameters in predicting the low-risk TdP and the high-risk TdP VF (+). The models were the following:

Model 1: HR-TdP > 220 /min and PI < 0.5 ,

Model 2: HR-TdP > 220 /min and RR pause > 1000 ms,

Model 3: HR-TdP > 220 /min and VRV-TdP < 30 ms,

Model 4: HR-TdP > 220 /min and number of beats > 20 .

All four models were characterized with very good negative predictive value (NPV $> 95\%$). Out of them, model 4 (HR-TdP > 220 /min and number of beats > 20) had the best overall diagnostic accuracy (91%), sensitivity (86%), specificity (92%), and NPV (98%) (Table 4).

DISCUSSION

We analyzed the characteristics of TdP in a-LQTS. In the vast majority of the cases, TdP is a self-terminating arrhythmia but sometimes it can degenerate into VF. This study analyzed electrocardiographic parameters to predict worse evolution in patients with TdP associated with a-LQTS. Prior literature, concerning this issue is scarce. Kirchhof et al., in a very elegant study, analyzed only electrocardiographic parameters that

could predict TdP in a-LQTS model but no characterization of TdP evolving into VF was provided. They showed abnormal T-U waves preceding TdP (97% of patients) and also larger T wave amplitude in comparison to the control group.⁴ The TdP initiating beat emerged from the T-U wave complex in 77% of the patients. The QRS duration of the first TdP beat was longer (175 ms) than in control group (145 ms), and the QRS angle was less steep before TdP than in other PVC-type noninitiating TdP. The authors concluded that the above mentioned parameters may help in identifying an imminent risk for TdP.⁴

Our analysis showed that some electrocardiographic parameters can be helpful to improve the characterization of TdP in order to identify the potential risk of its hemodynamic instability or progression to VF. This would allow with decision making regarding implanted cardioverter-defibrillators as the ultimate therapy after controlling for the acute event.

The main findings of our study showed that fast TdP (> 220 bpm) degenerates into VF. Fast TdPs are longer, are more stable with low ventricular rate variability, and present with shorter first cycle length than the slower episodes. Slower TdPs evolve into VF very rarely ($< 2\%$).

The Rate of TdP

When analyzing the characteristic of sustained tachyarrhythmias, one always would pay attention to the rate. However, in nonsustained arrhythmias like TdP, the data remain elusive. In our series, the TdP mean heart rate was 218 bpm, and episodes faster than 220 bpm were longer in their duration, had lower ventricular rate variability (were more stable), had shorter CI of initiating TdP beat, and shorter first cycle length interval within the TdP than the slower episodes with a heart rate < 220 bpm. Interestingly, only 2.5% of slower TdPs were converted into VF, and no one with a TdP rate < 206 bpm.

The Rate Stability of TdP

Two-thirds of all TdP episodes were presented with low ventricular rate variability < 30 ms. The "low"-VRV-TdP was the predictor of the VF event (+). Out of all the "high"-VRV-TdP episodes, only 4% of episodes evolved into VF. It should

Table 3. Electrocardiographic Characteristics of Low- and High-VRV Torsades de Pointes

	Number of beats in TdP	CI-PVC (1/min)	Min RR-TdP (ms)	Pause-RR (ms)	F-CL-TdP (ms)
Mean (SD)	18.7 (26.6)	510 (117)	235 (49)	1147 (335)	306 (55)
Low – VRV	21.3 (28)	499 (108)	228 (50)	1145 (339)	295 (46)
High – VRV	13.0 (21)	535 (134)	249 (42)	1151 (330)	328 (65)
P value	0.0001	0.099	0.009	0.92	0.002

Data are shown as mean value (SD). CI-PVC = coupling interval premature ventricular contraction; F-CL-TdP = first cycle length of TdP; min RR-TdP = minimal RR interval within TdP; pause-RR = pause RR interval; VRV = ventricular rate variability.

Table 4. Diagnostic Performance of Electrocardiographic Models in Predicting VF(+) Events

	DA	SN	SP	PPV	NPV	LR +	LR –
Model 1	76% (68;82%)	76% (52;91%)	76% (68;83%)	34% (21;50%)	95% (88;98%)	3.22 (2.17;4.71)	0.31 (0.16;0.67)
Model 2	83% (76;89%)	76% (52;91%)	85% (77;90%)	45% (28;63%)	95% (90;98%)	5.09 (3.15;8.21)	0.28 (0.13;0.60)
Model 3	73% (65;89%)	81% (58;94%)	71% (63;79%)	32% (19;46%)	95% (89;98%)	2.85 (2.02;4.03)	0.26 (0.10;0.64)
Model 4	85% (85;92%)	86% (63;97%)	92% (86;96%)	64% (44;81%)	97% (92;99%)	10.88 (5.85;20.23)	0.15 (0.05;0.44)

Model 1 = HR-TdP > 220/min and PI < 0.5; Model 2 = HR-TdP > 220/min and RR pause > 1000 ms; Model 3 = HR-TdP > 220/min and VRV-TdP < 30 ms; Model 4 = HR-TdP > 220/min and number of beats > 20.

DA = diagnostic accuracy; SN = sensitivity; SP = specificity; PPV = positive predictive value; NPV = negative predictive value; LR + = likelihood ratio of a positive test; LR – = likelihood ratio of a negative test.

be noticed that none of the “high”-VRV-TdP with VRV-TdP > 35 ms degenerated into VF.

The Hemodynamic Stability of TdP

About 14% of all TdP episodes were presented with hemodynamic instability. These episodes were faster, longer, and with less variability than stable episodes. The unstable episodes had the tendency to have shorter f-CL of TdP and longer pause-RR immediately before TdP. Additionally, the time from peak of TU complex to the depolarization of PVC initiating TdP was shorter in unstable versus stable TdPs.

The Mode of Onset and Termination of TdP

It is a common knowledge that S–L–S sequences are frequent in patients with TdP also known as “pause-dependent” with typical RR interval oscillations.^{2,3} In c-LQTS, it is believed that S–L–S plays a major role in the genesis of TdP.³ However, the data from the Registry of long QT syndrome (LQTS) showed that only 45% of episodes in c-LQTS were initiated by S–L–S.⁵ Nada et al. showed that in patients with c-LQTS, S–L–S was present in 65% of all TdP episodes, but 25% were with gradual increased sinus rate pattern and about 10% started with a “changed depolarization” defined as a sudden long-coupled PVC or fusion beat followed by short-coupled PVC.⁶ In the study by Kirchhof

et al., the initiation of TdP episodes was preceded by a longer RR interval than the prior beats but the RR interval was equally long before PVCs initiating and not initiating TdP.⁴ In our study, S–L–S was observed in 91%, the sudden onset was present in 8%, and 1% of all episodes started with increasing of the heart rate before TdP; what supports the hypothesis that in a-LQTS, the pause-dependency is the most frequent pattern of TdP initiation. The TdP was initiated in 61% with monomorphic PVC pattern. In turn, about 60% of all TdP episodes terminated with a deceleration mode. Only one in five episodes terminated with a gradual increase in the ventricular rate. The episodes of TdP with decel-mode of termination were longer but VRV was the same as in accel-mode.

The First Cycle Length and Coupling Interval of TdP

We found that the first cycle length of TdP could be an interesting marker in predicting evolution into VF. Namely, the shorter f-CL of TdP was observed in unstable, faster, and “low”-VRV-TdP episodes (see Tables 2–4). Locati et al. showed that the longer episodes of TdP had shorter f-CL-TdP.⁷ In turn, Leenhardt et al. were the first who confirmed that short coupled PVCs triggering TdP should be considered as a higher risk group in patients with structural normal hearts.⁸ We demonstrated in our work that the CI-PVC did not predict the VF(+) event.

QT Interval, U Wave, T–U Waves Amplitude Ratio, and Macrovolt T Wave Alternans

All these basic electrocardiographic parameters describing the repolarization process and its abnormalities did not discriminate TdP episodes for predicting instability or VF.

Antiarrhythmic Drugs

In our study, the drug-induced LQTS was observed in 19 (68%) patients. Fourteen out of 19 patients were assessed as amiodarone related. As in our work, in the German register of drug-induced LQTS and TdP, 60% of all validated LQTS/TdP cases were attributed to drug therapy. In this register, the cardiovascular drugs induced LQTS/TdP in 17 patients, including amiodarone in 10 patients.⁹ Amiodarone therapy contributes to approximately 2% of cases of drug-related proarrhythmia (0.7% of drug-related TdP). The low incidence of amiodarone-induced TdP may be associated with a more homogeneous repolarization across ventricular cells than other class III antiarrhythmic drugs. Older age, female sex, hypokalemia, and combined use of amiodarone with digitalis therapy are independent risk factors for TdP occurrence in patients under amiodarone therapy.^{10,11}

Practical Implications

Some electrocardiographic parameters could be helpful in predicting the deterioration of TdP into VF. The predictors of VF are as follows: the number of beats within TdP, heart rate of TdP, ventricular rate variability of TdP, minimal RR interval within TdP, and the PI. In a combining model of two ECG parameters in predicting the high-risk TdP quite satisfactory was only the increased heart rate of TdP > 220/min with the number of beats within episodes > 20.

Limitations

Several limitations should be acknowledged. We were unable to measure the dynamics of QTc, RR interval, or T wave alternans for minutes or hours before TdP episodes. This may explain, in part, why the number of patients with macro T-wave alternans is low. U wave analysis is better done observing the right precordial leads that

were not always available, leading to a possible underestimation. The small number of VF(+) event (n = 20) could result in the lack of significance differences between analyzed subgroups. Finally, one would desire the ECG analysis preceding TdP to be blinded to the final outcome of VF.

CONCLUSIONS

Some electrocardiographic parameters can be helpful in determining the risk of TdP evolving into VF. The slower ventricular rate (< 220 bpm), the higher rate instability (VRV > 30 ms), and the short episodes < 20 beats could predict benign evolution. Basic electrocardiographic parameters (QT interval, RR interval before TdP, U wave, and T–U wave amplitude ratio) describing the repolarization process and its abnormalities are not helpful in predicting the clinical course of TdP.

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